

A magazine published by MIZORAM PHARMACISTS' ASSOCIATION in collaboration with MIZORAM STATE PHARMACY COUNCIL



# THE MIZORAM PHARMACISTS • 2010

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Dr. H. LALHLENMAWIA PRESIDENT MIZORAM PHARMACISTS' ASSOCIATION

### MESSAGE

National Pharmacy Week 2010 kan thlen hian Pharmacists zawng zawngte chibai ka bûk a che u. He hun puala magazine buatsaih **'The Mizoram Pharmacists'** tihchhuah a lo ni leh ta hi ka lawm hle mai a, a buaipuitu Editorial Board te leh articles thawhtute chungah lawmthu ka sawi bawk e.

Pharmacists, hmun hrang hranga thawkte, kan hna theuhvah rinawmna leh taimakna vawng nung zel turin ka chah duh che u a. Kan thiamna leh ropuina a taka hmang chhuak thei ngei turin tan lak zual a pawimawh hle a ni. Ni tinin khawvelah technology thar a chhuak a, mahni thiamna tuai thar reng a ngai a ni tih hriain, inzir thar reng turin ka chah duh che u a ni.

Hun reiloteah B.Pharm (Pharmacy Practice) course D.Pharm-te tan zir theihin Pharmacy Council of India-in a buatsaih dawn a, D.Pharm zawng zawng ten B.Pharm (Pharmacy Practice) kan neih a tul dawn a ni. Vawiin atangin lo inbuatsaih lawk a tul hle mai.

Pharmacists kan nih angin damdawi thar ngaihven a, a nihna zirchiang hmasa thintu kan nih a ngai a, damdawi reng reng mi dangte zirtir turin kan hriat chian tawk a tul hle a ni.

Mizoram Pharmacists' Association member zawng zawngte tluang taka in hna thawk chhunzawm zel turin duhsakna ka hlan a che u.

Mizoram Pharmacists' Association dam reng rawh se.

Sd/-Dr. H. Lalhlenmawia





LALSAWMA PACHUAU PRESIDENT MIZORAM STATE PHARMACY COUNCIL

### MESSAGE

Mizoram State Pharmacy Council leh Mizoram Pharmacists' Association tangkawpin, National Pharmacy Week hmang tura hma kan la leh thei hi a lawmawm ka tiin, hemi atana tha leh zung sengtu zawng zawng chungah lawmthu ka sawi tak meuh meuh a ni. Kumina kan thupui **'Safety first with your medicine - ask your Pharmacists'** tih a ni zui leh zelte hian Mizoram mipuite fimkhurna thuchah min siam se, damdawi ei mai mai leh damdawi tha leh him ngaihtuah ve nachang min hriattir se a va duhawm em! Chutih rual chuan keini Pharmacists-te ngei hian rilru leh thinlung taka ngaihtuahin he kan thupui hlawhtlinna tur hian keimahni hma theuhah inpekna thar leh fimkhurna, taimakna min pe theuh sela, a va hlawhtlinthlak dawn em!

Kan pawl magazine, **'The Mizoram Pharmacists'** tihchhuah theih a ni lehzelte hian kan thawhhona thatzia leh tumruhna a tilangin ka hria a, hemi phênah hian mi bik, thawkrim fál leh hah bikte pawh an awm, anni zára hetiang puitlin thei chauh hi kan ni tih erawh hriatchian hle a ngai thung. An chungah lawmthu ka sawi a, article tha tak tak thawhtute zarah tunlai khawvêl tukverh atangin Pharmaceutical Services hmasawnna tak tak kan thlirho leh thei dawn ta a nih hi.

Ka lawm e.

(LALSAWMA PACHUAU)

# EDITORIAL

The Editorial Boards wishes to thank all the contributors of the articles and to the advertisers for **'The Mizoram Pharmacists 2010'**. Without you it would not have been possible to publish this magazine.

First of all, we would like to thank Mr. Lalrinsanga Sailo, Minister, Department of Health & Family Welfare, Government of Mizoram, Pu Lalsawma Pachuau, President, Mizoram State Pharmacy Council and Dr. H. Lalhlenmawia, President, Mizoram Pharmacists' Association for their wonderful and inspiring messages.

We express our sincere thanks to Committee members of Mizoram Pharmacists' Association, Mizoram State Pharmacy Council and Organizing Committee Member of National Pharmacy Week 2010 celebration at Aizawl for their encouragement, cooperation and constant support.

We also give thanks to all the people who directly or indirectly involve in bringing out this magazine.

Finally, we hope and prayed that this magazine will enlighten all the people and the knowledge it provide will be use for the betterment of the society and for the human race.

#### **Editorial Boards**

Editor-in-Chief		Pu Lalsawma Pachuau Senior Adviser, MPA		
Editor	:	Dr. H. Lalhlenmawia President, MPA		
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		<ul><li>a) A 2034 Binana</li><li>RIPANS</li><li>4) Office Bearers, MPA</li></ul>		

General Secretary Report

**Lalvuana** General Secretary Mizoram Pharmacists' Association



A hmasa berin National Pharmacy Week 2010 cum MPA Conference kan lo thleng leh thei hi ka lawm hle mai; he hun min hruai thlengtu Pathian hnenah lawmthu ka sawi a. Kan Chief Guest, Pu Lalrinliana Sailo, Hon'ble Minister, Health & FW, etc. he hun min hmanpui tur leh kan Week min hawnsak tura a hun hlu tak min pek avang te, kan Guest of Honour, Dr. Chawngthanliana, Director, RIPANS, Pharmacist hmakhaw ngaitu, he hun min hmanpui avangin an chungah lawmthu ka sawi a, kan mi sawm bikte zawng zawng chungah lawmthu ka sawi bawk a ni. Annual Magazine 'The Mizoram Pharmacists' mawihnai tak tichhuak theia a awm theihna tura buaipuitute zawng zawng chungah te, article leh thuchah (message) tha tak min rawn ziahsaktute chungah lawmthu ka sawi bawk e.

1. MPA dinhmun: MPA-ah hian Member thar eng emaw zat kan awm zel a, tunah hian member zawng zawng hi 210 vel kan awm a. MPA hi Pensioners te, Pharmacist thawk lai, Drugs Inspector, Lecturer, Professor, Private Hospital leh Community Services (Pharmacy hawng) mek te leh State danga hna hrang hrang thawk te, thiamna lamah Diploma atanga Ph.D thlenga Pharmacy lama neite infunkhawmna pawl a ni. Tuna kan hruaitute chu hengte hi an ni:

i)	President	:	Dr. H. Lalhlenmawia Sr. Lecturer, RIPANS		
ii)	Vice President	:	C. Vanthuama, Head Pharmacist, Civil Hospital, Aizawl		
iii)	Gen. Secretary	:	Lalvuana, Pharmacist, Civil Hospital, Aizawl		
iv)	Jt. Secretary	:	Zothanpuia, Lecturer, RIPANS		
v)	Treasurer	:	Lalhmingliani Pachuau, Quality Manager, MSACS		
vi)	Fin. Secretary	:	R. Rodingliana, Head Pharmacist, Civil Hospital, Aizawl		
vii)	Sr. Adviser	:	Pu Lalsawma Pachuau, ADC, DHS, Aizawl		
viii)	i) Executive Members 12 an awm bawk				

ix) MPA Member zat hi 204 niin, member thar kumin chhung hian 12 kan neih belh a, chutih rualin member pali ngawtin min boralsan a, mual min liamsan ta kan thiante hi kan ui hle a ni.

Kumin chhung hian OB Meeting tum 2 kan nei a, Executive committee vawi 4 neih a ni a, Pharmacist-te hmakhua leh Mizorama damdawi lama thiamna leh hmasawnna te ngaihtuahin rorel thin a ni.

2. Drugs Control Administration hi tihlen ni se, Drugs Control Staff-te hmalakna a theih anga tawiawmin hma lakpui a ni a, Mizoram Chief Minister hnenah pawh lehkha thehluh a ni a, hmalakna kal mek a ni. Hemi chungchangah hian kan Minister leh Chief Guest zahawm tak pawh hmuh a ni a, ani hnen atang pawh hian beiseina sang tak kan nei a, ani hma min lakpui avangin tunah hian a hlawhtlinna kan nghak mek a ni.

3. Procurement Section, DHS leh DHME-a Pharmacist dah tura kan hmalakna chu tunah hian DHME lamah chuan a hlawhtlinna kan hmu tawh a, Pharmacist dah a nih tak avangin kan lawm hle a ni. Hei hian Quality Control lamah pawh hma la chho zel tura kawng sialna a la nih chhoh zel beisei ila. Hei pawh hi kan Minister zahawm tak hma min lakpuina a ni tih ka sawi tel duh bawk a ni.

4. Vanduai thlak takin kumin hian kan member chatuan ram min pansan ta mi pali ngawt an awm a, kan pawl tan channa nasa tak a ni, thenkhatte phei chu kan pawl dan anga ràl theih lohte an ni lehnghal a, a pawi kan ti takzet a ni! Heng a hnuaia mite hi kan thawhpui chatuan ram min pansan ta, kan ui em emte chu an ni :

- i) Pu CH. Chawnghluna, Pharmacist, Hnahthial CHC, ni 5 January, 2010 khan Civil Hospital, Aizawl-ah min boralsan a, a ruang chungah pangpar dah a ni.
- ii) Pu Laltharzuala, Pharmacist, Phuldungsei PHC, ni 19 June, 2010 khan anmahni chenna inah min boralsan.
- iii) Pu Lalbuatsaiha, Pharmacist, Serchhip Hospital, ni 3 November, 2010 khan min boralsan.
- iv) Pu Lalnuntluanga, Superintending Pharmacist (Retd), Chhipphir khua chuan ni 12 November, 2010 khan Vaivenga Hospital, Aizawl-ah min boralsan a, a ruang chungah pangpar dahin thlah liam a ni.

Heng kan Pharmacist thawhpuite hi kan ui hle a, an kalsan tak chhungte Pathianin thlamuanna pein awmpui zel se kan duhsak tak meuh a ni.

5. National Pharmacy Week 2009 leh MPA Gen Conference hlawhtling taka hman a ni a, vawiina kan Chief Guest leh kan Minister ni bawk ho hian hlawk taka hman a ni. Magazine pawh hlawhtling taka tihchhuah a ni bawk. Kumin 2010 hian hmang leh thei turin nasa taka hma lak a ni a, hemi atan hian thil pawimawh tak tak ruahman a ni a – a) Magazine buatsaih a niin heng a hnuaia mite hi magazine lama mawhphurtute an ni:

i)	Editor-in-Chief	:	Pu Lalsawma Pachuau Senior Adviser, MPA
ii)	Editor	:	Dr. H. Lalhlenmawia President, MPA
iii)	Joint Editor	:	R. Lalawmpuii RIPANS
iv)	Cir. Manager	:	Pu C. Lalhmachhuana RIPANS
v)	Editorial Board Members	:	<ol> <li>Pu Lalhmingliana Drugs Inspector</li> <li>P.C. Lalawmpuii RIPANS</li> </ol>

- 3) Pu Zosangliana RIPANS
- 4) Office Bearers, MPA
- b) Kumin hian Local channel leh DDK-ah te Group Discussion, Drugs kaihhnawih heng – Herbal Drugs leh Zawlaidi chungchang thilah te kan nei a, hei hi Documentary film siamin video shooting te neiin kan buatsaih a. Mipui mimir tena damdawi lam leh Pharmacist-te dinhmun chiang zawka an lo hriat a, an hlawkpui ngei kan beisei bawk a ni.
- Kum 30 chuang chawl lova MPA Executive Member mawhphurhna lo chelhtu Pu C. Zoliana, Ramthar Veng, Aizawl hnenah chawimawina thuziak (citation) hlan a ni.

MPA dam reng rawh se.

Ka lawm e.

"A man of very moderate ability may be a good physician, if he devotes himself faithfully to the work" - ©liver Wendell Holmes

# WINE ... ZAWLAIDI

**Dr H. Lalhlenmawia** Department of Pharmacy, RIPANS hlenmawia@gmail.com

ine chu thil tui in chi, zu (ethanol) pai tel, grape atanga siam a ni. Grape rah hminte chu lakhawmin dawidimte nen dah pawlh a ni a, a hranpa-a zu siam thei chi thil dang, chini emaw, enzyme emaw te telh lovin grape-a chaw tha lo awm sate kha zu-ah a insiam ta thin a, chu chu wine a lo ni ta a ni. Grape káwrah hian dawidim ang chi, amahin a neih ve hrim hrim natural yeast chi khat a awm ve a, hei hian grape rah sawr, a kawrte nena dah pawlh hian, grape-a sugar leh carbohydrate te atangin zu an siam ve thin a, hei vang hian hmun tam takah chuan dawidim a hranpa-a telh kher loh pawhin zu a lo insiam thin. Grape kher lo pawh thei dang, apple leh berries angte atang pawhin dawidim telhin wine a siam ve theih tho a, mahse heng te hi chu a thei hming chawi tel khera sawi an ni thin. Entirnan, Apple wine, Elderberry wine, etc. Wine tia lam bik hi chu Grape atanga siam an ni bik a ni. Grape tam tak chuan zu tam tak siamna turin carbohydrate te leh sugar te an nei tam tawk lo va, wine zu pai tel tha tawk an nei lo fo thin. Hetiangah hi chuan spirit telh belh a ni thin a, chutiang hmanga uain siam chu Fortified wine an ti deuh bik thin.



#### Wine hi zu a ni em?

Wine hian zu a keng tel a, a awm zat erawh chu a chi hrang a zirin a inang lo thei. A nihna takah chuan wine hi zu a ni a, a thenah te phei chuan a zu pai hi a sang viau thin bawk. Tuna Mizorama wine kan neih Zawlaidi hi fortified wine niin 14% zu tel angin a bura intar (Label-ah) kan hmu a, a sang hle mai.

Wine-te hi table food ti a sawiin hmun thenkhatah chuan zu chi dang whiskey, rum, vodka, etc. te anga zu-a chhiar an ni chiah lo thin; hei hi a chhan ni bera lang chu wine-ah hi chuan grape rahin mihring tana chaw tha a pai chi hrang hrang, enzyme te, carbohydrate te, glucose te, protein te leh acid te kha wineah an awm tel thin vang niin a lang. Wine hi zu a ni kan tih rualin kan tarlan tak ang taksa tana chaw tha pawh tam tak a pai tel ve bawk a ni. Hengte avang hian food item-te zingah chhiar tel an ni ve thin bawk.

#### A va thúr ve?

Grape wine-te hi an thúr tlangpui thin, acid a tel tam thin avangin. Acid tel tam dan hi pH zawngin teh a ni tlangpui a, tuisik thianghlim tak mai hi pH 7 vel an ni a, pH a tlem khan acid a tam tial tial tihna a ni thin. Wine-te hian a tlangpuiin pH 3 atang a pH 4 thleng te an nei a, a chunga kan tarlan tawh fortified wine ni lo te phei chu an pH a hniam tlangpui vek a, thúr tura ngaih an ni tlangpui a ni. He an thúrna hi Acid chi hrang hrang awm vang a ni a, dan naranin Ascorbic acid (Vitamin-C), Formic acid, Citric acid, Malic acid, Succinic acid, Tartaric acid leh Acetic cid te an awm tlangpui. Heng acid-te hi grape rahin an neih sa te an ni hlawm a, a thente hi chu grape rah atanga zu an insiam (fermentation) avanga lo awm thar te an ni thin bawk. Heng acid-te hian wine ven him kawngah nasa takin an pui a, pH a san chuan wine hi a tha rei thei lo a, natna hrik ten a tichhe thuai thin. Heng bakah hian wine hi a thúr hian a tui zawk hle nia hriat a ni bawk. Chutih rualin heng acid-te hian taksa-ah harsatna an thlen nasa thei hle bawk. Pumpui ulcer te leh kawthalo te an thlen ve bawk thin a, control a tul hle a ni. Acid bikah hian Tartaric acid a tel tam phei chuan kawthalo a thlen nasa hle a ni.

Wine-te hi ruihna tura zu dang anga in a ni lo tlangpui a, a chhan chu zu dang nena khaikhin chuan acid a san em avang te leh thil dang carbohydrates leh protein ang te an awm thin vang a ni a; ruih hnêpna khawpa duh tan chuan zu mai ni lo thil dangte avangin taksaah harsatna a siam thin a, pumpui ulcer te a thlen hma em em a ni. Ruihna khawpa lo in thin tan chuan sim a tul hle a ni.

#### Wine tha lo a awm thei em?

Wine quality te hi a inang lo thei em em a, grape rah azir leh a siam uluk danah a quality a innghat thuk hle a ni. A tlangpuiin ram luma grape rah hian acid an nei tlem a, an thlum tha bik thin a, hmun vawta grep rah te hi an thúr bik a, acid an pai tam zawk thin. Hei vang hian wine hmun hrang hrang atanga siamte hi an tui dan a inang lo thei hle a, thenkhat an thúr viau laiin thenkhat te chu an thlum thin bawk. Hei vang hian hmun tam takah chuan wine tihtui nan chini te an pawlh belh teuh thin. Chini chu glucose-ah a chang leh a. hre miah lovin taksain a mawmawh aia tam daih glucose a lo ei phah thei thin a, zunthlum veite leh BP sang bikte tan phei chuan a hlauhawm thei hle thin a ni. Winete hi kan tarlan tawh angin Grape rah atanga siam a ni a, grape rahte hi rannungin an duh em em thin; hei vang hian hmun tam takah rannung thahna hlote an hman hial a ngai thin. A hun lova hman a nih chuan grape rahah khan túr hlauhawm tak tak, insecticide residue kan tih leh pesticide residue te a awm thei a, taksaah cancer te an thlen theih avangin a hlauhawm hle a ni. Heng bakah hian grape rahah te hian heavy metals kan tih mercury, lead, iron, silver, etc. te an awm ve thin a, heng heavy metals te hi taksa cancer thlen theitu an ni a, an lo tel ve ang tih a hlauhawm hle a ni. Grep atanga wine siam lai hian zu chi khat methanol lo insiam tel chang a awm ve thei bawk. Methanol hi a hlauhawm em em a, taksa chhungah hian formaldehyde-ah insiam lehin taksa tana túr hlauhawm takah a chang thin. Wine-te hian kan tarlan tak ang khan glucose te, carbohydrate te an pai vek a, hei vang hian natna hrik tam tak tan chuan nunna leh inthlah punna hmun tha takah a chang thei a, a siamna hmunah uluk a nih loh phei chuan natna hrik tam tak ei palh a awl hle a ni. Hmun tam takah chuan wine vawn thatna atan Potassium metabisulphite te telh an ni bawk thin. Hei hian Sulphur dioxide a siam a, a nihna tur ang tawk chauh a tel chuan wine a titui viau thei a, a tam lutuk chuan mihring tan a pawi viau thei bawk a ni. Grape rahah te hian túr chi khat Mycotoxin te an awm duh hle mai a, ei tel palh chuan luak, kawthalo leh khawsik te a siam thei bawk a ni. Heng lo pawh hi thil dang pawimawh tak tak a la awm nual a ni.

#### **Quality Control**

Ram changkang zawk, Europe te, USA te leh Australia-ah te chuan a chunga kan tarlan tawh thil chi hrang hrang te, mihring tana hlauhawm tur ang chi te chu hlauhawm lo tawk tura wine-a tel thei tur zat bithliah fel tak an nei thlap mai a, chutiang quality nei pha lote chu mipui ei tura hralh chhuah an khap tawp mai a ni. Wine hi zu chi dang, Whiskey, Rum, Vodka, etc. ang a ni ve lo va, grape rah atanga insiam, thlitfim, a tuina tur leh a that reina tur atana thil chi hrang hrang pawlh leh an nih avangin heng glucose, heavy metals, methanol, sulphur dioxide, acid, etc. ang te hi mihring tana hlauhawm tham an nei tel hma bik em em a, hei vang hian quality control tha taka neih a ngai a ni. Quality tha lo wine in palh a nih chuan mihring tana thil hlauhawm chi hrang hrang nasa takin kan ei a lo ni reng thei a ni.

#### A thatna lam ve thung

Grape rah káwrah hian enzyme chi khat Resveratrol an tih a awm a, he chemical hi rannunga zir chianna neih tawhah chuan BP sang tan te, diabetes tan leh cancer (a bikin vun leh chuap cancer) atan te a tha em em a ni tih hmuhchhuah a ni tawh a ni. Resveratrol te hi grape káwrah an awm a, grape rah atanga zu tlem a lo insiam a, thil dang nen an lo inchawhpawlh hnu chuan grape káwr atanga wine-ah kalin hun rei tak chhung chhe lovin an awm thei ta thin a ni. He Resveratrol avang hian ram thenkhat wine in nasa, France ang te hian a nawlpuiin Diabetes leh BP sang an vei tlem bik ni te-a rin a ni hial a ni. Hei lo pawh grape wine-ah hian, a bikin a rawng senah hian anthocyanin a awm tha hle a, hei hian taksaa thil bawlhhlawh awm, free radical-te a paih chhuak thei tih finfiah a ni bawk a; hei hian diabetes nasa takin a veng a, a bikin taksa a timám thain vun bawl leh chuar lakah nasa takin taksa a veng thei a ni. Wine hian carbohydrate te, protein te a ken tel nual avangin a dose tawk leka in a nih chuan taksa tan a thain chaw tha tam tak a supply a, a tichak thei hle a ni.

#### Zawlaidi lam ve hung

Thlirna a tam thei hle awm e. Thingtlang lam ten an thlai tharchhuah atanga siam a nih avangin an thawhrim hlawkna an tel thei ngei dawn niin a lang a, an lawmpuiawm hle mai. Mahse Mizoram chu ZU khapna state a ni miau mai a, wine hming chu eng ang pawh lo ni se, zu a neih zat 14% a ni miau mai si a, do loh theih loh, khap si lohah a chang ta a ni. Engpawh ni se, vawinah chuan kan bazarah te lei theihin a lo awm ta miau mai si a, kan in lo thei ta lo a ni. Heti laia ka'n sawi duh chu- wine a nih avangin mihring tan a thianghlim tawk tihna a ni lo. Quality tha lo tak leh hriselna tichhe thei wine a awm thei a ni tih kan hriat a tha hle mai. Hei vang hian sawrkar phalnain an siam a ni ta rau rau bawk a, sawrkar hian hma la se, quality tha tak mipuite ei turah hian siam chhuak se a va tha em. Mizoram mai hi target lo in, foreign ram te a hralh tlak tur quality hi awm thei se, zawlaidi chu Paris-ah te, London-a mi chengte pawhin in ve se, kan va hlawk leh zual dawn em!

Heti lo zawng pawh hian thlir ila... engvangin nge ZU hi 14% kher kher an neihtir? A tam lutuk a, mi a tirui dawn chiang a ni. Hei aia tlem daih, ruihna tham loh zu pai chung hian wine tui tak, fak tlak a siam theih chiang a ni.

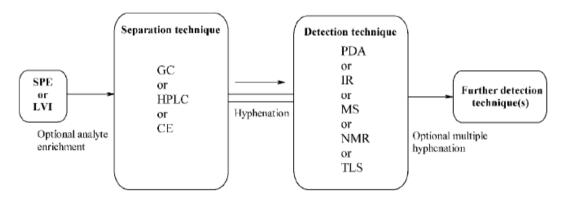
Zawlaidi chungchanga ka thupui ber fo mai chu mihring tana hlauhawm loh quality tha, khawvel hmun hrang hrangah pawh zawrh tlak tur siamin i in ve tawh ang u tih hi a ni.

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## A HYPHENATED LC-NMR TECHNIQUE

*R. Lalawmpuii* Department of Pharmacy RIPANS, Zemabawk, Aizawl

The technique developed from the coupling of a separation technique and on line spec troscopic detection technology is known as the hyphenated technique (Fig 1). Over the last two decades, the hyphenated techniques have received ever increasing attention as the principal means to solve many complex analytical problems. The power of combining separation technologies with spectroscopic technique has been demonstrated over the years for both quantitative and qualitative analysis of unknown compounds in complex natural product1.



#### Fig 1: Hyphenated technique

To obtain structural information leading to the identification of the compounds present in crude sample, liquid chromatography (LC), usually a high-performance liquid chromatography (HPLC), is linked to spectroscopic detection techniques ,e.g., nuclear magnetic resonance spectroscopy (NMR) or mass spectroscopy (MS) etc. resulting in the introduction of modern hyphenated techniques, e.g., LC-NMR, LC-MS.<sup>1</sup>HPLC is the most widely used analytical separation technique for the qualitative and quantitative determination of compounds in natural products extracts. Mass spectrometry (MS) and nuclear magnetic resonance (NMR) are the primary analytical techniques that provide structural information for the individually isolated compounds. The traditional way of studying natural products includes fractionation of a crude mixture or extracts, separation and isolation of the individual components using liquid chromatography and structure elucidation by using spectroscopic techniques(UV,IR,NMR,MS). This approach is technically demanding and time consuming and in many circumstances it may lead to well known compounds, which had been previously reported in the literature after a great deal of time and resources have been invested<sup>2</sup>. The potential of liquid chromatography directly coupling with nuclear magnetic resonance for a rapid and direct screening of crude plants extracts for useful products has recently gain considerable attention. The physical connection of HPLC (or LC) and MS (LC-MS) or NMR (LC-NMR) increases the capability of solving structural problems of mixtures of unknown compounds. Hence, this enables the identification of secondary metabolites at a very primary stage avoiding the time consuming isolation of pure components. Further using LC-coupled bioassay, the biological activity could be directly correlated to the identified compounds. These hyphenated techniques in combination lead to a rapid and efficient analysis of plants for compounds of phytochemical or pharmacological interest. Therefore, HPLC-NMR represents a potentially suitable technique in phytochemical research for the detailed on-line analysis of natural products<sup>3-6</sup>.

Among the spectroscopic technique available to date, NMR is probably the least sensitive, and yet it provides the most useful structural information towards the structure elucidation of natural products. The direct linking of HPLC with NMR spectroscopy has a success story and has transformed the technique from a research tool to the stage where routine analytical applications are possible<sup>1</sup>. Before undertaking NMR analysis of a complex mixture, separation of the individual components by chromatography is required. LC-MS is routinely used to analyze mixtures without prior isolation of its components. In many cases, NMR is needed for an unambiguous identification, because NMR provides a great deal of structural information about a compound of interest. In addition, new probe design which allow the use of gradient pulse sequences now provide the efficient and specific suppression of the NMR signals due to the HPLC solvent<sup>2</sup>.

The used of normal phase restricted the field of applications, so in most of the LC-NMR operations, reversed phase columns are used, employing a binary or tertiary solvent mixture with isocratic or gradient elution.

Recent advance in both hardware and software for the direct coupling of LC and NMR have given a new life to this hyphenated technique. These developments include new coils and flow cell design for high sensitivity, new RF system for multiple solvent suppression and improved dynamic range elution capability, and automatic peak-picking/storing capabilities. As a result, this method is a powerful tool used in many areas such as a natural product, organic molecules, bio-molecules, drug impurities, by-products, reaction mixtures and drug degradation products. The potential of HPLC-NMR for the investigation and structural elucidation of novel natural products has been enormously extended by the advent of powerful solvent suppression technique which generates high quality spectra and effectively obtains 1D on-flow and top-flow spectra and 2Dspectra of the stop-flow mode, such as WET-TOCSY, WET-COSY, WET-NOESY and others<sup>4, 7</sup>.

There are four general modes of operation for LC-NMR, such as on-flow, stop-flow, time-sliced, and loop collection which can be distinguished by the status of the sample during the measurement<sup>4</sup>.

#### PRINCIPLE OF LC-NMR COUPLING

Generally in LC-NMR system, the LC unit comprises auto sampler, LC pump, column, and non NMR detector (e.g., UV, DAD, EC, refractive index, or radioactivity). From the detector the flow is guided into the LC-NMR interference, which can be equipped with additional loops for the intermediate storage of selected LC peaks. The flow from the LC-NMR interface is then guided either to the flow cell NMR probe-head or to the waste receptacle. Following passage through the probe-head, the flow is routed to a fraction collector for recovery and further investigation of various fractions analyzed by NMR. A mass spectrometer can also be attached to the system via a splitter at the output NMR interface<sup>1</sup>.

The acquisition of a conventional NMR spectrum requires the dissolving of the sample of interest in a deuterated solvent, introduction of the solution into a cylindrical sample tube and placement of the sample in a conventional NMR probe within the NMR magnet. For LC-NMR, the probe must be modified to allow continuous flow of the solution under study. The major technical considerations of LC-NMR are NMR sensitivity, solvent suppression, NMR-and LC-compatible solvents and the volume of the chromatographic peak versus the volume of the NMR flow cell or LC-NMR sensitivity<sup>4</sup>. Fig 2 shows the schematic set up of the various LC-NMR modes.

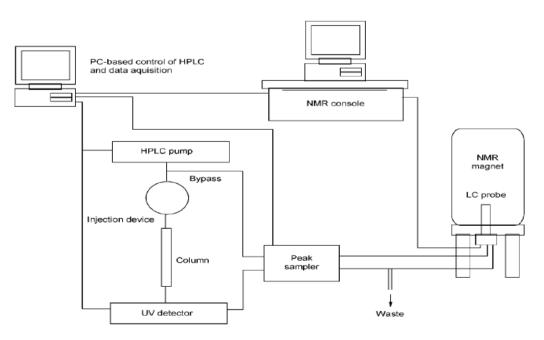


Fig 2: A typical LC-NMR system

There are different techniques which is related to LC-NMR to increase their sensitivity such as Cap LC-NMR or microflow NMR , Cryogenic technology in LC-NMR, LC-NMR/MS and LC-SPE-NMR etc.

#### APPLICATION OF LC-NMR

With the recent technological advances, the scope application of LC-NMR has increased. While applications to the field of drugs metabolisms become quite common. Report of the use of LC-NMR to identify natural product have been relatively rare. The first reports of the application of LC-NMR to natural products involved the characterization of isomeric mixtures produced by exposing a pure natural product to light or heat. LC-NMR was used to determine the structure of the photoisomerization product of the bioinsecticide azadirachtin and to characterize the geometric isomers of vitamin A acetate produced upon exposure to heat. The azadirachtin study employed stopped-flow LC-NMR measurements, while the vitamin A acetate study used on-flow measurements to detect the resonances of olefinic protons in order to determine cis or trans configurations of double bond<sup>2</sup>.

In the past few years, LC-NMR studies of natural products have progressed to include the characterization of individual components in crude, or partially purified, extracts. These applications demonstrate the full power of this hyphenated technique by eliminating the need to isolate individual components from a crude extract for subsequent NMR experiments. Then first report of this type of application was the characterization of the sesquiterpene lactones in Zaluzania grayana by on-flow and stopped-flow LC-NMR experiments<sup>8</sup>. Since this report, LC-NMR has been used to characterize a wide range of plant natural products, a testimony to the broad applicability of this technique. LC-NMR has been used to identify prenylated flavanones from Monotes engleri, monoterpene dimers from Lisianthius seemannii, lignans from Torreya jakii<sup>9</sup> and napthoquinones from Cordia linnaei. In addition, napthylisoquinoline and pyrrolizidine alkaloids, sesquiterpene lactones phenylphenalenones, taxanes, lignans, glycosides, and other compounds have been identified by data obtained from LC-NMR experiments. Most of these reports describe the identification of known members of these structure classes by LC-NMR. In a few cases LC-NMR has been used to determine structures of new analogues of known compounds. In these examples, stopped-flow measurements employing two-dimensional (2D) NMR experiments such as COSY (corellation spectroscopy), TOCSY (total correlation spectroscopy), GHSQC (gradient heteronuclear single quantum correlation), GHMBC (gradient heteronuclear multiple bond correlation), and NOESY (2D nuclear Overhauser effect spectroscopy) have been applied to determine structures of novel compounds. Most of the reports shows that the application of LC-NMR to the field of natural products has been to define structures of plant-derived metabolites, while very little use has been made by researchers investigating microbial or marine natural products<sup>2</sup>.

#### CONCLUSION

Use of hyphenated techniques is by far the most powerful strategy that an analyst can use to study complex mixtures of natural products. NMR spectral data obtained using LC-NMR provides structural information which other hyphenated methods cannot. LC-NMR is especially useful in instances where the data from LC-MS is incomplete or does not allow the confident identification of the desired component of a sample. LC-NMR coupling is well established with a series of available options for solving a variety of analytical problems. The different possible modes of operation and the various combinations of detectors and sample

manipulation techniques available ensure that restrictions on the applicability of LC-NMR can be reduced to a minimum<sup>4</sup>. The type of sample under study and the goals of the analysis determine the optimal choice of instrumentation and measurement mode. For the identification of major substances in simple mixtures, the on-flow techniques are more efficient. For detailed structure elucidation of the major peaks by means of 2D-NMR or 1D-NMR of minor peaks stopped flow and loop-storage method are necessary. When analyte concentration is limiting, sample manipulation techniques such as SPE, multiple trapping and the use of a cryogenic probe are appropriate. When the sample amount is limiting capLC-NMR is the method of choice. Detailed LC-NMR investigations of medicinal plants could contribute to new leads to drug development<sup>7</sup>.

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## ANTI- ARTHRITIC ACTIVITY OF METHANOLIC EXTRACT OF Dillenia pentagyna ON FCA INDUCED ARTHRITIS IN RATS

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#### **Abstract**

The intradermal injection of Freud's adjuvant (a thin suspension of dead tubercle bacilli in liquid paraffin) into foot pad of rats produces an inflamed "primary lesion", at the site of injection and then, after a delay of approximately 10 days. Inflamed "Secondary lesions" in areas of body remote from injection site.

The inflammation associated with both primary and secondary lesions in arthritis or arthritic rats is reduced by treatment with most of the compounds currently used in the chemotherapy of rheumatoid arthritis in human. Unfortunately, these agents which are in use do not interfere permanently with the disease process involved in the formation of secondary lesions and relapses occur after the treatment is ceased. The object of this paper is to describe some of the biological properties of methanolic extract of bark powder of the plant *Dillenia pentagyna* (Mizo: Kaihzawl). Unlike, other therapeutic agents, the extract did not show a significant reduction in inflammation due to arthritis, but has shown a marked regeneration of synovial cartilage in the infected rats.

#### Key Words

Freud's Complete Adjuvant, *Dillenia pentagyna*, Arthritis, Inflammation, Reactive Oxygen Species.

#### Introduction

Rheumatoid arthritis is a chronic systemic inflammatory disease predominantly affecting joints, and periarticular tissues. It is mainly characterized by synovitis and joint destruction, Current evidence indicates that the disease is an autoimmune disease.

Although, arthritis is classified as an autoimmune inflammatory, the disease compromises three basic interrelated pathological processes.

- i. Inflammation
- ii. Synovial Proliferation
- iii. Joint tissue destruction

Tumor necrosis factor alpha (TNF- $\alpha$ ), the product of macrophages has been demonstrated to play an important role in pathogenesis of the disease. Its effects include induction of pro-inflammatory mediators such as Interleukin-1, Nitric Oxides, Prostaglandins (PGs), methaloprotease and adhesive molecules.

The earliest lesion is vasculities, an inflammation of small blood vessels. The inflammation causes edema of synovicin and infiltration with mononeuclear cells, macrophages, lymphocytes and plasma cells. The activated macrophages, lymphocytes and fibroblast produce a variety of cytokine that promote further synovial proliferation and inflammation.

Joint damage occurs early in the case of Arthritis. The cartilage degranulation is now considered to be due to release of factor(s) capable of stimulating chondrocytes to degrade their own extracellular matrix. This factor from cellular or synovial lining is similar to Interleukin 1. The latter has been shown to stimulate release of lytic enzymes and PGE-2 from chondrocytes monolayers and inhibit synthesis of proteoglycans by articular cartilage. Thus IL-1 could contribute to cartilages and bone destruction and to fibrosis (Satoshkar, et.al., 2008).

#### **Reactive Oxygen Species and Arthritis**

Oxygen free radicals such as superoxides, Hydroxy radicals and related oxygen species such as Hydrogen peroxide and singlet oxygen are involved in the pathogenesis of many inflammation, granulocytes and macrophages produce large amounts of superoxides and hydrogen peroxide. It is well renowned that these oxygen free radicals have deleterious effect on biomembranes through the formation of lipid peroxides. Many cellular defense mechanisms are recruited against the toxic effects of these radicals in inflammation including serum sulphahydryl groups (-SH- groups), ceruloplasmin (CP), albumin and blood glutathione (GSH). (Fahim AT, et.al., 1994).

With respect to the toxic species of oxygen derived from inflammatory cells, it appears that  $O_2$  has little direct toxicity for cells or tissues. However, there is an accumulating body of evidence that O2? may contribute to the ultimate pathogenesis of injury following mobilization and activation of inflammatory cells. This may be related to transport of  $O_2$  across the anionic channels of cellular membranes, resulting in intracellular localization where reduction of ferritin associated (OH), formed from  $H_2O_2$ . It has also been shown that neutrophils mediated killing of endothelial cells is  $H_2O_2$  and iron dependent as demonstrated by the ability of catalase and deferroxamine to protect the cells from injury (Ward PA, et.al.,1988).

It is also found that Interleukin 1 and  $H_2O_2$  promote the phosphor-activation of the p38- mitagen activated protein kinase(p38MAPK). The p38MAPK pathway is particularly relevant target for antioxidant antagonism in chronic inflammatory diseases; p38MAPK regulates expression of inflammatory cytokine including IL-1 and largely regulates expression of iNOS and COX-2 (Robinson et.al., 1999).

#### Ethnobotanical Uses of Dillenia pentagyna

- i. Root: The root decoction is given in case of body pain twice daily till cure (Dubey et al., 2009)
- ii. Bark: One teaspoonful of bark powder is given three times a day in water for diabetes, for a period of three months. The powder is also given for the treatment of diarrhea and dysentery, three times a day till it cures. The bark powder is also given to the pregnant women for easy delivery and after delivery, it is given as tonic for the mother (Dubey, et.al, 2009)
- iii. Leaf: Leaf paste is applied to the wounds and infections. Leaf poultice is also used for the treatment of piles. Leaf powder is used for the treatment of breast cancer. (Dubey. et.al., 2009).
- iv. The fruit: The fruit extract of the plant is mixed with rhizome paste of ginger and used for the treatment of blood dysentery. (Sahu.et.al, 2010).

#### Materials and Methods

The studies were performed on albino rats of Sprague-Dawley strains whose weights were more than 100g. The animals were housed in standard laboratory conditions ( $24\pm2^{\circ}C$ ) and supplied with water and food.

#### Methods:

#### (i) Induction of Arthritis:

The albino rats were divided into 3 groups of four animals in each group. On the day 0, 0.1 ml of Freud's Complete Adjuvant was injected to the sub-planar area of the left hind limb. The dosing with the standard drug (Piroxicam) and the extracts (to be designated as DPE here after) was also started from that day itself, and continued for 14 consecutive days.

The control group received only distilled water (the vehicle) but the rest were treated accordingly. Measurement of rat paw volume is then continued for 14 test days (Newbould BB, 1965).

#### (ii) Measurement of Paw volume:

The rat paw edema due to adjuvant induced arthritis was measured continuously for 14 test days (Sundays and Saturdays inclusive). The measurement was done by using Plethysmometer (IITC Life sciences).

#### (iii) Histo Pathological Studies:

On the 14<sup>th</sup> day, the test subjects were sacrificed by ether narcosis. The hind limbs were removed and fixed in 10% buffered formalin. The limbs were decalcified in 5% formic acid, processed for paraffin embedding sectioned at  $5\mu$ m thick and subsequently stained with

Haematoxylin-Eosin for examination under a compound microscope. Sections were observed for the presence of hyperplasia of synovium pannus formation, and destruction of joint space.

#### <u>RESULTS</u>

#### (i) Measurement of Rat Paw Volume:

In the initial days, the DPE treated subjects has shown a marked decrease in inflammation. The magnitude of reduction was more than the standard drug in the 5-10 days of treatment. However, it failed to control the inflammation after the tenth day.

#### (ii) Evaluation of Histopathological slides:

The slides of the normal animals had no deformities in the joints. The slides of control group had shown marked signs of joints destructions which were evident from hyperplastic joint cartilages.

The slides of DPE showed a marked regeneration of cartilages around the joints.

#### DISCUSSION

The current pharmacotherapy of Arthritis is mainly based upon the symptomatic treatment of the disease. As, the disease is considered to be an autoimmune disease, the exact cause of the disease is indeterminate. Some workers suggested the genetically factors are responsible for the disease as in the cases like chromosomes 14 genes are responsible for chronicity of arthritis in rats (Wester L et.al., 2003). In the other hand, it is considered that free radicals are responsible for the symptoms of Arthritis (Fahim et.al., 1994; Ward PA, et.al., 1988).

The search for a new drug became a necessity as the paradigm of pathogenesis is changing from the classical views of autoimmunity towards the actions and involvement of genes and free radicals.

Freud's adjuvant induced arthritis has been reported to resemble human rheumatoid arthritis both in terms of histological and also in clinical manifestations (Brahn, 1991). Rheumatoid arthritis is characterized by persistent pro inflammatory signals leading to chronic inflammation of synovial joint and subsequent erosive destruction of articulate tissues.

Many cytokines have been described in animal models of inflammatory arthritis and in patients with rheumatoid arthritis. These small molecules mediate communication between cells, resulting in the attraction of inflammatory and immune cells into joints and activation of cells to release products that leads to tissue destruction (Arend WP, 2001).

Cytokines bind to specific receptors on cell surfaces, stimulating pathways of signal transduction that lead to increased or decreased transcription. Two signal transduction pathways that may be important in the rheumatoid synovium are the AP-1 and NK- B pathway. The latter appears particularly important in chronic inflammatory diseases, both in mediating the production of IL-1 and TNF- and their effects on target cells (Arend WP, 2001). Of par-

ticular interest, is the evidence that IL-1 and TNF can directly initiate oxidant production by phagosytes (Klebamoff SJ. et.al., 1986; Luger TA. et.al., 1983). In a time dependent and dose dependent manner contact of endothelial cells in vitro either with IL-1 or TNF causes some type of changes in the endothelial cells so as to enhance its susceptibility towards oxygen mediated damage (Varani J.et.al., 1988).

It has been shown that, there was a significant decrease in the level of serum -SH groups accompanied by an increase in serum ceruloplasmin blood glutathione and serum N-acetyl- -D-glucosamidase (NAG) during acute phases of Arthritis (Fahim et.al.,1995).

From the results obtained from the described work is that the methanolic extract of *Dillenia pentagyna* is effective in the regeneration of destructed joint spaces. The possible reasons may be due to its flavanol glycosides contents.

The latter is well known for its anti oxidant activity for a long period of time. The possible mechanism by which the extract shows anti arthritic activity is either by inhibition of cytokine NK- B pathway or by preventing p38MAPK pathway which is essential for effective free radical action.

However, it is of utmost importance to mention a fact about the plant and that is less work has done with it. Therefore the chemical constituents of the plant are to be explored extensively, so as to recover the active moiety responsible for such a remarkable biological effects. It is highly recommended to pursue a more comprehensive work over the plant with other animal models with other chemicals that can lead to the discovery of an effective drug candidate after the treatment of Arthritis.

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"The art of medicine consists of amusing the patients while Nature cures the disease"-Voltaire

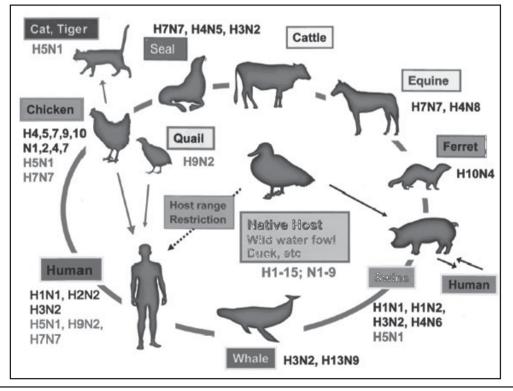
"When meditating over a disease, I never think of finding a remedy for it, but instead, a means of preventing it" -Louis Pasteur

"A skilful leech is better far than half a hundred men of war" -Samuel Butler



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vian influenza or bird flu is a form of influenza that strikes all birds. It is an acute infectious disease of the respiratory and gastrointestinal tract caused by a strain of influenza virus A which occurs in sporadic, epidemic and pandemic forms. All birds are thought to be susceptible to infection with avian influenza, though some species are more resistant to infection than others. Infection causes a wide spectrum of symptoms in birds,



ranging from bird illness to a highly contagious and rapidly fatal disease resulting in severe epidemics.

There are fifteen subtypes of influenza viruses known to infect birds. To date. all outbreaks of the highly pathogenic forms have been caused by influenza virus subtypes H5 and H7. Migratory water fowl, most notably wild ducks are the natural reservoir of avian influenza viruses and these birds are also the most resistant to infection. Domestic poultry including chickens and turkeys are particularly susceptible to epidemics of rapidly fatal influenza. The infected birds shed the virus in saliva. nasal secretions and feaces. Avian influenza viruses spread among susceptible birds when they have contact with contaminated nasal, respiratory and feacal material from the infected birds; feacal to oral transmission is the most common mode of spread.

There were three pandemics in the 20th century. All of them spread worldwide within one year of being detected. They are,

**1. 1918-1919, Spanish flu (A, H1N1):** The Spanish flu caused the highest number of known flu deaths; more than 5, 00,000 people died in the United States and 20 - 50 million people might have died worldwide. Many people died within the first few days of infection and other died of complications soon after. Nearly half of those who died were young healthy adults.

**2.1957-58, Asian flu (A, H2N2):** Asian flu caused about 70,000 deaths in the United States. It was first identified in China in late February 1957, the Asian flu spread to the United States by June 1957.

**3. 1968-69, Hong Kong flu (A, H3N2)**: The Hong Kong flu caused approximately 34,000 deaths in the United States. This virus was first detected in Hong Kong in early 1968 and

spread to the United States later that year. Type A (H3N2) viruses still circulate today.

During mid-December 2003, a number of Asian countries have reported outbreaks of highly pathogenic avian influenza virus in chicken and ducks. Infections in several species of wild birds and in pigs have also been reported. The rapid spread of highly pathogenic avian influenza, with outbreaks occurring at the same time in several countries, is historically unprecented and of great concern for human health as well as for agriculture.

Particularly alarming, in terms of risks for human health, is the detection of a highly pathogenic strain, known as "H5N1" as the cause of most of these outbreaks. H5N1 has jumped the species barrier, causing severe disease in humans, on two occasions in the recent past and had been detected in Vietnam and Thailand in 2003.

The symptoms of avian influenza in human have ranged from typical influenza like symptoms such as, fever, cough, sore throat and muscle aches to eye infection (conjunctivitis), pneumonia, viral pneumonia, acute respiratory distress and other severe and lifethreatening complications.

Recent research has shown that viruses of low pathogenicity can, after circulation for sometimes, short periods in a poultry population, mutate into highly pathogenic viruses. During 1983-84 epidemic in the United States of America, the H5N2 virus initially caused low mortality, but within six months it became highly pathogenic, with a mortality of about 90%. Control of the outbreak required destruction of more than 17 million birds at the cost of nearly US \$65 million. During 1999-2001 epidemic in Italy, the H7N1 virus initially of low pathogenicity, mutated within 9 months to a highly pathogenic form. More than 13 million birds died or were destroyed.

The quarantining of infected farms and destruction of infected or potentially exposed flocks are standard control measures aimed at preventing spread to other farms and eventual establishment of the virus in country's poultry population. Apart from being highly contagious, avian influenza viruses are readily transmitted from farm to farm by mechanical means such as by contaminated equipments, vehicles, feed, cages or clothing. So, stringent sanitary measures on farm can, however, confer some degree of protection.

In the absence of prompt control measures backed by good surveilance, epidemics can last for years. For example, an epidemic of H5N2 avian influenza, which began in Mexico in 1992, started with low pathogenicity, evolved to highly fatal form and was not controlled until 1995.

Based on historical patterns, influenza pandemics can be expected to occur, on average, three to four times each century when new virus subtype emerge and are readily transmitted from person to person. However, the occurrence of influenza pandemics is unpredictable. In the 20th century the great influenza pandemic of 1918-19 which caused an estimated 40 to 50 million deaths worldwide was followed by pandemics in 1957-58 and 1968-1969. Experts agree that another Influenza pandemic is enevitable and possibly imminent. Most influenza experts also agree that the prompt culling of Hong Kong entire poultry population in 1997 probably averted pandemics.

Several measures can help minimize the global public health risks that could arise from large outbreaks of highly pathogenic H5N1 Avian influenza in birds. An immediate priority is to stop further spread of epidemics in poultry populations. This strategy works to reduce opportunities for human exposure to the virus. Vaccination of persons at high risks of exposure to infected poultry using existing vaccines effective against currently circulating human influenza strains, can reduce the likelihood of co-infection of humans with avian and influenza strains, and thus reduce the risks that genes will be exchanged. Workers involved in the culling of poultry flocks must be protected by proper clothing and equipment against infection. These workers should also receive antiviral drugs as a prophylactic measure.

Influenza vaccination is the primary method for preventing influenza and its severe complications (viz. Inactivated Influenza Vaccine, Flu Shot and Live, Attenuated intranasal Influenza Vaccine, Nasal Spray). Antiviral drugs for influenza are adjunct to influenza vaccine for controlling and preventing influenza. There are four licensed influenza antiviral agents available. The four drugs are classified into two categories, the Adamantane derivatives (Amantadine and Rimantadine) and Neuraminidase inhibitors (Zanamivir and Oseltamivir).

The recent outbreaks of avian influenza in Asia (2003-2004) have been caused by the highly pathogenic H5N1 strain. There is evidence that this strain has a unique capacity to jump the species barriers and cause severe disease, with high mortality in humans. Avian influenza does not normally infect species other than birds. But it was first reported in humans in Hong Kong in 1997 with the H5N1 strain infecting 18 Humans, 6 of whom died. To date, the recent outbreak of avian influenza (H5N1) has caused more than 30 humans death, as reported. There is no evidence to date, human to human transmission of H5N1 strain. Apart from H5N1 strain, H9N2 and H7N7 stains also infect humans.

Currently there is no vaccine effective against H5N1 strain in humans. But current vaccines when administered to high risk groups protect against circulating human strains and thus reduce the risks that human at high risk of exposure to the bird virus that might become infected with human and avian viruses at the same time.

In uncomplicated cases of bird flu, symptom based therapy with Acetaminophen for the relief of headache and fever may be considered. Patients should be advised to rest and maintain hydration during acute illness. There is no evidence that the virus is passed through eating chicken or any poultry product till date since in the cooked poultry product the heat sterilizes the virus. Chicken products should be cooked thoroughly at a temperature of 100°C for a minimum duration of 10 minutes to make it safe.●

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"The Physicians look with another eyes on the medicinal herb than the grazing ox which swoops it in the comman grass" -Joseph Glanvill

"There seem to be a feeling that anything that is natural must be good. Strychnine is natural"-Isaac Asimov

"Health is the vital principle of bliss, And exercise, of health" - James Thomson

"Fat people who want to reduce should take their exercise on an empty stomach and sit down to their food out of breath. Thin people who want to get fat should do exactly the opposite and never take exercise on an empty stomach" -Hippocrates, Greek Physician

# STUDY OF ADVERSE DRUG REACTIONS IN WARDS OF A TERTIARY CARE HOSPITAL

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#### BACKGROUND

Patients' safety has gained momentum worldwide especially when the hospitals are expected to comply with the highest standard of quality in patient care. Pharmacovigilance aims to spot ADRs that had taken place through a keen review of the previously researched articles, other relevant publications and serve as a tool for the better use of drugs.

Drug-safety is the primary importance of any health care unit and a good pharmacovigilance can identify the risks or risk factors in a short possible time.

#### OBJECTIVE

The objectives of the study were:

- 1. To identify the Adverse Drug Reaction by Chart Review method.
- 2. To classify the Adverse Drug Reactions on the basis of Edward and Aronson's criteria.
- 3. To determine the prevalence of Adverse Drug Reactions with respect to various risk factors.
- 4. To determine the causality of the Adverse Drug Reactions by Naranjo's algorithm.
- 5. To determine the causality of the Adverse Drug Reactions by Karch & Lasagna criteria (used by the collaborating hospital).
- 6. To analyze the severity of the Adverse Drug Reaction by modified Hartwig method.
- 7. To analyze the preventability of the Adverse Drug Reaction by Thornton and Schumock criteria.

#### METHODOLOGY

This was a prospective study carried out in in-patients' ward of a private tertiary care hospital. Patients admitted to the hospital were evaluated for ADRs throughout their hospital stay. The patients were selected randomly on the basis of the inclusion and exclusion criteria given below.

#### Inclusion Criteria

• Patients of all age groups and of either sex.

#### Exclusion Criteria

• Patients' document with incomplete information.

In addition to the prescribed medications, the S.O.S. drugs were also taken into consideration. All the suspected ADRs that had occurred after admission as a possible result of drug(s) initiated or continued in hospital were studied

Data on the reported ADRs were evaluated to understand the pattern of the ADR with respect to patient demographics, nature of the reactions, characteristics of the drugs involved, and outcome of the reactions. The adverse drug reactions were identified; causality, severity and preventability were also analyzed

#### Causality assessment

The degree of association of an adverse effect with a drug was done with the help Naranjo's algorithm and Karch & Lasagna's criteria where in the former assigns the score to a set of questions. The total score for a particular drug-ADR combination is calculated and the association is termed into one of these categories- definite, probable, possible or doubtful and the latter which is a non-scoring system classified the criteria into- certain, probable, possible, unlikely, unclassified and unassessable.

#### Severity assessment

The severity of the ADR was assessed using adapted Hartwig severity scale.

#### Preventability assessment

It was assessed using Schumock and Thornton's criteria.

#### Statistical analysis

All the data was represented as average ( $\pm$ SEM) and percentages. The association of various risk factors with ADRs was analyzed using Chi square ( $^2$ ) test, t-test and ANOVA, odds ratio was used for the comparisons of these risk factors

#### RESULTS

The results were based on the data captured from in-patients' ward.

Table 1: Demographic characteristics

#### 1. Identification of ADRs

The ADRs were identified on the basis of the laboratory data, vital signs, and new symptoms of the patients after admission to the hospital and also through the spontaneous reporting of the physicians and nurses in the patients' record file. The type of ADRs, drug-class and individual drugs involved in ADRs were identified.

- 1.1 Hypotension The most common type of ADR
- 1.2 Cardiovascular drugs- leading class involved in ADR
- 1.3 Furosemide & Tramadol with the highest frequency of ADRs

#### 2. <u>Classification of ADRs</u>

The ADRs were classified using Edward and Aronson's criteria which was based on whether the ADR was a pharmacological effect and commonly seen, non-pharmacological and immunological, due to chronic use of the medication, delayed effect or failure of a therapy.

#### Type A reactions most commonly observed ADRS

#### 3. <u>Prevalence of ADRs</u>

The ADRs were also analyzed with respect to six risk factors namely; Gender, Age, Wards, Length of stay, Polypharmacy and Number of diagnosis.

3.1 Females show a higher prevalence of ADRs (OR=1.3; CI=0.9-1.7)

- 3.2 Geriatric patients have a higher prevalence of ADRs (OR=2.3; 95% CI=1.1-5.1)
- 3.3 Prevalence of ADRs was more in Cardiovascular ward (OR=1.1; 95% CI=0.8-1.5)
- 3.4 Increase length of stay increased the average number of ADRs (p<0.001)
- Patients with more than 5 diagnosis had a higher prevalence of ADRs (OR=1.1; Cl=0.7-1.8)
- 3.6 Polypharmacy has a direct impact on the number of ADRs (OR= 7.4; 95% CI=2.0-26.8; p<0.001)

#### 4. <u>Causality assessment of ADRs by Naranjo's scale</u>

Naranjo's scale was categorized into 4 groups; 0= doubtful, 1-4= possible, 5-8= probable and 9= definite.

#### Table 9: Causality assessment of ADRs (Naranjo's algorithm)

Scor	Score No. of patients		atients with ADRs		% ADR		
5. Causality assess		sment of ADRs by Ka	rch & lasag	na <sup>0</sup>			
1 – 4 Tal			10: Causality assessment of ADRs (Karch & Lasagna)			asagna)	
5 – 8	8		186	72.1			
≥9	Criter	ion	No <sub>10</sub> f patients wit	h ADRs	3.9	% ADR	
	Certa	ain	12			4.7	
	Proba	ble	134			51.9	
	Possible Unlikely Conditional Unassessable		100			38.7	
			12			4.7	
			0			0	
			0		0		

#### 6. <u>Severity assessment of ADRs</u>

Modified Hartwig's criteria were used for the determination of the severity level of the ADRs. This was classified as 1-2= mild, 3-4= moderate, 5-7b= severe

Criterion No. of patients with ADRs		% ADR
Mild	132	51.2
Moderate	123	47.7
Severe 3		1.1

#### Table 11: Severity assessment of ADRs

#### 7. <u>Preventability of ADRs</u>

In order to reduce the incidence of ADRs the preventability assessment was done. This was done using Schumock and Thornton's criteria. The preventability scale was categorized as definitely preventable, preventable and non-preventable.

#### Table: 12 Preventability assessment of ADRs

Criterion	No. of patients with ADRs	% ADR
Definitely preventable	3	1.2
Preventable	117	36.1
Non-preventable	202	62.7

"If you want Fame and fortune, invent a pill" -James Crichton

"In nature, oil and water dispersions are so well and widely distributed that it may seems as if emulsion formation is a most casual performance. But in reality, the production of a satisfactory commercial emulsion calls for an exacting blend of scientific knowledge, practical skill and intuition, commonly known as "flair". To master emulsion manufacture, it often seems, that one must be smarter than the emulsion, get up earlier in the morning, work harder and study more"-R.M.K. Cobb.

## **DRUGS STORE MANAGEMENT**

#### Lalvuana

Pharmacist, Civil Hospital, Aizawl

anagement han tih hian thil tamtak a huam thei a, mihring te enkawlna lam te, bungrua leh thildang enkawlna lam te, khawl leh hmanrua enkawlna te bakah pawl leh sorkar inenkawlna te pawh a huam thei awm e. Chuti ang hna thawk a, a kaihruaitu ber leh ruahmanna siamtu chu Manager an ti thin a, mite hokhawm a hna kawng khat atana ruahmantu leh duangtu a nih rualin a thununtu an ti bawk thin. Chutianga ruahmanna leh suangtuahna a taka hman theiha kalpui thiam chu management thiam an ni mai awm e.

Management chungchanga kan hriattur thenkhat han tarlang hmasa ila-

i) Planning: Hei hi ruahman thiamna ti ila; enge tih tur, engtikah nge, khawiah nge, engtin nge, tu innge ti ang tih leh engtin nge a hlutna leh hlawkna a lo lanchhuah dan tur tih ruahman thiamna a ni thei ang chu.

ii) Organising: Tum bulfuk tak nei a, chu mi tihlawhtling tura hmanrua leh a hnathawktu tur mihringte an hlutna hmang tangkai a, chhawpchhuak thiam leh huaihawt thiamna te,

iii) Staffing: Hnathawktu thlan dik te, mi tangkai tak leh mawhphurhtir thiam te, zirtir, training pek leh kaihhruai emaw chutianga tanpui thiamna,

iv) Direction : Tum lam nei rana inkaihhruaina leh chumi hawizawnga in kawhhmuhna chunga hnathawktu te kawh hmuh a, kaihhruai dan te,

v) Controlling: Tumna kan neihsa ang te ti hlawhtling tura endikna neih thin te, siamthat ngaite siam that leh a thaber tura kan duh dan anga kalpui tura ruahmanna siam angte kenkawh tlat te leh

vi) Co-ordination: Khing a chunga kan

han sawi tak zawng zawng te a tul dan anga hmankawp thiam leh lakkhawm thiamnate hi a pawimawh hle a ni.

Drugs store Management hi awlsam taka hriatthiam a nih theihnan hetiang hian a tawi thei angberin a pawimawh zual tak tak han tarlang dawn teh ang:

#### 1) A hmunhma:

Drug Store tur atan chuan hmun remchang tak thlan thiam a tul hle, a laili tur a ni a, Items hrang hrang dahkhawm nan a remchang tur a ni a, thil laksawn leh dah luh a remchang tur a ni, hmun hnawng lutuk leh sa lutuk leh eng lut nasa te hi a tha lo a ni.

#### 2) A chhunga hmanruate:

Almirah leh bin/rack chhuar te leh Fridge te Items hrang hrang tan a bikin Damdawi dahna phei chu a phui thain a him tawk tur a ni a, Locker nei leh nei lo te a awm tur a ni.

#### 3) A enkawltu:

A chunga management thiam kan sawi tak te kha Pharmacist-te hi Drugs Store

bikah chuan an ni a, Dan ang pawhin anni hi hman ngei tur a ni. Store room chu thil hrechiang leh hrethiam tur mithiam ngeiin a enkawl tur a ni a, Items tin te a indawt dan leh a awmze nei thei angberin a rem tlar diat ang a, a then phei chu kalh zel ngai te pawh a ni thei a, uluk takin a vawngtha ang a, a mamawhtu hnenah chauh fel taka ziakin a pe chhuak thin ang.

4) A enkawltu Pharmacist-te mawhphurhna lam hi han sawikai leh thuak dawn teh ang. Pharmacist chuan a Stock Items te hi class hrang hrangin a thliar hrang thei a, hetiangin :

a) ABC (Always Better Control) Analysis: Hetiang dan hmang hian kan Damdawi leh Items dang te chu thliarfel theih a duhawm hle. Hei hian sum lam renchemna a thlen bakah Items hrang hrang te chhinchhiah a ti awlsam bik a ni. Kan Items zingah hman tangkai em em leh man to tak, a loa awm theih loh te hi 'A' Class ah dah a ni a, chung atan chuan kan sum sen zawng zawng atanga za zela 70% hman a tul laiin, a items erawhchu tlem te a ni lawi si, kan stock item zinga za zela 10% chauh an ni thung. Kan mamawh leh hman tlanglawn tak tho si, a man pawh to lutuk lo, kan sum sen zawng zawng zat atanga za zela 15% vel tling phak, a items pawh tam tham ve tak ho hi 'B' Class ah dah a ni. Kan Items zingah chuan tlawm tak kan sum sen za zelah 10% chauh ngai leh hmun 75% awh vel daih ni si, enkawl uluk ngai hran lem lo te hi 'C' Class ah dah a ni leh a, hetiang hi ABC Analysis hmanga thliar hran dan chu a ni.

b) VED (Vital Essential Desirable) Analysis : Hetiang dan hi Thil thuhmunah te leh a chi hrangah te hman theih a ni. A awmzia chu Damdawiah chuan entirnan ; Quinine hi chi hrang hrangin siam a ni a, a tel lova awm theih miah loh chu Inj Quinine sulphate chu mamawhna a nasat em avangin Vital a ni a, Quinine HCl chu mamawhna a tlem deuh a, mahse neih tul ve tho si a nih avangin Essential a ni a, Quinine Ethyl carbonate phei chu hman a khat hle tawh avangin Desirable a ni tawh a ni. Hetiang hian Damdawi chi khat kher lo pawh thil kan neih te kha a pawimawh dan azir zela VED Analysis hmanga thliar theih a ni.

c) Identification of Materials in Stores: Kan thil enkawl te Damdawi leh thildangte awlsam taka hriathran dan tur han sawi leh ila; Hemi thu ah hian, Thil engemaw tan hmun a awm tur a ni a, chu thil chu ama hmunah chuan a awm tur a ni,' tih hi khawthlang lam tawng han hawh ve ta ila, a fiah deuh mah na, 'There should be place for everything and everything should be in its place.'Bungrua chu a len dan azir te, a chi hrang azir te leh kan hmanna tur azir tein kan thliar hrang leh thei bawk ang. Chung ang te chu hriat reng te a har thei a, chuvang chuan awlsam taka kan hriat theihnan chhinchhiahna (Coding) hmangin kan hre hrang leh thei dawn a ni. Entirnan; Alphabetic order hmang dawn ta ila, Code 'A' ah chuan Almirah, Atropine prepn etc te emaw coding atan chuan A/AI, A/At chutiang zelin. A awmna hmun (location coding) azirin, hetiangin; Bedside Locker chu Eye ward ah 10 awm ta se, BdL/EW-10 tih mai tur a ni. Hetianga tih hian items chi hrang hrangte an awmna hmun nen record a ti awlsam thei bawk a ni.

A dawt leh ah chuan, kan items enkawlte chu an hlutna a zir te, kan neih rei zawng emaw kawl rei theih chi anih leh nih loh azir tein kan Stock chu a kalpui leh theih a;

*i) First in First Out (FIFO):* Kan neih hmasak apiang chhut chhuah a, pek chhuah hmasak a hman emaw, a man to dan azira ngaihsak bik ngaite a awm thei. Bungrua rei tak kawl chi loh che reng mai chi dah reng lova a lut hmasa apiang a tahtawla hman hmasak ngai te an ni. *ii) Last in First Out (LIFO):* Hetah hian kan dawn hnuhnunber chu a pekchhuah hmasak berah atan chang a awm thin, a dahna tur hmun leh hmain azir loh vang te, kawl reia chhe mai thei te an awm thin avangin.

SI No	Name of Drugs	Period in month	Condition of storage
1	Ampicillin Capsules	24	normal room temp
2	Ampicillin Trihydrate	30	In a cool place (ie.10-25°C)
3	Chloramphenicol cap/tab	48	-do-
4	Streptomycin sulphate	48	not to exceed 20°C
5	Vitamin K	60	In a well closed container
			protected from light in a cool
			place
6	Insulin Preparations	24	At temp between 2-8°C not
			to freeze
7	Whole Human Blood	21 days	At temp between 4-6°C
8	BCG Vaccines	14 days	In cold place (ie. Below 8°C)
9	Adrenaline inj	12	-do-
10	Polio Vaccine	24	If stored at -20°C
		6	If stored at 0°C
		3	If stored at4°C

Damdawi thenkhat Storage Condition lo tarlang leh zawk ila:

Heng hi a tlangpui tak tak an ni a, hetiang ang standard storage condition kher hman tum hram a, a rem ngang lo a nih chuan kan damdawi te an chakna a tlahniam deuh dawn tihna a ni.

**Tlangkawmna:** Kan sawi tak zawng zawngte khi a hlawhtlinna chu a enkawltu Pharmacist te kutah a innghat lian hle a, a zira zir hetiang enkawl tura thiamna nei kan nih avangin mahni ngeiin remfel leh ruahman thiam angai a, tutee maw zir ve lem lo te kutah dah mai lovin mahni ngei kan pawimawh, chumi ti tur chuan management kan han tih tak a hi a pawimawh hle a ni. Chutih rualin kan chunga thu neituten kan Items te dan ang taka enkawl ngai an nih zia an hriat thiam ve a ngai hle a ni, chuti a nih loh chuan a hmun (store room) ringawt pawh remchang lo takah kan inbengbel a, tawt lutuka kan thil neih te kan enkawl fo chuan a bikin Damdawi te ngat phei chu a potency (chakna) hlauh vek thei anih bakah beisei loh chemicals hlauhawm zawk te a siamchhuah theih avangin min hriatthiampuina leh ngaihsakna a pawimawh hle a ni. Chuti ang taka Drugs Store Management lam chu thil tul anih chuan Pharmacist te tana Training neih thin dan te ngaihtuah ni thei se, Pharmacist chuan kan Ethics ah pawh damdawi Quality tha chauh ka pe ang tih kan neih kha a taka hman i tum zel ang u.

# HEALTH HAZARDS OF MOBILE PHONES

Mrs. Sh. Victoria Devi Lecturer, RIPANS Zemabawk, Aizawl

ne of the most common sights we see these days is that of people with their mobile phones next to their ears. A boon for better communication, cell phone usage nonetheless has many health hazards. Various studies indicate that the emissions from a cell phone can be extremely harmful, causing genetic damage, tumors, memory loss, and increased blood pressure and weakening of the immune system. This is alarming information, and one has to take account all these factors.



#### CELL PHONES AND HEALTH

Though there is no evidence of cells phones causing cancer or any such illness, but the suspicion, or fear of the same is not baseless either. The electromagnetic radiation from cell phones does have a potential link to cancer. The fact that this radiation is invisible, intangible, and enters and leaves our bodies without our knowledge makes it even more intimidating.

#### Possible Hazards:

- Two minutes of exposure to emissions from mobile phones can disable a safety barrier in blood causing proteins and toxins to leak into the brain, could increase chances of developing Alzheimer's multiple sclerosis and Parkinson's. (Scientists at Sweden's Lund University)
- Scientist say exposure to the phones' low level radiation causes red blood cells to leak hemoglobin and can lead to heart disease and kidney stones.
- Recent studies suggesting a link between cell-phone use and brain tumors, and the possibility that the microwaves could ignite petroleum fumes at gas stations.
- A cell phone unit, or communications tower, has so many thee radiation emanating gadgets. This can be a problem for its immediate environment.

#### Specific Health Concerns:

#### Cancer (Tumors)

Studies have been conducted suggesting that rats that have been exposed to microwaves similar to the sort generated by mobile phones but more powerful, showed breaks in their DNA which could indicate an adverse effect. Also, mice exposed to radiation for 18 months developed brain tumors. Though of course, these studies are not concrete proof.

#### **Blood pressure**

It was observed that people using cell phones were prone to high blood pressure. Again, there isn't any concrete evidence of the same.

#### Pregnancy

A study at the University of Montpellier in France was carried out on 6000 chick embryos and suggested that the heavily exposed chick eggs were five times less likely to survive than the control group. This study raised questions about possible effects on pregnant women but it has not yet appeared in peer-reviewed scientific literature or been reproduced, so its findings are difficult to assess.

#### Headaches, Heating Effects, Fatigue

A study brought out that longer the people used mobile phones, the more likely they were to report symptoms such as hot ears, burning skin, headaches and fatigue. The study did not include a control group (that is people who do not use mobile phones, to make a comparison); therefore the symptoms reported could have been caused by any number of other factors in the mobile phones users' environment, such as working with computers, stress, driving or reading.

#### Memory

There have been various studies into the connection between mobile phones and memory loss. A study looked into the effect of radiofrequency (RF) on the section of rats' brains that is linked with the memory. The results showed that RF could modify signals in the cells in a part of the brain that is responsible for learning and short term memory.

#### Posture (holding phone between raised shoulder and ear)

Some researchers claim that holding a mobile phone between the raised shoulder and ear could have a damaging effect on muscles, bones, tendons and discs. These problems would apply equally to a cordless phone or a landline phone as to a mobile phone and are the effect of bad posture.

#### MOBILE PHONES AND CHILDREN

Because of their smaller heads, thinner skulls and higher tissues conductivity, children may absorb more energy from a given phone than adults.

### **PREVENTION TIPS**

- Cell phones should be used for emergencies, and not for long conversations
- A small chip like cell phone microwave radiation protection device is available, which has ability to absorb electromagnetic energy waves from your mobile phone. It helps in reducing the potential harmful effects of these emissions to the human body.
- Using a mobile headset is a good idea; you don't have to hold phones next to your ears all the time.
- Use a hands free mobile car kit while driving, without taking your hands off the steering wheel.

### THE WHO (World Health Organization) RULES

- Mobile phone users should limit their exposure to harmful radio frequencies by cutting the length of calls.
- Hands free devices cut exposure by keeping the instrument away from the head and body.
- Driving cum mobile phone talking should be banned.
- Mobile phones should not be used in Intensive Care Units of Hospitals as they can pose a danger to patients by interfering with the working of pacemakers and defibrillators.
- People with hearing aids should not use mobile phones.
- Base stations, which have low powered antennae on their terrace to communicate with cell phones, should not be located near children's schools and playgrounds.

### CELL PHONES WHILE DRIVING

Studies indicate that a lot of car accidents have happened, while the driver was on the phone. This is because while driving, one obviously needs to concentrate, and talking on a phone doesn't help. Some countries like Portugal have banned the use of cell phones, which may not be very practical, as their main use is to be reachable while you are on the move. Thus, it is important to take certain precautions while driving:

- Position your phone within easy reach so that you don't have to take your eyes off the road.
- Get to know the features of your cell phone-speed dial, redial, voice mail; they can be your lifesaver. But don't dial and drive at the same time. Use a hands free kit.
- Avoid using a phone when road conditions are hazardous or traffic is heavy. You can let your voice mail take messages and then call back later.
- Don't engage in stressful conversations that may distract your attention from the road.

- Don't take notes or look up phones number whilst driving, wait till you can pull over.
- User abbreviated speed dialing. In fact, voice activated dialing is even better. It leaves both hands free. Frequently called numbers can be programmed.
- Have an answering machine installed that could take messages until you can return the calls. Let your co-passenger handle the calls if you are not travelling alone.

Globalization is the new mantra. In this age, it is very difficult not to have technology. But with technology, come certain hazards. The only way to beat these is again, better technology. Electromagnetic radiation is everywhere. More and more wireless communication services (cellular phones, paging, wireless Internet) are expected so is the artificial electromagnetic radiation. It seems that there is no way to reverse this trend. Scientist and engineers are developing better and safer wireless systems and devices. Smaller cell size, better base station antennas and other more advanced technologies will allow future cell phones to radiate much lower power. So, one can only hope that cell phone hazards will be reduced.

### NEED FOR PUBLIC AWARENESS

It is important to make people aware of the hidden dangers and lessen the use of mobile phones. The radio frequency electromagnetic field generated around the base station antenna may be harmful to general public and operator of maintenance personnel. The practice of installing antennas needs to be regulates in order to protect the general public from undesired effects caused by electromagnetic fields around the antenna.

As a precautionary measure, the mobile phone service providers or manufacturers should avoid promotional advertisements showing vulnerable segments such as children or pregnant women using mobile phones, the draft says.

Calling for raising the level of understanding about mobile phone technology and reduced mistrust and fears both real and perceived, the reports suggest developing an effective system of health information and communication as per WHO guidelines. More independent studies are welcome.

"The Government of India, especially The Ministry of Health, may initiate public awareness programmed in line with WHO recommendations," it says. Also plan to conduct independent studies in this regard. The study will include 4,000 participants and will be conducted under the ICMR guidance in association with JNU's School of Environmental Sciences and Obstetrics& Gynecology, neurology and biochemistry departments of AIIMS. Furthermore, the study will also analyze if the radio frequency wave radiations in India are compliant with the international standard.

Mobile phone radiations have linked to various disorders like depression and sleeping disorders. The present study will also try to pin point if the radio frequency wave radiation cause any effect on fertility of humans, on menstrual cycle, hormonal changes in women and the male reproductive system.

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"In the way of drugs I intend to take a phosphorus pill three times a day, preferably after meals, and a tonic composed of the tinctures of gentian, cinchona, calisaya, and cardamon compound. Into a teaspoonful of this, I shall mix tincture of nux vomica, beginnning with one drop and increasing it a drop each day until the maximum dose is reached. I shall drop this with a medicine- dropper, which can be procure at a trifling cost at any pharmac" - O. Henry

"Poisons and medicines are often times the same substances given with different intents" - Peter Mere Latam

# INTELLECTUAL PROPERTY RIGHTS

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he term intellectual property refers broadly to the creations of the human mind. Intel lectual property rights protect the interests of creators by giving them property rights over their creations.

The Convention Establishing the World Intellectual Property Organization (1967) does not seek to define intellectual property, but gives the following list of the subject matter protected by intellectual property rights:

- Literary, artistic and scientific works;
- Performances of performing artists, phonograms, and broadcasts;
- Inventions in all fields of human endeavor;
- ◀ Scientific discoveries;
- Industrial designs;
- Trademarks, service marks, and commercial names and designations;
- Protection against unfair competition; and "all other rights resulting from intellectual activity in the industrial, scientific, literary or artistic fields."

Intellectual property relates to items of information or knowledge, which can be incorporated in tangible objects at the same time in an unlimited number of copies at different locations anywhere in the world. The property is not in those copies but in the information or knowledge reflected in them. Intellectual property rights are also characterized by certain limitations, such as limited duration in the case of copyright and patents.

The importance of protecting intellectual property was first recognized in the Paris Convention for the Protection of Industrial Property in 1883 and the Berne Convention for the Protection of Literary and Artistic Works in 1886. Both treaties are administered by the World Intellectual Property Organization (WIPO).



Countries generally have laws to protect intellectual property for two main reasons. One is to give statutory expression to the moral and economic rights of creators in their creations and to the rights of the public in accessing those creations. The second is to promote creativity and the dissemination and application of its results, and to encourage fair trade, which would contribute to economic and social development.

### THE TWO BRANCHES OF INTELLECTUAL PROPERTY

Intellectual property is usually divided into two branches, namely copyright and industrial property.

### Copyright

Copyright relates to artistic creations, such as poems, novels, music, paintings, and cinematographic works. In most European languages other than English, copyright is known as author's rights. The expression copyright refers to the main act which, in respect of literary and artistic creations, may be made only by the author or with his authorization. That act is the making of copies of the literary or artistic work, such as a book, a painting, a sculpture, a photograph, or a motion picture. The second expression, author's rights refers to the person who is the creator of the artistic work, its author, thus underlining the fact, recognized in most laws, that the author has certain specific rights in his creation, such as the right to prevent a distorted reproduction, which only he can exercise, whereas other rights, such as the right to make copies, can be exercised by other persons, for example, a publisher who has obtained a license to this effect from the author.

### **Industrial Property**

The broad application of the term "industrial" is clearly set out in the Paris Convention for the Protection of Industrial Property (Article 1 (3)): "Industrial property shall be understood in the broadest sense and shall apply not only to industry and commerce proper, but likewise to agricultural and extractive industries and to all manufactured or natural products, for example, wines, grain, tobacco leaf, fruit, cattle, minerals, mineral waters, beer, flowers, and flour."

Industrial property takes a range of forms, these include patents to protect inventions; and industrial designs, which are aesthetic creations determining the appearance of industrial products. Industrial property also covers trademarks, service marks, layout-designs of integrated circuits, commercial names and designations, as well as geographical indications, and protection against unfair competition. Protection is directed against unauthorized use of such signs likely to mislead consumers, and against misleading practices in general.

### PATENTS FOR INVENTION

Most laws dealing with the protection of inventions do not actually define the notion of an invention. A number of countries, however, define inventions as new solutions to technical problems. The problem may be old or new, but the solution, in order to merit the name of invention, must be a new one. Merely discovering something that already exists in nature, such as a previously unknown plant variety, is not an invention. Human intervention must be added. So the process for extraction of a new substance from a plant may be an invention. An invention is not necessarily a complex item. The safety pin was an invention which solved an existing "technical" problem. New solutions are, in essence, ideas, and are protected as such. Thus protection of inventions under patent law does

not require that the invention be represented in a physical embodiment.

Patents, also referred to as patents for invention, are the most widespread means of protecting the rights of inventors. Simply put, a patent is the right granted to an inventor by a State, or by regional office acting for several States, which allows the inventor to exclude anyone else from commercially exploiting his invention for a limited period, generally 20 years. By granting an exclusive right, patents provide incentives to individuals, offering them recognition for their creativity and material reward for their marketable inventions. These incentives encourage innovation, which in turn contributes to the continuing enhancement of the quality of human life. In return for the exclusive right, the inventor must adequately disclose the patented invention to the public, so that others can gain the new knowledge and can further develop the technology. The disclosure of the invention is thus an essential consideration in any patent granting procedure. The patent system is so designed as to balance the interests of inventors and the interests of the general public.

The word patent, or letters patent, also denotes the document issued by the relevant government authority. In order to obtain a patent for an invention, the inventor, or the entity he works for, submits an application to the national or regional patent office. In the application the inventor must describe the invention in detail and compare it with previous existing technologies in the same field in order to demonstrate its newness.

Not all inventions are patentable. Laws generally require that an invention fulfill the following conditions, known as the requirements or conditions of patentability: Industrial Applicability (utility). The invention must be of practical use, or capable of some kind of industrial application.

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- Novelty. It must show some new characteristic that is not known in the body of existing knowledge (referred to as prior art) in its technical field.
- Inventive step (non-obviousness). It must show an inventive step that could not be deduced by a person with average knowledge of the technical field.
- Patentable subject matter. The invention must fall within the scope of patentable subject matter as defined by national law. This varies from one country to another. Many countries exclude from patentability such subject matter as scientific theories, mathematical methods, plant or animal varieties, discoveries of natural substances, methods for medical treatment (as opposed to medical products), and any invention where prevention of its commercial exploitation is necessary to protect public order, good morals or public health.

The conditions of novelty and inventive step (non-obviousness) must exist at a certain date, generally the date on which the application is filed. There is an exception to this rule, covered by an applicant's right of priority, regulated by the Paris Convention for the Protection of Industrial Property. This exception relates only to applications made in countries party to the Paris Convention. The rights of priority means that, having filed an application in one member country of the Paris Convention, the same applicant (or his successor in title) may, within a specified time period, apply for protection for the same invention in any of the other member countries. These later applications will be regarded as if they had been filed on the same day as the earliest application.

For example, if an inventor first files an application for patent protection in Japan, and later a second application, with respect to the same invention, in France, it is sufficient that the conditions of non-obviousness existed at the date on which the Japanese application was filed. In other words, the later, French application retains priority over any applications relating to the same invention filed by other applicants between the dates of the inventor's first and the second application. This is subject to the period between the two dates not exceeding 12 months.

It is customary to distinguish between inventions that consist of products and inventions that consist of processes. The creation of a new alloy is an example of a product invention. The invention of a new method or process of making a known or new alloy is a process invention. The corresponding patents are usually referred to respectively as a product patent and a process patent.

The persons to whom a patent is granted, is known as the patentee, the owner of the patent or the patent holder. Once a patent has been granted with respect to a particular country, anyone who wishes to exploit the invention commercially in that country must obtain the authorization of the patentee. In principle, anyone who exploits a patented invention without the patentee's authorization commits an illegal act. The protection is granted for a limited period, generally 20 years. Once a patent expires, the protection ends, and the invention enters the public domain. The patentee no longer holds exclusive rights to the invention, which then becomes available for commercial exploitation by others.

The rights conferred by a patent are not described in the patent itself. Those rights are described in the patent law of the country in which the patent is granted. The patent owner's exclusive rights generally consist of the following:

- In the case of a product patent, the right to prevent third parties without the owner's consent from making, using, offering for sale, selling or importing for these purposes the product;
- In the case of a process patent, the right to prevent third parties without the owner's consent from using the process; and to prevent third parties from using, offering for sale, selling or importing for these purposes the products which were obtained directly by that process.

The patentee is not given a statutory right to exploit his own invention, but rather a statutory right to prevent others from commercially exploiting it. He may give permission, or grant a license, to other parties to use the invention on mutually agreed terms. The patentee may also sell his right to the invention to someone else, who will then become the new owner of the patent.

There are certain exceptions to the principle that a patented invention cannot legally be exploited without the authorization of the owner of the patent. These exceptions take into account the balance between the legitimate interests of the patentee and those of the general public. Patent laws may provide for cases in which a patented invention may be exploited without the patentee's authorization, for example, in the wider public interest by or on behalf of the government, or on the basis of a compulsory license. A compulsory license is an authorization to exploit the invention given by a governmental authority. It is generally issued only in very special cases, defined in the law, and only where the entity wishing to exploit the patented invention is unable to obtain the authorization of the owner of the patent.

### UTILITY MODELS

While not as widespread as patents, utility models are also used to protect inventions. Utility models are found in the laws of more than 30 countries, as well as in the regional agreements of the African Regional Industrial Property Organization (ARIPO) and the Organisation africaine de la propriété intellectuelle (OAPI).

The expression "utility model" is simply a name given to a title of protection for certain inventions, such as inventions in the mechanical field. Utility models are usually sought for technically less complex inventions or for inventions that have a short commercial life. The procedure for obtaining protection for a utility model is usually shorter and simpler than for obtaining a patent, but utility models usually differ from patents for invention in the following main respects:

- The requirements for acquiring a utility model are less stringent than for patents. While the "novelty" requirement must always be met, that of "inventive step" or "non-obviousness" may be much less or even absent altogether. In practice, protection for utility models is often sought for innovations of a rather incremental nature, which may not meet the patentability criteria.
- The maximum term of protection provided by law for a utility model is generally shorter than the maximum

term of protection provided for a patent for invention (usually between 7 and 10 years).

The fees required for obtaining and maintaining the right are generally lower than those for patents.

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### **INDUSTRIAL DESIGNS**

An industrial design, in general terms, is the ornamental or aesthetic aspect of a useful article. This aspect may depend on the shape, pattern or color of the article. The design must have visual appeal and perform its intended function efficiently. Moreover, it must be able to be reproduced by industrial means; this is the essential purpose of the design, and is why the design is called industrial.

In a legal sense, industrial design refers to the right granted in many countries, pursuant to a registration system, to protect the original, ornamental and nonfunctional features of a product that result from design activity. So in registering their industrial designs, manufacturers protect one of the distinctive elements that determine market success. One of the basic aims of industrial design protection is to stimulate the design element of production. This is why industrial design laws usually only protect designs that can be used in industry or that can be produced on a large scale.

This condition of utility is a notable difference between industrial design protection and copyright, since the latter is only concerned with aesthetic creations.

Industrial designs can generally be protected if they are new or original. Designs may not be considered new or original if they do not significantly differ from known designs or their combinations. The legal protection offered by industrial designs concerns only the design that is applied to, or embodied in, articles or products. This protection does not prevent other manufacturers from producing or dealing in similar articles or products, as long as these do not embody or reproduce the protected design.

Industrial design registration protects against unauthorized exploitation of the design in industrial articles. It grants the owner of the design the exclusive right to make, import, sell, hire or offer for sale articles to which the design is applied or in which the design is embodied.

The term for an industrial design right varies from country to country. The usual maximum term is from 10 to 25 years, often divided into terms requiring the proprietor to renew the registration in order to obtain an extension of the term.

### TRADEMARKS

A trademark is a sign, or a combination of signs, which distinguishes the goods or services of one enterprise from those of another.

Such signs may use words, letters, numerals, pictures, shapes and colors, as well as any combination of the above. An increasing number of countries also allow for the registration of less traditional forms of trademark, such as three-dimensional signs (like the Coca-Cola bottle), audible signs (sounds, such as the roar of the lion that precedes films produced by MGM), or olfactory signs (smells, such as perfumes). But many countries have set limits as to what may be registered as a trademark, generally allowing only signs that are visually perceptible or can be represented graphically. A trademark is a sign used on goods or in connection with the marketing of goods. The trademark may appear not only on the goods themselves but also on the container or wrapper in which the goods are sold. When used in connection with the marketing of the goods the sign may appear in advertisements, for example in newspapers or on television, or in the windows of the shops in which the goods are sold.

In addition to trademarks identifying the commercial source of goods or services, several other categories of marks exist. Collective marks are owned by an association, such as an association representing accountants or engineers, whose members use the mark to identify themselves with a level of quality and other requirements set by the association. Certification marks, such as the Woolmark, are given for compliance with defined standards, but are not confined to any membership. A trademark used in connection with services is called a service mark. Service marks are used for example by hotels, restaurants, airlines, tourist agencies, car-rental agencies, laundries and cleaners. All that has been said about trademarks applies also to service marks.

Broadly speaking, a trademark performs the following four main functions. These relate to the distinguishing of marked goods or services, their commercial origin, their quality and their promotion in the market place:

To distinguish the products or services of one enterprise from those of other enterprises. For example, the word "apple" or the image of an apple cannot distinguish apples, but it is distinctive for computers. Trademarks do not only distinguish products or services as such, they distinguish them in their relationship to an enterprise from which the products or services originate.

- To refer to a particular enterprise, not necessarily known to the consumer, which offers the products or services on the market. Thus trademarks distinguish products or services from one source, from identical or similar products or services from other sources. This function is important in defining the scope of protection of trademarks.
- To refer to a particular quality of the product or service for which it is used, so that consumers can rely on the consistent quality of the goods offered under a mark. This function is commonly referred to as the guarantee function of trademarks.
- To promote the marketing and sale of products, and the marketing and rendering of services.

The owner of a registered trademark has an exclusive right in respect of his mark. It gives him the right to use the mark and to prevent unauthorized third parties from using the mark, or a confusingly similar mark, so as to prevent consumers and the public in general from being misled. The period of protection varies, but a trademark can be renewed indefinitely on payment of corresponding fees. Trademark protection is enforced by the courts, which in most systems have the authority to block trademark infringement.

### TRADE NAMES

Another category of industrial property covers commercial names and designations. A commercial or trade name is the name or designation that identifies an enterprise. In most countries, trade names may be registered with a government authority. However, under Article 8 of the Paris Convention for the Protection of Industrial Property a trade name must be protected without the obligation of filing or registration, whether or not it forms part of a trademark. Protection generally means that the trade name of one enterprise may not be used by another enterprise either as a trade name or as a trade or service mark; and that a name or designation similar to the trade name, if likely to mislead the public, may not be used by another enterprise.

### **GEOGRAPHICAL INDICATIONS**

A geographical indication is a sign used on goods that have a specific geographical origin and possess qualities or a reputation that are due to that place of origin. Agricultural products typically have qualities that derive from their place of production and are influenced by specific local factors, such as climate and soil. Whether a sign functions as an indication is a matter of national law and consumer perception. Geographical indications may be used for a wide variety of agricultural products, such as "Tuscany" for olive oil produced in a specific area of Italy, or "Roquefort" for cheese produced in a certain region of France. The use of geographical indications is not limited to agricultural products. They may also highlight particular qualities of a product, which are due to human factors found in the place of origin of the products, such as specific manufacturing skills and traditions. That place of origin may be a village or town, a region or a country. An example for the latter is Switzerland or Swiss, which is widely perceived as a geographical indication for products that are made in Switzerland, in particular for watches.

An appellation of origin is a special kind of geographical indication, used on prod-

ucts that have a specific quality that is exclusively or essentially due to the geographical environment in which the products are produced. The concept of geographical indication encompasses appellations of origin. Examples of appellations of origin which are protected in states party to the Lisbon Agreement for the Protection of Appellations of Origin and their International Registration include "Habana" for tobacco grown in the Havana region of Cuba, or "Tequila" for spirits produced in particular areas of Mexico.

Geographical indications are protected in accordance with national laws under a wide range of concepts, such as laws against unfair competition, consumer protection laws, laws for the protection of certification marks or special laws for the protection of geographical indications or appellations of origin. In essence, unauthorized parties may not use geographical indications if such use is likely to mislead the public as to the true origin of the product. Applicable sanctions range from court injunctions preventing the unauthorized use, to the payment of damages and fines or, in serious cases, imprisonment.

### PROTECTION AGAINST UNFAIR COMPETI-TION

The Paris Convention for the Protection of Industrial Property, Article 10bis, requires its member countries to provide protection of industrial property against unfair competition. This article is directed against acts of competition that are contrary to honest practices in industry or commerce. The Paris Convention lists the following as acts of unfair competition in relation to industrial property:

All acts of such a nature as to create confusion with the establishment, the

goods or the industrial or commercial activities of a competitor;

- False allegations in the course of trade of such a nature as to discredit the establishment, the goods or the industrial or commercial activities of a competitor;
- Indications or allegations, the uses of which in the course of trade are liable to mislead the public as to the characteristics of certain goods.

Protection against unfair competition supplements the protection of inventions, industrial designs, trademarks and geographical indications. It is particularly important for the protection of knowledge, technology or information which is not protected by a patent but which may be required in order to make the best use of a patented invention.

### THE ROLE OF WIPO

The World Intellectual Property Organization (WIPO) is an international organization dedicated to ensuring that the rights of creators and owners of intellectual property are protected worldwide and that inventors and authors are thus recognized and rewarded for their ingenuity. As a specialized agency of the United Nations, WIPO exists as a forum for its Member States to create and harmonize rules and practices to protect intellectual property rights. Most industrialized nations have protection systems that are centuries old. Many new and developing countries, however, are now building up their patent, trademark and copyright laws and systems. With the rapid globalization of trade during the last decade, WIPO plays a key role in helping these new systems evolve through treaty negotiation, legal and technical assistance, and training in various forms, including in the area of enforcement of intellectual property rights.

WIPO also provides international registration systems for patents, trademarks, appellations of origin and industrial designs. These greatly simplify the process for simultaneously seeking intellectual property protection in a large number of countries. Instead of having to file national applications in many languages, these systems enable applicants to file a single application, in one language, and to pay a single application fee. The WIPO-administered systems of international protection include four different mechanisms of protection for specific industrial property rights:

- The Patent Cooperation Treaty (PCT) for filing patent applications in multiple countries.
- The Madrid System for the International Registration of Marks for trade and service marks.
- The Hague System for the International Deposit for Industrial Designs.
- The Lisbon System for the International Registration of Appellations of Origin.

Anyone applying for a patent or registering a trademark or design, whether at the national or international level, needs to determine whether their creation is new or is owned or claimed by someone else. To make this determination, huge amounts of information must be searched. Four WIPO treaties have created classification systems, which organize information on different branches of industrial property into indexed, manageable structures for easy retrieval:

 Strasbourg Agreement Concerning the International Patent Classification.

- Nice Agreement Concerning the International Classification of Goods and Services for the Purposes of the Registration of Marks.
- Vienna Agreement Establishing an International Classification of the Figurative Elements of Marks.
- Locarno Agreement Establishing an International Classification for Industrial Designs.

WIPO also provides an Arbitration and Mediation Center, which offers services for the resolution of international commercial disputes between private parties involving intellectual property. The subject matter of these proceedings includes both contractual disputes (such as patent and software licenses, trademark coexistence agreements, and research and development agreements) and non-contractual disputes (such as patent infringement). The Center is also now recognized as the leading dispute resolution service provider for disputes arising out of the abusive registration and use of Internet domain names.

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# PHARMACEUTICAL INDUSTRY-A INDIA DINHMUN

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Pharmaceutical sciences hi mizoten kan hmelhriat loh lam tak ni in a lang. Pharmacy profession lama kan hriat deuh awm chu damdawiina kan pharmacist ho leh Drugs Inspector te hi an ni mai awm e. He pharmaceutical sciences hi India ram economy chawikangtu a nihna leh khawvel mithmuha India min phochhuaktu a nihna lam chu kan zingah chuan hriat a hlawh hmel lem loh hle. Amaherawh chu thiamna sang zelah pharma science lam zirte pawh kan lo pung ve zel a,



Mizoten kan hmelhriatna a la rei lo viau nachung hian mithiam pawh kan nei ve nual ta. Ph.D zir zo lai te kan nei ve ta reng mai. He article-ah hi chuan pharmacy ho hnathawh pakhat, damdawi siamchhuah lama India ram dinhmun tlangpui kan tarlang dawn a ni.

India ram hi ram lian tak, mihring cheng pawh tam tak kan ni a. Tun dinhmunah hian mihring tluklehdingawn (billion 1.13) vel bawr kan awm a ni. Mihring kan tam ang bawk hian damdawi mamawhna pawh a sanga, Pharma industry pawh kan ngah hle reng a ni. India ram damdawi siamna company (pharma company)-te hi an thangduang hle a, khawvel huap pawha pharma market thang chak ber pawl te zinga mi a ni. Kum khat chhunga India pharma company te turnover hi US dollar tluklehdingawn (billion) 4.5 vel lai a tling phak a ni. Kum 2006 chhung khan khawvela Pharma industry-te thanna rate chu 5% bawr vel a nih laiin India pharma company te thanna rate chu 10% chuang a tling phak hial a ni. A hnuaiah hian kum 2008-09 chhunga India pharma company thenkhatte annual turnover han tarlang ila.

Pharm. Industry	(in crores)
Ranbaxy	₹ 7400
Dr.Reddy's	₹ 6901
Cipla	₹ 5257
Sun Pharma	₹ 4272
Lupin	₹ 3866

India ramah hian damdawi siamna company lian zual (large scale) 300 chuang a awm a, tin, a laihawl leh te deuh (medium leh small scale) 10,000 chuang a awm bawk. A chunga kan tarlan company pangate kum khat chhung sum che vel pawh khitianga tam a nih chuan an vaia sum che vel chu tam tham tak tur a ni. Chuvangin pharma industry-te hian India ram economy-ah pawh dinhmun pawimawh tak an luah mek reng a ni. India pharma market hi production volume-ah chuan khawvel pumpuiah 4-na dinhmun a hauh mek a. Consumption value-ah chuan 13na dinhmunah a awm mek bawk. Kan dinhmun hi a chhe lem lo hle.

Tun kum 30 kal ta chhung khan India pharma company-te hi awm lo ata pharma khawvela hruaitu dinhmunah an rawn invawrh chhuak kan ti thei ang. A chhan kawng tam tak a awm ang a, a chhan lian tak pakhat nia lang chu kum 1970-a patent act hman tan a nih khan process patent (damdawi siam dan patent) kha product patent (siamchhuah sa patent) ai khan ngaih pawimawh a ni a. Chumi vang chuan India company-te chuan licensing fee pe lovin foreign company-te damdawi patent-te pawh a siam dan tidanglam (reverse engineering)-in an siam ve thei a. Heng damdawi an siamchhuah (generic drug)-te hi damdawi original (branded drug) tluk thova tha leh hna thawk an ni a. Hei hian nasa takin damdawi man a tihhniam phah ta a, chu chuan India pharma company-te hralhchhuah pawh a tihsan phah hle. Amaherawhchu, hei hian that lohna kawng lian tak pakhat a nei a, chu chu India pharma company ten damdawi siamchhuah leh hmuhchhuahna (research and development) lamah an hnufum phah hle a ni. Kum 2005-a patent (amendment) act hman tan a lo nih khan nasa takin pharma company-te pawh a

her danglam a. Procees patent mai ni lovin product patent pawh khauh takin lekkawh a lo ni ta a. Chu mai bakah kum 1995 January ni 1 atang khan reverse engineering pawh khap a lo ni ta bawk. Mahse hei hian India pharma company te a titlachhe hauh lo. Tlakchhiat ahnekin hma an sawn phah nasa hle zawk a ni. Chutia patent rules and regulation khauh taka kenkawh a lo nih takah chuan foreign pharma company tam tak ten India pharma company-te nen contract signin contract manufacturing leh outsourcing te hmangin India pharma company-te production a tihsan phah ve thung a. Hetianga foreign company ten India ram kher an rawn thlanna chhan hi eng dang vang ni lovin damdawi siamna tur raw material kan ngah vang te, industry dinna tur ram kan neih that vang te, mi thiam leh tawng thiam (english speaking) kan ngah vang te a ni. Tin, sawi leh sawi hnu, mihring kan tam a, hei hian market a tihthat phah bawk. Hei hian India ram damdawi thawnchhuah pawh nasa takin a tihsan phah a. India rama damdawi siamchhuah 40% hi ram danga thawnchhuah a lo ni ta a. Khawvel pumpuia bulk drug mamawh zat 40% hi India siamchhuah hian a lo phuhruk ta bawk. Tun hnai kum reilote chhung hian India damdawi thawnchhuah rate hi 20% aia sangin a pung hman bawk.

Mizoten kan hmelhriat ve deuh ramhmul damdawi (herbal drug) lam pawh hi a thangduang hle mai. India herbal drug market hlut zawng hi US dollar 62 billion lai a tling phak nia! Khawvel pum huap pawh hian herbal drug hmangtute an pung chak hle a. Herbal drug hmangtute hi 15%-a an pun laiin damdawi pangngai (modern pharmaceuticals) hmangtute hi 3% chauhin an pung thung. North-east India hi ramhmul damdawiah chuan kan hausa a, India ramah chuan resource nei tha ber area kan ni hial mai thei a ni. Hei hi hriain kan kawmthlang vai ho pawh hian min hmu tai titih der tawh niin a lang. India rama Pharmaceutical sciences zirna lar leh tha takte zinga mi National Institute of Pharmaceutical Education and Research (NIPER), Mohali-a Natural Product department te khuan major project-a neiin 'Survey and evaluation of pharmaceutical potential in North east India' tih chu an zo der tawh nghe nghe.

Keini Mizoram ngei pawh hi ramhmul damdawi kan neih thatzia chu inhrilh hriat kher ngai lovin a hre chiangtute vek kan ni. Heng kan hausaknate hi tun aia chak zawka hai chhuah dan te hi nei thei tawh ila chuan kan state pawh hian hma a sawn nasat phah ngeiin a rinawm. India pharma company thangduang tak hi lo ràl thlir ringawt a, India economy-in a that phahzia thu mahni tapchhak zawla lo sep rawtui ngawt lo hian pharma company te vanga hmasawnna te tel phatu kan nih ve hun hi a nghahhlelhawm mang e. Heng kan ramhmul damdawite hi hai chhuakin ram hmasawn nan kan hmang thei dawn nge, kum tin kan dan pangngai angin kan vât ang a, kan vah bak bak thlengin kan tikang duai duai zel mai dawn?●

"Good medicine is man's salvation; Excessive use gives aggravation"-Alexis Lawrence Romanoff

"There are no such things as incureable, there are only things for which man has not yet found a cure"-Bernard Baruch.

"A single untried popular remedy often throws the scientific doctor into hysterics"-Anonymous

"Surely every medicine is an innovation, and he that will not apply new remedies, must expect new evils" -Francis Bacon

# NIPER ATANGA KA THIL ZIRCHHUAHTE

### K.Thanzami

Asst. Professor Department of Pharmacy, RIPANS

um 2007, June thla, khawlum vanglai khan Punjab khawpui Chandigarh ka thleng ve rawih mai a. Chuta tang chuan ka M.S.Pharm zirna tur, India rama Pharmacy zirna in tha bera inchhal ngam, National Institute of Pharmaceutical Education and Research (NIPER) awmna, Chandigarh atanga hla lo te, Mohali chu ka pan ve leh a. He zirna ina kal dil (apply) tur hian national level exam pakhat, Graduate Aptitude Test-in Engineering (GATE), tuna Graduate Pharmacy Aptitude Test (GPAT) ni ta, hi paltlang phawt a ngai a. Chumi hnu chuan NIPER Joint Entrance Exam (JEE) paltlang leh a ngai a ni.He zirna in atang hian Master degree ka zirchhuah mai bakah thil dang tam tak ka zir chhuak a; heng thil dang ka zir chhuahte hi a ni tuna han tarlan ka tum ber chu.

NIPER-ah hian hmarchhak lampang mi, kal hmasa ber ka ni a, a tirah chuan a khawharthlak duh ang reng khawp mai. Mahse, B.Pharm ka zir laia ka classmate thin Bihari pakhat, ka kal hma kuma lo lut tawh, a lo awm ve hlauh mai a, hostel ka luh hmaa ka awmna tur, guest roomte min lo ngaihtuah sak vek a, ka buai tur leh lunglen tur a ti ziaawm ve khawp mai. Sawi tawh angin NIPER-ah hian hmarchhak mi an hmuh vawikhatna ka nih avangin a tirah chuan min duat uchuak khawp mai a, foreigner ang lek lek hian min hmu thinin ka hria; kan rama kan chaw ei thin leh kan nun dan min zawt uluk thei khawp mai. Chandigarh lampangah hmarchhak mi an thahnem ve tehreng nen, kan veng, Mohali lampangah chuan hmuh tur an tlem deuh aniang, dawra thiante nen kan han kal te hian, dawr nghaktu te hi an lo tawng puam ve ringawt zel a, nuih a za duh khawp mai.

Tichuan ka han awm rei ve deuh a, vai ho an sual, an phakar tih sawi uarna rama pianga seilian ka ni nangin vai ho fel zia ka hre chho a. Thian tam tak ka chhar chho zela, heng ka thiante hi India ram hmun hrang hrang atanga lokal te an ni hlawm a, a ram mi, Punjabi chu an tam lem lo. A tam zawkte chu thiam thei tak tak, an college/university kalnaa a ber kai (topper) te an ni hlawm. Chuvang chuan an thluak a tha em em vek mai a, mahse chu aia ka sawi duh chu an kalna tur (career path) ah hian an lo chiang em em mai a ni. Keini chuan NIPER te chu B.Pharm kan pass hnuah kan hre ve chauh a, anni ve thung erawh chuan B.Pharm zir an tum atang tawh khan Master degree zirna atan NIPER hi an lo thlang fel dim diam tawh a. An kal leh zel dan tur, PhD zir zel an tum emaw, hna zawn an tum emaw, India-ah nge foreign-ah awm an tum tihte an inngaihtuah fel lawk diam a, chumi tih hlawhtlin tum chuan theihtawpin an bei bawk thin. Keiniin a remchang chang kan zir a, zir theihna hmun ruak thei ang ang a zir kan tum hi chu an ang lo deuh. Tin, ka sawi duh leh pakhat chu zirlaiah mi tanpui an peih em em a, mahniin thiam bik a, midangin thiam ve lo se tih lampang hi an rilru ah a lang vak lovin ka hria. Tin, thil tha nia an hriat chu midang tan pawh an duhsak ve em em a, an inhrilh darh zung zung thin. Midang puih hi an inpeih em em a, puih kan ngai anih chuan hun an nei mai lo anih pawhin hun an neih theih dan tur an zawng hram hram thin. Han damloh nikhuate hian an bengvarin an tlawmngai thei em em a, a hrehawm tur ang aiin a hrehawm lo zawk thin a ni. Tin, ka fak leh duhna chu an rintlak em em mai khu a ni; miin thil ka lo ti ang an tih tawh chuan an rin ngam thlap a, 'ka theihnghilh' emaw 'ka hman leh lo' tih hi an nei ngai lo.

NIPER-a ka thil zirchhuah leh pakhat chu taimakna hi a ni. Hna hi an thawk nasa em em a; zirtirtu an ni emaw, zirlai an ni emaw, an hnaah an tui em em a. Hnathawh hun chhung (office hour) hi zing dar 9 atanga tlai dar 5 thleng ni mahse zirtirtute hi zan dar 10 thleng thlenga an awm chang a tam mai. Zirlaite phei chu zan dar 12 thleng laboratory-a hna thawh hi chu dan pangngai a ni a, zing dar 2 dar 3 thlen chang pawh hi a tam mai. Inrinni leh chawlhni hi a hming chuan chawlh a ni ve nangin zirlai leh zirtirtu tam zawkte chu department building-ah hmuh tur an awm thin. Mahse, hunawl han insiam chang chuan party, dinner eichhuah, cinema en leh han lenlam velte hi chu nuam an ti ve khawp mai, rilru berah erawh chuan an neih lem lo thung. Tin, an rilru a zau em em a, Hindu an ni emaw, Muslim an ni emaw, Jain an ni emaw, Sikh an ni emaw pawh ni se, an sakhaw hunpui (puja) te hi an inhlut pui thiam khawp mai a, an lawm mup mup vek zel mai. Christmas te pawh hi lawm an chak ve thin a, mahse a Kristian awmchhun ber hi Christmas hmanga in lama haw ka duh thin avang hian lawm ngaihna vak an hre lova, an lawm lo mai a ni.

Kan awmna hi Chandigarh-a Mizo ho awmna nen a inhlat deuh bakah inkhawm peih mi tak ka lo nih loh avangin Mizo zirlai dangte nen kan inhmu khat hle a. Kan inhmuh chhuna Mizo zirlai tam zawk awmte ka hmuh dan chu, phaia an awm chhan an zirlai aia thil ngaih pawimawh an nei ngah lutuk ni in ka hria. Kohhran lampang a ni emaw, zirlai pawl lampanga an chanvo a ni emaw, lenlam hrim hrim lampang ani emaw, ka hmuh ve dan chuan an zirlai tibuai khawpa inhmang an tam mah mah thin`. Tin, Mizo Kristian zirlai tamtak hian ringlo mi kan tihte atang hian zirtur tam tak kan neiin ka hria a. An sakhuaah an chiangin an pathiante hi an ring em em a, mahse keini Mizo te ang hian an nundan/zirlai/hnathawh tibuai thak khawpin an buaipui ve lem lo. An hnathawhah hian an rinna an tilang mai zawk thin. Tin, anmahni an invawng em em a, an taksa tana hrisello thil chu an ei/in lo ngamin an taksa tana tha tur hi an zawng hram hram zel thin. Keini Mizote angin zu, zuk leh hmuam an tih loh avangin fel leh tha ta luaah an in ngai ve lem lova, anmahni tana tha tur tih an hriat avanga ti lo mai zawk an ni. A chunga ka han tarlan tak thenkhat, NIPER-a ka thian ringlo mite(?) nundan leh awmdan tam tak atang khian keini ringtu inti te hian zirtur kan ngah hle in ka hria.

# LINGZHI - THE WONDER DRUG



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ABSTRACT: Ganoderma lucidum (Lingzhi or Reishi) is a medicinal fungus, which has been widely used in traditional Chinese medicine for a long time. It contains a variety of biological properties that promote good health and longevity. This review provides an insight into the history, availability and potential of this herbal drug in the field of modern medicine. It describes the pharmacologically active compounds and complex constituents of this mushroom and their possible reactions in the human body. Ganoderma lucidum has antitumor, antiviral, immunomodulatory, hypoglycemic and anti-oxidative activities which have been demonstrated in many studies. A brief account on its present day status is also discussed.

**KEYWORDS:** Ganoderma lucidum, Lingzhi, polysaccharides, triterpenes, diabetes, anti-tumor activities, immunomodulatory action.

### INTRODUCTION

Ganoderma lucidum is a medicinal fungus or mushroom indigenous to China <sup>1</sup>. Ganoderma is derived from 2 Greek words: ganos-shining or brighten and derma-skin, thus meaning 'shining skin'. It was used in traditional Chinese medicine since 4000 years back to promote good health. It is the oldest mushroom to be used in medicine. It is popular as 'Reishi' in Japan and 'Lingzhi' in China. Lingzhi in the Chinese language means 'herb of spiritual potency'.

Ganoderma mushrooms are tiny fungi that are unable to manufacture their nutrients through photosynthesis like green plants. In nature, they grow at the base and stumps of deciduous trees like Maple. They are found in steep and high mountain regions and are rare in the wild form. Ganoderma has about 200 species. According to the oldest Chinese medical book, 'The Chinese Herbal Materia Medica' Ganoderma species with high therapeutic value have been classified into 6 categories according to their shape, color and the body part which they affect. They are as follows:-

Red-heart, Purple-joints, Green-liver, White-lung and skin, Black-kidney and brain, Yellow-spleen.

Reishi or Lingzhi is a white rot basidiomycete with immunomodulatory, anti-ageing, detoxicant, cardiotonic and anti-tumor properties. The fruiting body of Reishi was first authenticated by Xiao Lan Mao, Journal of Microbiology, CAS.

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Reishi or lingzhi has been classified in Shen Nang's Materia Medica as a 'drug of high grade' i.e. a herb of high medicinal value and without toxicity. Lingzhi was known and valued by the ancient Chinese kings and queens. They would consume the mushroom and later murder the soldiers who brought it to them so as to guard the secret of their long life and healthy youthful skin from going to anyone else. At present Ganoderma lucidum is being produced by some Asian countries for commercial purposes. It was first successfully cultivated using PTC technique in1970 by Yukio Naoi of Kyoto University. Spore cultivation method is generally used. The 3 well known methods of cultivation are:

- 1. Natural Growth
- 2. Capsulated Cultivation
- 3. Logwood Cultivation.

### BASIC CELL CONSTITUENTS OF LINGZHI

Ganoderma lucidum possesses a large variety of bioactive compounds. The main chemical constituents are:-

- Polysaccharides
- Proteins
- Triterpenes
- Organic germanium

Other bioactive compounds have also been isolated and identified such as ergo sterols, coumarin, alkaloids, unsaturated fatty acids, vitamins and minerals.

Ganoderma lucidum Polysaccharides (GI-PS) also known as Ganopoly is the main efficacious ingredient of Reishi (Ley ss ex Fr) Karst. It has been extracted by hot water from the fruiting body of Ganoderma lucidum. The average yield of GI-PS is reported to be 0.82% in terms of the fruiting body. GI-PS is a polysaccharide-polypeptide with an average molecular weight of 584900 and has more than 17 amino acids. The ratio of polysaccharide to peptide is 93.51% : 6.49%. Polysaccharides consist of rhamnose, xylose, fructose, galactose, mannose and glucose with molar contents of 0.793 : 0.904 : 2.944 : 0.167 : 0.384 : 7.94 respectively. These sugars are linked together by B-glucosidic linkage. It is a hazelnut colored powder and soluble in water<sup>2</sup>. Ganoderan A and B are the main glucans.

Ganoderma lucidum proteins usually occur with polysaccharides as Ganoderma lucidum polysaccharide protein. The novel immuno modulatory protein known as Ling Zhi-8 (LZ-8) has been isolated<sup>3</sup>. Ganoderma lucidum proteoglycan has a carbohydrate: protein ratio of 10.4:1 Several triterpenes(>120) have been isolated and they are steroid hormones such as Ganoderic acid A, B, C, D, F, G, H, R, S, Y, Z 1. Other important ones are Ganoderiol F(a tetra cyclic triterpene)<sup>4</sup>,ganodermatriol, ganodermaiol, 26 oxygenosterols viz. Ganoderol A, Ganoderol B, Ganoderal A<sup>5</sup>.

Organic germanium is a compound which maintains or restores balance in the body. Germanium is dissolved in water and taken as medicin. According to physics theories and quantum biochemistry every organ in our body has an electric potential of its own and when the organ becomes dysfunctional the potential of the organ changes. Germanium restores the abnormal potential to normal since it is a semi-conductor. Its electrons seize away other substances easily.

**SECONDARY METABOLITES** :The hydro distillates and solvent extracts of fruiting bodies of

*Ganoderma lucidum* have been investigated. The oil constituents comprised of hydrocarbons, monoterpenes, and fatty acids<sup>6</sup>. Major volatile components are

- 1. trans-anethol
- 2. R-(-)-linalool
- 3. S-(+)-carvone
- 4. L-bisalobol

Two types of purified samples are obtained through consecutive separation process from cultivated broth of Ganoderma mycelium<sup>7</sup>. They are

- Water soluble sample (M.W. 1.2×10 6 Daltons)
- Water insoluble sample (M.W 1.0×10 6 Daltons)

The phenolic and alcoholic extracts of the fruiting body also produce significantly useful metabolites e.g.: methanol extract gives an L-Glucosidase inhibitor designated as SKG-38.

Active ingredients	Uses	Target system	
POLYSACCHARIDES	Anti-microbial, anti-viral, anti- fungal, anti-cancer Immune system		
PROTEINS	Anti-inflammatory, anti-platelet aggregation, coronary vasodilator, calming sedative effect, neuro- protective action	Immune system, Nervous system, Vascular system	
TRITERPENES	Anti-allergic, anti-stress, hepato- protective, anti-cholesterol, insulin like action, anti-hypertensive	Immune system, Endocrine system, Vascular system, Metabolic system	
ORGANIC GERMANIUM	Anti-oxidant, increases blood flow and oxygen supply, immune system support, protects bone density	Immune system, Vascular system, Skeletal system	
STEROLS	Hormone precursor, lowersHormone system,cholesterol synthesisMetabolic system		
ESSENTIAL FATTY ACIDS	Anti-inflammatory, regulates bodily processes, cell membrane integrity	Metabolic system, Immune system	

### KEY EFFECTS OF LINGZHI ON THE HUMAN BODY

According to the concept of Chinese traditional medicine Lingzhi affects the five important organs- heart, lung, liver, pancreas, and kidney and it can be served for their impairment control. The specific effects of Ganoderma lucidum are mentioned below:-

### 1. ANTI TUMOR ACTION:

Lingzhi enhances the body immune system and increases self-defense capability against tumor<sup>9</sup>. Ganoderic acids Z, Y, X, W, V, and T have been reported to have anti-cancer properties. Ganoderic acid A & C have been proved to inhibit Farnesyl Protein Transferase, an enzyme which participates in Rasdependent cell formation. These inhibitors play a role in potential therapeutic strategy for cancer treatment<sup>10</sup>.

### 2. HEPATO-PROTECTIONS AND DETOXI-FICATION:

Lingzhi is able to protect the liver from damage caused by a number of physiological and biological factors. According to an experiment which was conducted, Ganoderic acids R & S and Ganosporeric acid A in vitro have shown anti-hepatotoxic activity in galactosamine induced cytotoxic test with primarily cultured rat hepatocytes<sup>11</sup>. In vivo, two fractions of a total triterpenoid extract of G.lucidum (75% ethanol) can protect mice from hepatic necrosis induced by chloroform and D-galactosamine<sup>12</sup>.Effects are attributed to the ability of the triterpenoid extract to promote activity of scavenging enzymes for hepatic free radicals thus increasing anti-oxidation ability in mice<sup>13</sup>. Lingzhi also speeds up the metabolism of medicine and toxic substances in liver leading to curing of toxicated hepatitis and efficient detoxification. It relieves dizziness, fatigue, and related symptoms.

## 3. ANTI ATHEROGENIC AND CARDIO VASCULAR EFFECTS:

Reactive oxygen species and increasing blood lipids level are the key elements in pathogenesis of atherosclerosis. Control of cholesterol and other blood lipids reduces the risk of development and progression of atherosclerosis. Lingzhi reduces the levels of blood lipids, lipoproteins, and triglycerides in hypertensive subjects and high cholesterol diet rats14. It prevents the formation of atheromatous patches and reduces cholesterol in arterial walls thus softening blood vessels to prevent further damage. It also partially improves blood circulation and inhibits platelet aggregation contributing to stroke prevention. Lingzhi effectively dilates coronary artery, increases coronary flow and improves circulation in cardiac muscle capillaries. It is a valued anti-hypertensive.

### 4. HYPOGLYCEMIC EFFECTS:

Lingzhi is of immense use in the treatment of diabetes. G.lucidum serves as a substitute to insulin to inhibit release of fatty acids. It ameliorates symptoms in high glucose and high urine glucose subjects.Ganoderan A &B exhibit hypoglycemic effects and reduce diabetic symptoms<sup>15</sup>. Water soluble polysaccharides suppress insulin independent diabetes. A study was carried out in which 71 patients with confirmed type 2 diabetes were treated with Ganopoly (1800mg, 3 times daily for 12 weeks). At week 12 post-prandial glucose values had decreased to 11.8 mmol/L which was a significant difference compared to placebo group<sup>16</sup>.

### 5. IMMUNO-SUPRESSIVE AND ANTI-ALLERGIC ACTIONS:

Invasion of the body by an antigen elicits an immunological reaction that results in various malfunctions and immuno-pathological symptoms. Lingzhi has the ability to suppress these reactions and resume body order and function. It inhibits allergic reactions. Some compounds of G.lucidum viz. Ganoderic C & D inhibit histamine release from rat mice cells<sup>17</sup>. Several triterpenes show anti-complement activity against classical pathway of complement system with an IC 50 value of 5-40microM.eg: Ganoderiol F, Ganodermatriol, and Ganodermanondiol<sup>18</sup>. Ganoderic acids A, B, G, and H are effective in anti-inflammation. Many experiments and researches have depicted that G.lucidum stops the release of hyper susceptibility factors and prevent occurrence of allergic reactions. Therefore Lingzhi is effective in the treatment of illnesses caused by autoimmunity or hyperactivity mainly allergic asthma, chronic bronchitis, rheumatoid arthritis, skin allergies et al. Lingzhi exerts a beneficial immunomodulatory effects in patients with rheumatoid arthritis<sup>19</sup>. It was reported that administration of hot water extracts of a herbal formula containing Ganoderma lucidum as one of its components decreased herpes zoster pain with no post-herpetic neuralgia development after more than one year follow-up<sup>20</sup>.

### 6. ANTI-OXIDATIVE AND OTHER BIO-LOGICAL ACTIVITIES:

The anti-oxidative and free radical scavenging effects of the polysaccharides and triterpenes have been demonstrated in varied oxidative injury models including tert butyl hydro peroxide damaged mice peritoneal macrophages, alloxan-induced diabetes, cervical carcinoma rats and liver injury models<sup>21,22</sup>. Triterpenoids of this fungus are able to inhibit cholesterol synthesis and display atherosclerotic protection by inhibition of angiotensin converting enzyme<sup>23</sup>. The polysaccharides and polypeptides also delay ageing

of skin by enhancing synthesis of nucleic acids and proteins in blood plasma and bone marrow. Another factor that attributes to antiageing is the presence of anti-oxidant like material such as Super Oxide Dimutase (SOD). This anti-oxidant is needed to encounter damage to the body by free radicals such as Reactive Oxygen SpecieS (ROS). A fraction of the amino polysaccharide of Lingzhi behaves like SOD and protects against oxidative DNA damage<sup>24</sup>. The capacity of Ganoderma lucidum for skin protection has been exploited in beauty care and treatment.

### POSSIBLE UNDERLYING MECHANISMS OF ACTION OF LINGZHI

**IN CANCER:** The most attractive character of Lingzhi is its anti-tumor and immuno modulatory properties. The anti-tumor effect is brought about by enhancing the immune system. The water extract and polysaccharide fractions of G. lucidum modulate many components of the immune system such as the antigen-presenting cells, NK cells, T and B lymphocytes<sup>25</sup>. A number of experiments conducted in tumor bearing animals' in vivo as well as in vitro studies have enlightened us about the possible mechanism of these fungal extracts on anti-cancer actions<sup>26</sup>.

*GI* EFFECTS ON THE FUNCTION OF MONO-NUCLEAR PHAGOCYTE SYSTEM: The treatment of mice with the water extract from *Ganoderma lucidum* spores by s.c. injection resulted in a considerable increase in the activities of lysozome, acidic phosphatase, βglucoronidase and promoted the hydrogen peroxide formation<sup>27</sup>. This indicates that the water extracts of *GI* spores are able to activate macrophages. The Ganoderma polysaccharides increased the production of Interleukin (IL) 1 and tumor necrosis factor (TNF- ) in mouse peritoneal macrophages.

During the administration of crude GLE at 5, 10, and 20 g/kg by forced stomach tube feeding, TNF- mRNA expression in the peritoneal macrophages was also markedly increased. Thus the water extract and polysaccharide fractions could induce TNF- expression both in vivo and in vitro<sup>27</sup>. Exposure of human neutrophils to GI PS time dependently caused an increase in protein kinase C (PKC), p38 mitogen-activated protein kinase (MAPK), hematopoeitic cell kinase (HKC), and other tyrosine kinase Lyn activities which all contribute to the action of enhanced unspecific immune function<sup>28</sup>. Thus Ganopoly has the ability to enhance neutrophils function in phagocytosis and chemo taxis. They also inhibited spontaneous and Fas-induced neutrophils apoptosis in vitro<sup>29</sup>.

### GI EFFECTS ON DENDRITIC CELLS AND NATU-

**RAL KILLER CELLS:** Dendritic cells (DC) are pivotal for primary immune response. They are a kind of professional antigen-presenting cells. It has been shown that the *GI*-PS could increase the o-expression of CD11c and I-A/I-E molecules on DC surface, promote mRNAexpression of cytokine IL12 p40 in DC and augment protein production of IL -12 p40 in culture supernatants<sup>24</sup>. The lymphocyte proliferation of mixed lymphocyte culture (MLC) induced by matured DC was also enhanced by *GI*-PS.

**GI EFFECTS ON T LYMPHOCYTES:** Three kinds of GI-PS viz. BN3A, BN3B & BN3C increased the lymphocyte proliferation induced by Con A and IL-2 production in normal and aged mice in vitro.BN3A & BN3C could also antagonize the suppressive action of hydrocortisone on proliferation of mouse spleen cells<sup>30</sup>. They could also increase DNA synthesis in spleen cells of MLC by enhancing DNA polymerase induction in the young and aged mice. Moreover Gl increased the production of IFN- and markedly increased IFN- mRNA expression in T lymphocytes<sup>31</sup>.

GI EFFECTS ON B LYMPHOCYTES: The GI-PS significantly increased the lymphocyte proliferation induced by LPS<sup>32</sup>. A bioactive fraction isolated from the fruiting body of GI could stimulate the activation, proliferation and differentiation of B lymphocyte. This fraction known as GLIS is believed to be a new B-cell stimulating factor<sup>25</sup>. The immunomodulating effects of Lingzhi are so extensive because the polysaccharides particularly active -Dglucans could bind to the lymphocyte surfaces through specific receptors or serum specific proteins. This leads to alteration of the activities of the macrophages, T-helper, NK, and other effector cells. It has been reported that GI-PS showed the same basic -glucan structure with different types of glycosidic linkages. Some structural features such as -1, 3-linkages in the main glucan chain and further -1, 6-branch points are needed for immuno modulating and anti-tumor activities. The glucan containing mainly 1, 6-linkages has less activity. Glucan with higher molecular weight are also more effective than those with lower molecular weight<sup>33</sup>.

Three new lanostante-type aldehydes named as lucialdehyde A, B, C were isolated from the fruiting body of Gl. Lucialdehyde b, c show cytotoxic effect on Lewis Lung Carcinoma (LLC), T-47D, Sarcoma 180 and Meth-A tumor cell lines. Lucialdehyde exhibited the most potent cytotoxicity against the tested cell lines<sup>34</sup>.

Ganoderma lucidum mycelia activated NF-kappa beta by increasing the kappa beta DNA binding activity, thus enhancing innate immunity<sup>35</sup>. Gl extract was also found to inhibit proliferation pf SW480 human colorectal cancer cells<sup>36</sup>. Ganoderma lucidum

polysaccharides polypeptide inhibited the growth of vascular endothelial cells and induction of vascular endothelial growth factor (VEGF) in human lung cancer cells. Research has indicated that proliferation of HUVECs was inhibited by Ganoderma lucidum polysaccharides polypeptide in a dose-dependent manne<sup>37</sup>. Extract of Gl also showed the strongest 5 -reductase inhibitory activity. Treatment of the extract significantly inhibited testosterone-induced growth of the ventral prostate in castrated rats. Thus it is a useful ingredient for the treatment of Benign Prostatic Hyperplasia<sup>38</sup>.

### OTHER IMMUNO MODULATARY ACTIONS

Apart from enhancing immune action, could also down-regulate the excessive immune functions. The cytokine-modulating effect of *GI* PS is also tissue Ganoderma specific.

It was found that the proteoglycan isolated from GI mycelium (GLPG) had protective effects against carbon tetrachloride-induced cell injury in a dose-dependent manner<sup>39</sup>. This proteoglycan has 86.4% carbohydrate and has antioxidant activity. It decreased ALT & ASTactivities in CCl4-induced liver injury. This hepato-protective activity is due to its ability to scavenge free radicals induced by carbon tetra chloride (increased SOD activity). Carbon tetra chloride also induces TNF- secretion which contributes to the cellular damage in liver. GLPG down-regulated the CCl4induced TNF- level in plasma of mice thus inhibiting occurrence of inflammation, but the mechanism is still not known.

GI PG also contain anti-viral properties against herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2)<sup>40</sup>. It has been demonstrated that GLPG exerted its inhibitory effect against the virus by interacting with the positive charges on the virus or on the cell surface and thus inhibited viral penetration into the host cells.

Two lanostante-type triterpenes, lucidumol A and Ganoderic acid beta showed significant anti-human immunodeficiency virus (anti-HIV)-1 protease activity with IC50 value of 20-90  $\mu$ M<sup>41</sup>.

The immunomodulatory lectin, LZ-8 has immunosuppressive activity in vivo. It is composed of 110 amino acid residues. It could prevent the production of antibody to HBs antigen with high inhibition rate on intraperitoneal injection in mice<sup>3</sup>. A polysaccharide obtained from the sporoderm-broken spores of *Gl* (MW 1.26×105) was found to have a strong suppressing effect on antibody production and LPS induced lymphocyte proliferation in mice<sup>42</sup>. Ganoderma lucidum also displayed hepato-protective action against Hepatitis B virus<sup>43</sup>.

IN ANTI-OXIDATION: Oxidative stress has been linked with many diseases such as cancer, aging and atherosclerosis. Experimental studies have demonstrated that antioxidants and phytochemicals could prevent cancer metastasis and were suggested as adjuvants in cancer therapy<sup>44</sup>. Gl inhibited oxidative stress induced migration of MCF-7 breast cancer cells by the down regulation of MAPK signaling<sup>45</sup>. Other studies have shown that peptides isolated from GI possess potent antioxidant activity with little or no side effects. Ganoderma lucidum peptides blocked lipoxygenase activity and had scavenging effect towards hydroxyl radicals<sup>46</sup>. It also effectively guenched super oxide radical anion produced by pyrogallol auto-oxidation in a dosedependent manner. It pays a distinctive role in inhibition of per oxidation in biological systems through antioxidants, metal chelating and free radical scavenging properties activity. Gl exerts therapeutic effects against atherosclerosis by ameliorating inducible Nitrous oxide synthase (i NOS)-mediated NO overproduction in macrophages<sup>47</sup>. NO is a principle mediator in many physiological and pathological processes. Overproduction of NO via the inducible NOS has cytotoxic effects through formation of peroxynitrite with super oxide anion (oxidation). The i NOS is mainly expressed through macrophages and is able to produce large amounts of NO. The expression of i NOS is mainly regulated at expression level. The i NOS mediated NO production attributes to the development of atherosclerosis. Inhibitory effect of GI was mediated through its antioxidant action against LPS-induced super oxide anion in macrophages. Lingzhi extract (100µg/ml) completely abolished LPS-induced i NOS mRNA expression and NO production. Thus inducible NO synthase expression in macrophages is inhibited.

### CONCLUSION

At present, between 80 to 85% of all mushroom products are derived from their fruiting bodies that have been either commercially farmed or collected from the wild. With the increasing demand for better and up to grade health products from the public; it is a prior commitment of all competent pharmaceutical companies to come up with newer grade of drugs and their concepts. It is necessary that the marketed products are safe, essential, non-toxic, affordable and patient friendly.

Considering the fact that they are mushroom-extracts Ganoderma products are relatively cheap; method of production is economical and does not require complicated processes. They are marketed as

1) Spore powder capsules

2) Spore powder (shell broken, whole plant)

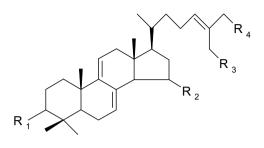
- 3) Tablets
- 4) Tea & Coffee
- 5) Slices
- 6) Soft oil capsules
- 7) Polish
- 8) Toothpaste , soap and shampoo

Attention should be emphasized on the legal regulations for authorization as a drug or dietary supplements. For utility of Gl as a drug, nutraceutical or other purposes the prerequisite is the continuous and uninterrupted production of either the fruiting bodies or mycelia in high accounts and in a standardized manner. Lingzhi therefore provides an alternative to health concerned citizens of this twenty-first century world to have a more promising and healthy lifestyle.

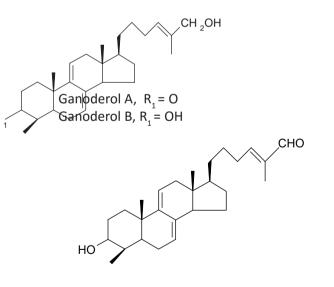
Ganoderic acid A,

 $R_{1} = R_{3} = R_{6} = O, R_{2} = R_{5} = -OH, R_{4} = H$ Ganoderic acid B,  $R_{1} = R_{3} = R_{5} = R_{6} = O, R_{2} = -OH, R_{4} = H$ Ganoderic acid C,  $R_{1} = R_{3} = R_{5} = R_{6} = O, R_{2} = -OH, R_{4} = H$ Ganoderic acid D,  $R_{1} = R_{3} = R_{5} = R_{6} = O, R_{2} = R_{4} = -OH$ Ganoderic acid F,  $R_{1} = R_{2} = R_{3} = R_{5} = R_{6} = O, R_{4} = -OH$ Ganoderic acid G,  $R_{1} = R_{2} = R_{4} = -OH, R_{3} = R_{5} = R_{6} = O$ Ganoderic acid H,  $R_{1} = -OH, R_{2} = R_{3} = R_{5} = R_{6} = O, R_{4} = -OAc$ Ganosporeric acid A,  $R_{1} = R_{2} = R_{3} = R_{4} = R_{5} = R_{6} = O$ 

### Ganodermanontriol R = OH Ganodermanondiol R = H



Ganoderiol F,  $R_1 = O, R_2 = H, R_3 = R_4 = OH$ Ganodermadiol ,  $R_1 = \beta$ -OH ,  $R_2 = R_3 = H, R_4 = OH$ 





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# <text>

besity is a chronic, relapsing, stigmatized, neurochemical disease that is more preva lent in developed/developing countries, and has become a growing health problem in many of the richest nations of the world and should now be considered as a chronic disease that is reaching an epidemic proportions.

### **Obesity definition:**

Obesity has been variously defined as 'an excess of body fat/adipose tissue mass.<sup>1</sup> It is a state of excess adipose tissue mass in the body. Obesity is more effectively defined by assessing its linkage to morbidity or mortality.<sup>2</sup> and is also evaluated by measuring the Body Mass Index.

### BMI (Body Mass Index):

It is a statistical measurement derived from body height and weight. Although it is not a direct measure of adiposity, but it is a most widely used method to measure or assess obesity, which is equal to weight/height2 (in kg/m<sup>2</sup>). Here, the weight of a person (in kilograms) is divided by the square of the height of that person (in meters). Thus, BMI is used as an indicator of whether or not a person is over or under weight.<sup>2</sup>

	BMI (kg/m <sup>2</sup> )	Obesity Class	Associated disease risk for type II diabetes, CVD and hypertension
UNDERWEIGHT	< 18.5		
NORMAL	18.5 - 24.9		
OVERWEIGHT	25 - 29.9		Increased
OBESITY	30 - 34.9	I	High
	35 – 39.9	Ш	Very high
EXTREME OBESITY			
	>40	III	Extremely high

CLASSIFICATION OF OVERWEIGHT AND OBESITY BY BMI. AND ASSOCIATED DISEASE RISK<sup>3</sup>

### WHY DO PEOPLE BECOME OBESE?

Multiple factors are involved in the development of obesity. These may be social, behavioral, environmental and genetics. The problem of obesity has become a global health problem in this present era. Some of the major reasons are as:

### 1) Food intake and Obesity:<sup>4</sup>

The type of food which we consume plays an important part in the development of obesity. Fats have more calories per gram and too much consuming of these foods also disturb the energy balance of the body as well. The increased food consumption which are consisted of carbohydrates (sugars) and also increased consumption of sweetened drinks as well as fast-foods has also contributed significantly to the carbohydrate intake. This leads to obesity.

### 2) Leading a sedentary lifestyle:<sup>4</sup>

In the present generation, we have seen the arrival of computers, televisions, video games, washing machines, dish-washers remote controls and many other modern convenient devices. With these convenient devices, there has been an increased in the sedentary lifestyle of majority of people and a decreased in the physical activity of majority of people. Decreased in physical activity i.e. decreased in the expenditure of energy thereby fail in reducing the fat storage and adjusting the energy balance of the body.

### 3) Drugs causing obesity:<sup>5</sup>

There are certain number of drugs commonly used in the treatment of psychosis, depression, and epilepsy which causes marked weight gain and may either diminish patient compliance or increase the risk of an adverse health outcome. Such drugs are:

**A) Antipsychotics:** Among the antipsychotics, risperidone, sertindole, olanzapine, and clozapine were found to cause weight gains ranging from 2.1-4.5 kg over the course of 10 week of treatment,

**B)** Antidepressants: Among the antidepressants, the risk for significant weight gain was highest for tricyclic drugs, nonselective monoamine oxidase inhibitors, and the novel agent mirtazapine.

**C)** Antiepileptics: Among the antiepileptics, valproate and gabapentin have been found to cause extreme weight gain in some individuals.

### 4) Obesity as a result of disorder of the homeostatic control of energy balance: <sup>1</sup>

It has been found that the plasma leptin is higher in obese individuals compared with non-obese subjects. Leptin (Greek 'leptos' meaning thin), is a protein hormone which has an important effects in regulating body weight, metabolism and reproductive function. It is approx. 16 kDa in mass and encoded by the obese (ob) gene. Leptin receptors are highly expressed in areas of the hypothalamus and are important body weight regulator.

The reason for obesity is due to resistance to leptin. Such resistance could be caused by defects in leptin synthesis, in its carriage in the circulation, in its transport into the CNS, in leptin receptors in the hypothalamus (as occurs in db/db mice) or in post-receptor signalling. There is some evidence that the action of a member of the family of suppressors of cytokine signalling, supressors of cytokine signaling (SOCS-3), may underlie or contribute to leptin resistance. Dysfunction of mediators other than leptin could be implicated in obesity. For example, TNF- $\alpha$ , another cytokine that can send information from fat tissue to brain, is increased in the adipose tissue of insulin-resistant obese individuals.

### 5) Genetic factors and obesity:<sup>6</sup>

It has been found that genetics has shown tremendous effect on the process of weight gain. Recent genetic studies have identified several different causative mutations underlying obesity. There are large number of genes in humans which are believed to affect the body weight and adiposity. Studies in twins and in adoptees and their families indicate that from 40% to as much as 80% of the variance of BMI can be attributed to genetic factors. The discovery that spontaneous mutations arising in single genes (e.g. the ob/ob genotype) produced obese phenotypes in mice led to a search for equivalent genes in humans. In general, however, human obesity should be regarded as a polygenic disorder involving the interaction of many genes. Other genes that appear to be involved include the

<sup>3</sup> adrenoceptor and the glucocorticoid receptor. Decreased function of the <sup>3</sup> adrenoceptor gene could be associated with impairment of lipolysis in white fat or with thermogenesis in brown fat. A mutation of this gene has been found to be associated with abdominal obesity, insulin resistance and early-onset type 2 diabetes in some subjects and a markedly increased propensity to gain weight in a separate group of morbidly obese subjects.

### PREVALENCE OF OBESITY IN INDIA

The prevalence of obesity in Indian population is over 20% in men and 30 % in women in urban areas and nearly 40 % have abdominal obesity. Study shows that 40% of adults in Indian cities and 17.3% in villages are obese<sup>6</sup>. In Punjab the frequency of obesity and overweight has found to be more in urban females than their rural female counterparts. A similar study reported that the prevalence of overweight (BMI > 25) was high among urban southern Indian children (17.8 % in boys, 15.8 in girls). The level of overall and central adiposity, as well as body fat was found to be high among Marwari's as compared with other ethnic populations of India. Prevalence of overweight of affluent children in Amritsar was as high or higher as high in some industrialized countries due to life-style changes and change in eating behaviour. Prevalence of overweight among affluent Bengali children in Kolkata was higher than those reported from other Asian countries7. In Chennai 1618% schoolchildren are obese, and in Cochin 15% of children are obese while 50% of adults are over-weight or obese<sup>6</sup>.

### TREATMENT OF OBESITY

- 1) Non- Pharmacological Approach
- 2) Pharmacological Approach and

### 1) NON- PHARMACOLOGICAL AP-PROACH:<sup>2</sup>

A) Diet therapy: For majority of overweight and obese patients, adjustment of the diet may be done to reduce caloric intake. This includes instructing patients in the modification of their diets to achieve a decrease in caloric intake. Ideally, caloric intake should be reduced only to the level that is required to maintain weight at a desired level. If this level of caloric intake is achieved, excess weight will gradually decrease.

B) Physical activity: An increase in physical activity is an important component of weight loss therapy. Sustained physical activity is most helpful in the prevention of weight regain. In addition, physical activity is beneficial for reducing risks for cardiovascular disease and type II diabetes. Extremely obese persons may need to start with simple exercises that can be intensified gradually. This decision should be based on a patient's age, symptoms, and concomitant risk factors. Some of these include fitness walking, cycling, rowing, cross-country skiing, aerobic dancing, and jumping rope. Jogging provides a high-intensity aerobic exercise, but it can lead to orthopedic injury. If jogging is desired, the patient's ability to do this must first be assessed. The availability of a safe environment for the jogger is also a necessity. Competitive sports, such as tennis and volleyball, can provide an enjoyable form of physical activity for many, but again, care must be

taken to avoid injury, especially in older people.

**C)** Surgery: Weight loss surgery is an option for weight reduction in patients with clinically severe obesity, i.e., a BMI 40, or a BMI 35 with co-morbid conditions. Weight loss surgery should be reserved for patients in whom other methods of treatment have failed and who have clinically severe obesity. Two types of operations have proven to be effective: Those that restrict gastric volume (banded called gastroplasty) and those that, in addition to limiting food intake, also alter digestion (Roux-en-Y gastric bypass).

### 2) PHARMACOLOGICAL APPROACH:<sup>8</sup>

Successful treatment which is defined as the sustained attainment of normal body weight without producing unacceptable treatment-induced morbidity is rarely achieved in clinical practice. Certain approaches produce only short-term weight loss. A carefully controlled diet and physical exercise are the main therapeutic approaches to obesity, but due to an increasing in the numbers of patients an anti-obesity drugs are often required. Such drugs could aim to suppress food intake, increase energy expenditure or increase lipolysis. Numerous pharmaceutical companies are working to provide effective anti-obesity agents. At present there are only two drugs licensed for the treatment of obesity, and are only really effective if given with a controlled diet and the tolerability of these drugs are of neither ideal. These drugs are:

A) Orlistat (which decreases fat absorption by preventing the breakdown of dietary fat in the gastrointestinal tract) and,

B) Sibutramine (which is mainly an inhibitor at the CNS sites that stimulate food intake).

### A) ORLISTAT (Xenical): Approved by FDA in April 1999

<u>Mechanism of action</u>: Orlistat is a pancreatic lipase inhibitor which reacts with serine residues at the active sites of gastric and pancreatic lipases, irreversibly inhibiting the enzymes and thereby preventing the breakdown of dietary fat to fatty acids and glycerols.

Orlistat is also reported to be effective in patients suffering from type II diabetes and other complications of obesity, to reduce leptin levels and blood pressure, to protect against weight loss-induced changes in biliary secretion, to delay gastric emptying and gastric secretion, to improve several important metabolic parameters, and not to interfere with the release or action of thyroid and other important hormones. It does not induce changes in energy expenditure. Its main actions are to reduce food intake and cause dose-dependent weight loss and the weight loss being associated with a decrease in obesity-related risk factors

<u>Unwanted effects</u>: Associated unwanted effects seen with Orlistat are Abdominal cramps, flatus with discharge and faecal incontinence. No significant drug interactions have been noted, except in the case of ciclosporin where reduced absorption of the latter drug has been reported.

### B) SIBUTRAMINE (Meridia): Approved by FDA in November 1997

Mechanism of action: Sibutramine is an inhibitor of neuronal 5-hydroxytryptamine (5-HT)/noradrenaline reuptake at the hypothalamic sites regulating food intake. Its main effects are to reduce food intake and cause dose-dependent weight loss, the weight loss is then associated with a decrease in obesityrelated risk factors. Sibutramine enhances satiety and is reported to produce a reduction in waist circumference which a reduction in visceral fat, a decrease in plasma triglycerides and very low-density lipoproteins, but an increase in high-density lipoproteins.

Unwanted effects: Sibutramine cause an increase in heart rate and blood pressure. Regular monitoring of these parameters is thereby essential. The drug is contraindicated if cardiovascular disease is present or if systolic or diastolic pressure is raised by 10 mmHg or more. Other unwanted effects are dry mouth, constipation and insomnia. Interactions with drugs that are metabolized by one of the P450 iso-enzymes can occur.

The weight reduction obtained with sibutramine alone is not easily maintained. To be effective in anti-obesity therapy it may need to be combined with other anti-obesity measures. Recent multicentre trial involving 499 obese patients was designed to assess the efficacy of sibutramine in maintaining weight loss over a period of 2 years. With oral sibutramine and an individualized management programme of diet, activity and behavioural advice, 77% of obese patients achieved weight loss and most maintained this with continuing treatment over the following 2 years.

### POTENTIAL NEW ANTI-OBESITY DRUGS

Drugs having potential anti-obesity properties are in phase III clinical trial, such drugs are mazindol (adrenergic agonist), posatirelin (a thyrotrophin-releasing hormone analogue) and sertraline (a selective serotonin uptake inhibitor, and some drugs which are still in phase II trial are buproprion (a dopamine re-uptake inhibitor, enterostatin, linitript (cholecystokinin A antagonist), pegylated leptin and AD 9677 (a 3adrenoceptor agonist)<sup>1</sup> Potential targets for new drugs agents that reduce food intake:

- reuptake inhibitors of 5-HT and noradrenaline at hypothalamic sites
- antagonists at receptors for melaninconcentrating hormone (MCH),\* NPY (Y5), corticotrophin-releasing hormone (CRH), galanin, orexins A and B
- binding proteins for CRH agonists at receptors for leptin, AGRP, cholecystokinin A, glucagon-like peptide 1 (GLP-1), Agents that increase energy expenditure or enhance lipolysis
- agonists at the <sub>3</sub>-adrenoceptor bombesin.

### ANTI-OBESITY DRUGS FROM HERBAL SOURCES

The search for plants having an antiobesity property has been going on for a decade and some of the examples of researches done on herbs for the possible activities are as:

A) Nelumbo nucifera: Investigation on the anti-obesity and hypolipidemic properties of Lotus (Nelumbo nucifera) was carried out by Du et al.9 using sprague dawley rats. Here obesity is induced to the animals by giving them a high-fat diet. It was found that the lotus leaf hot water extract supplemented with taurine showed antiobesity and hypolipidemic effect and was more effective than lotus leaf hot water extract alone.

**B)** Lagerstroemia speciosa: The leaves of Lagerstroemia speciosa, known as banaba, have been traditionally consumed in various forms for treatment of diabetes and kidney related diseases. Several in *vivo* and *in vitro* studies have also been conducted and confirmed the anti-diabetic activity10 as well. Research conducted on this plant found out that ellagitannin, an effective constituent of the banana extract has an anti-obesity property as well as an anti-diabetic property.

C) Corchorus olitorius L.: The leaves of molokheiya (Egyptian spinach) was investigated by Wang et al.11 for its antiobesity activity using LDLR mice fed high-fat diet.The antiobesity effect of polyphenolic compounds from molokheiya leaves was demonstrated and found that this effect is associated with reduction in oxidative stress and enhancement of beta-oxidation in the liver. So the researchers concluded that consumption of molokheiya leaves may be beneficial for preventing diet-induced obesity.●

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"Different sores must have different salves" - Chomas Fuller

"Oh Ye Gods, have ye ordeyned for every malady a medicine, for every sore a salve, for every paine a plaster"-John

## DIVINE DI ETARY REVISION

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any of us have heard the rationale for the'Genesis Diet'championed by many sincere and intelligent health experts. This diet is based on Gensis1:29, which gave Adam and Eve instructions to eat liberally from the plants foods lavishly provided in the Garden of Eden.

However, after huminity's Exodus from the Garden of Eden, the proteins unique to animal foods became increasingly important to a race now dependent on heavy labour, speed, and physical strength to survive. God codified approved animal protein sources as recorded in the Old Testament(Lev.11;Deut.14).

The foods approved by God as recorded in Lev.11 and Deut.14 supperceded 'the Genesis Diet' found in the first chapter of the Bible.God decleared "These are the animals which you may eat among all the animals that are on the Earth,"(Lev.11:2). Abraham, Moses, Jacob and Jesus ate Biblical clean meats.But they should avoid to eat unclean meats. The posible reason may be, the Hebrew words used to described "Unclean meats" can be translated as 'foul, polluted and putrid'. The same term were used to describe "Human waste" and other disgusting substances.Now that we all are not in the Garden of Eden, so we all need animal proteins.But we should follow God's instructions.(see Lev.11:3,4,7,8,9).

More and more, history and sciece are confirming that the Creator's provisions for mankinds need for food are still the best choice for ensuring health and quality of life today. If you follow the precise Biblical recommendations for the Creator's Sea-food, you can ensure health and avoid diseases. (see Lev. 11:9) Fish is a wonderfully rich source of protein, potassium, vitamins and minerals. Today the developed countries understand scientifically that Fish and Codliver oil : thin the blood, protect the arteries from damage, inhibit blood clots (antithrombotic), reduce blood triglycerides, lower LDL blood cholesterol, lower blood pressure, reduce risk of heart attack and stroke, reduce risk of lupus, relieve migraine headaches, fight inflamation, help regulate immune system, inhibit cancer in animals (and posibly humans), soothe brochial ashma, combat early kidney disease.

And I would like to quote about one 'unclean'meat that our top favourite food, i.e Pig or Swine in our State. Elmer Josephson who was a Pastor, Missionary and Cancer survivor of American said "The flesh of the swine is said by many authorities to be the prime cause of much of our American ill health, causing blood diseases, weakness of the stomach, liver troubles, eczema, tumors and cancer etc.". So, the Divine revisions of diet/food are very important for our today life. (I am writing this article with out any Denominational filling). If we follow the Divine dietary revision we will be improved and the said 'Health for all'will be achieved in our state.

## **OXYGEN FREE RADICALS, ARTHRITIS AND ANTI-OXIDANTS IN TREATMENT OF RHEUMATOID ARTHRITIS: A REVIEW**

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wo primary trends have dominated research on the pathology of the rheumatism or rheumatic disease over the past few decades: characterization of the mediators of inflammation and elucidation of the immunobiology of the host response. Inflammatory reactions often result in the activation and recruitment of pathogytic cells (e.g., neutrophils and/or tissues macrophage) whose product result in injury to the tissue. A vast amount of circumstantial evidence implicates oxygen derived free radicals, especially superoxide and hydroxyl radicals (and to lesser extent, hydrogen peroxide) as mediators of inflammation or tissue destruction in inflammatory or arthritic disease. As a result superoxides and free radicals might contribute in the biochemical changes observed during acute and chronic phases of study.

Free radicals (often referred to as radicals) are atoms, molecules or ions of unpaired electrons. Free radicals are not by products in general. In theoretical chemistry free radicals are called "Open shell" species while "Closed shells" is the term used for species that have only paired electrons. In brief free radicals are defined as any atom, group of atoms, or molecules with an unpaired electron occupying an outer orbit (Greencoald, RA, 1991). A general description of free radicals and its role towards the biological system are beyond the scope of this article. Nevertheless, a few more things about the generation are discussed here is.

(a) photon induced generation of free radicals

- (b) free radical chain reactions to new free radicals from existing free radicals
- (c) thermal chemical reactions generate free radicals

Regarding the human system, the second cited generation claims a promising status. In human body free radicals can only be generated from other existing free radicals. The oxygen molecule is converted into  $H_2O_2$ in electron transfer process in the synthesis of ATP. The resulting  $H_2O$  contains a highly energetic oxygen- oxygen bond and may be further converted to the free radicals by hemolytic cleavage of the O-O bond or another electron transfer chain.

The biologically relevant free radicals derived from oxygen are superoxide anion, singlet oxygen, hydroxyl radical and hydrogen peroxide. Of the mentioned groups, hydroxyl radicals, OH is the most highly reactive of the entire oxy radical. The bed global term applied to all four radical species as a class is "Oxygen derived free radicals" (Greenwald RA, 1991). ODFR can be generated in biological systems during various biological processes such as enzyme like xanthine oxidase, aldehyde oxidase generated superoxide as a part of their action; Mitochondria and chloroplast generate a steady flux of superoxide. It is also possible that the target cells such as endothelial cells may also provide a source of O<sub>2</sub>, perhaps in a manner analogous to hepatocytes undergoing H<sub>2</sub>O<sub>2</sub> mediated tissues injury (Rubin R, et. al., 1984)

With respect to the toxic species of oxygen derived from inflammatory cells, it appears that  $O_2$  has little direct toxicity for cells or tissues. But it may contribute to the ultimate pathogenesis of injury following mobilization and activation of inflammatory cells (Ward PA, et. al., 1988).

The most toxic oxy radical is hydroxyl radical, OH. It has been proposed that hydroxyl radical could be produced from the interaction of superoxide and hydrogen peroxide via a chemical process called Haber- Weiss reaction.

 $O_2^- + H_2^- O_2^- = O_2^+ OH_2^- + OH_2^-$ 

Another explanation which has now vastly accepted is interaction of metal ions in particular ferrous ion with hydrogen peroxide in what is known as Iron catalyzed Fenton reaction to produce hydroxyl radical (Ward PA, et.al., 1988, Greenwald RA, 1991).

Interest in oxygen derived free radicals as mediators of inflammation comes from identification of two relevant sources phagocytic cells, whose superoxide generating capability was recognized in 1973, and Ischemia/ Reperfusion Hypothesis. Both potential mechanisms are relevant in rheumatism.

#### PHAGOCYTIC CELLS

The biological generation of superoxide was brought to light of researchers attention by Mc Card and Fridovich in 1969 (Mc Cord JM, Fridovich I, 1969) but their initial observation were in enzymatic cell free systems. Later workers shown that leucocytes incubated with latex particles produced species that reduced cytochrome C and it was indeed the superoxide (Babior 1973)

In brief, phagocytic cells, when subjected to certain soluble stimuli or ingestion of particulate matters, undergo a "respiratory burst" characterized by a marked increase in oxygen consumption associated with increased glucose metabolism via HMP shunt. Simultaneously these cells generate both superoxide anion and Hydrogen peroxide. The cells capable of this response include polymorphoneuclear neutrophil (PMN), monocytes, peritoneal macrophage and alveolar macrophage. Neutrophils have long been known to be important sources of tissue destructive mediators involved in the inflammatory response. An evidence for this is in IgG-immune complex mediated vasculitis in the rat neutrophil depletion or complement depletion virtually abolishes all parameters (edema, vascular permeability, hemorrhage) of vascular damage (Cochrome CG, 1974). Some of the stimuli that can evoke the response include opsonized zymosan, C5a from the complement system, aggregated immunoglobulin (IgG), opsonized bacteria, the tumor promoter phorbol myristate acetate and N- formyl-L-methionyl-L-leucyl-L-phenylalanine (FMLP) (Greenwald RA, 1991, PA ward, et.al., 1988).

The sources of superoxide generation is a membrane associated nicotinamide-adenine dinucleotide phosphate, reduced (NADPH) (and perhaps NADH) oxidase (Greenwald RA, 1991).

PMNs and macrophages are obvious components of most acute and chronic inflammatory states. Aggregated immunoglobulins, bacterial products crystal and complement components are also clearly identifiable in many such conditions e.g., Rheumatoid joints. Thus this is highly plausible to conjecture that phagocytic cells within inflamed areas are probably secreting ODFR into their environment.

#### **ISCHEMIA- REPERFUSION HYPOTHESIS**

The second potential mechanism by which ODFR can be generated in vivo in human/animal disease is based on the observations of tissues deprived of oxygen temporarily and subjected to reflow of oxygen bearing blood (Weisfeldt ML, 1987, Mc Cord JM, 1985). In early, 1980s, a series of observations in various animal models of ischemia, showed that much of the tissue damage associated with circulatory compromise actually occurred after blood flow was established. The sources of radicals were identified in some of these systems as xanthine dehydrogenase that gets converted into xanthine oxidase when oxygen flow is cut off, when oxygen re enters the tissue, XO acts on purines such as xanthine or Hypoxanthine and superoxide is generated.

A group of British researchers (Blake DR, et.al., 1989, Woodruff T, et.al., 1986, Merry P et.al., 1989) has reasoned that the hypothesis can be extended to chronic joint inflammation as well. This is based on the observation that intra articular pressures (both resting and with exercise) are much in inflamed rheumatoid arthritis (RA) joints than in normal joints, even when corrected for the degree of effusion and synovial fluid oxygen tensions are lower than would be expected. Thus, the inflames RA joints is relatively ischaemic and anoxic (Levick JR, 1990).

#### FREE RADICALS AND SYNOVIAL FLUID CONDITIONS

The crucial role of Iron in catalyzing the secondary reactions of superoxides is apparent from the works of the earlier investigators. The type or category of Iron that can catalyse in the field of oxygen free radical is still a controversial thing. Lactoferrin can be found in inflamed joints expecting from stimulation of the secondary granules of PMN. However, the not so good catalytic activity of lactoferrin also runs beside it. The role of Iron as phoglistic agents has long been recognized (Blake DR et.al., 1984).

Using sensitive method based on the reaction of free iron with Bleomycin to produce a species that degrades DNA. Synovial fluid samples have been shown to contain sufficient iron to catalyze the necessary superoxide-hydroxyl conversion (Gutteridge JC, 1987, Rowley D et.al., 1984). Free iron in inflammatory synovial fluid has also been detected by the study of iron dependent ascorbate radicals (Buettner GR, Chamulitrat W, 1990). A detailed study of the iron/ ferritin content/saturation in RA tissue has shown ample supplies of potentially catalytic iron therein (Biemond P et.al., 1986). There appears to be little reason to doubt that synovial fluid. with or without contents of PMNs contains ingredients necessary for generation of free radicals.

#### CYTOKINES AND OXYGEN RADICALS FOR-MATIONS

Many cytokines have been described in the synovium in animal models of inflammatory arthritis and in patients with rheumatoids arthritis. These small molecules mediate communication between cells, resulting in attraction of inflammatory and immune cells into the joints and activation of cells to release product that leads to tissues destruction (Arend WP, 2001). Cytokines after binding to specific surface receptor stimulates two signal transduction pathwaysthe AP-1 and NF- B pathway. The latter appears to be particularly important in chronic inflammatory diseases.

An especially potent agonist of macrophages is bacterial liposaccharides. This product is especially effective in terms of its ability to cause macrophages to produce IL-1 and TNF- . The latter two can directly initiate oxidant production by phagocytes (Klebamoff SJ et.al., 1986, Luger TA et.al., 1983). The contact of macrophages with very low concentrations of these cytokines (e.g. < 10-9M) can "prime" Macrophages but not neutrophils for enhanced O<sub>2</sub> responses following addition of agonist such as IgG immune complexes (Warren JS et.al., 1988). Prolonged contact of endothelial cells with these cytokines in vitro enhances its susceptibility to oxygen radical mediated damage by activated neutrophils.

#### FREE RADICALS AS SIGNALING MOLECULES

The seminal work done Bacurle and Colleagues first showed that certain transcription factors of the NF- B/ rel family can be activated only not by receptor targeted ligands but also by the direct application of oxidizing and ionizing agents (Schreak, 1992). There is a hypothesis that  $H_2O_2$  acts through transient oxidative activation of protein Tyrosine Phosphatase (PTPs) which contain a nucleophilic

cystein as a calalytic element of the active site (Suo Goo Rhee, 1988).

It is found out that Interleukin-1 (IL1 ) and  $H_2O_2$  will promote the phosphoractivation of the p-38 mitogen activated protein kinase (p38MAPK) (Robinson et.al., 1999) in a manner that can be antagonized with sub millimolar quantities of NAC or nitrone based antioxidant phenyl-N-tert butyl nitrone (PBN). The PBN has been found efficacious in preventing Ischemia/Reperfusion injury).

The p38MAPK pathway is particularly relevant target for anti-oxidant antagonism in chronic inflammatory diseases; p38MAPK regulates expression of inflammatory cytokine using IL-1 and largely regulates the expression of NOs and COX-2.

#### EFFECTS OF FREE RADICALS ON TARGET TISSUES

#### 1. Hyaluronic Acid

HA is the dominant macromolecule of synovial fluid accounting for the viscosity (but not the lubricating functions) of the fluid. Rheumatologists have long observed that SF viscosity decreases in the presence of inflammation.

Degradation of HA can be produced in two ways: enzymatically by the special class of enzymes called Hyaluronidase, or by chemical interaction of macromolecule with a highly reactive chemical species such as free radical (Greenwals RA, 1991). There is no neutral hyaluronidase in PMN leucocytes and initial observation of Hyaluronidase activity in joints fluid by Bollet in 1963 (Bollet AJ, et.al, 1963) has not (and probably cannot) been confirmed (Greenwald RA, Moak SA, 1986).

Free radical mediated degradation of HA has been produced by:

- Action of XO on hypoxanthine or xanthine. (Mc Cord, 1974, Greenwald RA, Moy WW,1980, Hofmann H et.al., 1980; Betts HW et.al., 1984)
- (b) Action of single oxygen produced produced by exposure of a sensitizing dye to light (Andley UP, et.al., 1983)
- (c) Neutrophils (Greenwald RA, Hoak SA, 1986)

In view of the failure of several laboratories to detect hyaluronidase in the joint fluid (Greenwald RA, 1991), it is now readily accepted that free radicals are probably the mediators of HA degradation following inflammatory excitation of phagocytic cells. The reported effects on HA are depolymerisation, chemical changes to saccharide components.

#### 2. Collagens

Collagens are the major structural proteins of connective tissues accounting for the tensile strength of skin-ligaments, tendons etc. They are resistant to degradation. Only metal-dependent specific collagenases can make an initial clip in native collagen, after which other protease can finish the job.

Workers in leather industry reported that exposure of collagen to singlet oxygen reduced its viscosity impeded fibril formation and altered the primary amino acid composition (Venkatasubramanian K, Joseph KT, 1977). Collagen solutions when exposed to superoxide failed to get normally (Greenwald RA, Moy WW, 1979). Collagens in solution are degraded by exposure to ozone or Fenton Reagents (Kerr JS et.al., 1987). Treatment of collagen with ultraviolet light to generate singlet oxygen causes cross-linking and decreased solubility (Pathak MA et.al., 1990). In summary free radicals would appear to be agents capable of augmenting other systems for collagen break down and disposal by disrupting quaternary structure or making initial cleavages that lead to further enzymatic susceptibility.

Other substrate of rheumatic diseases relevance reported to be susceptible to action free radicals (Greenwald RA, 1991).

#### ANTI OXIDANTS

It is well renowned that the oxygen free radicals discussed earlier have deleterious effects on biomembranes through the formation of lipid peroxides (Babior BM et.al., 1973). Many cellular defense mechanisms are recruited against the toxic effect of these radicals in inflammation including serum sulpahydryl groups (-SH groups) (Lorber et.al., 1975). Ceruloplasmin (Goldstein IM, et.al., 1979), albumin, (Gutteridge JMC, 1986) and blood glutathione (Lands W, et.al., 1971). Moreover, the body employs enzymes such as Superoxide Dismutase (SOD) and catalase against the deleterious free radicals superoxides and Hydrogen peroxides.

From the earlier parts of discussion of the current article, it is very clear that body also does an effective function to prevent itself from the undesired harmful effects of free radicals. Interventions of SOD produce brief (1-2h) protection from the injury and during this period there is evidence of impairment of recruitment of neutrophils (Johnson KJ, Ward PA, 1981). The status of SOD therapy is widely studied by Robert A Greenwald in his papers in 1985. In this paper the preventive actions of SOD against XO-induced damages is described extensively. Nevertheless, the problem related with the administration of SOD is, it cannot be used by mouths and short half life of the enzyme.

In parallel studies, the role of natural products in the treatment of rheumatoid arthritis is studied extensively on the basis that some of the naturally occurring chemicals are potent free radicals scavengers. A mentioned above several defense mechanism are employed against free radicals such as tissue -SH groups, ceruloplasmin etc. During chronic inflammatory conditions, it is found that the levels of these substances varied in a spectacular manner.

In animal models of arthritis, there was significant decrease in the level of serum SH groups accompanied by an increase CP, blood GSH and NAG (serum N-acetyl- -Dglucosaminidase) during acute phases. In chronic phase, increase in serum CP and decrease in levels of blood GSH, plasma total proteins and albumin were significantly reduced (Fahim AT et.al., 1995). The workers also proved that administration of pumpkin seed oil elevate the levels of free radicals scavengers during adjuvant induced arthritis in rats.

Moreover, a plant product called Kalopanaxsaponin A and -I (KPS-I) were proven to a potent anti inflammatory and analgesic compound (Choi et.al., 2001). Late on, the workers found out that these compounds also have a significant free radical scavenging capacity which leads to the recovery of the destructed organs during RA.

The possible mechanism of action by which the oxygen free radical scavengers acts is still yet to be explored and a comprehensive work on it has to be done. Nonetheless from the earlier discussion, it is very clear that free radicals are involved in two main functions. Firstly, activating the NF- B pathways leading to the synthesis of inflammatory cytokines and secondly acting as signaling

pathways via p38MAPK pathways. So, if the scavengers of free radicals are effective, it can be suggested that the observed biological action may be due to their interference with the above mentioned pathways.

#### SUMMARY

After Mc Cords paper on the degradation of Hyaluronic acid, it became very clear that superoxide radicals and its relatives play a vital role in the progression of RA. Unfortunately, there was less information about this area than it is supposed to have. And therefore, a long term study is being suggested.

Nevertheless, several things became clearer and new things also came out to help the treatment of RA. In short it can write as follows:

- 1. There are at least (to note) two mechanism for the generation of free radicals in human body. The production of free radicals is also effected by factor like presence of metal ions such as Iron (though the role is a significant, the mechanism is still very unclear).
- 2. The free radicals can play a vital role in the biogenesis of inflammatory cytokine and also in the cell signaling pathways that lead to the inflammatory responses.
- 3. These chemical species have a marked deleterious effect on the biological systems especially towards the Hyaluronic acid. Collagen (however not so much), proteoglycans and connective tissues.
- 4. The employment of free radical scavengers such as serum -SH groups, ceruloplasmin, SOD make the basis of new treatment systems to RA. The

works of some of the naturally occurring free radical scavengers such as pumpkin seed oil were found to be very convincing.

Though, the present work is based on free radical biology, it is also good to add the role of genetic engineering to explore more detailed information about the chemical species. Workers has suggested that the chronicity of inflammation n animal models were controlled by genes of chromosomes 14 (Wester L et.al., 2003). So, in this regards another parallel work can also be done to find if there is any relationship between the said gene and free radical generation. Lastly, rheumatoid arthritis is still an autoimmune disease.

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# ZAWLAIDI

### (Table food... Alcohol... Quality Control...!?)

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nahlan leh Champhai tlangdungah, Mizoram leilung ngeia tha duh êm êm grape a awm an ti. Chu grape chu lo neituten an ching a, a rah atang chuan wine a siam theih tih hriain phur takin wine sawrkhurah chuan an bung ta tluk tluk mai. A hma in syntex leh thil dang an neih ang apiangah an siam mai thin a, mahse mihring eiah a tha lo tih an hriat vang ni mahna, Wine Industry an din ta rup mai. Mizoramin Industry lian, thingtlang mite din kan nei a lo ni ta reng mai!

Vawi tam tak sawrkarin loneitute khai chhuah tumin Policy chi hrang hrang (NLUP, MIP etc.) a siam tawh a. A mimala lo hlawhtlinpui tam tak awm mah se, khawkhatin an din chhuahpui tak hi kan hre lem lo. Chutih laiin Hnahlan khuate khi chuan grape hi an hlawhtlinpui dawn niin a lang tlat. Ka hriat ve dan chuan Horticulture Department lamin theih tawp an chhuahpui a, hetiang dinhmun hi thleng ta an ni awm e, tuna an grape khi a variety a tha lo pawh a ni mahna, tunah hian mithiamte chah chhuakin, tunlai thiamna hmangin grape quality thaah chantir an tum mek a ni awm e. A lawmawm hle mai.

#### Table food item em ni?

Wine a ni, zu a ni tih vel hi zawng, a chingfel theitute hian tifel mawlh teh se. Wine hi engvangin nge table food item tia an sawi thin? Grape rah hian a pang sir velah hian a maha awmsa natural yeast (Saccharomyces leh non-Saccharomyces) a nei a. Hei vang hian grape raha



awm carbohydrates thenkhatte kha ethanol-ah a insiam a, tichuan dawidim (veast) telh kher ngai loin 'zu' kan tih ethanol a lo insiam ta a ni. Chutiang zu leh thildang inpawlh vel chu 'grape wine' tiin sawi thin. Hetiang grape wine hian ethanol a nei tlem êm êm a, chuvang chuan hmun tam takah chuan dawidim an telh a, ethanol pai tam zawk wine a lo chhuak thin. Thenkhat chuan Dawidim hmang lovin a aiah spirit an telh ve leh thung a, hetiang hmanga siam hi Fortified wine an ti thin. Tuna Zawlaidi pawh hi Fortified wine niin ka lo hre ve a. grape rahah Engpawh nise, hian chawtha - carbohydrates te, proteins te, thau lam te, vitamin C te, organic acid chi hrang te, glucose te leh anthocyanin te a tam mai. Heng zawng zawng hi wine chuan a ken tel tâk vek avangin zu satliah a chhiar mai a ni ta lo va. Mihring tâna chaw tha a nihna changchawiin, 'Table food item' tiin an lo sawi ta a ni. Heng chaw tha tak tak a pai tel avang hian wine hi zu dang nen a inang thei lo a, ruih pawh a har bik thin. Heng zu dang Whiskey, Rum, Vodka etc. te hi chu distillation hmanga siam an ni a, acid leh chaw tha ho an keng tel ve lo a, ZU an ni tawp mai.

#### **Quality Control**

Grape wine a ni emaw, eng wine pawh ni se quality control an mamawh nasa khawp mai. Glucose leh sugar an neihte a sang viau thei a, acid an paite hi a tam uchuak thei bawk. Chu chuan pum natna leh ulcerte a thlen thei a, chu mai a ni lo, wine siamnaah hian a vawnthatna atân Potassium metabisulphite-te telh a ni thin. Hei hian

Sulphur dioxide a siam leh a, chu chuan wine quality a ti tha viau thei, mahse sulphur dioxide a tel tam lutuk chuan a hlauhawm leh thei viau lawi si. Heng bakah hian wine insiam lai hian zu ang chi tur hlauawm tak mai Methanol a insiam tel ve thei bawk, ei palh chuan formaldehyde-ah insiamin, thihna hial a thlen thei. Heng bakah Grape hian amahah hian tur chikhat Ochratoxin A a nei ve thei bawk, hei pawh hi hlauhawm tak a ni. Tin, diethylene glycol, Malvidol diglucoside te a insiam thei a, heng zawng zawng hi tur hlauhawm tak an ni thei bawk. Chu mai a la ni lo, Heavy metals kan tih -Iron, lead, Arsenic, Cadmium etc. te hi a siamna leh grape atang pawhin a tel thin a, arsenic phei chu tur hlauawm tak mai ani tih kan hre theuh awm e. Hei bakah heavy metals te hi cancer leh lung lam natna thlen thei an la ni lehnghal. Hei lo pawh Pesticide residues te pawh an la ti!! Heng thil zawng zawng hi a quality a thatna tur leh mipui kan him zawkna turin check vek a ngai a ni. Thlai zawng zawng hian heng kan tarlan takte hi an nei thei vek a, mihring tâna hlauhawm chin a awm vek bawk He kan Zawlaidiah hian eng ang chin nge a pai ve tak le? European Union chuan felfai takin an ram chhung a grape wine reng rengin a neih chin tur an bithliah fel thlap a. Chu aia sang an neih chuan mipui an intir ngai lo. Heng hi OIV Manual-ahte kan hmu thei a ni. Kan Excise Commissioner in quality control-ah Winery hmuna an laboratory kan ring tawk a ti tih Vanglaini ah ka lo chhiar a, heng zawng zawngte han enchiang tur chuan eng ang laboratory nge an neih ang tih ka ngaihtuah mai mai a. An laboratory ah chuan khawl chi hrang hrang UV-VIS Spectrophotometer,

HPLC, GC, AAS etc. tein an in thuam khup in ka ring a, tlawh a chakawm hle a ni. Chutih laia ka rilru a ka zawh chu Excise lam te chuan alcohol (ethanol) lam chauh an hma in ka ring a, khawnge Food and Drugs Administration lamte an awm ve.. mihring ei atan a thianghlim em tih lam te hi hriat kan va duh em!!

Mipuite pawh hian heti zawng hian i ngaihtuah ang u, quality tha lo wine kan in palh a nih chuan natna chi hrang hrang kan vei phah thei. Mizorama hralh chhuah tur pawh ni se, Europe-a mite aiin Mizo mipuite hi kan hlu lo bik hauh lo tih hria ila, ram changkangte ei ang quality hi min pe ve thei dawn lo a nih chuan zawrh chhuah loh law law hi a him zawk ngei ang.

#### Ethanol a pai zat?

Kan grape wine-ah hian 14% alcohol a awm niin an sawi a. Hei hi a sang khawp mai. Engatinge heti êm êm a sang ethanol an neihtir kher tih hi chhût tham a tling. Ruihna pawh thlen tham lo ethanol nei chung hian wine tui tak leh hrisel tak, chakna keng tel a siam theih dawn lawm ni? Ral phiar a lo phiar, mipui thuhmun fo thei lote zingah pawh a tlak dan a dang deuh tur.

#### Market lam hi?

Mizoramah chuan Zu khap a ni a. Sawrkar-in 'zu' nia a ngaih chuan engvanga Mizoram a hralh tum kher nge a nih? Quality tha tak siam ila, engvangin nge Zawlaidi, Mizoram kutchhuak hi Khawvel ram changkangten an in ve loh ang! A market pawh a hlawk dawn zawk asin. Sawrkar hian a duh chuan hma a la thei ngei ang. A tul chuan Society te pawhin hma la se, foreigna thawn chhuah tum hi a va tha êm.

Heng thil ngaihtuaha rilru ka lo sen lai takin, ka thian pakhat lo lengin 'quality control' chungchangah RIPANS, Pharmacy Department lamte hmang tangkai tura sawrkarin hmalakna a neih mek thute min rawn hrilh a,an ni hi damdawi leh hetiang lam analysis zirna hmunpui an ni a, a lawmawmin a thlamuanthlak ka ti hle. Mahse Zawlaidi hi kan in dawn a nih ngai chuan heng Laboratory test result-te hi i ngaichang hmasa phawt ang u. Hnam changkang zawkte nuih ruala nui pha ve tawh Mizote hian eng pawh eiin in dawn ila quality tha kan phut (demand) chu a hun ve ta e.●

## DAMDAWI THATNA LEH A HMAN DAN THA

#### **R. Lallianpuii** Department of Pharmacy, RIPANS Zemabawk, Aizawl

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Damdawi hi damna tura kan ei ni mah se mi thiamten a ei dan tur bi tuk (Dose) an siam vek a, he mi bak a ei tur tawk aia tam emaw ei lohna tura kan ei chuan tur(poison) a ni thei; chuvang chuan, damdawi thatna phawk chhuak tur chuan mawhphurhna mi tin hian kan nei sang hle a ni.

Damdawi chu a hmanna tur dik tak, dam lovin a mamawhna takah a hman tur ang tawk chiahin leh a man tlawm thei ang ber siin mi zawng zawng tana hman theihin a awm ngei tur a ni. Damdawi kan hman dan hi fimkhur a ngai hle a, mithiamten an chhut dan chuan damdawi zaa sawmnga vel hi a nih dan tur ang takin kan hmang lo a, chungte chu doctorin min chawh anga kan zawm loh vang te, keimahni duhthu leh rinthua kan ei mai mai thin avangin damdawiin a thawh tur ang tak a thawh theih loh phah thin a, chungte chuan nghawng chi hrang hrang a nei a ni.



(1) Ahmasa berah chuan taksaah harsatna (bad therapeutics) a thlen thei a, entirnan antibiotics penicillin kan tih angte hi duh duh dana ei tur a ni lo, a dose leh course dik taka ei tur a ni, a course eitur zat ei a nih loh chuan damlo chu dam angin lang mah se, a bikin Antibiotics bikah phei chuan taksaa natna hrikte an la thi kim lo thei a, a aia dose chak zawk hman leh a ngai thin a, hei hian damdawi hnathawh chak lohna (resistant) a \* thlen hial thei a ni.

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- (2) A pahnihnaah chuan taksaah nghawng tha lo a nei a, entirnan damdawi chu a dose dik taka pek a nih loh emaw, hman a ngaih tawh loh hnua rei tak hman a nihtein luhai, luak chhuak, thak leh chi dang dang a thlen thei a ni. Heng bakah hian taksa atanga a chhuah leh na kawngah Kal (Kidney) te a tichhe thei bawk, natna kan neih ngai loh aia nasa zawk kan vei hial thei a ni.
- (3) Damdawiah hian a chakna leh a thawh dan inang reng, mahse a man to zawk damdawi chawh a awm thei a, damlo harsa zawk te tan harsatna a thlen thei a ni. Hei hian tul lovah mipui te pawisa tam tak tak min sen thlawn tir fo a, kan economic in a tuar hial thei a ni.

A chunga kan sawilan takte khi damdawi hman a nih dan tur anga hman a nih loh avanga thleng thei thenkhatte chauh an la ni a, kan sawi kim seng lo ang, he mi kawnga invenga hma la tur chuan mipui leh damdawi lam thiammite mawhphurhna a awm ve ve a ni.

Damdawi kan tihte hi chi hnihin lo then dawn ta ila, (1) Doctor chawh ngai damdawi (Prescription Drugs) leh (2) Doctor lehkha tel lo va damdawi kan lei leh hmuh mai theih (Over the counter Drugs).

#### Eng ti angin nge Doctor chawh damdawi chu kan hman ang?

A hmasa berah chuan Doctorin damdawi min chawh reng rengin damlo ten tih ve tur kan nei a, chungte chu:-

 Damdawi chu eng atana tha nge tih leh eng angin nge a hlauhawm theih tih zawh tur a ni. Damdawi lo ei thin tawh neih chuan Doctor hrilh ngei ngei tur a ni.

- I damdawi ei tur chu a dose hniam zawka hman i duh chuan Doctor rawn tur a ni.
- Damdawi ei lo huat thin tawh neih chuan Doctor hrilh tur a ni.
- Damdawi ei lai emaw natna enkawl lai emaw nih chuan Doctor hrilh ngei ngei tur a ni.
  - Eng anga zingin nge Doctor chu hmuh a ngaih kan zawt bawk tur a ni, tichuan, kan damdawi ei dan leh a thawh dan ngun takin a check thei dawn a ni.

Damdawi min chawhte chu ngun takin kan vawng tha ang a, a hun taka eia, ei tur zat bituk damdawi ei thin tur a ni. Doctor hnen atanga hriattirna dawn reng reng, uluk taka chhinchhiah tur a ni. Doctorin min chawh anga hman a nih loh chuan taksaah nghawng tha lo a awm thei a, chumai bakah tum reng vang pawh ni lovin damdawi thenkhat a addict theih a, kan fimkhur a ngai hle a ni. Heng damdawi zinga a lar zual hmansual hlauhawm lo tarlang ila:

\*Opioids: chu damdawi nachhawkna dangin a chhawk theih tawh lohin nachhawkna atan hman thin a ni a, a hman danah fimkhur tur a ni, he damdawi hman lai hian damlo chuan zu a in tur a ni lo a, hritlang leh khuh damdawi (antihistamine) chi te a ei tel tur a ni lo.

\*Amphetamine: Asthma leh thawk lampang harsatna (respiratory problem) neite tan chawh thin a ni a, hritlang damdawi (decongestant) te nena ei pawlh loh tur a ni, B.P a tisang vak thei . Entirna sawi tur tamtak awm mah se tuna atan chuan kan tarlang vek seng dawn lo a ni.

Tunah chuan Doctor lehkha tel lova damdawi kan lei theih (Over the counter Drugs) te lo tarlang leh ila. Entir nan Paracetamol. Avil. thisen chaw. chloroquine. Quinine, vitamins, rulhut hlo (albendazole), ulgel te leh a dang tam tak a awm a, heng damdawi kan tarlan leh tarlan lohte pawh hi ei fimkhur an ngai tho a. A bik takin naupang, upa, raipuar leh nau hnute pe laite tan fimkhur lehzual a ngai a, Doctor emaw Pharmacist rawn chunga ei hi a him ber a ni. Natna benvawn nei leh enkawl mekte tan pawh heng damdawi hman dawn hian mi thiamte rawn hmasak a him ber zawk fo a ni. Heng damdawi Doctor lehkha tellova kan lei mai theih ang chi hote hi damlo na tak leh natna benyawn neite tana enkawlna tura tih a ni lo a, tlang hrileng leh natna sathliah enkawlna atan chauh a tih a ni. Amaherawh chu a ei dan leh a hman danah fimkhur a ngai em em a, a hman dan a dik lo chuan natna leh harsatna dang a thlen thei a ni.

#### Eng ti angin nge kan fimkhur ang?

#### \*Kum upate tan:

(1) Kum a lo upat chuan natna chi hrang hrang neite kan ni a, damdawi chi khat aia tam eite a lo ngai thin, chungah chuan damdawi nghawng tha lo emaw inhal a awm thei a, damdawi ei mai hmain mi thiamte rawn nachang hriat a tha.

(2)Damdawi dose sang hun rei tak ei chuan taksa tan a hlauhawm ve thei a ni. Entirnan ruh chuktuah natna nei tan nachhawkna an ei reng chuan pumpui lawng (ulcer) a thlen thei.

(3) Hritlang damdawite, khuh damdawite, thak damdawi (anti-histamine) ang hote hi hun rei tak kan ei chuan taksain a zo lo a, lu a hai a, khaw hmuh a fiah lo a, kachhung a ro duh a,zun leh ek thlengin harsatna an nei thei a ni.

#### \*Naupai leh naute hnute pe laite tan:

Nuin nau a pai laia damdawi thenkhat a eiin naute in a lo dawng ve thin a, chutiang bawkin nausen hnute hne laite hian hnute atangin nu damdawi ei an dawng a,chumi a nih avang chuan eng damdawi pawh ei hmain Doctor emaw Pharmacist emaw rawn hmasak a tha. Nau hrin hma thla thuma aspirin ei chuan nauteah leh nauvei laiin harsatna a thlen thei a ni. Naupai tirh thla thum chhunga nachhawkna thenkhat aspirin, diclofenac leh brufen te ei hian naute in lungnatna an vei hma bik a ni.

#### \*Natna benvawn neite tan:

Natna benvawn nei te tan hian OTC damdawi kan tih hote hi fimkhur taka an ei loh chuan an natna ti zual tuah an tang thei a ni.Entirna tlem lo pe ta ila–

#### i) Zunthlum neite tan:

Hnar ping damdawia kan hman thin te hian an natna a tizual thei a chuvangin kan hmang dawn a nih chuan doctor rawn hmasak a tha . Tin, khuh damdawi tui chi an ei dawn in chini (sugar free) telh lohna kan zawng hram hram tur a ni.

#### ii) Lung natna neite tan:

Antacid (digene leh ulgel) damdawi leh hritlang damdawi an ei dawnin, damdawi an lo ei thin nena inhal leh hal loh te doctor emaw pharmacist emaw zawh tur a ni.

#### iii) Kal natna neite tan:

Antacid an ei dawnin doctor emaw pharmacist emaw an rawn tur a ni.

#### iv) BP sang nei te tan :

Antacid leh hnar ping damdawi an ei dawn in doctor leh pharmacist an rawn tur a ni a, a chhan chu side effect a awm tam avang a ni.

#### \*Naupang tan:

Naupang te hi an taksa a la insiam puitlin loh avangin damdawi tamtak hi an taksaah a thawh dan hi puitlinga a thawh dan nen chuan a in ang vek lo a. OTC damdawi tamtak te hi naupanga an thawhdan zirchian loh a tam em em niin mi thiamte chuan an sawi ani. Naupang damdawi eiturah hian an kum zatin emaw an rih zawngin an dose hi an bithliah thin a. Entinan kum 2-6, kum 6-12 tih ang chi hian . Amaherawh chu naupang hi an pumrua a in thlau thei em em a, chuvang chuan an dose tur diktak hriat duh chuan an rihzawng atang a chhut thiam mithiam rawn tur a ni.

#### DAMDAWI VAWN THAT DAN

Chaw te chaw hmeh te ang tho hian damdawi hian hman tlak loh hun, chhiat hun a nei a. damdawite chu a vawn that dan tur ang taka kan vawn that chuan hun rei tak a hman thei a, kan vawn that loh erawh chuan a chhiat hun tur aia hmain a chhe thei a, turah(poison) a chang thei a. A tlangpuiin damdawi hi a siam atanga kum 2-3 chhung chu hman tlak leh him tura ngaih ani a. Amaherawh chu kan dahna hmunin a zir loh chuan chu aia hmain achhe thei ani. Damdawi tui hi vawikhat hman anih tawh chuan a dahna hmunin a zir loh a boruak lum tak, sa tak emaw hmun hnawng a dah a nih chuan hman chhunzawm loh hi a him ber a ni. Damdawi tui chite hi a mum leh powder aiin a chhe hma bik ani. Entirna thenkhat, damdawi him lo hman a hlauhawmna lo tarlang ila :

- 1. Tetracycline hi a thih tawh hnu chuan tur hlauhawm takah a chang thei a,kaltha lo a thlen thei a ni.
- 2. In danna contraceptive kan tih te hi a thih tawh hnua ei chuan naupai thei lohna a thlen thei .
- 3. Aspirin hi hunrei tak hnawnga a awm chuan acid ah a lo chang thei a, vinegar rim a nam thei ani.

 Mithlawr chi hote hi kan hawn hnuah a thlawrna hmawr hi kutin emaw thil dang engpoh kan siktir tur a ni lo.

Kan damdawi kawlte himtaka kan dah theih nan hengte hi kan zawm tur a ni;

- Damdawi chu hmun khatah dah khawm tur a ni a, a dahna hmun chu ro, vawt, niin an em lohna hmun ani tur a ni.
- 2. Naupang khawih phak lohna hmunah dah tur ani
- Damdawite chu a ma bur ah ngei vawnthat tur ani, ruah a, hmun dang a dah tur ani lo.
- 4. Damdawi kan neihte chu a hming chiang taka lang thei turin kan dah anga, ahman na tur kan hre lo anih chuan damdawi lam thiamte rawn a a hmanna tur dik taka hman a nih theih nan kan hriat thiam ang a ziah lan tur a ni.
- 5. Damdawi reng reng a hming ziah lanna company atanga an bel hi pawhthlak loh tur ani. Eng emaw palh avang a ahming ziah lanna a awm lo anih chuan hman loh a him ber ani.
- 6. A khattawkin kan damdawi kawl te chu a him leh him loh kan endik fo tur a ni a, engtika thi tur nge an nih hriat a tha.
- Dam dawi hman tlak lohte kan paihna hmun fimkhur tur ani a, naupang leh ran tena an hmuh phak lohvah kan paih tur a ni.

Damdawi chung chang reng rengah hriat thiam loh emaw, damdawi hriatchian kan duh emaw a nih chuan Mizoram State Pharmacy Council in a DRUGS INFORMATION CENTRE, K Lalhluna Building Zarkawt ah office hun chhung in eng lai pawh a zawh fiah theih a ni a,mahni kal lo pawhin phone number 2306497 ah zawh chian reng theih a ni.

# DAMDAWI VAWNTHAT

#### **Dr. H Lalhlenmawia** Department of Pharmacy, RIPANS

un lai khawvelah damdawi leh a kaihhnawih thilin nasa takin hma a sawn a, khawvelin damdawi pawimawhzia leh a hlauhawm si-zia te nasa takin an hre chho ta a; damdawi thar tam tak tak hmuhchhuah a ni chho zel bawk. Chutih laiin damna atana kan hman damdawite chu a hman sual chu sawi loh, kan vawn dan dik lo ringawt pawhin túr hlauhawm takah a chantir thei a ni tih kan hrechiang chho ta zel a, damdawi vawnthat kawngah inkaihhruaina mumal kan mamawh hle a ni. Hei hian Pharmacists pawimawhna leh tangkaina a tizual em em a, a chhan chu damdawi chemical nihphung zirchiang leh hrechiang bertute kan nih vang a ni. Ram changkang apiangah damdawi vawnthat hi an ngai pawimawh a, hmun changkang apiangah an uluk thin. Pharmacists-te hi Mizorama damdawi sawngbawl kawnga sawrkarin a rin ber leh innghahna kan ni a, damdawi chungchangah kan thiamnate hmang chhuak turin theihtawp kan chhuah a ngai a ni.

Heng a hnuaia kan tarlante hi damdawi vawnthat dan chungchang khawvelin a pawm te an ni a, zawm theih loh thil engmah a awm lo va, a tam zawk te hi chu kan practice lai mek an ni hlawmin ka ring. Kan zir ang a, sawiho ngai laite kan sawiho ang a, kan hnathawhna hmun theuhah practice kan tum bawk dawn nia. Kan thu zir tur laknate –

- Guide to good storage practices for Pharmaceuticals. Published by World Health Organisation in their Technical Report Series No 908, 2003.
- (2) Good Trade and Distribution Practice (GTDP) of Pharmaceutical starting materials. Geneva, WHO, 2002.



(3) Good manufacturing practices for pharmaceutical products. Published by WHO, 1999.

A hmasain WHO Technical report series No. 863 in damdawi vawnthat dan tur a hrilhfiah dan i lo thlir hmasa ang u –

#### Normal storage Condition:

Hmun ro, boruak thawveng, temperature 15-25 degree celcius. Rimchhia leh bawlhhlawh awm lohna hmun, ni éng emaw thil éng bik takin direct-a a chhun lohna.

Do not store over 30°C - from +2 to +30°C Do not store over 25°C - from +2 to 25°C Do not store over 15°C - from +2 to 15°C Do not store over 8°C- from +2 to 8°C Do not store below 8°C - from +8 to 25°C

Protect from moisture - not more than 60% RH in normal storage condition.

Protect from light - to be store in light resistant container.

#### DAMDAWI DAHKAWMA ENKAWL TU HRIATTUR PAWIMAWHTE

#### 1. MANAGEMENT AND PERSONNEL:

- Store enkawl turin helama thiamna bik nei qualified pharmacists a awm ngei ngei tur a ni.
- (b) Mahni invawn thianghlimna hmanrua kan kawl ngei ngei tur a ni. Eg, kut silfaina hmanrua, a tul thuta tuia inkhawh faina (shower), apron, etc. te kan nei ngei tur a ni.
- (c) Training /Intuaitharna an nei ngei ngei tur a ni.
- (d) Store enkawltu reng reng chuan kan hna thawh dan tlangpui leh kan tih turte ziakin kan dah ngei tur a ni.

#### PREMISES AND FACILITIES:

- (a) Store chhung a fai hle tur a ni. Hmun ro a ni ngei bawk tur a ni.
- (b) Store chhung chu damdawi tha taka dah theihna hmun tur tawka lian a ni tur a ni. Thil dah thatna hmun zingah heng dah thatna bik turte hi a hrangin a awm ngei tur a ni - bulk products, quarantined products, rejected products, inflammable materials, poisonous/danger materials.
- (c) Room chhung temperature hi 8°C -25°C a ni tur a ni a, humidity 60% RH aia sang a ni tur a ni lo. He miin a huam loh thilte dahna atan Refrigerator emaw, freezer emaw a awm ngei tur a ni.
- (d) Bungraw dahna chhuar (rack) tha tawk tak a awm tur a ni a, a pumpuia tihfai leh enfel awlsam tak a ni ngei tur a ni.
- (e) Chhuatah thil dah a awm tur a ni lo.
- (f) Thawktu bik ni lo luh phal tur a ni lo a, an luh ve mai mai lohna turin a danna tha tak siam tur.
- (g) Light a awm tha hle tur a ni a, emergency-a hman tur pawh a awm ngei tur a ni.
- (h) Store chhungah direct-in ni éng a lut tur a ni lo.
- Bang a mám thain tihfai reng theih a ni tur a ni. Tuihu leh bawlhhlawh dangte an lut ve tur a ni lo.
- (j) Boruak lak luhna leh circulation mumal takin a awm tur a ni.
- (k) Temperature leh humidity control-na system a awm ngei ngei tur a ni.

- (I) Store te hi hun bi neiin tihfai reng tur a ni a, a tihfai dan tur routine mumal tak siam thin tur a ni.A tihfaina tur bik hman rua pawh ziaka dah thlap tur a ni.
- (m) A tifaitu tur te hmarua hman dan ah training tha taka pek thin tur.

#### 3. RECEIPT OF INCOMING MATERIALS:

- Damdawi a lo thlen in Consignment
   leh invoice te a hmasa berah a inmil
   em tih kan endik vek tur a ni.
- (b) Label/Information a chuang a damdawi description, expiry date, batch number, quantity te kan check vek tur a ni, invoice nen a in anglo a awm chuan received ngawt lo in dahran (quarantined) tur a ni.
- (c) A consignment bik ah heng te hi uluk taka check vek tur ani- Container a inang tlang em? Chhe lai maw tha lo thei thil a awm em?
- (d) Damdawi kan dawn thar reng reng in heng te hi chiang taka record in kan vawng tha bawk tur a ni-Brand name, generic name, a vawn that dan tur, invenlawk ngai (precautionary measures) a awm em, accident thil ah eng tin nge first aid lak tur, eng ang dosage form nge, eng zat nge pack awm, batch number, manufacturing date, expiry date, damdawi store a dawn ni.
- (e) Damdawi kan dawn reng rengah Label a dik em tihchiang takin kan en hmasa tur a ni.
- (f) Container kal tlanga bawlhlawh lut thei a ni em tih te uluk taka kan check a tul hle a ni, chutiang an lo awm a nih chuan a case chin fel hma chu

quarantined tur a ni.

(g) Damdawi tha lo ni a ngaih leh damdawi tha te dah pawlh reng reng loh tur a ni.

#### 4. MATERIAL DISPATCH FROM STORE:

- (a) Dispatch record mumal takin kan vawng tur a ni a, hengte hi kan tilang ngei ngei tur a ni - Brand name, generic name, dosage form, strength, number of unit pack, manufacturing date, expiry date.
- (b) Damdawi vawn dan tur chiang takin kan tarlang bawk tur a ni.

#### 5. STOCK ROTATION AND CONTROL:

- (a) Damdawi stock-te hi hunbi mumal tak neiin kan check thin tur a ni. Kan record leh stock awm te an inmil dan kan check fo thin tur a ni.
- (b) Store-a damdawi kan dah laiin a chhe ve thei tho a, kan vawn dan te uluk takin a tha tawk em tih kan check fo tur a ni.
- (c) Damdawi kan dahthat reng reng chi hrang kan dah pawlh tur a ni lo.
- (d) Kan damdawi store-ah te expire tur a awm hnai em tih kan en fel fo tur a ni.

#### 6. STANDARD OPERATING PROCEDURE:

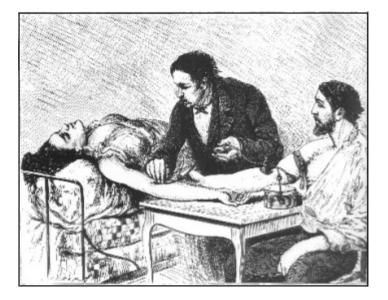
- (a) Eng damdawi pawh kan receive dawn apianga procedure mi tu pawh storea hnathawkin an hman tur kan nei ngei tur a ni.
- (b) Damdawi pek chhuah tur pawh a pe chhuaktu apiangin kan hman tur procedure mumal tak kan duang tur a ni.
- (c) Eng damdawi pawh rinhlelh kai a awm
   a, quarantined ngai ang chi a nih

chuan a tih dan tur record mumal tak kan neih a ngai a ni.

- (d) Store chhung tih fai dan a tifaituin step hrang hrang a tih tur indawt kan nei tur a ni.
- (e) Stock enfel hun apianga kan tih dan tur procedure fel fai leh record-na tur mumal kan nei ngei tur a ni.
- (f) Heng thil chi hrang hrang titute hian hna an thawh zawh apiangin check leh theih turin signature mumal tak an pe thin tur a ni ang.
- (g) Heng SOP-te hi revised reng tur an ni a, hmun langsar leh remchangah tar chhuah bawk tur a ni.

Heng a chunga kan han tarlan takte khi a tam zawk chu kan practice lai mek a niin a rinawm. Pharmacists ten kan hna thawhna hmun enkawl thianghlim leh a nihphung dik tak tura chei bawl hi kan tih tur a ni tih i hre thar leh ang u. Vawinah kan store-te a nih dan ang ni pha lo a awm maithei, heng thilah te kan ngawih reng chuan siam that a har tial tial dawnin a lang, a tuartu tur chu mipui leh ram a ni tih hrereng in theihtawp i chhuah zel ang u. Kan thiamna te hmang chhuak thei turin theihtawp chhuah ila, damdawi sawngbawlna kawngah chuan keini aia zir thûk an awm lo tih hriain mahni inrin tawkna nen, nasa taka hna kan thawh a ngai ani tih i hre thar bawk ang u.●

## **HISTORY OF BLOOD TRANSFUSION**



Lalhmingliani Pachuau Quality Manager, MSACS

From the earliest recorded, Blood has been a point of fascination and mystery. Earlier, Blood transfusion meant direct donor to patient transfusion. This practice however, was frequently disastrous because there was no quality knowledge of blood types and compatibility. The practice of blood transfusion, that is the transference of blood from the circulation of one individual to that of another for practical therapeutic purposes, is of relatively recent origin. Although it only became a practical possibility during and shortly after the Second World War the concept of 'transfusion' has a longer history.

## A glimpse of the gradual progress made in the history of blood transfusion:

**1492** - Pope Innocent VIII, in Rome, had an apoplectic stroke, and was mistakenly thought to be dead. His physician advised a blood transfusion as a therapeutic measure for the Pope's illness. Apparently, three 10year old shepherd boys were selected as donors and the blood of the dyeing Pope was passed into the veins of one of the boys, who gave him his own in exchange. The process was repeated with the other two boys. All three boys apparently died after the procedure and the Pope also did not benefit and died by end of that year.

**1615** - Andreas Libavius described his technique of Blood transfusion. It was unfortunately not adequately publicized.

**1628** - English physician William Harvey (1578-1657) discovered the circulation of Blood in human body.

**1665** - The first Blood transfusions of record take place. Animal experiments conducted by Richard Lower, an Oxford physician started as dog-to-dog experiments and proceeded to animal-to-human over the next two years. Dogs were kept alive by the transfusion of Blood from other dogs. **1667** - Jean-Baptiste Denis in France reported successful transfusions from sheep to humans.

**1818** - James Blundell, a British obstetrician, performed the first successful transfusion of human Blood to a patient for the treatment of postpartum hemorrhage. Using the patient's husband as a donor, he extracted a small amount of Blood from the husband's arm and, using a syringe, he successfully transfused to the wife. Between 1825 and 1830, he performed ten documented transfusions, five of which proved beneficial to his patients, and published these results. He also devised various instruments for performing Blood transfusions.

**1873 to 1880** - Physicians in the United States are documented, during these years, to have transfused milk (from cows and goats) to humans.

**1884** - Saline infusion replaced milk as a 'Blood substitute' due to increased frequency of adverse reaction to milk.

**1901** - Karl Landsteiner, an Austrian physician, and the most important individual in the field of Blood transfusion, documented the first three human Blood groups (based on substances present on the red Blood cells), A, B and O.

**1902** - A fourth main Blood type, AB was found by A. Decastrello and A. Sturli.

**1907** - Hektoen suggested that the safety of transfusion might be improved by cross-matching Blood between donors and patients to exclude incompatible mixtures. Reuben Ottenberg performed the first Blood transfusion using Blood typing and cross-matching. Ottenberg also recognized the "universal" utility of group O donors..

**1908** - French surgeon Alexis Carrel devised a way to prevent Blood clotting. His method involved joining an artery in the donor, directly to a vein in the recipient with surgical sutures. He first used this technique to save the life of the son of a friend, using the father as donor. This procedure, not feasible for Blood transfusion, paved the way for successful organ transplantation, for which Carrel received the Nobel Prize in 1912.

**1908** - Carlo Moreschi documented the antiglobulin reaction.

**1912** - Roger Lee, a Massachusetts General Hospital visiting physician, along with P. D. White, formulated and developed the 'Lee-White' clotting time. Lee further demonstrated that Blood from all groups can be given to group AB patients.

**1914** - Long-term anticoagulants, among them sodium citrate, were developed, allowing longer preservation of Blood.

**1916** - Francis Rous and J. R. Turner introduced a citrate-glucose solution that permitted storage of Blood for several days after collection. Also, as in the 1915 Lewisohn discoveries, this allowed for Blood to be stored in containers for later transfusion, and aided in the transition from the vein-to-vein method to direct transfusion. This discovery also directly led to the establishment of the first Blood 'depot' by the British during World War I. Oswald Robertson was credited as the creator of the Blood depots.

**1925** - Karl Landsteiner, in collaboration with Phillip Levine, discovered three more Blood groups: M, N and P. View Nobel Biography.

**1926** - The British Red Cross instituted the first human Blood transfusion service in the world.

**1932 -** The first facility functioning as a Blood bank was established in a Leningrad Russia hospital.

**1939 and 1940** - The Rh Blood group system was discovered by Karl Landsteiner, Alex Wiener, Philip Levine and R. E. Stetson and was soon recognized as the cause of the then majority of transfusion reactions. Known as the Rhesus (Rh) system, once this reliable test for this grouping had been established, transfusion reactions became rare. Identification of the Rh factor has stood next to ABO as another important breakthrough in Blood banking.

**1940** - Edwin Cohn, a professor of biological chemistry at Harvard Medical School, developed a cold ethanol fractionation; the process of breaking down plasma into components and products.

**1943** - The introduction by J.F. Loutit and P. L. Mollison of acid citrate dextrose (ACD) solution, which reduces the volume of anticoagulant, permitted transfusions of greater volumes of Blood and longer term Blood storage.

**1943** - P. Beeson published the classic description of transfusion-transmitted hepatitis.

**1945** - Coombs, Mourant and Race described the use of antihuman globulin (the "Coombs Test") to identify "incomplete" antibodies.

**1950** - The use of glycerol cryoprotectant for freezing red Blood cells became widespread.

**1950** - Carl Walter and W. P. Murphy, Jr., introduced the plastic bag for Blood collection. This replaced breakable glass bottles with rugged plastic bags. This technical development enabled the evolution of a collection system capable of safer and easier preparation of multiple Blood components from a single unit of whole Blood.

**1954 -** The Blood product Cryoprecipitate (now AHF) was developed for people suffering from haemophilia.

**1962 -** The United States reported approximately 4,400 hospital Blood banks, 123 community Blood centers and 55 American Red Cross Blood centers, collecting, in aggregate total, as many as six million units of Blood per year.

**1964** - Plasmapheresis was introduced as a means of collecting Plasma for fractionation.

**1967 -** Rh immune globulin was commercially introduced to prevent Rh disease in the newborns of Rh-negative women.

**1971** - Hepatitis B surface antigen (HBsAg) testing of donated Blood began in the United States.

**1972** - Aphaeresis was used to extract one cellular component, returning the rest of the Blood to the donor.

**1979** - A new anticoagulant preservative, CPDA-1, which extends the shelf life of whole Blood and red Blood cells to 35 days, increasing the Blood supply and facilitating resource sharing among Blood banks is introduced.

**1983** - Newly introduced Blood additive solutions resulted in extend shelf life of treated red Blood cells to 42 days.

**1985** - The first Blood screening test to detect the probable presence of HIV was licensed and implemented by Blood banks in the United States. **1992 -** Testing of donor Blood for HIV-1 and HIV-2 antibodies (anti-HIV-1 and anti-HIV-2) was implemented.

**1999 -** The Blood manufacturing community began implementation of Nucleic Acid Amplification Testing (NAT) under the FDA's Investigational New Drug (IND) application process. NAT employs a testing technology that directly detects the genetic materials of viruses like HCV and HIV.

#### HISTORY OF BLOOD TRANSFUSION IN INDIA

**1939** - Indian Red Cross Society formed a Blood bank Committee to support the transfusion centre with equipment and donors.

**1942** - India's first Blood Bank established on March 6, 1942 at the All India institute of Hygiene and public Health, 110 Central avenue Calcutta to meet the war need.

**1988 -** Mandatory testing of Blood for HIV was implemented under Drugs & Cosmetic Act, 1940

**1992** - Blood Safety Programme implemented by National AIDS Control Organisation

**1998** - Professional blood donation was banned following Supreme Court order w.e.f 1st January, 1998.

**2001 -** Mandatory testing of Blood for HCV was implemented under Drugs & Cosmetic Act,1940 w.e.f 1st June, 2001

**2002** - National Blood policy prepared by NACO & NBTC, Govt of India.

Jesus said to them, 'I tell you the truth, unless you eat the flesh of the son of Man and drink his blood; you have no life in you. Whoever eats my flesh and drinks my blood has eternal life, and I will raise him up at the last day. For my flesh is real food and my blood is real drink John 6 : 53-55

### PHARMACY COUNCIL OF INDIA DIAMOND JUBILEE CELEBRATION 2010 & NATIONAL SEMINAR

*C. Vanthuama* Vice President, MPA



harmacy Council of india hi Pharmacy E ducation leh Pharmacy Profession bulpui a ni a, Council ropui leh changtlung tak a ni. President leh Vice President tih loh chu O.B. post a awm hran lo va. Secretary hna zawng zawng hi Registrar leh a staff-ten an thawk vek a, Treasurer leh Finance secretary hna zawng zawng hi Account Branch staff-ten an thawk vek bawk a. Heng thawktute hi P.C.I. staff (employee) an ni. Central-a kan Council khu Presidential form of Council a tih theih hialin ka hria; a kalphung pawh a ngelnghetin a felfai hmel hle a ni.

Ni 9&10 July, 2010 khan Pharmacy Council Diamond Jubilee Celebration leh National Seminar, Vigyan Bhavan, New delhi-ah neih a ni a. Hetah hian India ram state hrang hranga Council-te kal tura tih a ni bawk a. Mizoram State Pharmacy Council atangin mi panga – Pu Lalsawma Pachuau, Asst. Drugs Controller, Dr. H. Lalhlenmawia, Asst. Professor, Nl. P.C. Lalawmpuii, Asst. Professor, Nl. Esther Lalduhawmi Hnamte, Registrar te tirh kan nih angin kan zu kal a. A mimal takin ka hlawkpui hle mai. State pawn lam boruak zu chhim bakah Pharmacy



Council of India ningkhawng tam tak ka zu hmu a, ka rin aiin kawng engkimah a lo ropui a ni.

Ni 8 July, 2010, chawhnu dar 2:55-ah Lengpui Airport atangin kan chhuak a, Kolkataah darkar hnih lai kan chawlh hnuin kan chhuak leh a, Delhi chu 7:20 pm-ah kan thleng ta a. Kan thlenna, The Summit Hotel, 54/9-D, Kishangarh, New Delhi-70-ah kan indah luh fel meuh chuan 9:30 pm a lo ri der a. Chutichuan zinkawng hlimawm leh nuam tak chu chawlhsan rihin tui takin zanmu kan chhing ta hlawm a.

Ni 9 July, 2010 khawvar eng mawi tak mai chu Siamtu Pathianin a rawn her chhuahtir a. Keini ho chu kan thlenna The Summit Hotel atang chuan 7:30 am-ah P.C.I. office-a in-report turin kan chhuak a. Fel taka thil tulte kan tih zawh vek hnuah chuan Diamond Jubilee Celebration leh National Seminar neihna tur hmun Vigyan Bhawan, Maulana Azad Road kan pan ta vang vang a, 9:55 am-ah kan thleng ta a. Reception Counter-ah registration tia badge mawi tak kan awrh hnu chuan main hall-ah kan lut dawn ta a. Hall luhkapuiah chuan airport aia uluk zawk mahin kan taksa chu a pumin metal detector-in min check vek a, cell phone leh camera pawh ken luh an phal lo va, reception counter-ah kan dah vek a ni.

Sawi nâk emaw ka hre lo va, han ziah lan ka duh em em mai chu Mizoram State Pharmacy Council-a kan President te pahnih, Pu Lalsawma Pachuau leh Dr. H. Lalhlenmawia te an tlangtlak that dan hi a ni. India rama Pharmacy Education leh Drugs Control lama hotu lian leh senior pui puiten an lo lawmin an lo chibai lawp lawp thin a, tam tak phei chuan an hmingin an lo ko fak fak thei a. Pu Sawma phei chu Vai ho ngaihsan zawngin a awm thiam nge ni, 'Lalsawma, my friend,' tia patling leh patling, âwm leh âwm insi thlap a, dàra bán bât liam hnâwpa lo pawma lo warm welcome-tu mi sawmpahnih (Isua zirtir zat) ngawt an awm a. Ka rilrua a lo lan dan chuan kan President an lo welcome a ni ringawt lo va, Mizoram State Pharmacy Council min lo



welocome niin ka hria a, an sirah ngawi rengin ka lo tlangnel phah ve em em a ni.

Bhawan chhung chu kan han lut a, pangpar leh electric eng mawi taka chei leh air conditioned nuam ruih mai a lo ni a. Hall no. 1-6 a awm a (mi 200 leng te, 300 leng te, 500 leng te, etc.), National leh International level meeting pawimawh tak takte pawh he Bhawan chhungah hian an lo nei tawh thin a ni. Tichuan, Pharmacy Council member thutna tura rem bikah chuan kan President-te pahnih (Pu Sawma leh Pu Mawia) te chu an thu a, Maawmi, Esther-i leh kei chu delegates thutna tura siamah chuan kan thu a/ Dar 11:00 am a lo rik chiah chuan kan Chief Guest, Hon'ble President of India, Her Excellency Smt. Pratibha Devisingh Patil, a thusawi ringawt pawha India ram nghawr nghing dawt dawt thei, nu te reuhte ni lawi si chu a lo thleng a. Pharmacist 1000 rual kan din thup lai chuan kan hnung lam atangin band party-in music tang et awtin India hnam hla (Jana gana mana...) hall chhung khawk rum rumin an han play a; Inaugural function tan nghal a ni a. Delhi tlanga zaithiam leh musician lar ten an violin tumin opening song an sa a. Tichuan Prof. B. Suresh, President, PCI, kan Chief Guest, Hon'ble President of India, Pratibha Devisingh Patil leh kan Guest of Honour. Central Cabinet Health Minister, Shri Ghulam Nadi Azad te thusawi ropui tak tak ngaihthlak a nih hnuin Inaugural Function chu kan zo ta a.

Dar 12:30 pm-ah Scientific session tan a ni a. P CI President Chairman a ni a, Dr. Mike Rouse, Asst. Executive Director, International and Political Affairs chu speaker a ni. Tunlai khawvel changkang zela Pharmaceutical Sciences zirna leh hnathawh lo sang zel chanchin ngaihnawm leh ropui takin a sawi a; zawhna leh chhanna hun neih zui nghal a ni a. Dat 1:30 pm-ah lunch break kan nei a, ei-in a 'cial a ni tawp mai - a tui ber pawh a hriat theih loh, dam tlang thep thawpa chhungkaw kima eiho atan a itawm ngei mai. Mi thawlna lam, VIP ho eina lamah ruai buatsaihtuten keini tem ho min nawr chho va, a fuh lehzual a ni awm e. Antam thlak pawlh tih ang vel lam a ni lo, tuifinriat kaikuang fry, etc. tih vel a ni nuaih mai. Hriat chian a duh chuan Pu K. Zakamlova, Bungtlang South pharmacist-in min zawt chiang se.

Dar 2:30 pm-ah Scientific Session neih chhunzawm a ni a. Heta tang hian stream 1 leh stream 2-ah kan inthen a. Hengte hi speaker-te an ni – 1. Dr. Krishna Kumar, Professor, School of Pharmacy, Haward University, Washington DC; 2. Shri Subodh Priolker, General Manager, Colorcon (South Asia); 3. Dr. B. Suresh, Vice Chancellor, JSS University,

Mysore; 4. Dr. T.K. Ravi, Principal, College of Pharmacy, SRIPMS, Coimbatore, Tamil Nadu; 5. Shri Raj Vaidya, Chief Pharmacist, The Hindu Pharmacy, Panaii: 6. Dr. Jibon C. Gogoi, Institute of Pharmacy, Assam Medical College; 7. Sri Prafull D. Seth, Vice President, International Pharmaceutical Federation; 8. Prof. C.K. Kokate, Vice Chancellor, KLE University, Belgaum, Karnataka, etc. Sawrkara thawk Pharmacist (D.Pharm) te B.Pharm-a hlankaina tur bridge course siam tum mek thu te (hetah hian Mathematics harsa pui pui leh Pharmaceutical Chemistry harsa pui pui tel lo tura duan a ni ang), Pharm D (Doctor of Pharmacy) course zirna chungchang te, Pharmaceuticals Industry-in Pharmacy Education/Technology sang zel a mamawh dan te, hriatna leh thiamna sang zel nei tura Pharmacist-te intuaihriam thar a tul thu te, Pharmacy Practice - A Global Perspective tih te, Recent Trends in Pharmaceutical Sciences and Research, etc. te ngaihnawm tak takin an sawi a, zawhna leh chhanna hun neih zui nghal a ni. Tichuan, ni 10, July, 2010, 6:00 pm-ah farewell thingpui kan in a, khua a lo thim chuai chuai ta a, kan sarual tin ta a ni.

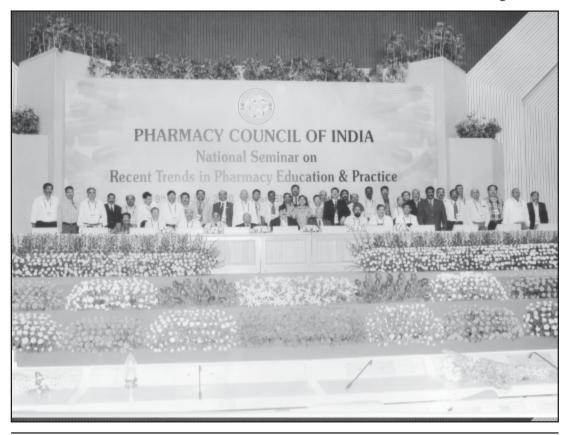
Zan dar 8:00-ah PCI President-in Central Council member-te tan FICCI-ah zanriah a buatsaih a. Member ka ni ve lo nain, kan President ten an ruala kal ve turin min ti a. He hunah hian PCI member ni lo awm chhun ka ni awm e. Thil hi a lo tam em em khawp a, squash atangin squash lo thlengin in tur chi hrang hrang leh ei tur tuihnai chi tinreng mai, nai 0 (au!) pawh sen ngai lo... "I duh em? I duh em?" Vai YMA emaw ni te hian an lo ti deuh reng mai a, mahnia va inthlit mai tur pawh a tam mai. Hemi zan kher kher hi chuan ka nupui aiin Pu Huala, Supd. Pharmacist ka ngai vawng vawng mai!

Ni 11 July, 2010 hian PCI member-te chauh meeting neih a ni a. He hunah hian PCI

Vice President thlanna neih nghal tur a ni bawk a. Hetah hian kan President-te pahnih (Pu Sawma leh Pu Mawia) an tel a, keini delegates ho erawh chuan free time neiin khua kan lo chuan mai mai a. Tichuan, ni 12 July, 2010-ah kan lo haw ta a. Mahse Lengpui Airport-ah chuan chhum zing nasa avangin kan tum thei lo va, dar 3:20 pm-ah Kolkata-ah riak thla turin min letpui ta vuah vuah mai a. Hotel senso tur leh ka wallet thêp tawh si ziate ka ngaihtuah neuh neuh a, ka huphurhin ka lungngai ru hle mai a. Mahse, vanneihthlak takin hetiang thlawhna tum theih loh avanga let leh ho hi chu Air India-in 5-Star hotel-ah a thlawn vekin an lo thleng thin a lo ni a. Room nuam em emah min dah a, ei-in lah chu President dinner siam zan ang deuh tho a ni a; in tur chi hrang hrang leh ei tur chi hrang hrang, pawisa sen pakhat pawh sen ngai lovin a lo awm

leh teuh pek a. Mumang chu a ni si lo. Pu Huala bawk chu ka han phone leh pek a, engtin tak ngai ang maw?! Mut a tui duh ngei mai. Hnung lama sa barh nge, rina lohva ui buk sa tih pawh ka hrethiam lo. Pu Sapa, Champhai Pharmacist-in a hrilhfiah dik thiam ngei ang!

PCI Diamond Jubilee Celebration leh National Seminar function changkang leh ropuia kan tel ve thei te, Hon'ble President of India live-a kan hmu thei te hi kan vannei mang e, tiin Maawmi, Esther-i leh kei chuan kan sawiho sep sep a ni. ka buaipui hah pawh ngai lovin ticket, etc. te min tihfelsak vek a. Kawngah pawh chinchang hre ve ang takin hotute zarah ka awm ve mai mai a. Fapa mal duat, a pa bula thlamuang taka a zin hi ka inchan ber a. Kan zinkawng thui tak, hlimawm em em chu tawpin ni 13 July, 2010 khan Pathian hruainain kan lo haw thleng ta a ni.



## QUANTITATIVE DETERMINATION OF CURCUMIN CONTENT IN TURMERIC POWDER OBTAINED FROM SELECTED AREAS OF NE INDIA BY RP- HPLC

Laldinchhana, Sonjit Das, Trelya K Marak, Dr H Lalhlenmawia

Department of Pharmacy, Regional Institute of Paramedical and Nursing Sciences, Zemabawk, Aizawl Mizoram

#### INTRODUCTION

Curcumin is the main chemical constituents of turmeric (*Curcuma longa*) and is obtained from dried as well as fresh rhizomes of Curcuma longa. It has been defined by standard organization (ISO 5562-1983) and British standards(BS 6147:1983). There are three kinds of curcumin such as,

- 1) Diferuloylmethane
- 2) p-Hydroxycinnamoylferuloylmethane
- 3) p,p-Dihydroxydicinnamoylmethane

Cucumin can be used for various purposes like colouring agent, as a condiment, antiulcer agent, anti-inflammatory agent, antioxidant, anthelmintic etc.

Here, it has been highlight the quantitative determination of curcumin (Diferuloylmethane) content in the given samples by reverse phase-HPLC, which is mainly based on the comparision of characteristic peaks of standard curcumin and the given samples.

#### MATERIALS AND METHOD

#### **Collection of samples**

The dried powder samples were collected from four different places which were listed as follows:

- Mizoram Assam
- Meghalaya Rasoi Brand

#### Materials

The following materials are used for analysis:

Methanol HPLC grade obtained from Merck. Methanol AR obtained from S.d fine chemicals,Water HPLC grade obtained from Merck,Standard Curcumin (CAS 458-37-7) obtained from Sigma,UV-VIS Spectrophotometer V-530 JASCO, HPLC W 2489 WATER USA,Silica Gel G for TLC obtained from Merck.

#### Extraction of curcumin from crude samples

5gm of the powdered sample collected was cold macerated with 70ml methanol for 7days. It was then filtered through Whatman filter paper No.1. After filtration the volume of the filtrate obtained from different samples are as follows

Mizoram	-	59ml
Assam	-	55ml
Meghalaya	-	57ml
Rasoi Brand	-	61ml

#### Thin layer chromatography studies

TLC plate was manually prepared by using Silica Gel G and the elution characteristic of standard curcumin and extract were studied with different solvent composition of Methanol and water.

#### UV-VIS spectrophotometric studies of curcumin

Curcumin was dissolved in methanol and the maximum absortion spectrum was found by using UV-VIS Spectrophotometer which is indicated by a characteristic peak in the spectrum.

#### HPLC characterization of pure curcumin and crude extract

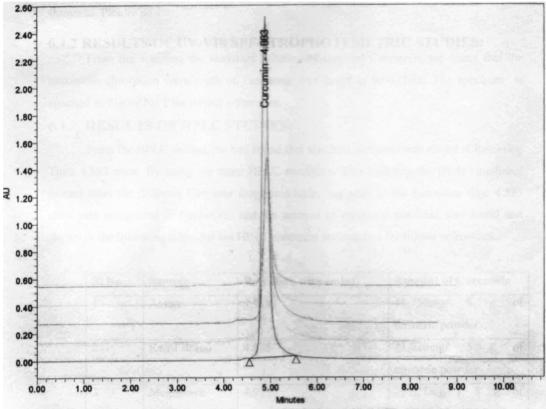
**Standard Curcumin:** The standard curcumin was injected into the HPLC and the required HPLC condition was set as follows: (mobile phase and absorption wavelength was determined from the above studies)

Flow rate	-	1ml/min
Wavelenght	-	427nm
Mobile phase	-	methanol : water (8:2)
Column	-	reverse phase column
Run time	-	10mins

#### Curcumin crude extract

- 1) 1ml of the sample solution was pipetted out in a measuring cylinder and to this 1ml of methanol was added which is then diluted upto 10ml using methanol. This will give 100mg/ml.
- 2) The sample is then injected into the HPLC and allowed to run it for around 10mins.

3) The exact content of curcumin in the given samlple was calculated from the graph given by HPLC.



Sample Name: curcumin std; Date Acquired: 5/20/2010 11:19:25 AM IST; Vial: 1; Injection: 1 Sample Name: Curcumin - Assam; Date Acquired: 5/21/2010 2:04:17 PM IST; Vial: 1; Injection: 3 Sample Name: Curcumin (Marketed); Date Acquired: 5/21/2010 2:13:44 PM IST; Vial: 1; Injection: 4 Sample Name: Curcumin (Mizoram); Date Acquired: 5/21/2010 2:24:04 PM IST; Vial: 1; Injection: 5 Sample Name: Curcumin (Meghalaya); Date Acquired: 5/21/2010 2:32:57 PM IST; Vial: 1; Injection: 6

Peak Summary with Statistics

Name: Curcumin

	Sample Name	Vial	Inj	Name	Retention Time (min)	Area	% Area	Height	Amount	Units
1	curcumin std	1	1	Curcumin	4.883	25762440	100.00	2453948	100.0	mcg/mL
1	2 Curcumin - Assam	1	3	Curcumin	4.918	22185321	100.00	1476067	85.6	mcg/mL
-	3 Curcumin (Marketed)	1	4	Curcumin	4.925	18731241	100.00	1220000	72.3	mcg/mL
	Curcumin (Mizoram)	1	5	Curcumin	4.933	10094334	100.00	814869	39.0	mcg/mL
5	Curcumin (Meghalaya	) 1	6	Curcumin	4.931	10461268	100.00	905728	40.4	mcg/mL

Reported b)

Report Method: Peak Summary Report Report Method ID: 1009 Page: 1 of 2 דוטופטו ואמויום. שועלבדווש איטופכל

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1:54:08 PM Asia/Calcutta

#### RESULTS

#### TLC studies

From the TLC with the composition of different mobile phase, it has been found that the ratio of Methanol is to Water at 8:2 had shown the best elution of curcumin.

#### **UV-VIS Spectrophotometric studies**

From scanning the methanol solution of standard Curcumin, the maximum absorption wavelength of Curcumin was found to be 427nm.

#### **HPLC studies**

From the HPLC studies, it shows that standard curcumin was eluted at Retention Time 4.883 mins. By using the same HPLC condition, after injecting the crude methanol extract

from different turmeric powder available, any peak in the Retention time 4.883 mins was recognized as Curcumin, and the amount of curcumin available was found and shown in the following table. The spectrum of HPLC are given in Fig 1.

#### CONCLUSION

From the above table it can be concluded that, the highest amount of curcumin was present in turmeric powder obtained from Assam.

As we have seen, the curcumin content is different for different samples. This can be due to various factors like geographical conditions, particle size, presence of impurities etc. Since the particle size is not determined, large particle size may also result in poor extraction of curcumin from the given samples.

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