IJCP

International Journal of Community Pharmacy

Volume 1 Number 2 May-August 2008

An official publication of Association of Community Pharmacists of India and Manipal University, India

Address: International Journal of Community Pharmacy
Manipal College of Pharmaceutical Sciences
Manipal University
Manipal – 576 104
India

E-mail: ijcp.acpi@manipal.edu

MESSAGE

The role of a modern day pharmacist goes beyond that of a neighborhood storekeeper and a care giver. He has to be an effective communicator and ready to don the mantle of societal leadership. The practice of Community Pharmacy can thus be viewed as one that provides the practitioner an opportunity to address a larger audience. Advocacy, consumerism, community pharmacy education, "pharmaceutical writing" are some definite activities that come to my mind while keying in my thoughts.

There cannot be a better person to teach the consumer the correct usage of pharmaceutical products, the misuse of medicines, the harms of self medication and the harmful affects of drugs, than a Community Pharmacist. The knowledge that he has acquired and his strong link with the community gives him a unique position of strength to address this oft neglected area. As science and drug discovery processes advance rapidly, when newer drug delivery systems are invented and perfected, when the effectiveness of certain medications and regimens are questioned and newer side effects are ascribed to products already in use; the gap between what is known to the scientific community and the lay public widens. Community Pharmacists should be the ones to bridge this gap.

Meta analyses and Systematic Reviews get published in scientific journals but the message rarely percolates down to the people who really matter. Scientific writing of pharmaceutical findings can be pursued as a career to be followed with passion. These and other related activities will make the profession truly community centric.

Dr. H. Vinod Bhat
Registrar (International Programs) and
Executive Director (Planning)
Manipal University

EDITORIAL

The patient care in community is becoming critical due to change in how diseases affect the health. The advent of diseases like Diabetes, Hypertension in epidemic proportions has changed the disease map world wide. India is known as the world capital for chronic diseases. There is increased burden on hospital care due to increased number of patients seeking intensive health care. The changed scenario has added pressure on health care resources and provider. The patients are left to take care of themselves, before they become seriously ill.

The diseases like Diabetes and Hypertension are asymptomatic initially make the patient to neglect the care which latter on results into a causality. They are collectively called life style based demands, community based approaches, one to one interaction of patient to health care provider in order to intervene effectively. The medicines alone are being mere tolls, just mere provision of drugs, wont improves the health of the patients. There is need for constant encouragement advice and reinforcement of the principles of healthy practices. The developed countries have changed the style of healthcare provision to meet the expectations of health care of a community. They are well developed pharmacists who take care of the patient needs and help the patient in management of diseases before they become seriously ill. In fact they contribute greatly in minimization of morbidity of diseases. It is proven beyond doubt that the Community Pharmacist being the right man to play the role in above crisis of poor health cares provision.

We are happy to present our second issue before you, which contain experiences of community-based services. We hope in coming days community services will emerge as a major force to resolve the issue of patient non-compliance. The provision of Pharmaceutical care in a community will bring in positive changes in health care delivery. The beginnings of services are to be made throughout the country so that Indian patients are secure and get the benefits of modern medicine from Kashmir to Kanyakumari. The simplest way to popularize the pharmaceutical care is through the pharmaceutical educational institutions. The teacher, students and practicing pharmacists have to collectively work towards provision of pharmaceutical care to the patients and every dispensed prescription.

Dr. N. Udupa
Editor-in-Chief

MESSAGE FROM ACPI

The Community Pharmacy in many developing countries has refused to grow beyond its business model. The Pharmacist in developing countries has remained obscure in direct health care of the patient. The pharmacists in developing countries are divided nuclear societies leaving the patient in dark regarding the pharmaceutical care. Many a time the patients are so confused about the using of the drugs, they have taken into granted a health care with out pharmacist is usual scenario. Looking at the lacunae in health care, WHO in collaboration with FIP come out with a concept of global pharmaceutical care. The apex health bodies of the world are strongly advocating that a balanced health care is provided by inputs from multidisciplinary approach by basic professions of health care. The Doctors, Pharmacist and Nurses are the basic professions to provide balanced health care by team work. However in many developing countries, due to disparities in professions, the services of health care are incomplete. The responsibilities of pharmacist include the total care for the patients as for the drugs and its usage are considered. There should be a fallow up of patient, how the therapy is envisaged and weather expected outcomes of therapy is achieved?

There is need to reorient pharmacy services in the existing system. The best way is to approach patients, document their health details and educate them about intelligent way of using medicines and as well as regarding life style changes which could help in improving their health.

Dr. Anantha Nagappa Naik
President
Association of Community Pharmacists of India

Novel Drug Design for Treatment of Cancer: A New Perspective

Mundada Atish S.[*1], Avari Jasmine G.[1], Bhattad Mona J.[2], Nath Nirmal M. [2] Sinha Ramaa C[3].

[1]University Department of Pharmaceutical Sciences, R.T.M. Nagpur University, Amravati Road, Nagpur- 440033.
[2]University Department of Biochemistry, R.T.M. Nagpur University, L.I.T. Campus, Nagpur- 440033.
[3]Bharati Vidyapeeth's College of Pharmacy, Sector-8, C.B.D., Belapur, Navi Mumbai.
*Corresponding author

atishmundada@rediffmail.com

Abstract:

Cancer, one of the major causes of death in the developed nations is a quintessentially dreaded disease caused due to the anomalous behavior of the cells. Out of myriads of options available today, chemotherapy has become increasingly important inspite of the fact that patients ultimately succumb to death because of its untoward side effects. But, on the brighter side, today we can list a number of neoplasms like Hodgkin's lymphoma, choriocarcinoma, Burkitt's lymphoma that can be cured by chemotherapy alone or in combination with other methods. Despite of these impressive advances, there is a sobering realization that many of the most prevalent forms of cancer still resist chemotherapeutic intervention. In the present review article, we tried to gauge the real challenges faced by the researchers in new drug design in treating cancer, aiming towards an amicable solution in the form of a complete cure rather than a better cure.

Keywords: cancer treatment, bio-marker, drug design.

Introduction:

Cancer, one of the major causes of death today, is a disease in which there is an uncontrolled multiplication and spread within the body of abnormal forms of the body's own cells. In most of the cases, the cause is multifactorial. Out of the various approaches to deal with cancer like surgery, radiation, immunotherapy, chemotherapy, biological response modifiers, etc., chemotherapy is becoming increasingly important in the recent years. Although it has prolonged the life, patients ultimately succumb to death due to the two reasons:

1. The serious and fatal toxicities involved in chemotherapy
2. Recurrence of the cancer

Indubitably this fact per se, sheds light on the current antineoplastic agents and their shortcomings[1]. On a brighter side, in spite of

the shortcomings, certain impressive advances have manifested in the form of complete cures for certain carcinomas like Burkitt's Lymphoma, Choriocarcinoma, Hodgkin's disease, Lymphosarcoma[2,3]. However, many of the most prevalent forms of cancer still resist the effective chemotherapeutic intervention. Hence the gamut of challenges confronted by researchers is right from harnessing the novel molecular targets like "transcription factors", "matrix metalloproteins" to "enzyme catalyzed therapeutic activation", etc.

In this article, we tried to focus on the real challenges in new drug design for treating cancer. The various areas that the researchers need to look into are as follows:

1. Transcription factors and neoplasia, which are the vistas in novel drug design.
2. Development of other novel tools and drugs as anticancer agents-
    - Cellular invasions and its regulation
    - ECTA (Enzyme Catalyzed Therapeutic Activation)
3. Work on novel molecular targets in cancer chemotherapy-
    - Targeting genome beyond the topoisomerase with camptothecins
    - Combination of the DNA damaging agents and checkpoint 1 inhibitors
    - G-quadruplex interacting agents are more than simple telomerase inhibitors
4. Biomarkers: a revolution sorely needed.
5. Novel oncogenic protein kinase inhibitors for cancer
6. Resistance in cancer: a target in drug discovery.
7. Use of stem cells since they can guide the drug to the tumor.

1. **Transcription Factors and Neoplasia, which are the Vistas in Novel Drug Design**

The fundamental role of gene transcription and the recognition of transcription factors as important control elements of cell growth have guided the researchers for these proteins as potential pharmaceutical targets for therapeutic intervention in cancer. The vast array of information available about these transcription factors, their molecular architecture and mode of action in various biological contexts, combined with the new opportunities offered by the

flourishing techniques of structure based drug design, computer aided modeling and functional genomics/proteomics are creating an exciting scenery for the development of a novel generation of highly selective drugs.

This transcription factor based therapeutic approach may revolutionize the anticancer drug options and will add significantly to the current clinical armamentarium.

1) Transcription factors (TFs) plays a pivotal role in the gene transcription process.
2) The enormous advances in genetic engineering techniques over the last decade have made possible their identification and elucidation of their structure and the signaling pathways that modulate their function.
3) Aberrations in their biochemical properties or the regulatory mechanisms that fine tune their activity, because of either genetic defects or abnormal internal/external cues; can lead to a variety of clinical entities from developmental disorders and diseases to several malignancies.
4) Focusing on cancer mutations and deregulated functioning of transcription factors encoded by or related to certain proto-oncogenes[4] and tumor suppressor genes[5] are currently involved in various types of malignant transformation.

So the challenge lies in the discovery of small molecular compounds aimed at particular transcriptional targets that participate in the development and progression of the cancer phenotype. Thus looking at the prospective benefits these small molecule drugs will offer, we should await the results if the researchers take it up as a challenge & harness the dormant information. This might represent the future perspective in substituting the classic cytotoxic and hormonal anticancer agents of the past by more selective drugs with greater efficacy and negligible side effects. Thus the in-depth understanding of the transcriptional networks underlying tumor genesis is of vital importance for the designing of new anticancer drugs. A decisive advantage of such an approach would be the reduced likelihood of the outgrowth of resistant cells, a major liability in contemporary forms of cancer chemotherapy

Approaches like structure based ligand design methodologies hold great promise in the synthesis of small molecule drugs that may alter the activity of the cancer associated transcription factors. As an ever growing number of solved TFs 3D

structures are being added to the data pool, one future challenge of the structure based drug design will be undoubtedly to apply the arsenal of available tools like new computer programs, algorithms for conformational analysis, ligand docking, structural alignment, enormous progress in the molecular biology providing 3D structure and SAR of the therapeutically relevant biopolymers to design transcription factor targeted low molecular mass agents that would modulate specific functions with high selectivity.

2. Development of other Novel Tools and Drugs as Anticancer Agents

The over manifestation of cancer usually occur at later stages of the disease process when the invasive potential has already been implemented. By the time of diagnosis, a high proportion of patients have occult or clinically detectable metastasis[6]. The capacity of the conventional cytotoxic approaches against this advanced accelerating disease has unfortunately been limited. Invasion is an active translocation of neoplastic cells across tissue boundaries and through the host cellular and extra cellular matrix barriers. Under this hypothesis, agents or treatments that maintain the integrity of the epithelial basement membrane may be an alternate approach to retard invasion or angiogenesis.

In malignant tumors, such anti proliferative therapy is the only possible strategy today despite its inevitable side effects on the normal proliferative cells such as the digestive tract and the immune system.

- **Cellular invasion and its regulation:**

Significant evidence has accumulated to directly implicate the members of the matrix metalloproteins (MMPs) in tumor cell invasion[7] and metastasis formation. MMPs are the zinc containing enzymes that are capable of degrading and remodeling many proteinaceous components of the extra cellular matrix. A number of synthetic and natural inhibitors for MMPs have been found and tested for possible usefulness.

All the MMPs inhibitors contain a zinc binding function (ZBF) in order to block the zinc atom from fulfilling its catalytic role at the enzyme's catalytic site. The inhibitors so far synthesized have raised serious doubts about their clinical use because of unfavorable pharmacokinetics and chronic toxicities. So the challenges to the researchers herein lies to design novel MMPs inhibitors which are more specific to a particular class out of 4 main classes of MMPs. Recent evidence shows a positive

correlation between MMP-2 activity and tumor cell invasion.

- **Enzyme catalyzed therapeutic activation technology:**

Many conventional drugs are enzyme inhibitors. They work by inhibiting a diseased cell's key enzyme, a protein that promotes or catalyses a specific biochemical reaction involved in cell growth or metabolism. But diseased cells can outsmart this approach by mutating or increasing the production of this enzyme transforming it into a resistant enzyme immune to higher drug doses. This cycle of drug resistance culminates in life threatening drug toxicity to the patient until the drug is no longer useful. Therefore the challenge to researchers is to discover and develop drug molecules capable of breaking the cycle of drug resistance while minimizing damage to the healthy cells.

A pharmaceutical developer New Biotics has already started finding drugs to treat cancer and infectious diseases. They are applying ECTA technology to develop a new generation of pharmaceuticals that transform drug resistance into therapeutic advantage. Unlike conventional agents that kill diseased cells by enzyme inhibition with toxic effects and drug resistance, ECTA provides a solution to this problem with powerful drugs that carry a potent toxin hidden within their chemical structure.

Released and activated by the diseased cell's resistance enzyme, the toxin causes the cell to self destruct with minimal toxicity to the patient. Although the ECTA drug may enter the normal cells, the diseased cells are more susceptible to the drug and its hidden payload because they have much higher concentrations of the resistance enzymes. In this way a diseased cell is tricked into committing suicide by a drug that acts as a substrate rather than inhibitor of the enzyme.

3. Works on the Novel Molecular Targets in Cancer Chemotherapy waiting for Discovery

Despite of the advances in the past decade, the medicinal cancer therapy is hampered by problems of severe unwanted side effects and the development of resistance[8]. Many established anti-cancer drugs are directed towards targets that are not specific for cancer but to the essential biomolecules in the living cells. Because cancer cells carry not only one but multiple genetic alterations which are more characteristic for the individual patient than for the tumor entity, an individualized medical approach could improve the success of a tumor therapy. A

prerequisite for personalized tumor therapy is an up gradation of an array of anti-cancer drugs directed to different molecular targets. Therefore, a systematic search for anti-cancer drug targets for the inter-disciplinary application of methods from bio-informatics, bio-chemistry, chemistry, tumor biology and related sciences should contribute to a research priority. Various such targets waiting to be harnessed to their fullest potential according to the author are as follows:

- **Targeting the genome beyond topoisomerase with camptothecins:**

Camptothecins selectively target topoisomerase I[9] (top I). Camptothecins represent a paradigm for targeting macro-molecular interactions. Camptothecins slow down the dissociation of two macromolecules- top I and DNA. Although, top I is the only primary target of camptothecins, the mechanisms of camptothecins rest beyond the formation of cleavage complexes. Indeed, top I cleavage complexes lead to replication (and transcription) mediated DNA damage. It is likely that DNA damage can be repaired more efficiently in normal than in cancer cells that are intrinsically deficient for DNA repair and cell cycle checkpoints. If specific deficiencies are associated with clinical responses, their detection should guide therapeutic decisions. Furthermore, targeting DNA repair and checkpoints might increase the selectivity of top I inhibitors for tumors and thereby increasing anti-tumor activity while reducing the side effects of top I inhibitors.

- **G-quadraplex interacting agents are more than simple telomere inhibitors:**

G-quadraplex is a poor substrate for telomerase activity and different classes of molecule ligands that selectively stabilize this structure and inhibit telomerase activity. These ligands differ from the catalytic inhibitors of telomerase by several points. Developing these with a special emphasis on their biological activities as potential anti-tumor agents is going to be a big tool for research.

- **Combination of the DNA damaging agents with checkpoint 1 inhibitors:**

During the cell cycle that leads to mitosis, checkpoints are activated in response to DNA damage. The checkpoints control the ability of cells to arrest cell cycle allowing time to repair the DNA. In more than 50% of cancer cells, the G1 checkpoint is inactive due to mutations of p53[10]. Therefore, the combination of a DNA damaging agent with

a G1 checkpoint inhibitor should force selectively cancer cells into a premature and lethal mitosis. This approach which has recently drawn considerable interest in researchers is also a challenge.

4. Bio-Markers – a Revolution Sorely Needed

Bio-markers measure the drug-induced changes in the patient's blood or tissue. Such changes can confirm drug activity and thereby help selecting patients which are more likely to respond to the treatment. These biochemicals are revolutionizing cancer drug development. After 20 years of study, we have begun to see the clinical benefits for patients from drugs that are designed to exploit the cancer gene-based targets. These drugs cannot be optimally developed using approaches designed for the more traditional cytotoxic chemotherapies. Maximum tolerated dose may not indicate optimal dose; dose-limiting toxicity may not be proliferation linked and myelo-suppression side-effects cannot be used as surrogate markers of cyto-toxicity. These facts highlight the need to find and develop the pharmacodynamic and prognostic markers to confirm that new agents have their desired biochemical effects as well as to establish optimal dosing. A bio-marker that reveals apoptosis in tumor cells, demonstrate that an experimental agent is killing the tumor cells. Thus biomarkers avoid the long delays required to reach a clinical end-point.

At present the bio-markers are used in two ways, firstly, prognostic markers that are preferably identified through the DNA microarray chips could match new classes of drugs with the molecular profile of individual tumors. If a drug is targeted specifically against cells that have a particular mutation, translocation, or gene over-expression, then testing tumor tissues to determine whether that molecular profile is present in a tumor could help clinicians avoid prescribing an in-effective treatment.

The second approach which consist of pharmacodynamic markers, tell us whether drug is having its intended bio-chemical effect, and if so, to what extent or how extensive it is. In the long term strategy, these pharmacodynamic effects could be used as surrogate markers for clinical response. There are many hurdles in developing bio-marker based drugs. Markers need to be identified early in a drug's life-cycle, since their use spans the pre-clinical and clinical phases of evaluation. Also in many cases it may help to develop and

validate a diagnostic agent in parallel with a therapeutic agent, although this might increase the complexity of the developmental process.

The FDA is recognizing the growing importance of the bio-markers in oncology, although its views and their eventual impacts on regulatory requirements are still evolving. Using bio-markers based on proteomic and pharmacogenomic tools allows targeted drug development, a revolution that builds on the successes of targeted drug design, in particular computer-aided design tools used together with X-ray crystal structures of the novel target proteins. Bio-markers can lead to the development of less toxic drugs as well as drugs that are more suitable for specific patients. Bio-markers can pave the way for a new vision of the cancer therapy, where cancer could be controlled for life. This new era promises drugs that can better meet patient's needs than the current armamentarium.

Successful cancer treatment of the future is being developed with a focus on the molecular targets underlying the pathophysiology of neoplasia. Prominent targets which have emerged are mutated in the course of a cancer's development and mediate activation or release from suppression of pathways mediating proliferation or apoptosis. These are arguably pathogenic targets. However, equally important are targets which can be defined on the basis of large scale analysis technique of gene or protein expression in tumors which define targets as a result of tumor's differentiation state or tissue of origin ('ontogenic' targets); targets mediating drug uptake; metabolism ('pharmacologic' targets) and 'micro environmental targets' mediating the alteration of tumor stromal elements.

Hence the authors feel that irrespective of the nature of the molecular targets, which is the focus of new therapeutic efforts, ideally target definition in susceptible tumors or patients would be the part of the development plan. In addition, an understanding of the therapeutic index which might be achieved in the host versus tumor tissues using a surrogate or an actual marker and monitoring the drug effect would be available from animal models.

5. Novel Oncogenic Protein Kinase Inhibitors for Cancer Therapy - a Challenge

Small molecule drug discovery for cancer therapy is making extraordinary progress

especially to the realm of advancing novel oncogenic protein kinase inhibitor lead compounds providing significant impetus to both basic research and clinical testing. In this perspective structure and mechanism based drug design are highlighted. Also, evolving concepts in novel oncogenic protein kinase inhibitor drug discovery is highlighted relative to therapeutic target selectivity including the recent identification of oncogenic kinase mutants effecting drug-resistance or enhanced drug susceptibility to small-molecule inhibitors.

6. Resistance in Cancer: a Target for Drug Discovery

Resistance remains a major problem in the clinical utility of cancer chemotherapy. However it also represents a tumor cell phenotype that is in many ways different, and thus distinguishable from the majority of normal cells. Two approaches to the targeting of resistant cells are described involving intratumoral P450 expression, mechanisms of drug efflux and defective DNA repair. It is suggested that the view of the solid tumor as a complex organ rather than a collection of individual cells will inform future drug development in order to overcome and target multiple mechanisms.

7. Use of the Stem Cells in Drug Delivery to Tumors

Texas researchers claimed to have perfected a method by which they can deliver cancer treatment directly into tumors, bypassing the healthy tissue. The study was done on mice but human trials would begin soon. The research team used the benefits of a known anti-cancer therapy, interferon beta, which can kill cancer cells. In practice, this therapy has proven problems. It causes toxic side effects and its benefits disappear within minutes of patients getting their shots. Attempts were made to circumvent these problems by manipulating a certain type of stem cell to encode the interferon beta gene. The stem cells then move like guided missiles, targeting tumor cells.

Thus, patients would be infused with the stem-cell delivered anti-cancer treatment. The targeted delivery of anti-cancer therapy to tumors is built upon the well known strategy employed in the healing of the wound. The specialized stem cells known as mesenchymal stem cells, comes from bone marrow and help maintain healthy connective tissues. When new tissue is needed to heal wounds or form scars those special stem cells swell in number.

Even though they are tumors, the malignant cells act just like "never healing wounds". Half the tumors are made up of stromal cells that provide structural support. For the body, forming that tumor support structure is much like healing wounds and forming scars. They enter the specialized stem cells, giving them the clues they need to take on the construction duties of stromal cells delivers the cancer busting ability directly to tumors. The research team did not see the engineered stem cells drift into healthy organs like lungs, liver, spleen, kidney or muscles.

Conclusion:

Despite the fact that assiduous and laudable research has already commenced in this direction, the author feels the dire need of a panacea for various carcinomas, is a formidable challenge for the future research. Not only the modus operandi of various novel molecular targets in cancer is known today but also the new opportunities offered by the flourishing techniques of structure based drug design and computer aided modeling are opening a plethora of alternatives as well as options. Thus we hope that an impeccable cure does not remain a pie in the sky but a believable reality so that the patients suffering from this dreadful disease can heave a sigh of relief and rekindle their hopes of living their lives without bearing the torturous side effects of the anticancer therapy.

Acknowledgement:

Authors are grateful to Mr. Sharad C. Chandak, Glenmark Pharmaceuticals, Sinnar, India, for his unending support during the preparation of this review article.

References:

1. Calabresi P, Chabner BA. Chemotherapy of Neoplastic diseases. In: Goodman and Gilman editors. The Pharmaceutical Basis of Therapeutics. 9th edition, 1994,pp.1225-1287.
2. Viter De VT, Hubbard, SM. Hodgkin's disease. New England Journal of Medicine 1993:328-560.
3. William A. Antineoplastic agents. In: Wilson and Gisvold editors. Textbook of Organic Medicinal and Pharmaceutical Chemistry, 11th edition, 1993,pp.390-543.
4. Braun MM, Caporaso NE, Page WE, Hoover RN. Genetic component of lung cancer: cohort study of twins. Lancet 1994;344:440-443.

5. Cavence WK, White RL. The genetic basis of cancer. Scientific American 1995:272-79.
6. Ruoslahti E. How cancer spreads. Scientific American 1996: 72-77.
7. Aznavoorian S, Murphy AN, Steeler-Stevenson WG, Liotta LA. Molecular aspects of tumor invasion and metastasis. Cancer 1993;71:1368-1382.
8. Carmichael J. Cancer Chemotherapy: identifying novel anticancer drugs. Br Med J 1994;308:1288-1290.
9. Editorial. DNA topoisomerases – new twists to tumor therapy. Lancet 1988;1: 511-513.
10. Stewart BW. Mechanisms of apoptosis: integration of genetic, biochemical, and cellular indicators. J National Cancer Institute 1994;86:1286-1295.

Cassia: A Wonder Gift to Medical Sciences

Papiya Mitra Mazumder[1], V. Percha[2], Mamta Farswan[2*], Aman Upaganlawar[3]

[1]Birla Institute of Technology, Mesra, Ranchi, Jharkhand, India
[2]Department of Pharmaceutical Sciences, SBS (PG) Institute of Biomedical Sciences, Balawala, Dehradun, India,
[3]Department of Pharmacology, The Maharaja Sayajirao University, Baroda, Gujarat, India
[*] Corresponding author
mamta_fr2002@yahoo.co.in

Abstract:

Since the advent of modern drug remedies, traditional medicine has greatly receded in occidental societies. Moreover only a limited number of medicinal plants have received detailed scientific scrutiny, thereby prompting the World Health Organization to recommend that this area could be comprehensively investigated. Plants belonging to *Cassia* species are used extensively in various parts of the world against a wide range of ailments, the synergistic action of its metabolite being probably responsible for the plant's beneficial effects. This species of plants are

reported to contain alkaloids, sitosterols, anthraquinone glycosides, tannins and flavonoids. Various species of Cassia are reported to have laxative, purgative, antidiabetic, anti-inflammatory, antimicrobial, antifungal, hepatoprotective, antipyretic, antineoplastic, antimalarial, antiasthmatic, antiviral and wound healing properties. In the Ayurvedic system of medicine these plants were also used for the treatment of fever and headache. This paper reviews the phytochemical and pharmacological activities of the various species of *Cassia,* considering the fact that there are about hundreds of species of this genus which are distributed all around the world and many of them which occur in India. This paper also appraises the hypoglycemic, antioxidant and free radical properties of plant parts**.**

Key words: Phytoconstituents, hypoglycemia, *Cassia*, anthraquinones, laxatives.

Introduction:

A medicinal plant is one whose one or more of its organs contains substances that can be used for therapeutic purposes or which are precursors for the synthesis of useful drugs. For the past two decades, there has been an increasing interest in the investigation of different extracts obtained from traditional medicinal plants as potential sources of new therapeutic agents[1]. Traditional or indigenous drugs used by different ethnic groups of the world for the treatment of diseases have special significance of having been tested on long time scale. They are relatively safe, easily available and affordable to masses. Traditional drugs have given important lead in drug search, resulting in the discovery of novel molecules such as, Artemisinine for the cure of multi-drug resistant malaria, Silymarin for hepatoprotection and Vincristine and Vinblastine for certain type of cancers have already been isolated from plants and sincere efforts for curing immunity related problems, AIDS, Alzheimer's and diabetes are on their way[2]. Due to these varieties of reasons, the popularity of complimentary medicines is on an increase. Traditional plant therapies coupled with dietary measures as prescribed in Ayurvedic and other indigenous system of medication are good supplement for the treatment of diseases nowadays[3-5].

The World Health Organization in 1980 has recommended the evaluation of the effectiveness of plants in conditions where there is lack of safe synthetic drugs[3]. Today we are witnessing a great deal of public

interest in the use of herbal remedies. There are many herbs, which are predominantly used to treat cardiovascular diseases, liver disorders, central nervous system, digestive and metabolic diseases. Herbal drugs, their extracts and compounds isolated from them have demonstrated a broad spectrum of biological activities. Ethanopharmacological studies on such herbs/medicinally important plants are an area of interest for the investigators throughout the world. One such species, *Cassia* invites attention of researcher's world wide for its pharmacological activities ranging from antidiabetic to antiviral.

Cassia, is a large genus of around 500 species of flowering plants in the family Leguminosae and is widely distributed throughout Asia including India, Mauritius, China, East Africa, South Africa, America, Mexico, West Indies and Brazil. There are hundreds of species of *Cassia* which occurs with more than 1000 names. Some important species are *Cassia fistula, Cassia grandis, Cassia hirsutica, Cassia sieberiena, Cassia alata , Cassia tora, Cassia occidentalis, C. auriculata, C. Nigricans*[6]. From a pharmaceutical perspective the presence of anthranoides with strong laxative and purgative effects is of particular interest and characteristic of this genus. *Cassia* species have been of medical interest due to their good therapeutic value in folk medicine. Abo and Eluojoba showed that the leaves and pods of *Cassia fistula, Cassia spectabilis* and *Cassia podocarpa* possess laxative and antimicrobial activities[7-8]. The extracts of flowers and seeds of *C. auriculata* were found to possess antidiabetic activity[9]. Manonmania evaluated the antioxidant activity of *C. fistula*[10].

Dalziell and Benjamin evaluated the use of leaves of *C. nigricans* as appetizers, febrifuges and for treating skin diseases such as ringworm, scabies and eczema[11]. The anti-inflammatory and hepatoprotective activity of *Cassia occidentalis, C. fistula* and *C. sophera* are also reported[12-14]. *C. sophora, C. italica, C. pumila* are reported to have CNS depressant, anxiolytic and hypnotic activity[15-17]. The seeds of *Cassia tora* have good binding and suspending property and also used as a substitute for coffee. Barakol was isolated from *Cassia siamea* having anxiolytic and purgative activity. *Cassia mimosoides* is reported to have antiobesity activity[18]. *Cassia tora, C. auriculata, C. fistula, C. alata* were reported to have antidiabetic and antioxidant activity[19-22].

Taxonomical classification of the genus Cassia

Scientific classification

Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Rosidae
(Unranked)	Eurosids I
Order	Fabales
Family	Leguminosae
Subfamily	Caesalpinioideae
Tribe	Cassieae
Subtribe	Cassinae
Genus	*Cassia* L.

Some species of Cassia, their habitat, distribution and common names:

Name of the species	**Habit**	**Distribution**	**Common name**
Cassia alata L.	Shrub	Wide	Ringworm shrub
Cassia angustifolia Vahl.	Shrub	Wide	Arabian senna, Indian senna
Cassia auriculata L	Shrub	Malaysia	Mataran tea, Tanner's tea
Cassia bakeriana Craib.	Tree	Mandalay	
Cassia bicapsularis L.	Shrub	Cultivated	Dan-kywe
Cassia corymbosa Lam.	Shrub	Mandalay	

Cassia didymobotrya Fresen.	Shrub	Mandalay	
Cassia fistula L.	Tree	Wide	Indian laburnum, Purging cassia
Cassia glauca Lam.	Small tree	Cultivated	Pyiban-nyo, Pyiban-shwe
Cassia grandis L. f.	Tree	Cultivated	Horse cassia Pink shower
Cassia italica (Mill.) L.	Shrub	Wide	Dan-gywe
Cassia javanica L.	Shrub	Cultivated	Pink shower or White shower tree
Cassia javanica	Shrub	Myanmar	Pwabet
Cassia mimosoides	Shrub	Mandalay	Mezali
Cassia marginata Roxb.	Small tree	Cultivated	Red cassia
Cassia obtusa Roxb.	Shrub	Wide	Negro coffee, Wild coffee
Cassia occidentalis L.	Shrub	Wide	Country senna
Cassia pumila Lam.	Shrub	Yangon	
Cassia senna L.	Shrub	Wide	Alexandrian senna
Cassia sophera L.	Shrub	Mandalay	Foetid cassia
Cassia spectabilis DC.	Small tree	Cultivated	Panama-ngu
Cassia tora L.	Shrub	Wide	Metal seed, Ngusat
Cassia hirsuta L.	Herb	Myanmar	Kandauk
Cassia siamea Lam.	Tree	Myanmar	Mejari, Mezali, Siamese cassia

Phytochemistry and pharmacological activities of different parts of *Cassia* species:

Name of the species	Plant parts	Chemical Constituents	Pharmacological activity
Cassia fistula	Heart wood	Fistucacidin(3,4,7,8,4'-pentahydroxyflavan[12]	
	Bark	Oxyanthraquinone, Dihydroxyanthraquinone	Antitumour hepatoprotective
	Leaves	Procyanidin B2, biflavonoids, triflavonoids, rhein, rhein glucoside, sennoside A, sennoside B, chrysophanol, physcion epiafzelechin 3-O-B-D-glucopyranoside, 7 biflavonoids and two triflavonoids, (-)-epiafzelechin,(-)-epicatechin and procyanidin[23-26]	Wound Healing, Antioxidant[19], antitumor, hepatoprotective[12], hypoglycemic, antibacterial, antidiabetic
		Kaempferol, eucopelargonidin tetramer (with free glycol unit), rhein, fistulin, alkaloids, triterpenes, flavonoids[28]	Antioxidant[20] antifungal[27]

Flowers	Rhein, volatile oil, waxy and resinous Derivatives flavonoids, fistulin[29]	
Fruit pulp	kaempferol and rhein Chrysophanol[29]	
Seeds	Fistulic acid, 3-formyl-1-hydroxy-8- methoxy anthaquinone1,8-dihydroxy-3-anthraquinone carboxylic acid was isolated from the pods[31-32]	Anti-tumour activity of *C. fistula*[30]
Pods	Rhamnetin-3-O-gentiobioside	
Roots		Cardioprotection[33]

***Cassia occidentalis* L.**	Leaves	Anthraquinones, A bianthraquinone, flavonoid glycosides matteucinol 7-rhamnoside Chysophanol and emodin[34-38]	Yellow fever, headache, conjunctivitis
	Root	chrysophanol, emodin, pinselin, questin, germichrysone, methylgermitorosone singueanol-I pinselin and 1,7-dihydroxy-3-methylxanthone, 1,8-dihydroxyanthraquinone.2 new bis (tetrahydro) anthracene derivativeoccidentalol-1 and occidentalol-II were isolated from the roots	Anti-inflammatory, antibacterial, antimalarial antimutagenicity, hepatoprotective[39,40,13]
	Aerial parts	C-glycosidic flavonoids, cassiaoccidentalins A, B and C Anthraquinones[41]	purgatives and laxative

			purgatives and laxative[41]
	Seeds		
Cassia alata	Bark	Sennosides anthraquinoids, aloe-emodin, chrysophanol, chrysophanic acid, and rhein (cassic acid), adenine and the flavonoids[43-45] Kaempferol 3-O-gentiobioside (K3G)	Antifungal[42]
	Leaves		antibacterial
	Flower, root, stem bark		Antibacterial[46], antimutagenic, antifungal, analgesic, antiinflammatory and hypoglycaemic[21]
***Cassia italica* Miller.**	Leaves	Coumarins, flavonoids, B -sitosterol coumarins, arotenoids, flavonoids, anthraquinones, tannins, sugars, reduced compounds, mucilage, sterols and triterpens. B -sitosterol, stigmasterol, α-amyrin, 1,5-dihydroxy-3-Me-anthraquinone[48-49] The contents of sennosides and	Antimicrobial and antitumor activity, purgative[47]

		rhein glycosides in leaves, pods, and callus of Cassia italica were investigated[50]	
	Pods	Sennosides and rhein glycosides	CNS depressant, antinociceptive and sedative[15]
	Whole plant		Anti-inflammatory, antipyretic, analgesic antineoplastic and antiviral activities.
Cassia tora	Roots	1,3,5-trihydroxy-6-7-dimethoxy-2-methylanthroquinone and beta-sitosterol	Anti-inflammatory
	Leaves	Emodin, tricontan-1-0l, stigmasterol, □-sitosteral-□-D-glucoside, freindlen, palmitic, stearic, succinic and d-tartaric acids uridine, quercitrin and isoquercitrin	Antinociceptive and smooth muscle contracting activities[52]
		Isolated are aloe-emodin, 1,8-dihydroxy-3-(hydroxymethyl)-anthraquinone	
	Seeds	Naptho-alpha-pyrone-toralactune, chrysophanol,	

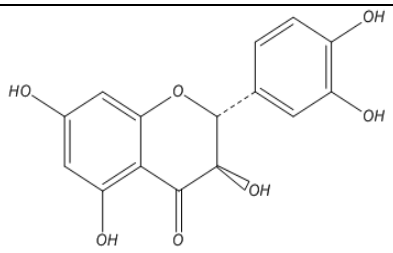
		physcion, emodin, rubrofusarin, cchrysophonic acid-9-anthrone, nor-rubrofusarin gentiobioside, aloe emodin, rhein, emodin	
			The purgative, antioxidant, antibacterial antipsoriatic activity[53]
Cassa auriculata	Leaves	Anthraquinones	Antidiabetic
	Flowers	Anthraquinones, aloe emodin and sitosterols	Antidiabetic, antioxidant[22]
	Whole plant and Pods		Antidiabetic and laxative[54-55]
Cassia sophora	Heartwood	Sopheranin (1, 3, 6, 8-tetrahydroxy 2-methyl 7-vinyl anthraquinone) has been isolated, beta-sitosterol, chrysophanol, physcion and emodin[56]	

		Cycloartane triterpene glycoside named Cyclosophoside A, was isolated[54-55]	
	Seed		Analgesic, anticonvulsant effect, hypnotic, hypoglycemic activity, hepatoprotective activity[14,16]
Cassia javanica	Seed	Chrysophanol, physcion, 1,5-dihydroxy 4,7-dimethoxy 2-methyl anthraquinone 3-O-alpha-L(-) rhamnopyranoside and 1,3,6,7,8-pentahydroxy-4-methoxy 2-methyl anthraquinone have been isolated[59]	
Cassia podocarpa	Leaves and fruits	Anthraquinones	Gonorrhea and pile, fever, control insects, virus and their infections,virucidal Purgative, laxative and Antispasmodic[60-62]
Cassia absus	Leaf	Quersetin, rutin, alkaloids	Wound healing
	Root	Anthraquinoness, chrysophanol, aloe emodin, chaksine	
		Sitosterol, chaksine, flavonoides, triterpenoides	
			Astringent, cathartic,

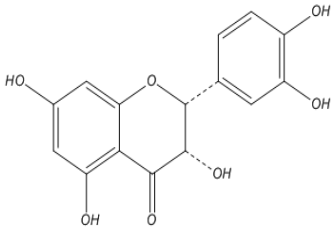
	Seeds		opthalmia, infections
Cassia siamea	Flowers	Anthraquinones and sitosterol Catechin[63]	Antioxidant, antispasmodic[64]
	Whole plant	Two novel alkaloids with tricyclic skeleton, cassiarins A, and B , have been isolated[66]	Antispasmodic, fever and purgative[65]
	Leaves		Anxiolytic Antispasmodic
***Cassia angustifolia* Vahl.**	Leaves	Glucoside, sennosides, kaempferin, chrysophenic acid, aloe emodin and rhein	Purgative, cathartic, vermifuge[62]
	Fruits and pods	Glycerides of rhein, chrysophenic acid, sennoside β and ά	Laxative
***Cassia mimosoides* L.**	Roots	Physcion	Anthelmintic, antifungal
	Leaves	Emodin and its glycerides, emodic acid	Asthma, typhoid, stomach trouble, antiobesity[18]
Cassia grandis	Whole plant		Anti-dermatophyte activity Fungicidal and fungistatic[67]
***Cassia pumila* L.**	Whole plant	Anthraquinones, diterpenes, alkaloids[68]	CNS depressant, diuretic, spasmolytic[68] and antipyretic

***Cassia glauca* L**	Leaves and stem	Anthraquinone glycoside, 3-hydroxy-6-methoxy 3 methyl anthraquinone, B sitosterol, lupeol	Antidiabetic, pollution tolerant, CNS depressant[69]
		Catechin, dulcitol, 3-methoxy epigalactocatechin,	
	Bark	Y-sitosteroline, digitolutein were isolated, chrysophanol	Purgative, antimalarial
	Seed		
***Cassia uniflora* Mill.**	seeds	Proteins, polyphenols, ά galactosidase[62]	
***Cassia spectabilis* DC.**	Flowers	Chrysophanol, emodin, isorhamnetin- 5-glucoside, kaempferol, alkaloids[62]	

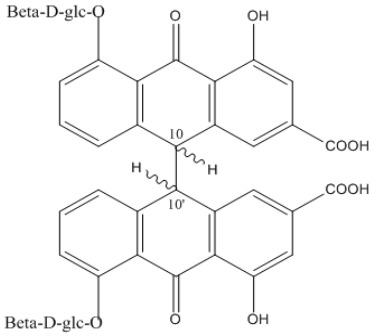
Structures of some of the phytoconstituents from *Cassia* species.



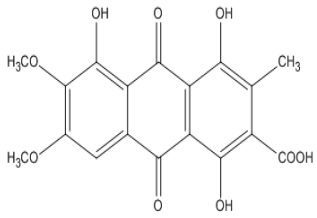
(+) Catechin



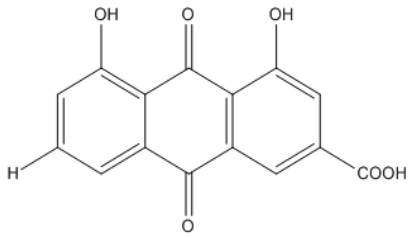
(-) Epicatechin



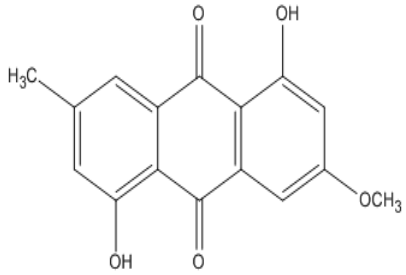
	C-10
Sennoside A	R
Sennoside B	R



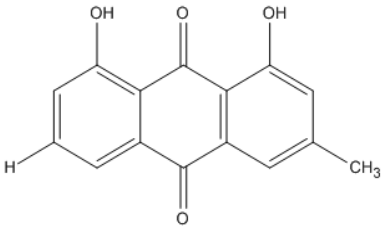
Fistulic Acid



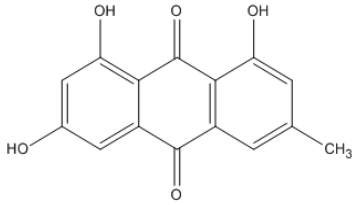
Rhein



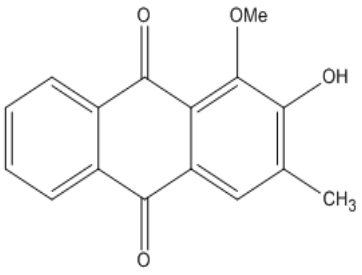
Cassia italica



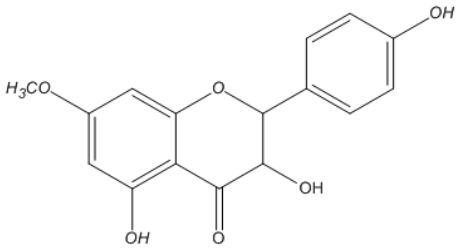
Chrysophanol



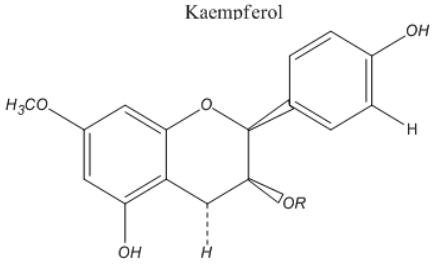
Emodin



Digitoluein



Kaempferol



(+) Epiafazelechin

Conclusion:

In the present review, we have made an attempt to congregate the botanical, phytochemical, ethnopharmacological, pharmacological and taxonomical information on *Cassia*, a species of medicinal herb used in the Indian system of medicine. Survey of literature revealed the presence of glycosides, alkaloids, flavonoids, triterpenoids and sterols in different species of Cassia. It also revealed a broad spectrum of pharmacological activity of the species. This species exhibited a wide range of activities ranging from antidiabetic, antioxidant, anti-inflammatory, antibacterial, antitumor, anxiolytic and cardioprotection have been studied. Presence of wide range of chemical compounds indicates that the active constituents isolated from the species could serve as a "lead" for the development of novel agents having good efficacy in various pathological disorders. An extensive survey of literature revealed that *Cassia* is an important source of many pharmacologically and medicinally important chemicals. Although many studies have claimed the use of some species of *Cassia* for the treatment of various diseases but still the pharmacological potential of the other plants species of the genus are required to be explored.

Acknowledgement:

The authors are immensely thankful to Dr. D. Sasmal, Head of the department, Birla Institute of Technology, Mesra, Ranchi for the support and guidance for writing this article.

References

1. G.H.S. Bonjar and P.R Farrokhi. Antibacillus activity of some plants used in traditional medicine of Iran. Niger. *J. Nat. Prod. Med* 8: 34–39 (2004)
2. H. Sagrawat, A.S. Mann and M.D.Kharya. Pharmacological potential of Eugenia jambolana:

A review. *Pharmacognosy Magazine* 2(6): 96 (2006).

3. D.M. Eisenberg, R.C. Kesseler, C. Foster, F.E. Norlock, D.R. Calkins and Delbanco T L. Unconventional medicine in the United States: Prevalence, costs, and patterns of use. *New Engl.J. Med* 328: 246-252 (1993).
4. A.H. Maclenan, D.H. Wilson and A.W. Taylor. Prevalence and cost of alternative medicine in Australia. *Lancet* 347: 569-573 (1996)
5. V.P. Upadhayay and K. Pandey. In Ayurvedic approach to diabetes mellitus and its management byindigenous resources. Diabetes Mellitus in Developing Countries, (Interprint New Delhi,) (1984) pp. 375-377.
6. R. G. Ayo1, J. O. Amupitan and Yimin Zhao. Cytotoxicity and antimicrobial studies of 1, 6, 8-trihydroxy-3-methyl-anthraquinone (emodin) isolated from the leaves of *Cassia nigricans*. *African Journal of Biotechnology* Vol. 6 (11), 1276-1279, (2007).
7. K.A. Abo, A.A. Adeyemi and I.A. Jegede. Spectrophotometric estimation of anthraquinone content and antimicrobial potential of extracts of some *Cassia* species used in herbal medicine in Ibadan. *Sci. Forum* 3(2): 57–63 (2000)
8. A.A. Eluojoba, A.T. Abere and S.A. Adelusi. Laxative activities of *Cassia* pods sourced from Nigeria. *Niger. J. Nat. Prod. Med* 3: 51–53 (1999)
9. S.S. Jalalpure, M. B. Patil, P. Aruna, B. N. Shah and M.D. Salahuddin. Antidiabetic activity of *Cassia auriculata* seeds in alloxan induced diabetic rats. *Niger. J. Nat. Prod. Med* 8: 22–23 (2004)
10. G. Manonmani, V. Bhavapriyaa, S. Kalpanaa, S. Govindasamya and T. Apparananthamb. Antioxidant activity of *Cassia fistula* (Linn.) flowers in alloxan induced diabetic rats. *Journal of Ethnopharmacol* 97: 39–42 (2005).
11. T.V. Benjamin. Investigation of *Cassia alata*, a plant used in Nigeria in the treatment of skin

diseases. *J. Afri. Med. Plants* 3: 135–136 (1980)

12. T. Bhakta, P.K. Mukherjee, K. Mukherjee, S.S. Banerjee, C. Mandal, K. Tapan, P.M. Maity and B.P. Saha. Evaluation of hepatoprotective activity of *Cassia fistula* leaf extract
13. M. A. Jafri, M. S. Jalis, K. Javed and S. Singh. Hepatoprotective activity of leaves of *Cassia occidentalis* against paracetamol and ethyl alcohol intoxication in rats. *J Ethnopharmacol* 66 (3): 355-61 (1999)
14. H.M. Burkill. The useful plants of west tropical Africa, Vol 3 (1985)
15. S.C Jain, R.A. Sharma and R.Jain. Sennosides in *Cassia italica* in vivo and in vitro. *Fitoterapia* 67 (1): 82 (1996)
16. A. Bilal, N.A. khan, A. Ghufran and M. Inamuddin. hepatoprotective effect of seeds of *Cassia sophera* against CCl4 induced hepatic damage in albino rats. *Pharmacog mag.* 1(2): 80-86 (2005)
17. H. Morita, S. Oshimi, Y. Hirasawa, K. Koyama, W. Ekasari, G. Indrayanto and N. Zaini. Cassiarins A and B, Novel Antiplasmodial Alkaloids from *Cassia siamea*. *Org Lett* (9): 17685627 (2007).
18. A. Caceres, B.R. Lopez, M.A. Giron and H. Logemann. Plants used in Guatemala for the treatment of dermatophytic infections. 1. Screening for antimycotic activity of 44 plant extracts. *J Ethnopharmacol* 31(3):263-76 (1991).
19. G.C. Yen, P.D. Duh and D.Y. Chuang. Antioxidant activity of anthraquinones and anthrone. *Food Chem* 70: 437-441 (2000).
20. Luximon-Ramma, T. Bahorun, M.A. Soobrattee and O.I. Aruoma. Antioxidant activities of phenolic, proanthocyanidins, and flavonoid components in extracts of *Cassia fistula*. *J. Agric. Food Chem* (50):5042-5047 (2002).
21. M. Nazirizadeh and G.H. Amin. Chemical information including known chemo-types Studies of drugs from Senna (*Cassia italica*) plants in Iran. *Iran. J.*

Chem. Chem. Eng 5: 68-72 (1985).

22. A.R. Juvekar and G.V. Halade. Hypoglycemic activity of *Cassia auriculata* in neonatal streptozotocin induced non-insulin dependent diabetes mellitus. *Journal of natural remedies* Vol/1: 14-18 (2006).
23. T.V. Padmanabha Rao and V. Venkateswarlu "Fistucacidin" from the bark and heartwood of *Cassia fistula* Linn. *Bull. Nat. Ins. Sci* 31: 28-33 (1965).
24. M. Rani and S.B. Kalidhar. A new anthraquinone derivative from Cassia fistula Linn. Pods. *Indian J. Chem* 37B: 1314-1315. (1998)
25. Y. Kashiwada , K. Toshika , R. Chen, G. Nonaka and I. Nishioka. Tannins and related compounds. XCIII. Occurrence of enantiomeric proanthocyanidins in the Leguminosae plants, *Cassia fistula L.; Cassia Javanica L. Chem. Pharm. Bull* 38: 888-893 (1996).
26. N.N. Kaji , M.L. Khorana and M.M. Sanghavi. Studies on *Cassia fistula* Linn. *Indian J. Pharm* 30: 8-11 (1968).
27. V. Duraipandiyan and S. Ignacimuthu. Antibacterial and antifungal activity of *Cassia fistula* L.: An ethnomedicinal plant. *Journal of Ethnopharmacology* 112 (3): 590-594 2007
28. A. Kumar, C.S. Pande and R.K. Kaul. Chemical examination of *Cassia fistula* flowers. Indian J. Chem 4: 460 (1966).
29. P. Liptak and I. Szentagali. A *Cassia fistula* hat_anyaga. *Ber. Ungar. Pharm. Ges*. 13: 61-63(1937).
30. R.K. Khanna and S. Chandra. Forest/Domestic waste as a source of natural dyes. *J. Econ. Bot* 20: 497-500 (1996).
31. F.K. Modi , M.L. Khorana. A study of *Cassia fistula* pulp. *Indian J. Pharm* 4: 61-63 (1952).
32. T.R. Misra, R.S. Singh, H.S. Pandey and B.K. Singh. A new diterpene from *Cassia fistula* pods. *Fitoterapia* LXVIII (58):375 (1997).
33. T. Chaminda, J. Munasinghe, C.K. Seneviratne, M.I. Thabrew

and A.M. Abeysekera. Antiradical and antilipoperoxidative effects of some plant extracts used by Sri Lankan traditional medical practitioners for cardioprotection. *Phytother. Res* 15: 519-523 (2001)

34. M.M. Vaishnav and K.R.Gupta. Rhamnetin 3-O-gentiobioside from *Cassia fistula* roots. *Fitoterapia* LXVII: 78-79 (1996).
35. R. Anton and P. Duquenois. Contribution to the chemical study of *Cassia occidentalis* L. *Ann Pharm Fr* (1968)
36. B.S. Ginde, B.D. Hosangadi, N.A. Kudav, K.V. Nayak and A.B. Kulkarni. Chemical investigations on *Cassia occidentalis I*. Isolation and structure of cassiollin, a new xanthone. *J. Chem. Soc* 9: 1285-9 (1970)
37. E.J.Adjanohoun, L. Assi Ake, J.J. Floret, S. Guindo, M. Koumaré, A.M.R. Ahyi and J. Raynal. Médecine traditionnelle et pharmacopée contribution aux études ethnobotaniques et floristiques au Mali, Edition Agence de Coopération Culturelle et Technique (ACCT), Paris; 26 (1985).
38. P.P Rai and M. Ashok. Anthraquinone glycosides from plant parts of *Cassia occidentalis*. *Indian J. Pharm. Sci* 45(2), 87-8. (1983).
39. C. Perez and C. Anesini. In vitro antibacterial activity of Argentine folk medicinal plants against Salmonella typhi. *J Ethnopharmacol* 44(10): 41-6(1994).
40. N. Sharma, P. Trikha, M. Athar and S. Raisuddin. In vitro inhibition of carcinogen-induced mutagenicity by *Cassia occidentalis* and *Emblica officinalis. Drug Chem Toxicol* 23(3): 477-84 (2000).
41. H. Tsutomu,U.Hiroshi, I. Hideyuki, S. Sumiko, T. Tomofusa and Y. Takashi. Phenolic constituents of C*assia* seeds and antibacterial effect of some Naphthalenes and anthraquinones on methicillin resistant S. aureus. *Chem.*

Pharm. Bull 47 (8): 1121-1127(1999)

42. S. Palanichamy, M. Nagarajan and M. Devasagayam. Effect of *Cassia alata* leaf extract on hyperglycemic rats. *J Ethnopharmacol* 22(1):81-90 (1988)
43. J. Harrison and C. Garro. 1977. "Study on anthraquinone derivatives from *Cassia alata* L. (Leguminosae). *Rev Per Bioquim* 1 (1): 31 -33 (1977)
44. C. Rao and G. Subhashini. "Saponins and leucoanthocyanins in *Cassia L*." Current Science, 55(6): 320 -321 (1986).H. Moriyama, T. Iizuka, M. Nagai, H. Miyataka and T. Satoh. 2003. Antiinflammatory activity of heat-treated *Cassia alata* leaf extract and its flavonoid glycoside. *Yakugaku Zasshi* 123(7): 607-11 (2003).
45. M.N. Somchit, I Reezal, I. E. Nur and A.R. Mutalib. In vitro antimicrobial activity of ethanol and water extracts of *Cassia alata*. *J Ethnopharmacol*. 84(1):1-4 (2003)
46. M. R.Khan, M. Kihara and A.D. Omoloso. Antimicrobial activity of *Cassia alata*. *Fitoterapia* 72*(*5): 561-4 (2001).
47. B.H.Ali, A.K. Bashir and M.O.M. Tanira. Some effects of *Cassia italica* on the central nervous system in mice. *J. Pharm. Pharmacol* 49 (5): 500-504 (1997).
48. M. Kazmi, A. Malik, S.A. Hameed, N. Ali and S. Noor. An anthraquinone derivative from *Cassia italica*. *Phytochemistry* 36 (3):761-763 (1994).
49. M. Assane, R. Nydyema, E. Bassene, A. Sere and O. Gaye. Purgative activity of *Cassia italica. Dakar Med*. 392:125-8 (1994).
50. S.C. Jain, R. Jain, R.A. Sharma and F. Capasso. Pharmacological investigation of *Cassia italica*. *J Ethnopharmacol* 58 (2):135-42 (1997).
51. M. Kazmi, A. Malik, S.A. Hameed, N. Ali and S. Noor. An anthraquinone derivative from *Cassia italica*. *Phytochemistry* 36 (3):761-763 (1994).

52. S. Malhotra, A.P. Singh and A.S. Sandhu. Effect of indigenous herbal drug [CT-s125] in Psoriasis? A clinical evaluation Research Studies. (2005).
53. M. Latha and L. Pari. antihyperglycemic effect of *C. auriculata* in experimental diabetes and its effect on key metabolic enzymes involved in carbohydrate metabolism. *Clinical and experimental pharmacology and physiology* 30: 38-43 (2003)
54. H.M. Suresh, B.C. Hatapakki, S.J. Shivkumar, C.S. Hallikeri, B.M. Swamy and V.K. Chandur. Laxative activity of *Cassia auriculata* pods in rats, *J. natural remedies* Vol-7: 150-154 (2007)
55. S Malhotra, K Misra. A New Anthraquinone from *Cassia sophera* Heartwood. *Planta Med* 46 (12):247-9 1 (1982)
56. Yan Zhao, Jin-Ping Liu, Dan Lu and Ping-Ya Li. A novel cycloartane triterpene glycoside from the seeds of *Cassia sophera L. Nat Prod Res* 21 (6):494-9 (2007).
57. A. Bilal, N.A. Khan and H.A. Inamuddin. Pharmacological investigation of *Cassia sophera, linn.* var. purpurea, roxb. *Medical Journal of Islamic World Academy of Sciences* 15 (3): 105-109, (2005).
58. A.M. Khan, A.H. Khan, M.S. Akhtar, B. Ahmad, A. Sher and W. Ahmed. Pharmacological screening of *Cassia sophera* for Hypoglycemic activity in normal and Diabetic Rabbits. *Proceeding Shaikh Zayed Postgrad Med Inst* 16(1):1-4 (2002).
59. A.A. Akinremi, O.R. Omobuwajo and A.A. Elujoba. Pharmacological standards for the fruits of *Cassia fistula* and *C. podocarpa*. *Nig. J. Nat. Prod. Med* 4: 23-27(2000).
60. R.O. Akomolafe, I.O. Adeoshun, A.O. Ayoka, A.A. Elujoba and E.O. Iwalewa. An *in vitro* study of the effects of *Cassia podocarpa* fruit on the intestinal motility of rats. *Phytomedicine* 11 (2-3): 249-254 (2004).
61. P.K. Warrier PK, Indian Medicinal plants, Vol. 2. Orient Longman, (1996) P-30.

62. C. Deachapunya, W. Thongsaard and S. Poonyachoti. Barakol suppresses norepinephrine-induced inhibition of spontaneous longitudinal smooth muscle contractions in isolated rat small intestine. *Journal of Ethnopharmacol* 101(1-3): 227-232 (2005).
63. E.O. Ajaiyeoba, J.S. Ashidi, L.C. Okpako, P.J. Houghton and W.C. Wright. Antiplasmodial compounds from *Cassia siamea* stem bark extract. *Phytother Res (*17) : 17705142 (2007)
64. C. Deachapunya, W. Thongsaard and S. Poonyachoti. Barakol suppresses norepinephrine-induced inhibition of spontaneous longitudinal smooth muscle contractions in isolated rat small intestine. *Journal of Ethnopharmacol* 101(1-3): 227-232 (2005).
65. M.O. Amamoto, S. Shimura, Y. Itoh , T. Ohsaka and M. Egawa. Anti-obesity effects of lipase inhibitor CT-II, an extract from edible herbs, Nomame Herba, on rats fed a high-fat diet. *International journal of obesity* 24: 758-764 (2000).
66. A. Caceres, B.R. Lopez, M.A. Giron and H. Logemann. Plants used in Guatemala for the treatment of dermatophytic infections. 1. Screening for antimycotic activity of 44 plant extracts. *J Ethnopharmacol* 31(3):263-76 (1991).
67. F.T. Fatawi, F.A. Hussaini and A. Shoeb. Spasmolytic anthraquinones from *Cassia pumila. Fitoterapia*. 57 (4): 271 (1986).
68. Rai and Roy, *J Bangladesh Academic Science* 15: 193 (1991)
69. Sundararaj and Balasubramaniyam. *Indian J Chem* 106 (18B): 292 (1979)

Infection Control Training Need Assessment among Health Care Providers in Selected Hospitals of Dakshina Kannada Districts of Karnataka, South India

Christopher Sudhaker[*1], Kishore Gnana Sam[2]

1-Manipal College of Nursing, Manipal

2-Manipal College of Pharmaceutical Sciences, Manipal

[*]Corresponding author
Chris.sudhakar@manipal.edu

Abstract:

Objective: To assess the need for infection control training of health care providers, in long-term care facilities.

Methodology: The need assessment survey questionnaire, were distributed to 614 nurses working in 8 selected hospitals of Udupi district and Mangalore (DK) district. The quota sampling method was used.

Results: There was 100% agreement by the respondents that infection control training is relevant, to prevent hospital associated infections. Majority (98.04%) agreed that infection control training should be mandatory to the nurses and majority (91.85) preferred that they require infection control training. Majority of them preferred group discussion (83.38) demonstration (79.31), video (79.31) self study (77.03) and only 16.61% preferred the lecture as their preferred mode of teaching and learning. There were 100% agreement with the topics like infection transmission in the health care setting, misconception about disease transmission, importance of following infection control, methods of infection control, standard precautions (universal precautions), hand washing and use of gloves, disinfection, aseptic technique management of sharps sterilization and waste management.

Conclusion: This opportunity can be utilized by the hospital pharmacists, to initiate continuing education programs and develop standard guidelines to effectively control nosocomial infections. The first step of a well-designed infection control program is to design standard protocols and train health care providers. Ultimately controlling infection is everyone's business and when it comes to infection control, knowledge is really a power.

Key Words: Infection Control; Training need assessment; continuing education program

Introduction:

The Centers for Disease Control and Prevention (CDC) has estimated that there are at least two million health care-associated infections each year. Of these, 90,000 people die and, most importantly, a third of these deaths are probably preventable. The infectious problems that we are likely to face, even in the near future, are really frightening and human lives are actually at stake. This is a great challenge that we must all rise to control nosocomial infection and effective training is the need of the hour.[1]

Hospital associated infections occur in about 5% to 10% of hospital admissions worldwide. In India the hospital associated infections rate is alarming and is estimated to be about 30% to 35% of all hospital admissions. According to Ganguly et al., Only 0.49 percent of the population in India has access to essential drugs this makes compliance and treatment very grueling task for majority of the population.[2] Whereas Pakistan and Bangladesh, known for their poor performance in the health sector, have a much higher rate with 50 to 79 percent of their population having access to essential medications. [3]

In developing countries like India, hospital infection control programmes are nonexistent or, at best, in their infancy. The main causes postulated for the development and spread of hospital associated infections in India are the indiscriminate use of antibiotics, failure of many hospitals to follow basic infection control methods like washing of hands, overall lack of hygiene in public hospitals and the poor state of government hospitals. India has neither stringent laws on the sale and utility of antimicrobials, nor notification systems, to record infections like Methicillin Resistant Staphylococcus Aureus (MRSA).[4]

Infection control education has been a core component of infection control programs since they were established and remains a constant feature of the modern healthcare context.[5] While debate continues regarding the extent and quality of infection control education as a component of undergraduate healthcare professional curricula. Heath care professionals are accountable to providing safe and ethical care to the public. This process ensures that all members of the healthcare team are provided with basic infection control education and training on entry to the healthcare organization. Hence an infection control training need assessment survey was conducted to assess

the need and type of appropriate training method required to deliver infection control education.

Methodology:

The present study was a descriptive, questionnaire survey, aimed to assess the training needs of staff nurses on infection control, the mode of delivery preferred by them, allocation of educational contents, factors facilitating their infection control education and the strategies to deliver the infection control education to the nurses working in the selected hospitals.

The need assessment was carried out using survey questionnaire among nurses of 8 hospitals of South Karnataka, India. Survey research can be defined as a non-experimental research that focuses on obtaining information regarding the activities, beliefs, preferences, and attitudes of people via direct questioning of a sample of respondents.[6] Large number of infection control researchers have utilized survey methods, examined the student's willingness to follow hand washing guidelines and their opinions in the long term care and the educational activity.[7] The survey was designed to assess the training strategies, and identify resource sensitive solutions to hospital infection control problems in countries with limited resources.

Tools

The researcher developed need assessment survey questionnaire. The content validity for the tool was done by 9 experts from different fields of health science including hospital administration. The tool was pre-tested at Dr. A.V. Baliga hospital Doddanagudde, Udupi, Karnataka, during Dec 2005. Average time taken for the data collection using knowledge questionnaire was 40-45 minutes.

Sample and Sampling

Upon obtaining the permission from the institutions and approval from ethical committee, the researcher distributed the need assessment survey questionnaire to the nurses working in hospitals of Udupi district and Mangalore (DK) district. The study included all the different settings like rural, suburban, referral and government hospitals to have the equal opportunities and assess the different opinions. This survey was conducted during November-December, 2005 at KMC hospital Mangalore, Attavar, Ambedkar circle Mangalore, Dr. TMA Pai hospital Udupi, Government general hospital Udupi, Government maternity and childrens' hospital Udupi, Dr. TMA Pai

Rotary hospital, Karkala and Government hospital nurses attending training Programs conducted by department of Microbiology KMC Manipal at Udupi, and Kasturba Hospital, Manipal. A total of 700 questionnaire were distributed depend on the strength of the nursing personnel in the hospital. The sample size was predetermined as rural 5% suburban 25% government 10% and referral 60%.(Quota sampling technique). Only 643 responders returned the completed questionnaire. After eliminating partly filled and incomplete questionnaire the final sample was 614. The data of the need analysis was analyzed using descriptive statistics.

Results:

The data presented in table 1 shows that there was 100% agreement by the respondents that infection control training is important to prevent hospital associated infections. Majority (98.04%) agree that infection control training should be made mandatory to the nurses and majority (91.85%) expressed their opinion as that they require infection control training. Majority of the responders (83.38%) selected group discussion, while other techniques preferred were demonstration (79.31%), video (79.31%) self study (77.03%) and only 16.61% selected lecture as their preferred mode of teaching and learning. There were 100% agreement with the topics like infection transmission in the health care setting, Misconception about disease transmission, Importance of following infection control, Methods of infection control, Standard precautions (universal precautions), Hand washing and use of gloves, Disinfection, Aseptic technique management of sharps sterilization and waste management. In the area of common policies and procedure (51.62%), infection control regulations, guidelines, (38.11%) and in the area of employee health the response was (34.54%). Hence areas which received an opinion based score of > 75% were selected for the preparation of training manual. The data on the need of infection control training is depicted in Fig:1 and the preferred method of teaching is depicted in Fig 2.

Discussion:

Result of need assessment survey showed that there was 100% agreement by the respondents that infection control training is important to prevent hospital associated infections. Majority (98.04%) of the respondents agree that infection control training should be mandatory to the nurses and majority (91.85) selected that they

require infection control training. Majority of the nurses selected group discussion (83.38) demonstration (79.31), video (79.31) self study (77.03) and only16.61% selected lecture as their preferred mode of teaching and learning.

Many research studies recommend to coordinate education programs with other consistent strategies and processes, effective teaching and learning practice has to be identified by the learner's need. Systematic reviews conducted by Rowe, et al. 2006.[8] from low and middle income countries, non-systematic reviews of studies from industrialized and low and middle income countries, revealed several trends: dissemination of written guidelines without additional interventions was generally ineffective; supervision and audit with feedback was generally quite effective; non-traditional training methods such as computer-based training might be less expensive than and as effective as traditional methods, multiple determinants of performance might be more likely to improve performance than single interventions. Few studies have compared different interventions in the same setting or the same intervention in multiple settings. Because the determinants of behavior are varied and complex, and the reach and effect of any one strategy will be limited, there is a need for coordinated multi-strategy approaches to achieve the necessary intensity of efforts to yield sustained behavior change in the long term Need assessment of the target group is one of the important methods to develop the need based education.

It determine the effectiveness of a customized intervention about infection control.[9] The participation of learners, with others, in the design and implementation can help to ensure their specific needs and concerns being met in a culturally and socially appropriate way. It can also foster commitment or ownership of the program, which can enhance sustainability. Study conducted by Zelle, 1999 on Developing and Implementing a Pharmacy Infection Control Program revealed that development of complete infection control plan for pharmacist and program will protect employees who provide pharmaceutical care and services as well as the residents who receive them.[10] A solid plan and a thorough understanding of the program by all staff members are vital elements to the implementation of a successful pharmacy infection control program.

Conclusion:

The result of this study can be utilized by the pharmacy professionals who work in the hospital settings to provide education to develop their infection control practices. The American Society of Health-System Pharmacists (ASHP) believes that pharmacists have a responsibility to participate in infection control education and providing education for health professionals on topics such as antimicrobial use and resistance, decontaminating agents (disinfectants, antiseptics, and sterilants), aseptic technique , sterilization methods. They can also educate and counsel inpatients, ambulatory care patients, and home care patients in the following areas: adherence to prescribed directions for antimicrobial use, storing and handling medications and administration devices, and other infection control procedures (e.g., medical waste disposal proper hand-washing techniques). The main purpose of a well-designed infection control program is to reduce the spread of infections. This begins by education and identifying infections and controlling the spread of infections to other patients and staff members. Ultimately controlling infection is everyone's business and when it comes to infection control, knowledge is really a power.

Table-1, Learning need assessment analysis of the nurses on infection control training

N=614

Content	Frequency	Percentage (%)
Importance of infection control training prevent HAI	614	100
Infection control training should be mandatory	602	98.04
Requiring Infection control training	564	91.85
Method of teaching		
Class room lectures	102	16.61
Self study handbooks	473	77.03
Case study	365	59.44

Role play	448	72.96
Group discussion	512	83.38
Video	478	77.85
Demonstration	487	79.31
Topics to be included		
Definitions and meaning of HAI	614	100
Infection transmission in the health care setting	614	100
Misconception about disease transmission	614	100
Importance of following infection control	614	100
Methods of infection control	614	100
Standard precautions (universal precautions)	614	100
Hand washing and use of gloves	614	100
Disinfection	614	100
Aseptic technique	614	100
Management of sharps	614	100
Decontamination	463	75.40
Sterilization and storage	614	100
Waste management	614	100
Common policies and procedure	317	51.62
Surveillance (unit level)	459	74.75
Identify the predictors of HAI	461	75.04
Infection control regulations, guidelines,	234	38.11
Employee health	212	34.54
Prevention of sharp injury	561	91.36

Exposure prophylaxis	561	91.36
How to educate peers and patients regarding HAI	562	91.53

Reference:

1. 'Leary's. DS. In: Opening Comments at the Infection Control Conference by Joint Commission -; 2003; November 17, 2003; 2003.
2. Ganguly P.S. YK, Abida Malik. Association of the Nosocomial infections and Hospital Procedures. Indian Journal of Community Medicine 2000-01 - 2000-03;25(1).
3. Bal. The Budget has promoted private healthcare at the cost of public sector. In: www.expresshealthcaremgmt.com; 2003.
4. Shaheen R. Hospital Infection Control Programme: An Overview ,2005-0. Indian Journal for the Practicing Doctor, 2002; Vol. 2,(No. 3 2005-07 -08).
5. Streeter S, Dunn, H., Lepper, M. 'Hospital Infection - A Necessary Risk?' American Journal of Nursing 1967;67(3):526-533.
6. Polit D.F. BCT, Hungler B.P. Nursing Research, Methods, Appraisal and Utilisation,. 5th Edition. ed. Philadelphia.: Lippincott,; 2001.
7. Cardo D, Orouke, EJ. Abstr Intersci Conf Antimicrob Agents. In: Chemother Intersci Conf Antimicrob Agents; 2001 Dec 16-19; 41; Atlanta; 2001.
8. Rowe A K, D; Lanata, C.F.; Victoria, C.G. How can we achieve and maintain high-quality performance of health workers in low-resource settings. The Lancet. 2005;36(05).
9. Calabro K, K. Bright, K. Kouzekanani. Long-term Effectiveness of Infection Control Training among Fourth-year Medical Students. Med Educ 2000.
10. Zelle,P Developing and Implementing a Pharmacy Infection Control Program American Society of Consultant Pharmacists, Inc1999,.

A Survey of Labeling Guidelines on Few Marketed Ayurvedic Medicines

Aswatha Ram H.N* and Venkatesha V.A.

Department of Pharmacognosy,
ManipalCollege of Pharmaceutical Sciences,
Manipal University, Manipal–576 104,

*Corresponding author
aswatharam@gmail.com

Abstract: Herbal medicines are becoming popular and the sale has increased considerably over the last ten years in the industrialized countries. The growing demand is probably due to the belief that herbal medicines are innocuous and naturally superior to synthetic drugs. The labeling information on these medicines should essentially comprise essential details about the product, which the doctor and patient must be aware of for the proper usage. In 1996, the WHO framed product information guidelines for the proper use of herbal products. In this study, a survey was carried out based on the above guidelines for a few marketed herbal medicines manufactured by popular Indian herbal industries. The information on the labels and the product inserts were thoroughly studied before arriving at any conclusion. Labels of a few medicines lack some of the important information viz., indications which include drug interaction, safe usage during pregnancy/lactation and expiry date. Thus it is imperative that these necessary details should be included either on the label or product inserts.

Key words: Herbal medicines, WHO guidelines, Indications, Regulatory authorities

Introduction:

Herbal medicines have been gaining importance not only in the developing world but more so in the developed countries. Sales of herbal medicines have grown dramatically since the FDA's decision to categorize them as Dietary Supplements in 1994. In 1998, several mainstream pharmaceutical companies started manufacturing and marketing herbal products. Herbal preparations such as herbal teas, tablets, capsules containing the parts of the plants or their extracts are widely used and accepted forms. The WHO has in recent years looked into the safety aspects of such preparations and has framed product consumer information which is essential for its proper usage. Ayurveda and Siddha are indigenous systems of medicine in India and various herbs are used in the

preparation of Ayurvedic formulations and Siddha medicines respectively. However these preparations continue to be marketed without proper labeling of the essential information regarding its usage etc., and no attempt has been made by the regulatory authorities to set things right. In this article an attempt has been made to bring to the fore the present scenario of labeling of such alternative medicines.

Safety of herbal medicines:

The safety of herbal remedies is of particular importance since many products are self prescribed and patients usually do not inform their doctors that herbal medicines are being taken. Many of these products are also sold as dietary supplements but scientific information on their safety and effective usage is hard to find[1]. The efficacy and harmlessness of herbal medicines depend not only on the remedy and its usage, but also on consumer-related parameters[2] together with a thorough understanding of product information by the prescriber and the consumer as framed by the WHO.

List of labeling guidelines framed by WHO[3]:

1. Name of the product
2. Quantitative list of active ingredient(s)
3. Dosage form
4. Indications
   - dosage (if appropriate, specified for the children and the elderly)
   - mode of administration
   - duration of use
   - major adverse effects, if any
   - overdosage information
   - contraindictions, warnings, precautions and major drug interactions
   - use during pregnancy and lactation
5. Expiry date
6. Lot number
7. Holder of the marketing authorisation.

Labeling and Packing of Ayurvedic (including Siddha) or Unani Drugs[4]:

Manner of Labeling: The following particulars shall be either printed or written in indelible ink and shall appear in a conspicuous manner on the label of the innermost container of any Ayurvedic (including Siddha) or Unani drug and on any other covering in which the container is packed, namely:-

(i) The name of the drug. For this purpose the name shall be the same as mentioned in the authoritative books included in the First Schedule of the Act.

(ii) A correct statement of the net content in terms of weight, measure or number as the case may be. The weight and volume shall be expressed in metric system.

(iii) The name and address of the manufacturer.

(iv) The number of the license under which the drug is manufactured, the figure representing the manufacturing license number being preceded by the words 'Manufacturing Licence Number' or 'Mfg. Lic. No.' or "M.L.".

(v) A distinctive batch number, that is to say, the number by reference to which details of manufacture of the particular batch from which the substance in the container is taken are recorded and are available for inspection, the figure representing the batch number being preceded by the words "Batch No." or "Batch" or "Lot Number" or "Lot No." or "Lot" or any distinguishing prefix.

(vi) The date of manufacture. For this purpose the date of manufacture shall be the date of completion of the final products, or the date of bottling or packing for issue.

(vii) The words "Ayurvedic medicine" or "Siddha medicine" or "Unani medicine" as the case may be.

(viii) The words "For External Use Only' if the medicine is for external application.

(ix) Every drug intended for distribution to the medical profession as a free sample shall, while complying with the labeling provisions under clauses (i) to (viii), further bear on the label of the container the words "Physicians sample. Not to be sold" which shall be over-printed.

A survey of labeling information of Ayurvedic and Siddha medicine in the light of the WHO prescribed guidelines lacked some pertinent essential labeling information which are as follows.

Herbal medicines and drug interactions:

Herbal medicines interact with synthetic drugs and thereby affect the drug action by quantitative alterations, either by increasing or decreasing the amount of the drug

available to have an effect. For example, patients who are taking herbs concurrently with warfarin have to be very careful[5] because it interacts with aspirin, ibuprofen, vitamin K and green tea. Antidiabetic herbs may interfere with antidiabetic drugs by enhancing hypoglycemic effects. The dose of the herbs and drugs should be balanced very carefully to control blood glucose levels[6].

Contraindications of herbal preparations during pregnancy:

The use of some herbs is prohibited during pregnancy which include *Abrus precatorius, Achyranthus aspera, Adhatoda vasaka, Hibiscus species, Ricinus communis* and *Gossypium* species[7]. Breast-feeding mothers who use herbals should consult a physician or pharmacist who has information concerning the safety of herbal medication[8]. For example, herbal medicines containing the following herbs either alone or in combination should be avoided during pregnancy. Senna, cascara, rhubarb and aloes are used as laxatives. Their use is prohibited during breast-feeding due to anthraquininone constituents that may cause potassium deficiency[9].

Licorice root is used in the treatment of peptic ulcer/duodenal ulcers. The active components glycyrrhizic and glycyrrhetinic acids account for anti-inflammatory and anti-allergic effects. However, the components of licorice root possess mineralocorticoid properties leading to toxic effect such as sodium and water retention, hypokalemia and hypertension which can lead to cardiac arrest[10].

Rauwolfia contains reserpine used in hypertension. It is also used as CNS depressant. It is, therefore, contraindicated in breast-feeding. Ginseng may cause estrogenic side effects as well as platelets changes. Until more information is known, ginseng root should be avoided in the lactating mother[11].

Shelf life of Ayurvedic tablets/pills:

Every product has a definite shelf life which depends on various physical, chemical, environmental and biological factors[12]. If stored properly vati/gutika formulations retain their potency for up to two years from the date of manufacture[13].

With this in view, we have carried out a random survey on a few herbal medicines manufactured and marketed by popular companies in India. The product information on the label and product inserts were thoroughly studied.

Conclusion: We have found that many of the formulations lacked one or more of the above necessary information i.e. mainly indications on their label/inserts. Most often information provided is rarely adequate. Only 10-20% of the companies provide the requisite information. Thus, it is imperative that the Ayurvedic, Siddha and Unani Technical Advisory board, Central - Drugs Control Department, Ministry of Health - Government of India and other drug regulating authorities look into this aspect and implement the minimal labeling requirements for marketing herbal medicines namely indications like drug interactions, safety aspects during pregnancy and expiry either on the label or by product inserts.

References:

1. Fossati C, Fanzio G. Laclin Terap, 1985;112:249.

2. Raffaele Capasso, Angelo A. Izzo, Lusia Pinto, Teresa Bifulaco, Carmen Vitobello, Nicola Mascolo, Phytotherapy and quality of herbal medicines. Phytoterapia 2000;71:558-565.

3. World Health Organisation. WHO technical reports 1996, No.863, 183 (Annex II).

4. Bharati HK. A manual of Drugs and Pharmacy Laws in India. 2nd ed. Indore:Sadhana Mandir,1984:604-605.

5. Fetrow CW, Avila JR. Professional handbook of Complimentary and Alternative medicine. Pennsylvania:Springhouse Corp, 1999.

6. Miller LG, Herbal medicinal selected clinical considerations focusing on known or potential drug herb interaction. Arch Intern Med 1998;156:2200.

7. Chaudhri RD. Herbal drug industry - A practical approach to Industrial Pharmacognosy. New Delhi: Eastern publishers, 1999.

8. Hardy ML. Herbs of special interest to women. J Am Pharm Assoc 2000; 40:234.

9. Blumenthal M, Gruenwald J, Hall T, Riggins C, Rister R. The complete E monographs therapeutic guide to herbal medicine. Austin, TX: American Botanical Society, 1998.

10. Conn JW, Rovner DR, Cohen EL. Licorice-induced Pseudoaldosteronism, Hypertension, Hypokalemia, Aldosteronopenia and Suppressed Plasma Renin Activity, JAMA 1968;205:492.

11. Howard CR, Lawrence CA. Drugs and Breast feeding. Clin Perinatiol 1999;26:447.

12. Chauhan SK, Singh BP, Tyagi A, garwal S. Accelerated stabiltiy studies of a

polyherbal preparation (Eumil) capsule. Ind J Pharm Sci 2000;62(3):181-184.
13. Vaidya Bhagawan Dash. Fundamentals of Ayurvedic medicine. 1st ed. Delhi: Sri Satguru publications, 1999:206.

Hepatoprotective Activity of Herbohep a Polyherbal Phytomedicine

Ganjiwale R.O*., Wadher S. J., Kharche N. V., Yeole P.G.

Institute Of Pharmaceutical Education and Reaserch, Borgaon (Meghe), Wardha (M.S.) 442 001

*Corresponding author: Email: niks_s24@rediffmail.com

Abstract:

Herbohep, a polyherbal formulation composed of 3 herbal extract mixtures such as Katuki, Kalmegh and Bhumyamalaki was evaluated for carbon tetrachloride(CCl_4)induced hepatotoxicity. Hepatotoxicity was induced in Albino rats by intraperitoneal injection of CCl_4 (0.7 ml/kg/day, p.o.).Different doses of Herbohep formulation were administered to the experimental rats (250 and 500 mg/kg/day).The hepatoprotective effect of these doses was evaluated by the assay of liver function biochemical parameters (SGOT, SGPT, ALP, serum total Protein, serum cholesterol, serum bilirubin). In higher dose (500 mg/kg/day, p.o.)treated animals,the toxic effect of CCl_4 was controlled significantly by restoration of the levels of SGOT, SGPT, ALP,serum total protein, cholesterol, Bilirubin as compare to normal and the standard drug Silymarin treated groups. 500 mg/kg/day,p.o.of Herbohep formulation possesses significant hepatoprotective activity against carbon tetrachloride (CCl_4) induced hepatotoxicity in albino rats as compare to other dose.

Keywords: Hepatoprotective activity, Herbohep formulation, serum marker enzymes.

1 Introduction:

Liver is the most important organ concerned with the biochemical activities in the human body. It has great capacity to detoxicate toxic substances and synthesize useful principles. Therefore, damage to the liver inflicted by hepatotoxic agents is of grave consequences. There is an ever increasing need of an agent which could protect it from such damage. In view of severe undesirable side effects of synthetic agents, there is growing focus to follow systematic research methodology and to evaluate scientific basis

for the traditional herbal medicines which are claimed to possess hepatoprotective activity (Shahani, 1999).

Conventional or synthetic drugs used in the treatment of liver diseases are sometimes inadequate and can have serious adverse effects. So there is a worldwide trend to go back to traditional medicinal plants. Many natural products of herbal origin are in use for the treatment of liver ailments (Venkateswaran et al., 1997; Latha et al., 1999; Mitra et al., 2000; Dhuley and Naik, 1997).

Herbohep is one of the Herbal formulation containing Katuki (*Picrorhiza kurroa)*, Kalmegh (Andrographis paniculata) and Bhumyamalaki (*Phyllanthus niruri).*In the present investigation Herbohep, a polyherbal formulation consisting of medicinal plants derived from the traditional system of medicine in India, Ayurveda, has been evaluated for its hepatoprotective action. The hepatotoxin used was CCl_4 because CCl_4-induced liver dysfunction in rats simulates liver cirrhosis in man (Pérez-Tamayo, 1983; Wensing et al., 1990).

2 Materials and Methods:

The Herbohep tablets were procured from local market of Wardha, Maharashtra, India.

2.1. Dose of Herbohep Tablet (Achliya et al., 2004; Mitra et al., 2000),

The Herbohep tablet was administered to the experimental rats in two doses i.e. 250 mg/kg, p. o. and 500 mg/kg p. o. by dispersing Distilled water.

2.2. Animals

The hepatoprotective study was conducted on albino rats (150- 250 gm), with prior approval from the Institutional Animal Ethical Committee (Registration No.535/ 02/a/CPCSEA /Jan2002) of Institute of Pharmaceutical Education & Research, Wardha, in house breed. They were kept at standard animal housing conditions (Temperature 23 ± 10 C and relative humidity 55 ± 10%) and 12 hour light/ dark cycle. The animals were maintained on standard diet in large specious polypropylene cages and supplied with water ad -*libitum*. They were used for studies after an acclimatization period of 10 days in laboratory environment activity.

2.3. Assessment of hepatoprotective activity (Prasanna, 2002)

To assess the hepatoprotective activity the animals were divided into normal, toxicant, standard and test groups. The method consists of three steps:

Normal levels of serum Glutamate Pyruvate Transaminase (SGPT) and serum Glutamate Oxaloacetate Transaminase (SGOT), Alkaline Phosphatase (ALP), Total protein, Bilirubin and Cholesterol were determined by withdrawing blood samples directly by puncturing the Retro-orbital plexus on the first day of study. Collected blood was centrifuged at 2500 rpm for separation of serum. Serum was analysed on semi-autoanalyser (MERCK Microlab-300) for following parameters like SGPT, SGOT, ALP, Total protein, Bilirubin and Cholesterol.

To the animals 0.7ml per kg body weight of carbon tetrachloride (CCL_4) was administered intraperitoneally for five days. On the sixth day enzymatic levels were noted.

After intoxication with CCl_4, Herbohep and Standard Silymarin were administered for five days. On the 11th day the serum levels were recorded. For determination of significant intergroup difference each parameter was analyzed separately.

2.4. Biochemical Parameters Measurement

Biochemical Parameters measurement of SGPT, SGOT, ALP, Bilirubin, Cholesterol and Total proteins were carried out.

Animal Group: Albino rats of either sex were divided into following group with six animals in each group. (Gautam et al., 2007)

Group I : Normal, received normal rat fed & water

Group II : Control, CCl_4 intoxicated (0.7ml/kg by Intraperitonial injection)

Group III : Standard drug treated, (Silymarin, 100 mg/kg, orally)

Group IV : Herbohep treated (250 mg/kg, orally)

Group V : Herbohep treated (500 mg/kg, orally)

2.5. Statistical analysis

The results are expressed as Mean ± SD of six animals from each group. The data were evaluated by one way ANOVA followed by Dunnett's test (Hukkeri and Karadi, 2004)

3. Results:

The administration of CCl_4 to the animals resulted in a marked increase in SGOT, SGPT, ALP, Cholesterol, Bilirubin and significant decrease in enzyme level of serum total protein. (Sood, 2004)

Table - 1 Effect of Various doses on Various Serum Level in hepatotoxic Rats.

Sr. No.	Groups	SGOT [mg/dl]	SGPT [mg/dl]	Serum ALP [U/l]	Serum Total Protein [mg/dl]	Serum Cholesterol [mg/dl]	Serum Bilirubin [mg/dl]
1.	Normal[GR.I]	194.91 ±8.485	85.63 ±0.205	176.10 ± 0.332	7.15 ±0.21	67.32 ±2.341	0.86 ±0.014
2.	Control[GR.II]	338.26 ±1.414*	138.72 ±1.195*	509.16 ± 0.530*	4.09 ±0.19*	124.88 ±1.428*	2.305 ±0.009*
3.	Hepatotoxic +Standard [GR.III]	220.69 ± 1.605**	97.4 ±1.174**	229.70 ± 0.077**	6.09 ±0.31**	96.66 ±0.961**	0.933 ±0.014**
4.	Hepatotoxic+HH (250mg/kg) [GR.IV]	248.69 ±1.223**	107.01 ±0.622**	250.94 ± 0.848**	5.67 ±0.25**	103.16 ±0.410**	1.24 ±0.003**
5.	Hepatotoxic+ HH (500mg/kg) [GR.V]	213.93 ±0.558**	95.87 ±0.148**	230.55 ± 1.697**	6.25 ±0.19**	90.43±0.634 **	1.1 ±0.042**

Values are given as Mean ± SD of six rats in each group.

Control was compared with the normal, $p < 0.01^{*}$

Experimental groups were compared with the control, $p < 0.01^{**}$

The toxic effect of CCl_4 was controlled in the animals treated with the different doses of herbohep by way of reversal of the levels of the liver function biochemistry similar to that of the standard drug silymarin.Among the different doses treated groups significant hepatoprotective activity was observed in those treated with 500mg/kg.

4. Discussion:

The CCl_4 has been used as a tool to induce hepatotoxicity in experimental animals (Goodman and Gilman, 2002).This toxic chemical caused peroxidative degradation in the adipose tissue resulting in fatty infiltration of the hepatocytes.

Administration of different doses of Herbohep tablet formulation showed significant hepatoprotective activity, which was comparable with the standard drug silymarin.The effect was more pronounced with 500mg/kg.Other dose 250mg/kg of showed moderate activity.

Liver damage and recovery from damage was assessed by measuring serum marker enzymes, biochemical changes in liver Injury produced by CCl_4 seems to be mediated by a reactive metabolite, trichloromethyl free radical ($\cdot CCl_3$) formed by the hemolytic cleavage of CCl_4 or by an even more reactive species, trichloromethylperoxy free radical ($CCl_3COO\cdot$) formed by the reaction of $\cdot CCl_3$ with O2. This biotransformation is catalyzed by a cytochrome P450-dependent monooxygenase. The toxicity produced by CCl_4 is though to be due to the reaction of free radicals ($\cdot CCl_3$ or $CCl_3COO\cdot$) with lipids and proteins, however, the relative importance of interactions with various tissue constituents in producing injury is controversial. The free radical causes the peroxidation of the polyenoic lipids of the endoplasmic reticulum and generation of secondary free radicals derived from these lipids, a chain reaction. This destructive lipid peroxidation leads to breakdown of membrane structure and function; as a result there is elevation of enzyme levels in plasma. (Bhat and Madyastha, 2000).

Assessment of liver function was made by estimating the activities of SGOT, SGPT, ALP, Cholesterol, Bilirubin and Total protein. SGPT and SGOT are the

enzymes originally present in higher concentration in cytoplasm. When there is hepatic injury, these enzymes leak into the blood stream in conformity with the extent of liver damage. The elevated levels of these marker enzymes in CCl_4 induced hepatic injury in rats in the present study corresponded to the extensive liver damage induced by the toxin.

Any decrease in the level of the above enzymes would indicate reversal of the induced toxicity of the liver. The Herbohep tablet had shown significant decrease in enzyme level of SGOT, SGPT, ALP, Cholesterol, Bilirubin and significant increase in enzyme level of Total protein ($P< 0.01$). The effect was more pronounced with 500mg/kg.than other dose 250mg/kg of showed moderate activity.Thus hepatoprotective action of this Herbohep tablet is likely to be due to its ability to induce microsomal enzymes there by inhibition of the lipid peroxidation induced by CCl_4. On the basis of our results it can be concluded that Herbohep has antihepatotoxic activity against CCl_4 induction.

References:

1. Achliya G.S., Wadokar S.G., Dorle A.K., (2004), "Evaluation of Amalkadi Ghrita against carbon tetrachloride-induced hepatic damage in rat", Journal of Ethanopharmacology, 90, 2229-2232.
2. Bhat, V.B., Madyastha, K.M., 2000. C-phycocyanin: a potent peroxyl radical scavenger in vivo and in vitro. Biochemical and Biophysical Research Communications 275, 20–25.
3. Dhuley, J.N., Naik, S.R., 1997. Protective effect of Rhinax, a herbal formulation against CCl4-induced liver injury and survival in rats.Journal of Ethnopharmacology 56, 159–164.
4. Gautam, S. P., Ganjiwale, R. O., (2007), "Hepatoprotective activity of Tecomella undulata leaves", IJGP, 1(3-4), 24-27

5. Goodman Gilman's, (2002). The Pharmacological Basis Of Therapeutics, 9th Edn., (International Edition), Published by McGraw-Hill Health Professions Division, Pp- 1678-1680
6. Hukkeri, V. I., Karadi, R.V., (2004). Hepatoprotective activity of fruit pulp of *Annona reticulata* in carbon tetrachloride induced toxicity, Indian Drugs 41(11), 684-685.
7. Latha, U., Rajesh, M.G., Latha, M.S., 1999. Hepatoprotective effect of an ayurvedic medicine. Indian Drugs 36, 470–473.
8. Mitra, S.K., Seshadri, S.J., Venkataranganna, M.V., Gopumadhavan, S.,Venkatesh Udupa, U., Sarma, D.N.K., 2000. Effect of HD-03-a herbal formulation in galactosamine-induced hepatopathy in rats. Indian Journal of Physiology and Pharmacology 44, 82–86.
9. Pérez-Tamayo, R., 1983. Is cirrhosis of the liver experimentally produced by CCl4 an adequate model of human cirrhosis? Hepatology 3, 112–120
10. Prasanna Habbu, Hukkeri, V.I., Hunasagi, B.S., Marihal, S.C., Kulkarni, R.V., Patil, C.C., (2002). Screening of *Hedychium spicatum* for hepatoprotective activity in albino rats, Indian Drugs, 39 (2) 117-119
11. Shahani, S., 1999. Evaluation of hepatoprotective efficacy of APCL-A polyherbal formulation in vivo in rats. Indian Drugs 36, 628–631.
12. Sood, R., (1994). Medical Laboratory Technology Methods and Interpretations, 4th Edn., Jaypee Brothers, Medical Publishers(P) LTD, 399-430.
13. Venkateswaran, S., Pari, L., Viswanathan, P., Menon, V.P., 1997. Protective effect of Livex, a herbal

formulation against erythromycin estolate-induced hepatotoxicity in rats. Journal of Ethnopharmacology 57, 161–167.

14. Wensing, G., Sabra, R., Branch, R.A., 1990. Renal and systemic hemodynamics in experimental cirrhosis in rats: relation to hepatic function.Hepatology 12, 13–19.

Perception Analysis about Banned Drugs among the Physicians in Udupi District of South India

Divya Saxena*[1], Shilpa Dua[2], Jyoti Choudhari[2]

Corresponding author

div1406@gmail.com

[1]Manipal College of Pharmaceutical Sciences, Manipal

[2] Shri Baba Masthnath College of Pharmaceutical Science and Research, Rohtak, India

Abstract:

India has become a dumping ground for banned drugs; also the business for production of banned drugs is blooming. Not many people know about these banned drugs and consume them causing a lot of damage to themselves. As the study is wide and contain a number of banned molecules it is difficult to search out the specific data relevant to the subject. Some of the available data containing market of banned drugs are-

More than 20 Indian companies produce rofecoxib, the top five brands accounting for annual sales of 400 million rupees. Chloramphenicol, makes up about 11% of antibiotic use, and is still one of the popular antibiotics available over the counter without a prescription. Neurobion by Merck which ranks 4th in sales at $ 7.16 million. Surbex by Abbot 15th at $ 3.37 million. Betnesal-N by Glaxo 36th at $ 2.12 million. Lederplex syrup/capsules by Lederle 40th at $ 2.06 million. Terramycin by Pfizer 29th at $ 2.37 million. Hydryllin cough syrup by Serale 30th at $ 2.34million.

This study was aimed to understand and analyse the perception level of banned drugs among the physicians in Udupi district of Karnataka. In this

study we attempted to reveal the information about general awareness regarding the banned drugs among physicians was also an objective of study. The study was expected to help to analyse whether the physicians agree that the drugs banned abroad should also be banned in India. Information was collected regarding the banned drugs from secondary sources including internet, journals, magazines and bulletin etc. Information was also collected from primary data collection method (questionnaire). Questionnaire was framed including closed and open ended questions. Responses were collected from general physicians from the selected area. Data obtained by the questionnaire was analysed by percentage method. Conclusion was derived from the interpretation of data and analysing the results.

Objectives of the Study:

This study was aimed to understand and analyse the perception level of banned drugs among the physicians in Udupi district of Karnataka. And to study the physicians view about banned drugs are primary objectives of study. Creating awareness about the banned drugs among physicians was also an objective of study.

Importance of study:

The study was expected to help to analyse whether the physicians agree that the drugs banned abroad should also be banned in India. Study would bring into light the need to ban the drugs having fatal side effects. It also help to reveal the lacuna in the system where in the banned drugs are still available and used in market.

Research Design:

Secondary data analysis:

Secondary data is collected from the work or the survey done on the topic. It is available in the journals, internet and other available sources.

Primary data collection:

Primary data was collected by means of the questionnaire. The questionnaire was presented to the physicians and there views about the topic were recorded and analysed. The questionnaire was prepared with close and open ended questions.

Questionnaire design:

A Questionnaire of nine questions was setup, where by the in-depth knowledge can be attained upon proper

analysis of the subject. The questionnaire was designed using the close ended questions.

Sampling frame:

Sampling Process: The sampling process used during the survey is nonprobability, quota type process (two stage sampling technique in first stage the controlled categories are made in the next stage sample elements are selected based on convenience or judgment.

Respondents: The questionnaire was presented to physicians (general practioners M.D)

Sampling unit: The physicians from private clinics, hospitals, nursing homes from Udupi district were selected as samples.

Sampling size: A sample size of 20 respondents is selected to secure maximum accuracy in the results**.**

Plan of data analysis:

The data attained by the questionnaire is analysed by means of the percentage method. Where in the 20 respondents are extrapolated to 100. The results thus obtained are depicted in the form of the charts.

List of Banned Drugs in India[1,2,3]

Till date the Indian government has banned several FDCs and imposed restriction on many drugs and their combinations with other drugs for its manufacturing and marketing in India. Following is the list-

1. Amidopyrine
2. Phenacetin
3. Sulphanilamide
4. Practolol
5. Methapyrilence and its salts
6. Penicillin skin/ eye ointment
7. Tetracycline liquid
8. Oxytetracycline liquid oral preparation
9. Demeclocycline liquid oral preparation
10. Methaqualone
11. FDC of chloramiphericol with other drugs for internal use
12. FDC of Ergot with any drugs
13. FDC of Vitamins with anti-inflammatory agents and tranquilisers
14. FDC of Atropine with analgesics and antipyretics
15. FDC of Yohimbine and strychnine with Testosterone and vitamins.
16. FDC of iron with Strychnine, Arsenic and Yohimbine.
17. Chloral hydrate

18. FDC of sodium bromide with other drugs.

19. FDC of Tetracycline with vitamin C.

20. FDC of antihistamins with antidiarrhoeals.

21. FDC of Penicillins with Sulfonamides

22. FDC of vitamins with analgesics

23. FDC of prophylactic vitamins with Anti TB drugs except isoniazid with Pyridoxine Hydrochloride (Vitamin B6).

24. FDC of Strychnine and Caffeine in Tonic.

25. FDC of Hydroxy Quinolines groups of drugs with other drugs and liquid oral antidiarroheal or any other dosage form for paediatric use except for external use.

26. FDC of corticosteroid for internal use

27. FDC of Anabolic steroid with other drugs.

28. Combination of high dose of Estrogen and Progesterone (low dose combination is allowed for its use as contraceptive)

29. FDC of Sedatives/ hypnotics/ anxiolytics with analegesic and antipyretics.

30. FDC of anti-TB drugs except the under-stated combinations.

I II

(a) (I) Pyrizinamide 1000mg; 1500mg

(II) Rifampicin 450mg; 600mg

(III) Isoniazid 300mg; 300mg

(b) (I) Ethambutol 600mg; 800mg

(II) Isoniazid 200mg; 300mg.

31. FDC of Histamin H2 receptor antagonists with antacid except any combination approved by DCGI.

32. Patent and proprietary medicines having alcohol more than 20% except preparation listed in IP.

33. All preparations containing chloroform exceeding 0.5% w/w or v/v whichever is appropriate.

34. FDC of anthelmintics with cathartics or purgatives except for piperazine.

35. FDC containing more than one antihistaminic drug.

36. FDC of Salbutamol or any other bronchodilator with central acting antitussives and/ or antihistamines.

37. FDC of Laxatives and/ or antispasmodic drugs in enzyme preparations.

38. FDC if metoclopramide with other drugs except with Aspirin/ Paracetamol.

39. FDC of centrally acting antitussives with antihistamin as having atropine like activity in expectorent.
40. Preparations claiming to combat cough associated with asthma that contain a centrally acting antitusive and/ or antihistamine.
41. Liquid oral tonic having glycerol phosphates and other phosphates and/ or CNS stimulants and such preparations having alcohol more than 20%.
42. FDC containing Pectin and/ or Kaolin with any drug which is systemically absorbed through GI tract.
43. Toothpaste/ toothpowder containing tobacco.
44. Dovers powder IP Dovers Powder IP Tablets.
45. Antidiarrohoeal preparations containing kaolin/ pectin/ attapulgite/ activated charcoal.
46. Antidiarrohoeal preparations having phthalye sulphathiozole, Sulphaguinidine, succinic sulphathiozole, Neomycin, streptromycin, dihydro streptomycin or their salt.
47. Antidiarrhoeal formulation in any form for Pediatric use containing Diphenoxylate or Loperamide or Atropine or belladonna including their salts, esters or metabolites or their extracts or alkaloids.
48. FDC of antidiarrhoeals with electrolytes,
49. Oral Rehydration salts (ORS)-other than conforming to WHO formula or Pharmacapoeial preparation.
50. FDC of Analgin with any other drugs.
51. FDC of Dextropropoxyphene with any other drug except with antispasmodics and or NSAID
52. FDC of Phenylbutazone or Oxyphenbutazone with other drugs.
53. FDC of allopathic drugs with Ayurvedic, Siddha or Unani drugs.
54. Mepacrine Hydrochloride (Quinacrine and its salts) in any dosage form for use for female sterilization or contraception.
55. Fenfluramine and Dexfenfluramine.
56. FDC of streptomycin with penicillin.
57. FDC of Vitamin B1, B6 & B12.
58. Fixed dose combination of Nitrofuratoin and Trimethoprim.
59. Fixed dose combination of Phenobarbitone with any antiasthamatic drugs.

60. Fixed dose combination of Phenobarbitone with Hyoscin and/or Hyoscyamine.
61. Fixed dose combination of Phenobarbitone with Ergotamine and/or
Belladona.
62. Fixed dose combination of Haloperidol with any anti-cholinergic agent including Propentheline Bromide.
63. Fixed dose combination of Nalidixic acid with any antiramoebics including Metronidazole.
64. Fixed dose combination of Loperamide Hydrochloride with Furazolidone.
65. Fixed dose combination of Cyproheptadine with Lysine or Peptone.
66. Fixed dose combination of Diazepam and Diphenhydramine Hydrochloride.
67. Cisapride- Only qualified gastro-enterologists such as super specilists holding DM in gastro-enterology are permitted to prescribe cisapride.
68. Astemizole
69. Terfenadine
70. Sildenafil citrate. To be prescribed by endocrinologists, Urologists and Psychiatrist only.

Results and Discussion:

Most of the physicians are aware of the fact that some drugs are banned in India. 96% responded in a positive manner. Whereas only 4% said they were unaware about the information. Majority of physicians cited that they were aware of only 1-30 drugs that are banned. Most of them did not know the exact or the approximate number of banned drugs. Study shows that only 4% of the surveyed physicians actually had the correct information. Most of the physicians agree that cases of side effects due to banned drug come across them. This shows that these drugs are easily available in market even if these are banned. About 76% cases are accounted to face side effects. Most of the patients told the physicians that they are comfortable using the drug and would like to go with it as the drug shows effect and has fewer side effects. About 64% respondents told that they will like to go with such drug. The physicians told that most of the time they advice the patient to change the treatment while some of them prefer to prescribe by the risk - benefit ratio; duration of treatment and

other factors. Most of them (88%) are of opinion that combined doses should be banned as well. While some of them were of opinion that the drug interaction should be the criteria to Ban the drugs in India. If the drug has potential to treat disease and is comparatively less side effects it should not be banned. There was almost an equal response from the doctors. Some doctors feel that the drugs banned abroad should be immediately banned in India as well. Whereas few respondents feel that the ADR's should be made the criteria to Bann. Simply banning drugs as they are not acceptable abroad is not a genuine reason.

In the view of 62% respondents journals are the best source which the physicians prefer to update their latest knowledge about in banned drugs. Most of the physicians said that government is not making many efforts. Majority of the doctors feel that a demographic and ethnic factor does affect the metabolic activities of the individual. Therefore such factors should be kept in mind while prescribing a drug. Thus a drug acceptable in U.S may not be acceptable in Indians as they vary in the metabolic activities.

Majority of the physicians blame the government 26 out of 100 for the cited situation most of them told they don't receive the copy of IMA newsletter. Lack of awareness programs ranks second in lead, deteriorating the situation. Most of the physician opined that government need to play a vital role in restricting the Banned drugs (28 out of 100). As well as the manufacturers should stop producing the drugs banned by the government. 20% said that there is a need of pharmacovigilance program. Whereas most of them agreed that all the three are required.

Conclusion:

The study shows:

- That most of the physicians are aware but not sure that which and how many of them are banned. Thus they have only limited knowledge.
- This limited knowledge is due to the lack of awareness programs and government measures (Although the

government claims that each year a copy of IMA newsletter is send to the physicians containing information about the banned drugs).

- Physicians opined that if the "drugs are banned abroad they should also be banned in India also" should not be the sole criteria to ban the drugs.
- There should be pharmacovigilance programs so monitor ADR's and the "Benefit- Risk ratio" of a drug should be used to ban the drug.
- Most of the physicians state that the combination or the fixed dose formulations containing banned drug should also be banned as they may be harmful.
- Physicians cite that if once the drug is declared as banned strict measures should be followed so that the drug is made completely out of market.

Recommendations:

- An urgent screening and listing of all the drugs in the market is required.
- Identification of hazardous and also irrational and non-essential drugs is required.
- Withdrawal of these drugs should take place immediately.
- Deterrent punishments for those who continue to sell banned drugs and challenge the decision of the Drug Controller and the drug related laws.
- Consultative Committee should be formed and strictly imposed.
- A separate bulletin containing information about the banned drugs should be published and made available to all the physicians and chemists.
- More pharmacovigilance centre should be set up to monitor the effect of drug on Indians.

Limitations of study:

1. Topic is perceived as controversial subject so physicians do not respond easily
2. Limited sample size

References:

1. http://www1.sapdesignguild.org/resources/optical_illusions/intro_definition.html
2. http://www.investorwords.com/208/analysis.html
3. http://www.expresspharmaonline.com/20051115/market01.shtml
4. http://www.medindia.com/news/healthwatch/overthecounterdrugs.asp?str=3 date 19/8/07
5. http://www.pharmabiz.com/article/detnews.asp?articleid=17397&sectionid=46 date 18/8/2007
6. http://www.indianpad.com/story/20605 date 14 Aug 2007
7. http://www.locostindia.com/CHAPTER_3/Rationality%20of%20Drugs_3.htmdated 16aug2007
8. http://www.pakistaneconomist.com/database1/cover/c96-45.asp dated 16th Aug 2007

Assessment of Patient's Perception on Medication Counseling using Patient Information Leaflets

M.Surulivel Rajan*[1], GVM. Krishna[2], Anitha.G. Reddy[2], Jnana Prasuna.N[2], Ajay Kumar.N[2].

*Corresponding author

msvrajan@rdiffmail.com

[1]Department of Pharmacy Practice, MCOPS, Manipal

[2]College of Pharmacy, SRMC&RI (DU), Chennai.

Abstract:

Patient counseling has been well established in developed countries as a responsibility of a pharmacist. In India patient counseling is a new concept and this is slowly recognized as a responsibility of the pharmacist. Use of patient information leaflet for counseling appears to have better effect on patient understanding of therapy and compliance. This study aimed to find patients' perception on counseling when patient information leaflets were used for counseling. Patient information leaflets were prepared for14 cardiovascular drugs in English and Telugu. Patient counseling

was carried out in clinics and pharmacies in Vijayawada and Guntur in Andhra Pradesh. Before counseling, patients' baseline medication knowledge was assessed using a standard questionnaire and after counseling patients' perception was assessed using their feed back. Totally 35 patients were counseled. Baseline medication scores of males were higher than females and education level was found to have important role in the baseline medication knowledge. All the patients felt that the counseling was useful. Patients expressed satisfaction over the Patient Information leaflets and are willing to receive similar counseling in future. The study showed that patients perceive counseling is useful and are willing to receive counseling from pharmacists. Community pharmacists can seize the opportunity to provide patient oriented services and establish themselves as healthcare providers from mere traders.

Keywords: Patient counseling, Patient information leaflets

Introduction:

Pharmacists in developed countries have focus on patient centric approach. During early nineties 'Pharmaceutical care' has evolved into a concept that drove changes within the profession. Pharmaceutical care is defined as the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve the patient's quality of life[1]. One of the important components of pharmaceutical care is patient medication counseling with suitable counseling aids like printed information leaflets. Printed information leaflets were also appearing to have positive effect on compliance when distributed to targeted patient group[2.] Use of counseling aids such as patient information leaflets (PILs) is accepted as one of the best ways to improve patient's understanding. PILs are used to outline key information to assist patients and their caregivers in the effective and safe use of a medicine[3]. Patients who receive PILs regarding medicines generally have improved awareness of medication use, are more likely to be completely satisfied with their treatment, know the name of their medicine, and are more aware of the possible adverse drug reactions[4].

In India, profession of pharmacy practice is evolving slowly and in the past decade much attention has been given by the professional leaders on the aspect of Hospital and Clinical Pharmacy. Postgraduate course in pharmacy practice has come up in various institutions in our country. These changes have led to the attitudinal changes in young pharmacists. In a recent survey conducted among pharmacists in Karnataka and Kerala, young pharmacists have opined that the patient counselling is the responsibility of practicing pharmacists[5].

In Indian health care setup, most of the physicians either in government or private practice are busy because of high patient load. Medical practitioners may not have time to counsel the patients regarding medications. Pharmacists are also either busy or they do not have adequate knowledge and training in medication counselling. Moreover there are no incentives for pharmacist to take up patient medication counselling. The acceptability of the patients in receiving counseling from a pharmacist is also not known.

Aim of the study:

This study was planned to assess the patient's perception on medication counselling by the pharmacist using counselling aid particularly using medication information leaflet in English and local language of the patients. It was also planned to assess the basic medication knowledge of the patients to identify target group of patients who will need more help and support by the pharmacist.

Methodology:

Most commonly used cardiovascular drugs were selected. Totally 14 drugs were selected for inclusion into study. Drug information leaflets were prepared using United States Pharmacopoeia drug information[6] for the patients as a model (Table 1). Drug information leaflets were translated in Telugu language (Fig.1) Medication knowledge assessment questionnaire (Table 2) was adopted from the one, which was designed by Vitalina Rhozenfeld et al[7]. The questionnaire contained a total of six questions, which a patient must know before use of medication. Each question carried a maximum of 4 points and depending upon the response, patient will get

scores. A patient who has answered all the questions correctly gets maximum points.

Final year pharmacy students who have taken up this project were trained on the aspects of medication counselling and knowledge assessment of patients. These pharmacy students went to the pharmacies and clinics in Vijayawada and Guntur in Andhra Pradesh. The patients who were prescribed the medications, which were in the selected list, were included for counselling. The demographic data was collected regarding patients in a designed proforma. Patient's medication knowledge score was assessed using the standard questionnaire. After assessing the medication knowledge patients were counseled using information leaflets in Telugu which is the local language. After counselling patients were provided with a copy of information leaflet and their feed back was collected.

Results and Discussion:

Demographic characters:

A total of 35 patients were included. Their medication knowledge was assessed prior to counselling. Out of 35 patients, 19 (45.75%) were males and 16 (45.7%) were females. When education qualification of patients were analyzed, 16 (45.7%) were found to be graduates and 11 (31.42%) were high school level and 7 patients were of middle school level and one patient was illiterate. Among the different age groups, 24 patients (65.7%) were in the age group of 41-60 years and followed by the age group <40 years having 7 patients (20%). There were 4 patients (14.28%) in the age group of 61 years and above.

Factors affecting baseline medication knowledge:

The average medication knowledge score of male patients was 13.10±3.99 and 10.87±4.2 for females. This may be because level of education was more with males compared to females. When stratified according to education, the medication knowledge for graduates was 14.18±3.72 and for high /higher secondary school level it was 11.14±5.6. The average score for the middle school level was 10.09±2.3 and the medication score for the illiterate was 7. This pattern of scores implied that the level of education definitely play a role in the baseline medication knowledge. This result is similar to

studies of other authors who conducted similar studies[8].

Feedback:

All the 35 patients did not receive this type of information on medicine in the past. All the patients have got information on medicines from physicians and they would prefer the information by the pharmacist in the future. All patients felt that the information leaflets were useful. Illiterate patients wanted information leaflets because their literate family members can go through the information and explain them.

This study shows that counseling patients on medications by pharmacists can increase the satisfaction of patients and this reinforces the results of other reported studies[9]. Patients feedback suggests this type of information to be given for all the medicines they were taking; counseling through telephone and to have pictorial representations in the patient information leaflets for better understanding. If pharmacists come forward to give counselling and discuss about the health related issues with the patients, pharmacist services are appreciated by patients.

Conclusion:

An attempt to study the perception of patients on medication counselling was made. In this study, it has been found that female and illiterate patients did not have sufficient knowledge about their disease and medications. Pharmacists can target this group of patients for counselling. Pharmacists need to be trained and equipped for this task. This will help to change the image of the pharmacist from a 'seller' to a 'health care professional'.

Referernces:

1. Robert S. Beardley. Advancing pharmacist's contribution to enhancing compliance. J Pharmacoepidemiol 1995;3:49-61.
2. Seals TD, Keith MR. Influence of patient information leaflet on anticonvulsant drug compliance in prison. Am J Health-Syst Pharm 1997; 54 (22):585-87.
3. Ruth Ferguson. Communication Skills. In: A Textbook of Clinical Pharmacy Practice, Parthasarathi G, Karin Nyfort-Hansen, Milap C

Nahata (Eds). 1st edn; Orient Longman, India 2004: 32.

4. I.C.K. Wong. Readability of patient information PILs on antiepileptic drugs in the UK. Seizure 1999; 8:35-37.
5. Ramesh Adepu, Nagavi BG, Mahendra Kumar BJ. Patient counselling, practicing pharmacists' perceptions from two south Indian states. Ind J Pharm Sci 2004;66(1):44.
6. USPDI (1997). Advice for patient drug information in lay language, USP DI Vol. II, 18th edn , United States Pharmacopoeia.
7. Vitalina Rhozenfeld, Jean-Marie Pflamm, Kulvinder K. Singh, Michelle K. Brazil, Judy WM. Cheng. Assessing the impact of medication consultations with medication event monitoring system. Hosp Pharm 1999;34:539-549.
8. Ponnusankar S, Surulivel Rajan M, Anandamoorthy N Suresh B. Assessment of impact of medication counseling on patients' medication knowledge and compliance in an outpatient clinic in south India. Patient Edu Counsel 2004:54:55-60.
9. Mc. Cann S. Weinman. J. Empowering the patient in the consultation. Patient. Edu. Counsel. 1996; 27:227-234.

Table 1. Model Patient Information Leaflet for Nitrates

NITRATES – ORAL

Other names: Etithrityl tetra nitrate, Isosorbide di nitrate, Nitroglycerin

Description:

This medicine is used to treat symptoms of chest pain. It acts by relaxing blood vessels and increasing blood supply and oxygen to heart and reduces its workload.

Before using this medicine:

- Tell your doctor if you are allergic to this medication.
- This medicine should not be taken during pregnancy unless recommended by your doctor.
- Signs and symptoms of over dose may occur in the elderly who may be more sensitive.

Other medical problems:

- Make sure you tell your doctor if you have any other medical problems.

Proper use of this medicine:

- Take this medicine exactly as directed by your doctor.
- Check with your doctor if you need a fast acting medicine to relieve the pain of a chest pain attack.
- Take this medicine with a full glass of water on an empty stomach.

Side effects:

- Dizziness, Light-headedness, nausea or vomiting, restlessness, dryness of mouth, head ache. If you notice any of the above mentioned symptoms contact your doctor.

Missed doses:

- If you miss a dose of this medicine, take it as soon as possible and if the next scheduled dose is within 2 hours, skip the missed dose and go back to your regular dosing schedule. Never double the doses to compensate for the missed doses.

Storage:

- Keep out of the reach of children.
- Store away from heat and direct light.
- Do not store this medicine in moist places.

Precautions while using this medicine: If you are taking this medicine regularly, do not suddenly stop using this medicine. Check with your doctor for the best way to reduce the dose of the medication.

Table 2. Patient Medication Knowledge Assessment Form

QUESTIONS	SCORES			
	1	2	3	4
What is the name of the medication? Can you identify this medication?				
What are the timings of this medication and directions?				
What this medication is for?				
What is the dose of this medication?				
Do you know how long you have to take this medication?				
Do you know what other food/medications you have to avoid while taking this medication?				

Trends in Labeling of Ethical Pharmaceuticals in India

Anantha Naik Nagappa*, Namita Kumari Srivastava, Manju Varghese, Sapna Kamlesh Rupani, Sudhapalli Poojee

Dept of Pharmacy Management, Manipal College of Pharmaceutical Sciences

Manipal, 576104 India.

*Corresponding author
anantha1232000@gmail.com

Ethical (prescription only) pharmaceuticals label is compilation of information about a product provided by a manufacturer approved by drug controller of India . Label contians necessary information for safe and effective use of and is written primarily to health care professionals. Pharmaceutical labels are important aspect of product as they carry information related to the product identity product usage and shelf life apart from source and regulatory information. It is observed that in India the pharmaceutical labels are not comprehensive as regulatory guidelines covers partial aspects of

labellings and leaving the product usage and related information for the patients, being optional. In order to establish the current styles and status of labellings this study was undertaken. The study involved critical evaluation of labels of ethical pharmaceuticals in the Indian Market. The observational study regarding contents and quality of presentation of labels was conducted based on the assessment of the following parameters viz., Font size, therapeutic indication, storage condition, dose, auxiliary labels, expiry date, other regulatory labels and package inserts.

It was found that the labels in the Indian market are grossly inadequate from the point of view of the patient and health care professional . The study establishes the need to form national guidelines with proper regulations. The labeling guidelines should be implemented uniformly throughout the nation. This could help in avoiding medication error and assist in quality use of medicines.

According to the United States Pharmacopoeia (USP), the term "labeling" designates all labels and other written, printed, or graphic matter upon an immediate container of an article or upon, or in, any package or wrapper in which it is enclosed, except any outer shipping container. The term "label" designates that part of labeling upon the immediate container.

As per the Federal Food, Drugs and Cosmetics act, Section 201, the term "label" means a display of written, printed, or graphic matter upon the immediate container of any article; and a requirement made by or under authority of this chapter that any word, statement, or other information appear on the label shall not be considered to be complied with unless such word, statement, or other information also appears on the outside container or wrapper, if any there be, of the retail package of such article, or is easily legible through the outside container or wrapper. The term "immediate container" does not include package liners. The term "labeling" means all labels and other written, printed, or graphic matter upon any article or any

of its containers or wrappers, or accompanying such article.

Labelling entails much more than the information that appears on a bottle or package. It is a concise and comprehensive statement of the best information about a drug's quality, efficacy and safety. Quality refers to the precise chemical composition of the drug, the strength and physical form in which it is supplied, and the rules for its storage and handling. Efficacy refers to the medical conditions for which it is indicated and the therapeutic effects of use, as well as the proper dosing for the accepted indications. Safety refers to potential side effects, contraindications and other consequences of use, including rules for monitoring patients with various special conditions.

Labelling is intended as a guide to patients aswell both for medical apart from health care professionals. It is presented as a textual narrative, but it also contains important detailed data elements. They prove to be useful to the patients by way of providing the necessary information to help take correct decisions whilst the use of the product and also help to avoid confusion regarding its use. As products are usually handled in the ambulatory/out patient care set-up, the primary aim should be also to provide information to the patients. It was found that the labels in the Indian scenario are good only for the use of doctors and pharmacists who have background knowledge on the use of drugs. A prescription drug product label (also known as a professional label, package insert, direction circular, and package circular) is a compilation of information about a product written by the manufacturer and approved by FDA. Labeling, or prescription information is a requirement for all approved drug and biological drug products.

In most developed countries the regulatory agencies have established comprhensive guidelines and rules for the content and format of labelling. For example in the United States these are set out in the Code of Federal Regulations under Title 21 concerning The Food and Drug Act. 21 CFR 201.56 defines the major topical sections to be included as:

- Description
- Clinical Pharmacology

- Indications And Usage
- Contraindications
- Warnings
- Precautions
- Adverse Reactions
- Drug Abuse and Dependence
- Over-dosage
- Dosage and Administration
- How Supplied

FDA has designed new labeling to help health care practitioners easily find, read, and convey information important for the safe and effective use of prescription drugs. Legal requirements for the labeling of medicines in the Great Britain are explained in *Medicines, Ethics and Practice: A Guide for Pharmacists.* These regulations also specify that the label must clearly state precise instructions for use by the patient and the cautionary and advisory labels *(refer table- 01)* where appropriate. In the India, the labeling of ethical pharmaceuticals are to be in accordance with guidelines mentioned in the *Drugs and Cosmetics Rules, 1945* and *Drugs and Magic Remedies Act, 1954*

The Drugs and Magic Remedies (objectionable advertisements) Act, 1954 controls and prohibits certain classes of advertisements relating to drugs and magic remedies. According to the Act, *Advertisement* includes all notices, circulars, labels, wrappers, or other documents and all announcements made orally or by means of producing or transmitting light, sound or smoke.

The rules specify the indication of the proper name of the drug in a more conspicuous manner than the brand name, a correct statement of the net contents, the content of active ingredients, the address and name of the manufacturer, a distinctive batch number, manufacturing license number, expiry particulars, information related to storage or manner of use, and general information like 'Physician's sample, not for sale'. However, there are no specific rules regarding the inclusion of auxiliary (cautionary and advisory) labels, therapeutic indication, dose, side effects, and other relevant information regarding the drug on the package

label. The *warning* labels for prescription drugs include:

Schedule- H: To be sold by retail on the prescription of a Registered Medical Practitioner only.

Auxiliary labels (Cautionary and Advisory labels) are essential for avoiding hazards of medication errors, in order to achieve the desired therapeutic goals. See Table 1.

Standard cautionary and advisory labels offer advice but are not exhaustive. The labels are not a substitute for adequate counselling by prescribers and dispensers (most medicines are dispensed by pharmacists) but are intended to reinforce essential information the patient needs to know.

Table 1 Requirements of Ideal Labellings

Recommended label wording can offer advice about:

- Timing of doses in relation to food.
- Completing the course of treatment.
- What to do if a dose is missed.
- The correct storage of a medicine.
- Dissolution of the medicine in water before taking it.
- Limits to the number of tablets that should be taken in a given time.

Recommended label wording can offer warnings about:

- Effects of the medicine on driving or work (e.g. through drowsiness).
- Foods or medicines that should be avoided.
- Avoidance of exposure of the skin to sunlight or sun lamps.
- Medicines that can discolor the urine.
- Medicines that can stain clothes or skin.

According to the study, it was found that most of the labels on the dispensed medications lacked cautionary and/or advisory labels with the exception of a few. The absence of these linformation in abels can often leads to serious concequences and may also decrease the efficacy of the drug therapy. In some cases the absorption of a drug might be affected due to drug-drug

interactions or drug-food interactions of which the patient under the medication might be unaware of. For instance, consumption of calcium containing products renders the tetracyclin therapy a falure. For those patients who are on asprin or paracetamol must be adviced not to take any other paracetamol containing products as it might lead to overdose, which might ultimately lead to kidney damage due to over dosage

Preparations that may cause the patient's urine to turn an unusual colour, like Rifampicin, must bear a label that cautions the patient of the same, which would otherwise lead to patient noncompliance and ultimately lead to failure of the therapy. Such errors in therapy can be avoided by including a simple advisory and/or cautionary label. The incorporation of these labels will not only reduce the occurance of errors, but inturn also optimise the drug therapy. The ammendments in regulatory reforms which would update the labellings covering such details for pharmaceuticals with specific requirements which is a nescessity for safe and qulaity use of medicine.The main objective of the study is to conscientiously and critically analyse labels of pharmaceuticals, identify any discrepancies in labelling. It also involves giving suggestions to the various cautionary and advisory labels that need to be present for specific drugs for better patient awareness to ultimately improve patient compliance.

A case study for diazepam tabelts was carried out as an example to suggest changes in the labeling pattern in order to make the label more informative. The information on the current label of one of the brands of diazepam tablets that is available in the Indian market was noted down and compared with the drug information mentioned in the British National Formulary 2007. Observational study was also carried out for labels of tablets (N= 100) from the shelves of the medical stores . The summary of this study is given in Table no 3

Table 2: Recommended wording of cautionary and advisory labels

Warnings • May cause drowsiness • May cause drowsiness. If affected do not drive or operate machinery. Avoid alcoholic drink • May cause drowsiness. If affected do not drive or operate machinery • Avoid alcoholic drink • Follow the printed instructions you have been given with this medicine • Causes drowsiness which may continue the next day. If affected do not drive or operate machinery. Avoid alcoholic drink • This medicine may colour the urine
Instruction for usage • Take at regular intervals. Complete the prescribed course unless otherwise directed • Dissolve or mix with water before taking • Allow to dissolve under the tongue. Do not transfer from this container. Keep tightly closed. Discard 8 weeks after opening • …with or after food • …half to one hour before food • …an hour before food or on an empty stomach • …sucked or chewed • …swallowed whole, not chewed • …dissolved under the tongue • …with plenty of water • To be spread thinly…

Dos and don'ts

- Do not take indigestion remedies at the same time of day as this medicine
- Do not take indigestion remedies or medicines containing iron or zinc at the same time of day as this medicine
- Do not take milk, indigestion remedies, or medicines containing iron or zinc at the same time of day as this medicine
- Do not stop taking this medicine except on your doctor's advice
- Avoid exposure of skin to direct sunlight or sun lamps
- Do not take anything containing aspirin while taking this medicine
- Caution flammable: keep away from fire or flames
- Do not take more than…in 24 hours
- Do not take more than…in 24 hours or…in any one week
- Do not take more than 2 at any one time. Do not take more than 8 in 24 hours
- Do not take with any other Paracetamol products
- Contains aspirin and Paracetamol. Do not take with any other Paracetamol products
- Contains aspirin
- Contains an aspirin-like medicine

The absence of relevant information on the labels may lead to physician prescribing multiple drugs which may interact with each other. This can lead to serious health hazards and patient non-compliance which may lead to ineffective therapy!

CASE STUDY OF DIAZEPAM TABLETS

The following details were found to be present on the label of the below mentioned drug:

Brand name: X

Generic name: Diazepam tablets I.P

Each uncoated tablet contains Diazepam I.P 5mg

Dosage: According to medical prescription

Storage: Store protected from light

Schedule H drug: Warning: To be sold by retail on the prescription of a *Registered Medical Practitioner* only.

The above label was found to be lacking in terms of providing important information regarding indications, cautions, interactions, contra-indications, side effects, over-dose, dose, etc of diazepam tablets. The package insert was also found to be absent. We suggest the following information also be present, if not entirely on the label, then as a package insert accompanying every carton in which the medication is packed.

DIAZEPAM

Indications: short-term use in anxiety or insomnia, adjunct in acute alcohol withdrawal; status epilepticus; febrile convulsions; muscle spasms; peri-operative use

Cautions: respiratory disease, muscle weakness and myasthenia gravis, history of drug or alcohol abuse, marked personality disorder, pregnancy, breast-feeding; reduce dose in elderly and debilitated, and in hepatic impairment, renal impairment; avoid prolonged use (and abrupt withdrawal thereafter); special precautions for intravenous injection; porphyria; when given parenterally, close observation required until full recovery from sedation

Interactions:

- Enhanced hypotensive effect when anxiolytics and hypnotics given with ACE Inhibitors
- Enhanced hypotensive effect when anxiolytics and hypnotics given with adrenergic neurone blockers
- Increased sedative effect when anxiolytics and hypnotics given with alcohol
- Enhanced hypotensive and sedative effects when anxiolytics and hypnotics given with alpha blockers
- Increased sedative effect when anxiolytics and hypnotics given with general anaesthetics
- Increased sedative effect when anxiolytics and hypnotics given with opioid analgesics

- Enhanced hypotensive effect when anxiolytics and hypnotics given with angiotensin-II receptor antagonists

Contra-indications: respiratory depression; marked neuromuscular respirator weakness including unstable myasthenia gravis; acute pulmonary insufficiency; sleep apnoea syndrome; severe hepatic impairment; not for chronic psychosis; should not be used alone in depression or in anxiety with depression; avoid injections containing benzyl alcohol in neonates

Side effects: drowsiness and lightheadedness the next day; confusion and ataxia (especially in the elderly); amnesia; dependence; paradoxical increase in aggression; muscle weakness; *occasionally*; headache, vertigo, hypotension, salivation changes, gastro-intestinal disturbances, visual disturbances, dysarthria, tremor, changes in libido, incontinence, urinary retention; blood disorders and jaundice reported; skin reactions; on intravenous injection, pain, thrombophlebitis, and rarely apnoea

Over-dosage: Benzodiazepines taken alone cause drowsiness, ataxia, dysarthria, and occasionally minor and short-lived depression of consciousness. Activated charcoal can be given within one hour of ingesting a significant quantity of benzodiazepine. Benzodiazepines potentiate the effects of other central nervous system depressants taken concomitantly. Use of the benzodiazepine antagonist flumazenil can be hazardous, particularly in mixed overdoses involving tricyclic antidepressants or in benzodiazepine-dependant patients. Flumazenil should be used on **expert advice** only.

Dose:

- By mouth, anxiety, 2 mg 3 times daily increased if necessary to 15-30 mg daily in divided doses;

  Elderly (or debilitated) half adult dose

  Insomnia associated with anxiety, 5-15 mg at bedtime

  Child night terrors and somnambulism, 1-5 mg at bedtime

Font Size Generic name Vs Trade name	1	2	3	4	5
• By intramuscular injection or slow intravenous injection (into a large vein, at a rate of not more than 5 mg/minute), for severe acute anxiety, control of acute panic attacks, and acute alcohol withdrawal, 10 mg, repeated if necessary after not less than 4 hours Note Only use intramuscular route when oral and intravenous routes not possible • By rectum as rectal solution, acute anxiety and agitation, 500 micrograms/kg repeated after 12 hours as required; elderly 250 micrograms/kg; child not recommended. As suppositories, anxiety when oral route not appropriate, 10-30 mg (higher dose divided); dose form not appropriate for less than 10 mg. Suggestion: The information regarding dose and cautions can be printed on the label, whereas the rest of the important information can be included in the package insert					

FONT SIZE: Generic Vs Trade name

KEY: 5- Big and clear

4- Big and unclear

3- Equal and clear

2- Equal and unclear

1- Small and unclear

Percentage: 5- 56%

4- 15%

3- 14%

2- 0%

1- 15%

THERAPEUTIC INDICATION

Therapeutic Indication	1	0
Number of Drugs	5	95

KEY: 1-Present

0-Absent

Percentage: 1- 5%

0- 95%

STORAGE CONDITIONS

Storage conditions	1	0
Number of Drugs	100	0

KEY: 1-Present

0-Absent

Percentage: 1- 100%

0- 0%

DOSE

Dose	1	0
Number of Drugs	5	95

KEY: 1-Present

0-Absent

Percentage: 1- 5%

0- 95%

AUXILIARY LABELS

Auxiliary Labels	1	0
Number of Drugs	36	64

KEY: 1-Present

0-Absent

Percentage: 1- 36%

0- 64%

EXPIRY DATE

Expiry date	1	0
Number of Drugs	93	7

KEY: 1-Clear

0-Not clear

Percentage: 1- 93%

0- 7%

OTHER REGULATIONS

Other regulations	1	0
Number of drugs	100	0

KEY: 1-Present

0-Absent

Percentage: 1- 100%

0- 0%

PACKAGE INSERTS

Package Inserts	1	0
Number of Drugs	28	72

KEY: 1-Present

0-Absent

Percentage: 1- 28%

0- 72%

Results:

It was found that most of the drugs that were surveyed complied with the regulations laid down by the Drugs and Cosmetics Rules 1945 with respect to the font of the generic name being bigger than the brand name, and was also clearly visible. Some drugs complying with the regulations of font size, however, did not meet the clarity criteria. Some of the others did not meet either of the set criteria. It was found that 71% of the labels surveyed complied with the criteria and stated the generic name of the drug in a font size that was bigger than that of the trade name. It was observed that 78.9% of the time the generic name of the drug was clearly visible. 14% of the labels surveyed specified the generic name in the same font size as that of the trade name, which were also optimally conspicuous. 15% of the labels were noted to be non-compliant with the rules by stating the generic name of the drug in font size smaller than the font size of the trade name.

Of the total surveyed tablet labels, 30% of the labels lacked clarity mainly due to the colour of the ink used or the aluminum foil packaging. Although mentioning of therapeutic indications and dose on the labels is not specified by the regulations, very few labels, only 5% did contain the aforesaid parameters and were ranked higher and considered better labels than the ones that did not. Storage conditions were mentioned on each and every one of the surveyed tablet labels and it scored

a 100%. The expiry date mentioned on the labels was evaluated for its clarity and visibility. Though it was mentioned on all the labels, in some of the labels it was very difficult to detect and read. These consituted only 7% of the labels that were surveyed. The other regulatory requirements like batch number, manufacturing licence number, etc was mentioned in all the labels. Package inserts were present in 28% of the cartons only. Majority of the boxes did not contain them.

Conclusion:

Labels of ethical pharmaceuticals in India are inadequate in terms of providing information to the patient and health care professionals. This can be the root cause of many medication errors and failure in therapy. In the developed countries the labels are being regulated to ensure a safe and quality use of medicines. However, labels in developing countries like India are not uniform and are inadequate in terms of information. There is a need for upgrading the existent regulations to be at par with developing countries as the same pharmaceuticals are used in therapeutics. There should be stringent norms and regulations regarding the inclusion of dose, indications, appropriate auxiliary (cautionary and advisory) labels, side effects, contra-indications, interactions as part of a label on every package.This will help the physician to make rational decisions regarding drug use, reduce the non-compliance amongst patients especially those in ambulatory care, and provide sufficient information to all other health care professionals to support and ensure ***quality use*** of medicines.

Bibliography

1. Indian Pharma Reference Guide 2007-08 , Kongposh Publications, New delhi, India.
2. British national Formulary 53, March 2007,BMJ and RPS Publishing group, London, U.K.

Table 3 summary of observational study of 100 tablets labellings

KEY: 5- Big and clear

4- Big and unclear

3- Equal and clear

Parameters	1	0
Therapeutic indication	5%	95%
Storage conditions	100%	0%
Dose	5%	95%

2- Equal and unclear

1- Small and unclear

KEY: 1-Present

0-Absent

Expiry date	1	0
Number of Drugs	93%	7%

KEY: 1-Clear

0-Not clear

Upcoming Conferencees and Workshops Around the Globe

Compilation by Mr. Dinesh Kumar C.
Department of Pharmacognosy, Manipal College of Pharmaceutical Sciences, Manipal

July 2008

IBC's Beyond Antibodies
28 - 29 July 2008, La Jolla, CA, USA.
IBC's 3rd Annual Beyond Antibodies conference on July 28-29, 2008 in La Jolla, CA will discuss recent scientific as well as business developments in antibody alternatives. Attend and review data from companies with antibody alternatives in clinical and preclinical stages.

August 2008

Drug Discovery & Development of Innovative Therapeutics
04 - 07 August 2008, Boston, MA, USA
Practical, Actionable Ideas for Accelerating Discovery and Early Development. The Drug Discovery & Development of Innovative Therapeutics (DDT) World Congress is the ONLY international event that compares applications of translational medicine and transforming technologies across multiple therapeutic areas to help you find new ways to achieve POC quickly. View the full program agenda online at www.drugdisc.com.

THE 11TH IRANIAN PHARMACEUTICAL SCIENCES CONFERENCE (IPSC2008)
18th August 2008 - 21st August 2008, Faculty of Pharmacy, Kerman University of Medical Sciences, Kerman, Iran; www.ipsc2008.ir

WORLD CONGRESS OF PHARMACY AND PHARMACEUTICAL SCIENCES 2008, 68TH INTERNATIONAL CONGRESS OF FIP
29th August 2008 - 4th September 2008, Basel, Switzerland, www.fip.org/basel2008/

XXth International Symposium on Medicinal Chemistry
31 August 2008 - 04 September 2008, Vienna, Austria
The XXth EFMC-ISMC will cover drug discovery advances in all therapeutic areas as well as the most recent advances in lead identification strategies, drug design and profiling technologies. The conference will also illustrate the impact of the "omics" area on the interfaces between chemistry, informatics and biology.

September 2008

IQP - INTEGRATED QUANTITATIVE PHARMACOLOGY: CONCEPTS AND APPLICATIONS
1st September 2008 - 7th November 2008 at the Department of Pharmacology, University of Gothenburg in Gothenburg, Sweden [2059]
Contact: Patrik Aronsson, Telephone: + 46 - 31 - 786 3440; Fax: + 46 - 31 - 82 10 85
Email: patrik.aronsson@pharm.gu.se.
Website: http://www.pharmguse.net/advanced/advanced-courses.html

EU DRUGS REGULATION FROM DISCOVERY TO MARKETING AND BEYOND
2nd September 2008 - 5th September 2008 at the Venue: The Cavendish Hotel in London, United Kingdom [2104], Contact: Judith Black / Leigh White
Telephone: 44 1483 730071; Fax: 44 1483 730008
Email: info@management-forum.co.uk;

Website: http://www.management-forum.co.uk/html/con_semin_section/con_display_event.asp?event=824

COMPUTERIZED SYSTEMS IN CLINICAL RESEARCH: CURRENT QUALITY AND DATA INTEGRITY CONCEPTS

8th September 2008 - 12th September 2008 at the DIA in Horsham, PA, USA [2149]
Contact: Marketing Manager, Telephone: +1.215.442.6100; Fax: +1.215.442.6199
Email: dia@diahome.org; Website: http://www.diahome.org

World Drug Manufacturing Summit

09 - 11 September 2008, Dusseldorf, Germany
The World Drug Manufacturing Summit brings together the leading pharmaceutical and biotech manufacturing professionals to network and discuss issues at the cutting edge of lean production methods and transformational change in a tightly regulated environment. To view the full programme and to register, visit the website http://www.wdmsummit.com or call +44 (0) 207 202 7558

13TH ANNUAL SUMMIT ON THE MEDICAID DRUG REBATE PROGRAM

Sep 15, 2008 - Sep 17, 2008, Marriot Downtown Chicago Magnificent Mile Chicago, Illinois United States.
Event website: http://www.iirusa.com/medicaiddrugrebates/14340.xml
Phone: 888-670-8200
Have a question about this event? Customer Service representatives are available to help from 8 AM - 6 PM EST Call 888-670-8200.

EXPOPHARM 2008

Sep 18, 2008 - Sep 21, 2008, International Pharmaceutical Trade Fair Munich, Germany
Email address: besucher@expopharm.de
Event website: http://www.expopharm.de/en/index.html
Phone: +49 (0)6196 - 928 412; Fax: +49 (0)6196 - 928 40

ADVERSE DRUG EVENTS IN PREMARKETING CLINICAL TRIALS AND POSTMARKETING PHARMACOVIGILANCE: THE COMPLIANCE, MEDICAL ASSESSMENT AND RISK MANAGEMENT CONTINUUM

18th September 2008 - 19th September 2008 at the Sheraton Philadelphia City Center Hotel in Philadelphia, PA, USA [2184]
This Program was Developed by the Clinical Safety and Pharmacovigilance Special Interest Area Community.
Contact: Marketing Manager, Telephone: +1.215.442.6100; Fax: +1.215.442.6199
Email: dia@diahome.org; Website: http://www.diahome.org

HOSPITAL PHARMACY OPTIMIZATION

Sep 22, 2008 - Sep 23, 2008, Las Vegas, Nevada United States
Email address: info@worldrg.com;
Event website: http://www.worldrg.com/showConference.cfm?confCode=HW08026
Phone: 1-800-647-7600

BRITISH PHARMACEUTICAL CONFERENCE (BPC)

27th September 2008 - 29th September 2008, Manchester Central, Manchester, UK
Event website: bpc2008.org

PHARMACY 2008
Sep 30, 2008 - Oct 02, 2008, Exhibition Centre Lenexpo St. Petersburg, Russia
Contact person: Tatiana Petina, Email address: med@primexpo.ru
Event website: http://www.primexpo.ru/hospital/eng/index2.shtml?red=
Phone: +7 (812) 380-6006, Fax: +7 (812) 380-6001

14TH INTERNATIONAL PHARMACEUTICAL TECHNOLOGY SYMPOSIUM
8th September 2008 - 10th September 2008
Kervansaray Lara, Antalya, Turkey, www.ipts-hacettepe.org

2ND ANNUAL PAIN THERAPEUTICS SUMMIT 2008
Oct 06, 2008 - Oct 07, 2008
"Commercial and Scientific Perspectives on Pain Management and New Product Development", , New Jersey United States
Email address: sales@arrowheadpublishers.net
Event website: http://www.arrowheadpublishers.com/conferences/paintherapeutics2008/
Phone: +13122443703/+18663971376

ANNUAL SYMPOSIUM FOR NURSES AND PHARMACISTS SPECIALIZING IN ONCOLOGY: ASSESSING AND MANAGING SIDE EFFECTS IN THE ERA OF TARGETED THERAPIES
Oct 25, 2008 - Oct 25, 2008,
Renaissance Dallas Hotel Dallas, Texas United States
Email address: cme@pergrouplp.com
Event website: http://www.cancerconferences.com/multi_disease/nursephysician_symposium/
Phone: (888) 949-0045, Fax: (214) 367-3305