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HIGHLIGHTS FROM THE INTERNATIONAL CONFERENCE ON NEW DEVELOPMENTS IN DRUG DISCOVERY FROM NATURAL PRODUCTS AND TRADITIONAL MEDICINES

NATURAL PRODUCTS AND TRADITIONAL MEDICINES: OLD KEYS FOR NEWER PATHOLOGIES

A. Kuhad, K. Chopra

Pharmacology Research Laboratory, University Institute of Pharmaceutical Sciences, UGC Center of Advanced Study, Panjab University, Chandigarh-160 014, India. Correspondence: dr_chopra_k@yahoo.com; anurag_pu@yahoo.com

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ABSTRACT

The International Conference on New Developments in Drug Discovery from Natural Products and Traditional Medicines (DDNP-TM 2008) was held on November 16-20, 2008 at the National Institute of Pharmaceutical Education and Research (NIPER), SAS Nagar (Punjab), India. The event focused on the discovery of new biological pathways, novel chemical entities as lead scaffolds, phytopharmaceuticals, nutraceuticals and functional foods, infectious diseases, lifestyle and metabolic disorders, oncological, inflammatory and immunological disorders, marine natural products, the synthesis of bioactive molecules, traditional medicines and in silico approaches. This conference provided an excellent platform for the networking of international and national researchers and the pharmaceutical industry to reap benefits from Mother Nature's Combi-Lab.

INTRODUCTION

Natural products have long been regarded as the mainstay of drug discovery programs. India, with its rich biodiversity and millenarian traditional medicine system of Ayurveda, offers a unique opportunity for drug discovery from natural sources. In the past few decades, the scientific community has focused on the mechanistic evaluation of the multiple activities of natural molecules. Prof. K.K. Bhutani, Head, Department of Natural Products, NIPER, organized the International Conference on New Developments in Drug Discovery from Natural Products and Traditional Medicines (DDNP-TM 2008) in November of last year at the National Institute of Pharmaceutical Education and Research (NIPER), SAS Nagar (Punjab), India. Prof. Harkishan Singh, NIPER visionary, and Prof. Sukhdev Singh, Visiting Professor, B.R.A. Centre for Biomedical Research, were guests of honor. More than 500 delegates from different regions of the world attended the conference to share their new ideas, build networks and foster friendships. There were around 10 exhibition booths for showcasing new products and recent technologies developed by leading companies.

Prof. Sukh Dev gave an overview on the traditional system of Ayurvedic medicine. Five thousand years ago in the magnificent Himalayas, one of the greatest sages of India, Srila Vyasadeva, wrote down the Vedas for the first time, which included a branch called Ayurveda, or "the science of life" ("Ayur" means life and "Veda" means science). The Vedas came from an oral tradition that reached back into antiquity. Srila Vyasadev entrusted the original copies of the texts to his most erudite and enlightened disciples, who, along with other great sages, inaugurated a very long sacrificial ceremony for hundreds of years for the purification and blessing of the entire world. During that time, they studied and discussed these ancient texts with their own disciples, who wrote commentaries and expanded and developed the original and eternal truths without altering them. During the years after the conclusion of this sacrifice, copies of these perfect Vedic texts were placed in various temples and libraries throughout India. They were written down in the original Sanskrit language for the benefit of the general population. (Sanskrit is the father of Latin and most of the world's languages.) (1).

As far as the science of life –Ayurveda— was concerned, volumes of wisdom poured forth like the rains during the monsoon season. Besides Vyasadeva's information about hundreds of herbal drugs in

the Vedas, there were subsequent descriptions by other sages like Sushruta and Charaka on how to perform prosthetic surgery to replace limbs, cosmetic surgery on the nose and elsewhere, cesarean section, and even brain surgery. Everything was described in great detail and archeological research has uncovered evidence that proves that some of these operations were performed successfully between 3,000 and 5,000 years ago. The great sage Charaka provided information in Ayurveda about the development of the child within the womb week by week, month by month, limb by limb, from conception to birth, which equals our modern medical texts in accuracy.

There is information about atomic energy, gynecology, pediatrics, surgery, anatomy, herbal drugs, Ayurvedic dieting and nutrition. All are described in the most simple and profound manner so as to make it easy to obtain a basic working knowledge of this great science of life – Ayurveda. We know this sounds incredible and you may be wondering: How is it possible to have one system embrace all systems? How would it be applied? The answer is simple. The first step is to ascertain the individual's "biological mode" and then treat the person accordingly (1).

SCIENTIFIC TOPICS

Approximately 10 different scientific aspects of natural product-based drug discovery were discussed in 18 plenary lectures, 33 invited lectures, 22 oral and 172 poster presentations. Various reports were presented on natural herbs, marine natural products, phytopharmaceuticals, nutraceuticals and functional foods that promoted health and attenuated or delayed the onset of several disorders, including infectious diseases, cancer, immunological, lifestyle and metabolic disorders (Table I). The deliberations of the conference were focused on drug discovery aspects of both natural products and traditional medicine, with the objective of developing modern medicines for health benefits.

Novel chemical entities as lead scaffolds

Dr. Bhutani indicated in his welcome note that, in spite of past success in new chemical entity (NCE) generation from natural products for drug discovery and development, there has been a decrease in the generation of NCEs by pharmaceutical companies. This decrease could be reversed if researchers embrace traditional medicines with an open mind. Drug discovery and development from natural products must take into account the full spectrum of traditional knowledge and requires conducting research in two basic forms: the discovery of NCEs from plants and the development of marketable formulations based on traditional medicine formulae. Pharmaceutical companies base their discovery of new drugs on NCEs only. Expectations of low toxicity in humans for plants used traditionally are not unreasonable, as these plants have been thoroughly tested over the ages. Natural products with higher molecular weights and rotatable bonds with stereogenic centers are more readily absorbed compared to synthetic drugs (2).

Bioprospecting is another strategy for effective and economical drug discovery. It is currently estimated that of a total of approximately 420,000 plant species that exist in nature, over 248,000 species of higher plants have been identified, and of these, 12,000 plants are known to have medicinal properties. However, less than 10% of all plants have been investigated from a phytochemical or pharmacological point of view. A total of 11,145 medicinal plants are found in India and China, but only a very small number have been systematically investigated. Therefore, many traditionally used and chemically less investigated plants can be exploited for a rich pool of new active compounds for drug discovery programs. However, there are many pressing issues, such as sustainable development taking into account the supply and demand for new raw materials, and stability and safety issues that require attention for the development of traditional medicines. From India, three drugs have qualified based on their mode of action: flavopiridol, forskolin and guggulsterone. The Food and Drug Administration (FDA) in the U.S. and the Committee on Herbal Medicinal Products (CHMP) in Europe have introduced a simplified registration protocol for traditional herbal medicinal products. The FDA has been reluctant to approve multiple-agent drugs until recently in 2006, when the first such drug, sinecatechins (MediGene), a topical antiviral composition prepared from catechins extracted from green tea (*Camellia sinensis*), was approved.

Marine natural products

Various presentations focused on cyanobacteria, which create a fascinating diversity of natural product structures using an equally fascinating diversity of biosynthetic enzymes. Marine cyanobacteria are an exceptionally rich source of novel peptide and integrated peptide/polyketide-type natural products. Many of these natural products are potentially toxic to mammalian cells, and this has furthered exploration as a source of new anticancer lead compounds. Marine natural products that are in clinical and advanced preclinical trials as anticancer agents include bryostatin, ecteinascidin, discodermolide and E-7389. Cyanobacterial secondary metabolites also have anti-inflammatory and antimicrobial properties (3).

Methods and techniques

The discovery of newer methods and techniques has paved the way for new drug discovery. Nowadays, the concept of "differential smart screens", which entails screening extract activities against pairs of receptor sites, is applied. The comparison of the ratios of the binding affinity for the two receptor sites for a known selective ligand and for an extract helps to predict which extracts contain components with the best activity. This technique is gaining attention, as the screening of well-defined compounds is time-consuming and expensive. However, this technique is applicable for a limited number of targets. With the help of antisense RNA techniques, a large number of therapeutic targets are being discovered. The discovery and characterization of the novel antibiotics platensimycin and platencin were done using a combination of whole-cell screens and antisense technology. Another approach termed "chemical genetics profiling" uses a panel of yeast strains with selective mutations that highlight sensitivities to particular drugs. A database is created which records the activities of a wide range of known compounds, whereby it is possible to investigate mixtures of compounds or drugs with known mechanisms. Stichloroside and theopalauamide, two structurally unrelated compounds that would not have been expected to act via the same biological target, have been discovered using this technique. More recently, a metagenomics approach has been used to access a wider range of synthetic capabilities from bacteria. This

Table I. *A comprehensive summary of studies on natural products presented at DDNP-TM 2008.*

Ref.	Natural intervention/dose	Study design	Outcome
7	*Murraya koenigii*/ 200 mg/kg p.o. for 30 days	Assessment of antidiabetic and antioxidant activity in streptozotocin (STZ)-induced diabetic rats	Presence of biologically active ingredients such as alkaloids, flavonoids, triterpenoids, glycosides and phenolic compounds responsible for antihyperglycemic and antioxidant activity
8	Luteolin/1.2 mg/kg p.o. for 3 weeks	Effect on the status of drug-metabolizing enzymes on azoxymethane-induced colon cancer in BALB/c mice	Reduction in phase I metabolizing enzymes and enhanced phase II metabolizing enzymes along with increased expression of glutathione *S*-transferase α and μ
9	Astaxanthin/ 25 mg/kg p.o. for 16 weeks	Chemopreventive effect against 1,2-dimethylhydrazine-induced experimental colon carcinogenesis	Increased enzymatic and nonenzymatic antioxidant activity, decreased lipid peroxidation, inhibited COX-2 expression
10	Morin/500 ppm b.i.d. for 13 weeks	Effect on DMBA-induced mammary carcinoma	Morin alleviates mammary carcinogenesis by modulating membrane damage and protecting against oxidative damage-induced DNA fragmentation by scavenging free radicals generated by DMBA
11	*Ocimum sanctum*/ 100 mg/kg p.o. for 16 weeks	Effect on DMBA-induced lung cancer	*O. sanctum* extract treatment prevented weight loss in mice with neoplasia, accompanied by decrease in lung tumor count and decrease in serum tumor markers
12	Epigallocatechin-3-gallate/ 20 mg/kg p.o. for 28 days	Effect on bleomycin-induced experimental pulmonary fibrosis	Epigallocatechin-3-gallate supplementation restored lipid peroxidation, myeloperoxidase, hydroxyproline, iNOS, NF-κB, TNF, IL-1β & IL-6 activity
13	Apigenin	Cytotoxic effect of apigenin against *Leishmania donovani* (therapeutics for Kala-azar)	Produced programmed cell death in the promastigote form of *L. donovani*
14	Diallyl sulfide/ 100 mg/kg i.p. for 7 days	Effect on cisplatin-induced nephrotoxicity	Diallyl sulfide prevented lipid peroxidation, restored enzymatic and nonenzymatic antioxidant levels, inhibited NF-κB & COX-2 expression
15	Siddha medicinal plant	Indoleamine 2,3-dioxygenase-inhibitory activity	Plants from Sapindaceae family identified as potent inhibitors of indoleamine 2,3-dioxygenase activity
16	*Diospyros lanceifolia, Nephrolepis cardifolia, Sarcandra glabra, Begonia picta*	Biological activity against *Escherichia coli, Staphylococcus aureus & Pseudomonas aureus*	Ethanolic extracts & fractions of the roots of *D. lanceifolia* (plumbagin & 7-methyljuglone) showed significant activity against *E. coli & S. aureus*; tubers of *N. cordifolia* showed some activity against *S. aureus*
17	*Rumex nepalensis* Spreng	Identification of antioxidant compounds. The fractionation of ethyl acetate extract resulted in isolation of anthraquinones chrysophanol, physcion, emodin, chrysophanol-8-*O*-β-D-glucopyranoside and naphthalene derivatives nepodin and nepodin-1-*O*-β-D-glucopyranoside	Nepodin showed 85% inhibition of DPPH radical-scavenging activity, with an IC_{50} of 11.67 μM. Nepodin has better antioxidant activity compared to trolox (IC_{50} = 15.72 μM)
18	*Vitex negundo*/ 125, 250 & 500 mg/kg p.o.	Anticonvulsant activity against maximal electroshock (MES) seizures and pentylenetetrazol (PTZ)-induced seizures	*V. negundo* oil (α-humulene) at doses of 250 mg/kg and above suppressed tonic MES-induced convulsions and mortality. However, all doses of oil suppressed PTZ-induced convulsions and mortality without producing any sedation and motor impairment
19	*Helicteres isora*	In vitro antioxidant activity against nitric oxide and DPPH-inhibitory activity; antimicrobial activity against *E. coli, S. aureus & Candida albicans*	*H. isora* had potent antioxidant and antimicrobial activity
20	*Sesbania grandiflora*/ 200 & 400 mg/kg p.o.	In vitro antioxidant and in vivo anti-inflammatory activities evaluated	Methanolic and hydroalcoholic extracts showed significant antioxidant activity in nitric oxide- and DPPH-inhibitory assays. Hydroalcoholic extract significantly inhibited inflammation in carrageenan-induced paw edema & cotton pellet-induced granuloma pouch models

Continued

Table I (Cont.). *A comprehensive summary of studies on natural products presented at DDNP-TM 2008.*

Ref.	Natural intervention/dose	Study design	Outcome
21	Lycopene/1, 2 & 4 mg/kg p.o. for 4 weeks	Evaluated the effect of lycopene on renal function and reno-inflammatory cascade in STZ-induced diabetes	After 8 weeks of STZ injection, rats showed marked disruption of renal function, increased oxidative-nitrosative stress, cytokines, caspase-3 activity in cytoplasmic lysate and NF-κB in nuclear lysate of kidneys. Interestingly, coadministration of lycopene significantly and dose-dependently prevented biochemical and molecular changes associated with diabetes. Moreover, diabetic rats treated with insulin-lycopene combination showed a more pronounced effect on molecular parameters compared to their per se groups
22	2-(Un)substituted-3-amino-5-aryl-6-benzylpyrazolo[3,4-*d*]pyrimidin-4-(5*H*)-ones/2.5, 5 & 10 mg/kg i.p.	2-(Un)substituted-3-amino-5-aryl-6-benzylpyrazolo-[3,4-*d*]pyrimidin-4-(5*H*)-ones were synthesized by condensation of 2-benzyl-3-aryl-5-cyano-6-thiomethylpyrimidin-4(3*H*)-ones independently with hydrazine hydrate/phenyl hydrazine in the presence of dimethylformamide and catalytic amounts of anhydrous potassium carbonate, and analgesic activity was evaluated	2-(Un)substituted-3-amino-5-aryl-6-benzylpyrazolo[3,4-*d*]pyrimidin-4-(5*H*)-ones exhibited good analgesic activity in the hot plate test and against acetic acid-induced writhing, and phenyl substitution at the 2-position was favorable for analgesic activity
23	*Anethum graveolens, Foeniculum vulgare, Trachyspermum ammi, Elettaria cardamomum, Viola adorata*	Antibacterial and phytochemical evaluation	Gram-positive bacteria showed greater sensitivity compared to Gram-negative bacteria (MIC 2-8% [aqueous] & 0.5-1.5% [acetone]. Quantitative analysis showed presence of alkaloids (1.1-4.23%), flavonoids (3.5-15.8%) & saponins (0.5-0.7%)
24	*Gardenia gummifera*/10-50 mg/mL	In vitro anthelmintic activity	Petroleum ether, ethyl acetate and methanol fractions were evaluated against *Pheretima posthuma*. The test extracts induced paralysis and also death of worms even at a concentration of 10 mg/mL
25	*Madhuca latifolia*/100-500 µg/mL	In vitro antioxidant activity using DPPH assay	The extract showed antioxidant activity with an IC_{50} value of 61.30 µg/mL
26	*Caesalpinia digyna*	In vitro antimycobacterial activity against *Mycobacterium smegmatis* (ATCC 14468)	The crude methanolic extract showed weak inhibition of *M. smegmatis* (MIC = 512 µg/mL), whereas fraction B (eluted with 10% methanol) showed significant antimycobacterial activity (MIC = 64 µg/mL). Fraction B contains four homoisoflavonoids (eucomine, bonducellin, dihydobonducellin & intricatinol), two isoflavonoids (genistein & daidzein) and two flavonoids (eriodictyol & quercetin)
27	*Coleus forskohlii*	In vitro anti-HIV activity	Chloroform, ethyl acetate and butanol extract showed 58%, 38% & 0% inhibition, respectively, of p24 antigen in CEM-GFP cells infected with HIV-1
28	Morin/500 mg/kg p.o. for 16 weeks	Evaluated against diethylnitrosamine (DEN)-induced liver carcinogenesis	Morin-induced apoptosis in DEN-treated rats was confirmed by DNA fragmentation, caspase-3 and -9, Bcl-2, Bax, NF-κB p65 subunit
29	*Morindia citrifolia*/ 10% p.o. for 1 month	Evaluated against DEN-induced liver carcinogenesis	Decreased lipid peroxidation, increased antioxidant enzyme activity in both liver and serum of DEN-treated rats
30	*Clitoria ternatea*/2.5-10 mg/mL	In vitro antioxidant and antimicrobial activity	Moderate antifungal activity against *C. albicans* (50-55% inhibition) was observed at 10 mg/mL
31	*Casuarina equisitifolia*/ 200 & 400 mg/kg p.o.	Evaluated against CCl_4-induced hepatotoxicity	*C. equisitifolia* restored serum transaminases, alkaline phosphatase, total protein, albumin, triglyceride, glucose and cholesterol levels
32	*Mangifera indica*/600-1200 µg/disk	Antibacterial activity against some clinically isolated bacteria	*M. indica* showed potent antibacterial activity

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Table I (Cont.). *A comprehensive summary of studies on natural products presented at DDNP-TM 2008.*

Ref.	Natural intervention/dose	Study design	Outcome
33	*Polyalthia longifolia*/ 540-3240 mg/kg p.o.	Acute toxicity of methanolic extract of *P. longifolia* evaluated per OECD guidelines	No deaths, no reduction in body weight or changes in biochemical parameters were observed after 14 days, indicating that *P. longifolia* is safe up to 3240 mg/kg
34	*Calotropis gigantae*	In vitro antifilarial activity studied on spontaneous movements of the whole worm and nerve muscle complex of *Setaria cervi*	Alcoholic extract caused inhibition of spontaneous movements of the whole worm and nerve muscle complex
35	*Murray paniculata*/ 150 & 300 mg/kg p.o. for 3 weeks	Antioxidant activity against STZ-induced oxidative stress	A dose of 300 mg/kg produced significant reductions in TBARS and hydroperoxides both in liver and kidney. GPx, catalase and GSH activities were also restored
36	Diapal tablets (Neem, Turmeric, Fenugreek, Arjun, Triphala, etc.)	Repeated-dose (250 mg/kg) oral toxicity study in rats for 90 days	No mortality, no change in physical, hematological and biochemical parameters
37	*Anacardium occidentale*	Aqueous, ethanolic and petroleum ether extracts evaluated for in vitro antioxidant activity in Griess and DPPH assays	IC_{50} values for dried aqueous & ethanolic extracts were found to be 658.3 and 1002.3 µg/mL, respectively
38	*Butea monosperma*/ 100 & 200 mg/kg	Evaluated hepatoprotective activity against CCl_4-induced hepatotoxicity	Restored liver function test and biochemical parameters
39	*Ichnocarpus frutescens*/ 100-300 mg/kg p.o.	Antioxidant and anti-inflammatory activities evaluated	A dose of 100 mg/kg produced 54.63% inhibition of carrageenan-induced paw edema whereas 300 mg/kg produced 22.64% inhibition of granuloma formation in the cotton pellet-induced granuloma pouch model
40	*Ruta graveolens*	Anticonvulsant activity against PTZ- and electrically induced convulsions	Treatment significantly delayed onset and reduced duration of seizures
41	*Arisaema leschenaultia*	In vitro antioxidant activity evaluated in DPPH assay	IC_{50} value was 20 µg/mL compared to 28 µg/mL for BHT
42	Punarnavashtak kwath/ 100 mg/kg p.o. for 45 days	Evaluation of hepatoprotective activity	Significantly restored physical, biochemical and histopathological changes
43	Jeevanti/300 mg/kg p.o.	Evaluation of anti-inflammatory activity and mechanism of action of Jeevanti (*Leptadenia reticulata, Dendrobium macraei & Marsdenia volubilis*)	Methanol extract produced anti-inflammatory effect in the carrageenan-induced paw edema model along with in vivo antioxidant activity. In vitro studies indicated involvement of cyclo-oxygenase pathway
44	*Sphaeranthus indicus*	Antiasthamatic activity evaluated	Inhibited oxidative stress, inflammation and other hematological parameters in histamine- and ovalbumin-induced bronchospasm
45	*Celosia argentea*	Anticancer activity evaluated	Mitotic index was reduced from 95 to 69 after 1 h and to 64 after 3 h
46	*Solanum xanthocarpum*/ 200 & 300 mg/kg p.o.	Mechanism of anti-inflammatory activity studied	Found to be a mast cell stabilizer against compound 48/80 (potent mast cell degranulator)
47	*Boerhaavia diffusa*	Cytotoxic activity evaluated against HeLa cells	Produced 70% cell death at 300 µg/mL and 40% cell death at 200 µg/mL
48	*Acacia catechu*/200 mg/kg	Anticarcinogenic activity evaluated	Methanolic extract inhibited the growth of KB cells by 83%, U-87 MG cells by 73%, HeLa cells by 66%, MCF7 cells by 63% and NCL-H46 cells by 58% at a concentration of 200 µg/mL
49	*Tepheosia purpurea*	Hypoglycemic and antidiabetic effects of alcoholic, aqueous & petroleum ether extracts	Alcoholic extract produced significant decrease in normal blood glucose levels; alcoholic and water extracts significantly decreased fasting blood glucose levels in diabetic rats
50	*Mimosa pudica*	Study of anti-inflammatory and analgesic properties	Showed anti-inflammatory and analgesic activity in carrageenan-induced paw edema and tail flick tests, respectively
51	*Bauhinia variegate, Bidens chinensis, Mimosa pudica, Moringa oleifera, Ricinus communis, Tinospora cordifolia*	Antimycobacterial activity studied against *M. smegmatis* (ATCC 14468)	*B. variegate, M. oleifera, R. communis, T. cordifolia* showed significant antimycobacterial activity compared to isoniazid

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Table I (Cont.). *A comprehensive summary of studies on natural products presented at DDNP-TM 2008.*

Ref.	Natural intervention/dose	Study design	Outcome
52	*Coccinia indica*/25-300 mg/kg p.o.	Investigation of anti-inflammatory (carrageenan-induced paw edema) and analgesic (tail flick test) effect	A dose of 200 mg/kg produced 78% inhibition of carrageenan-induced paw edema. A dose of 300 mg/kg produced greater analgesic effect than ibuprofen, which is comparable to morphine
53	*Solanum xanthocarpum*	In vitro proinflammatory cytokine- and nitric oxide-inhibitory effects	Ethyl acetate and methanol extracts showed good inhibitory effect on proinflammatory cytokines, e.g., TNF-α, IL-1β and NO production, in RAW 264.7 cells stimulated by lipopolysaccharide in vitro
54	*Pterocarpus santalinus*/ 100, 250 & 500 mg/kg p.o.	Analgesic, anti-inflammatory and antioxidant activity	Produced dose-dependent central and peripheral analgesic and anti-inflammatory effects; in vitro antioxidant effect at 500 µg/mL
55	*Thespesia populnea*/ 400 mg/kg p.o.	Antihistaminic activity	Significant activity was observed (ethanolic extract) against histamine-induced bronchospasm in guinea pigs and systemic anaphylaxis in rats, and significant protection against mast cell degranulation
56	Lycopene/10 mg/kg p.o. for 5 days	Investigation of anti-ischemic activity in hepatic ischemia–reperfusion injury	Restored liver function, prevented lipid peroxidation and normalized tissue antioxidant level
57	Methi, *Boswellia serrata, Acacia catechu*	Antiarthritic effect	In a model of arthritis, combination of the three drugs exhibited 48.75% inhibition and combination of two drugs such as Methi & *B. serrata, A catechu & B. serrata* and Methi & *A. catechu* exhibited 44.58%, 36.25% and 29.16% inhibition, respectively, of paw edema after 21 days
58	*Wrightia tinctoria*/ 200-400 mg/kg p.o.	Immunomodulatory effect on cellular (delayed-type hypersensitivity reaction) and nonspecific immunity (carbon clearance assay)	Produced dose-dependent increase in the rate of carbon clearance, as well as phagocytic activity
59	*Lepidium sativum*/ 50, 100 & 200 mg/kg p.o.	Antidiarrheal activity evaluated in castor oil-induced diarrhea, prostaglandin E_2-induced enteropooling in rats and charcoal meal test in mice	Showed significant and dose-dependent reduction in cumulative wet fecal mass, PGE_2-induced secretions and decreased movement of charcoal, indicating antimotility activity
60	*Dolichos lablab*/ 400 & 800 mg/kg p.o.	Analgesic and anti-inflammatory activity	Showed mild analgesic activity in hot plate test and significant inhibition of paw volume in carrageenan-induced paw edema model
61	*Borassus flabellifer*	Antidiabetic effect of alcoholic and aqueous extracts of *B. flabellifer* evaluated	Improved glucose tolerance in oral glucose tolerance test in normal, alloxan-induced and dexamethasone-induced diabetic rats
62	*Cedrus deodara*/ 200 & 400 mg/kg p.o.	Hypoglycemic and antidiabetic activity	Petroleum ether, alcoholic and aqueous extracts showed significant reduction in fasting blood glucose level, as well as after glucose (2 g/kg) loading
63, 64	*Thespesia populnea*/ 1, 3 & 10 mg/kg p.o. *Spathodia companulata*/ 50, 100 & 200 mg/kg p.o.	Antidiarrheal activity of precipitate of residual fraction of aqueous extract	Showed significant, dose-dependent reduction of cumulative wet fecal mass in castor oil-induced model, inhibition of PGE_2-induced secretions and decreased movement of charcoal in charcoal meal test
65	Bis(gingenrolinato) oxovanadium/ 6, 12 & 24 mg/kg p.o.	Antidiabetic evaluation	Produced dose-dependent reduction in plasma glucose, serum triglycerides, cholesterol and LDL, and increased liver glycogen and HDL

involves sampling the entire bacterial DNA from an environmental sample and cloning the DNA in host organisms such as *Escherichia coli*. These recombinant bacteria are cultured and tested for the expression of bioactive metabolites. The metagenomics approach has led to the discovery of novel compounds, the turbomycins, with antibacterial activity (2).

Phytopharmaceuticals

Natural plant products, or Nature's combinatorial library, have a long history of providing drugs, especially anticancer drugs; 61% of all the new drugs introduced worldwide during 1981-2002 can be traced to or were inspired by natural products. Plant-derived clinically used anticancer agents include vinblastine, vincristine, etopo-

side, teniposide, paclitaxel, docetaxel, topotecan and irinotecan. Natural products are more drug-like than most synthetic compounds, demonstrating both by statistical and various other analyses the importance of natural products as pharmaceuticals (4).

Inflammatory and immunological disorders

Dr. Bharat B. Aggarwal explained the pathological role of inflammation in numerous diseases through activation of nuclear factor NF-kappa-B (NF-κB) and STAT3. Phytochemicals that suppress inflammation mediated through these pathways may be useful as therapeutics for these disorders (5).

Natural products in vaccine adjuvant discovery

Dr. Manish Gautam reported that, despite two centuries of vaccine use, very few adjuvants are licensed for human use. Alum is not always the appropriate choice due to its limitations in engaging cellular immunity. With the discovery of QS-21 and MPL there is resurgent interest in the chemical diversity offered by natural products for the discovery of newer adjuvants. The herbal extract SIIL-3 potentiated diphtheria-neutralizing antibody titers and interferon gamma/IL-4 ratios, ensuring higher survival rates even with higher dilutions of diphtheria vaccine, suggesting immunoadjuvant potential. Under immunocompromised conditions, SIIL-3, in contrast to alum, resulted in significant recovery of CD4/CD8 counts, interferon gamma/IL-4 ratios and antigen-specific responses. SIIL-3 is being explored for its potential as a safe, effective and economical vaccine adjuvant (6).

CONCLUSIONS

No single healthcare system provides solutions to all health problems. Therefore, the world is moving towards "medical pluralism" to embrace the unmet health needs of society. Research inputs to provide a scientific basis for Ayurveda are needed in order to provide unique advantages for the pharmaceutical industry for enhancing drug discovery programs in India, as well as abroad.

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REFERENCES

1. Dev, S. *Ayurveda material medica: A treasure trove of biologically active molecules.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, 6-18.
2. Bhutani, K.K. *International Conference on Newer Developments in Drug Discovery from Natural Products and Traditional Medicine - An overview.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, 1-5.
3. Gerwick, W., Byrum, T., Carland, T. et al. *Integrating chemical and biochemical approaches to natural products drug discovery from marine cyanobacteria.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, 33-43.
4. Kingston, D.G.I., Cao, S., Hou, Y. et al. *Biodiversity conservation and drug discovery: Can they be combined?* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, 19-32.
5. Aggarwal, B.B., Danda, D., Bokyung, S. *Targeting inflammatory pathways for prevention and treatment of chronic diseases by phytopharmaceuticals derived from traditional medicine.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, 56-65.
6. Gautam, M., Mishra, S., Patil, D. et al. *Natural products in vaccine adjuvant discovery.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst OP-18.
7. Arulselvan, P., Subramanian, S. *Assessment of antidiabetic and antioxidant nature of Murraya koenigii leaves extract in streptozotocin-induced diabetic rat model.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-1.
8. Kumar, P.A., Sudhandiran, G. *Luteolin upregulates glutathione-S-transferases-α and μ on azoxymethane-induced colon carcinogenesis.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-2.
9. Nagendraprabhu, P., Kumar, P.A., Sudhandiran, G. *Chemopreventive efficacy of astaxanthin, a dietary carotenoid, against 1,2-dimethyl hydrazine induced experimental colon carcinogenesis.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-3.
10. Kumar, R.N., Raja, S.B., Sivaramakrishnan, V., Devaraj, S.N. *Mitigation of 7,12-dimethylbenz(a)anthracene induced mammary carcinoma by morin.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-4.
11. Kumar, V.R.P., Sivaramakrishanan, V., Devaraj, S.V. *Antineoplastic effect of Ocimum sanctum Linn against benzo(a)pyrene induced lung cancer - An in vivo study.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-5.
12. Sriram, N., Kalayarasam, S., Sudhandiran, G. *Epigallocatechin-3-gallate, a green tea polyphenol, abrogates inflammation during bleomycin-induced experimental pulmonary fibrosis.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-6.
13. Kumar A.S., Sudhandiran, G. *Apigenin, a dietary flavonoid, increases reactive oxygen species and induces apoptosis in Leishmania donovani promastigotes.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-7.
14. Kumar, J.A., Mani, V.M., Kalayarasan, S., Sriram, N., Sudhandiran, G. *Antioxidant and anti-inflammatory effect of diallyl sulphide, against cisplatin induced nephrotoxicity in Wistar rats.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-8.
15. Kuzhiumparambil, U., Ramakrishnan, V., Kohen, J., Vemulpad, S., Jamie, J. *Indoleamine 2,3-dioxygenase inhibitory activity of Siddha medicinal plant.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India), 2008, Abst PP-11.
16. Meyanungsang, Jamie, J., Vemulpad, S., et al. *Studies on ethanomedicinal plants of Nagaland and their phytochemical analysis.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-12.
17. Gautam, R., Karkhile, K.V., Bhutani, K.K., Jachak, S.M. *Identification of antioxidant compounds from roots of Rumex nepalensis Spreng*. Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-13.
18. Saneja, A., Lal, S., Jain, S. *Evaluation of anticonvulsant activity of the essential oil of fruits of Vitex negundo.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-15.
19. Itankar, P.R., Pathak, R.S., Patil, A.T. *Evaluation of antioxidant and antimicrobial potential of Helicteres isora Linn. leaves.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-16.
20. Itankar, P.R., Arora, S.K., Patil, A.T. *Phytochemical study, isolation of active constituents and evaluation of antiinflammatory and antioxidant activity*

of Sesbania grandiflora Linn. Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-17.

21. Kuhad, A., Bishnoi, M., Chopra, K. *Lycopene, a potent carotenoid ameliorates diabetic nephropathy in rats.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-18.
22. Baheti, K.G., Ganorkar, S.B., Yewale, S.B., Dehghan, M.H., Modani, S. *Synthesis and analgesic activity of 2-(un)substituted-3-amino-5-aryl-6-benzylpyrazolo[3,4-d]pyrimidine-4-(5H)-ones.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-19.
23. Kaur, G.J., Arora, D.S. *Antibacterial and phytochemical evaluation of some traditional medicinal plants.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-21.
24. Kamble, M.A., Itankar, P.R., Patil, A.T. *In-vitro antihelminthic activity of Gardenia gummifera gum extract.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-22.
25. Jaiswal, A.R., Jatav, C.P., Itankar, P.R., Patil, A.T. *Antioxidant activity of alcoholic extracts of Madhuca latifolia flowers.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-23.
26. Agrahari, U.C., Srivastava, A., Lechner, D., Bucar, F., Jachak, S.M. *Phytochemical investigation on Caesalpinia digyna Rottl. and evaluation of antimycobacterial activity in vitro.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-27.
27. Bodiwala, H.S., Sabde, S., Mitra, D., Bhutani, K.K., Singh, I.P. *Anti HIV diterpenes from Coleus forskohlii.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India), 2008 Abst PP-30.
28. Sivaramakrishnan, V., Niranjali, D.S. *Amelioration of cellular liver carcinogenesis and modulation of apoptosis mediated by morin.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-31.
29. Kumar, P.M., Niranjali, D.S. *Protective effects of Indian Morinda citrifolia against DEN (N-nitrosodiethylamine) induced hepatic injury in male Wistar rats.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-32.
30. Panda, R.K., Itankar, P.R., Patil, A.T. *In-vitro antioxidant and antimicrobial activity of leaf and root extract of Clitoria ternatea Linn.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-33.
31. Vaghasiya, Y., Parekh, J., Chanda, S. *Evaluation of hepatoprotective effect of Casuarina equisitifolia Linn on carbon tetrachloride induced toxicity in rats.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-34.
32. Vaghasiya, H., Vaghasiya, Y., Chanda, S. *Antibacterial activity of methanol extract of Mangifera indica Linn seeds against some clinically isolated bacteria.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-35.
33. Dave, R., Vaghasiya, Y., Shukla, V., Chanda, S. *Acute oral toxicity of methanolic extract of Polyalthia longifolia var. pendulla leaf in Wistar albino rats.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-36.
34. Rizvi, W., Kumar, A., Kumar, R. *In-vitro antifilarial activity in alcoholic extract of leaves of Calotropis gigantea Linn.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-37.
35. Ojha, S.K., Rao, C.V., Kumar, M.V. *Action of Murraya paniculata against streptozotocin-induced oxidative stress.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-42.
36. Nidhiya, I.S.R., Tatke, P., Despande, S.G. *Repeated dose oral toxicity study of an antidiabetic herbal formulation in rats.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-47.
37. Jaiswal, Y.S., Tatke, P.A., Vaidya, A. *Antioxidant activities of various extracts of leaves of Anacardium occidentale.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-49.
38. Gupta, A., Pandey, S., Surana, V., Shah, D.R., Maithili, V. *Evaluation of hepatoprotective activity of bark Butea monosperma Lam. Taub.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-51.
39. Pandurangan, A., Khosa, R.L., Hemalatha, S. *Evaluation of anti-inflammatory and antioxidant activity of Ichnocarpus frutescens root.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-57.
40. More, R., Gadgoli, C. *Studies on anticonvulsant activity of Ruta graveolens.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-67.
41. Gunde, M.C., Pathak, A.K., Amnerkar, N.D. et al. *Phytochemical investigation and in vitro evaluation of Arisaema leschenaultia Blume extracts for antioxidant property.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-73.
42. Shah, V., Doshi, D., Shah, M., Bhatt, P. *Evaluation of hepatoprotective activity of classical ayurvedic formulation punarnavashtak kwath against ethanol induced hepatotoxicity in rats.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-82.
43. Prajapati, C., Shah, B., Kapadia, N., Shah, M., Santani, D.D. *Evaluation of anti-inflammatory activity and mechanism of action of jeevanti: Leptadenia reticulata, Dendrobium macraei and Marsdenia volubilis.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-83.
44. Shah, U., Prajapati, M., Saluja, A., Shah, M., Shah, S. *Antiasthmatic activity of methanolic extract of Sphaeranthus indicus.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-84.
45. Rukhsana, A.R., Shubhashri, M., Nirmal, S., Ayesha, S. *Evaluation of anticancer activity of aerial parts of Celosia argentea Linn.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-90.
46. Karkare, V.P., Parmar, S.K., Gangwal, A., Sanandia, J.R., Sheth, N.R. *Membrane stabilizing activity a possible mechanism of action for the anti-inflammatory activity of Solanum xanthocarpum.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-93.
47. Srivastava, R., Dwarkanath, B.S., Saluja, D., Chopra, M. *Inhibition of cell proliferation and induction of apoptosis by Boerhaavia diffusa ethanolic root extract.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-98.
48. Alam, S., Tiwari, M. *Evaluation of the potential anticarcinogenic activity of the extracts of the extracts of the bark of Acacia catechu.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-99.
49. Kumar, R., Murugananthan, G., Joshi, N.C., Deep, P. *Hypoglycemic and anti-diabetic effects of Tepheosia purpurea root extracts.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-100.
50. Jadhav, V.D., Parameswaram, S. *Study of anticariogenic properties of Mimosa pudica roots.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-106.
51. Srivastava, A., Bairwa, K., Lechner, D., Bucar, F., Jachak, S.M. *Screening of some selected Indian medicinal plants for antimycobacterial activity in vitro.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-108.

52. Niazi, J., Goel, R.K., Bansal, Y. *Bioactivity guided fractionation of ethanolic extract of Coccinia indica and isolation of an anti-inflammatory and analgesic constituents.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-109.

53. Paul, A.T., Singh, A., Bhutani, K.K. *In vitro pro-inflammatory cytokine and nitric oxide inhibitory effects of Solanum xanthocarpum Schard and Wend.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-111.

54. Kumar, D., Singh, J., Rashmi, Yadav, N., Kaushik, D., Kumar, S. *Analgesic, anti-inflammatory and antioxidant activities of Pterocarpus santalinus.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India), 2008 Abst PP-121.

55. Patel, D.G., Patel, V.M., Patel, N.J., Patel, N. *Investigation of anti-histaminic activity of ethanolic extract of Thespesia populnea bark.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-123.

56. Patel, V.M., Tripathi, P., Patel, N.J., Patel, D.G. *Investigation of anti-ischemic activity of lycopene in hepatic ischemia reperfusion injury in rats.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-125.

57. Patel, N.G., Vyas, A.S., Panchal, A.H., Patel, R.K., Bhatt, C.J. *Anti-arthritic and vascular protective effect of methi, Boswellia serrate and Acacia catechu in combination and alone on arthritic rats.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-126.

58. Deep, P., Murugananthan, G., Thabah, P., Kumar, R. *Immunomodulatory effect of extracts of Wrightia tinctoria bark.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-129.

59. Manohar, D., Lakshman, K., Shylaja, H., Viswanatha, G.L., Rajesh, S., Nandakumar, K. *Antidiarrheal activity of methanolic extracts of seeds of Lepidium sativum.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-130.

60. Baig, Y., Maurya, V., Manohar, D., Lakshaman, K. *Phytochemical investigation and evaluation of leaves of Dolichos lablab for anti-inflammatory and analgesic activity.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-131.

61. Bhadala, S.L., Debnath, T., Srinath, R. *Anti-diabetic effects of root extracts of Borassus flabellifer.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-134.

62. Sharma, B., Raghav, P., Nandkumar, K. *Hypoglycemic and anti-diabetic activity of Cedrus deodara.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-135.

63. Reddy, S., Patel, B., Kumar, N.K. *Antidiarrhoeal activity of precipitate of residual fraction of aqueous extract of Thespesia populnea in laboratory animals.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-136.

64. Rajesh, S., Praveen, S., Divanji, M., Viswanatha, G.L., Shylaja, H., Nandkumar, K., Mukund, H. *Antidiarrheal activity of alcoholic and aqueous extracts of stem bark of Spathodia companulata in rodents.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-137.

65. Padhye, S.B., Takawale A.R., Ghaisas, M.M., Phanse, M.A., Dandavate, P.R. *Bis(gingenrolinato) oxovanadium (IV) attenuates diabetic alterations in alloxane diabetic rats.* Int Conf New Dev Drug Dis Nat Prod Trad Med (DDNP-TM) (Nov 16-20, India) 2008, Abst PP-143.