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### Guest Editor

**Dr. Deprasad Chattopadhyay**

**ICMR Virus Unit, Kolkata, India**



**Cover figures:** Scattered: Structures of different ethnomedicinal phytophores used for disease management.

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## The Guest Editor



Dr Debprasad Chattopadhyay did his Ph.D. in Pharmaceutical Microbiology from Jadavpur University, Kolkata in 1989 after his M.Sc. and then moved to London Hospital Medical College, London as a Visiting Fellow. After a brief training at London under Late Professor J.D. Williams and Dr Jette Elisabeth Kristiansen at Satens Serum Institute, Copenhagen he returned to India and joined the Indian Institute of Chemical Biology (CSIR), Kolkata and then in the Regional Medical Research Centre (Indian Council of Medical Research), Port Blair in 1993 as a Research Scientist. In 1997 he moved to ICMR Virus Unit, Kolkata, at which he is presently working as an Assistant Director (Scientist). He made significant contribution in public health research, particularly in antimicrobial drug development. His in depth studies on ethnomedicinal practices of the Onge, Nicobarese, and Shompen tribes of Andaman & Nicobar Island (by establishing personal relationship with them), help in recording the endemic, threatened and rare flowering plants of Bay Islands. Utilizing the tribal Knowledge-base, he has investigated the scientific basis of those medicaments and identified four herbal leads with antimicrobial, anti-inflammatory, antipyretic, antipsychotic and sperm motility-inhibiting activities. His group has purified and characterized a bioflavonoid that can inhibit the *in vitro* proliferation of *Plasmodium falciparum*, the agent of deadly malaria, and is highly effective against the chloroquine-resistant *P. falciparum* strain. His another contribution is the demonstration of antibacterial activity of methdilazine, a phenothiazine, that produce synergism with aminoglycoside antibiotics. This combination is useful in controlling bacterial resistance as methdilazine alters membrane permeability of bacteria thereby facilitate the entry of antibiotics within the bacterial cell. He has contributed more than 50 research papers, 5 chapters and 5 Review in highly prestigious International Journals like *Biotechnology Annual Review*, *Mini Review in Medicinal Chemistry*, *New Biotechnology* etc., and Books like *Modern Phytomedicine: Turning Medicinal Plants into Drugs*; *New Strategies Combating Bacterial Infection* (Wiley-VCH, Germany), *Evaluation of Herbal Medicinal Products: Perspectives of Quality, Safety and Efficacy* (Royal Pharmaceutical Press, Great Britain) etc. and is the editor of the reference book *Ethnomedicine, A Source of Complementary Therapeutics* (Research Signpost, India) and *Phytotherapy in Diabetes and Hypertension* (Bentham Science, USA). He is associated with 18 International peer reviewed Journals as Reviewer and Editorial Board Member of three Journals, published by Bentham Science, Elsevier Science, Global Science Book Publications, Academic Press etc. As Guest Faculty, Examiner, paper setter, Ph.D. guide he is attached with Universities like Jadavpur University, Kolkata; Aligarh Muslim University, Aligarh, Dr MGR University, Chennai etc. He has received awards from the Indian Association of Medical Microbiologists (1988), CSIR Research Associateship (1989-1992), Dr R.V. Rajam Medal from the Indian Association for the Study of Sexually transmitted Diseases & AIDS (1998), International Society of Chemotherapy (1991), Overseas Award from the World Conference on Dosing of Antiinfectives, Germany (2004), Professor Amiya Bose Oration Award from Indian Dietetic Association (2008 and 2009), Indian Science Communicator Award in 2<sup>nd</sup> Rastriya Vigyan Sancharak Sammelan 2009 by the Department of Science & Technology, Government of India. Dr Chattopadhyay also chaired the scientific session in the *International Conference on Drug Delivery and Drug Targeting Research*, Kolkata in 2008, and International conference on *Herbal Medicine Evaluation of Quality, Efficacy and Safety*, Bangalore in 2009. He is the member of different Selection Committee for Government funded research projects, and for the selection of teaching faculty of University and Colleges. He has four patents in his credit and handled several projects of national importance, including ethnomedicinal projects with grass root innovators.

## Foreword: Ethnomedicinal Phytophores

Evolution of primitive ancestors to modern human being across time represents a fascinating story in the parlance of biology. However, the journey was not trouble free. In our sustenance and perpetuation many odds like disease posed serious threat towards very survival. Many a times history has witnessed epidemics those led to loss of huge lives across continents, that impose high economic, social and psychological costs. Therefore, it was important to prevent diseases, maintain health and to restore the health of those who fall ill. Every human community responded to this challenge by developing a system for health care. Hence, the medicinal system reflects the interaction and synergy of social and cultural system. Since prehistoric times, human beings have found remedies within their habitat and have adopted different therapeutic strategies depending upon climatic, phytogeographic, floral and faunal characteristics as well as their cultural and socio-structural typologies. Traditional systems thus, contain beliefs and practices in order to avoid, prevent or avert ailments, which constitute traditional preventive medicine that are quite different from those of scientific medicine. The medicinal systems based on cultural framework have created a new discipline of “ethnomedicine”. Thus, *Ethnomedicine* (eth·no·med·i·cine/eth”no-med ĩ-sin) or ethnic medicine or “folk medicine” is the medical systems based on the cultural beliefs and practices of specific ethnic groups or particular culture and concern about the care and treatment of illness. The study of etiology of disease, practitioners and their role in health care, and types of treatment administered are the purview of ethnomedicine, which helps in the search for new cures and wellness among indigenous people. At large, ethnomedicine is a sub-field of ethnobotany or medical anthropology of all cultures either written (e.g. Traditional Chinese Medicine, Ayurveda), or orally transmitted over the centuries. In the scientific arena, it deals with the use of several health promoting practices and natural products for the maintenance of optimal physical and emotional health, as well as prevention and treatment of diseases.

According to Barsh (1999) “traditional” imply repetition from generation to generation and ethnomedicinal system has developed on careful observation by traditional healers in a given generation of indigenous people, compare their personal experiences with what they have been told by their teachers and neighbours, conduct experiments to test the reliability of their knowledge, aa well as to enhance and improvise their findings. The “tradition” about traditional knowledge is not its antiquity but the way of acquiring and use, which is unique to each indigenous culture. In almost all ethnomedicinal endeavour, causes are commonly described as “natural” and “magical” or “supernatural”, and illness caused by angry deities, ghosts, ancestors and witches fall into the first category; while those due to an upset in body humors and consequently lose of bodily equilibrium fall into second. This stands in contrast to that of natural causes (naturalistic), where illness is explained in impersonal, systemic terms. The intrusion of heat or cold into or their loss from the body upsets the basic equilibrium; the balance of humors off the *dosha* of Ayurveda, and the *Yin* and *Yang* of Chinese medicine must be restored if the patient is to recover. The natural environment is a living incubator where the components like land, sea, atmosphere, the flora and the fauna are linked and interact with human being in an intrinsic manner. Therefore, plants play a participatory role in healing. A healer’s power is determined by the magnitude of his understanding of the natural laws for the benefit of patients and the whole community.

Ethnomedicine plays an important role in many cultures as healing traditions over centuries. The belief that health and sickness depends upon a correspondence of body’s internal environment and the surrounding atmosphere, much like Hippocrates and Galen taught over 2,000 years ago. It embraces on the belief that the earth plays a vital role in one’s spiritual, emotional, and physical well-being, and these methods are effective in many cases as biomedical treatment. The western medicine is much more technical and analytical, while traditional practices are much more holistic. Good health, disease, success or misfortune are not seen as random but arise as a result of the individuals’ actions and the balance or imbalance between the individual and the social environment. Use of herbal medicines in Africa, South America and Asia,

represents a long history of human interactions with the environment. Plants used in traditional medicine contain a wide range of metabolites that can be used to treat chronic as well as infectious diseases. A vast knowledge about the use of plants against different illnesses may be expected to have accumulated in areas where the use of plants is still of great importance. The medicinal value of plants lies in either alone or in combination of some phytochemicals or *phytophores* that produce a definite physiological action on the human body. The most important of these bioactive compounds are alkaloids, flavanoids, tannins and phenolics. Herbs or its components used in traditional medicines are usually less or non-toxic due to time tested selection, and traditional dosage in liquid form to encourage the use of extremely low concentration of the active ingredients. However, the problem of toxicity arises due to human manipulation to increase the accumulation of the active compound for increased bioactivity. Therapeutically active molecules in plants exists in a mixture with other phytochemicals like tannins, carbohydrates, amino acids, proteins, vitamins, trace metals, etc. Moreover, the human body is well acquainted to these natural extracts, most of which, in other forms, are consumed as food. Thus, usually these herbs do not upset or inflict toxicity in the body, but help in maintaining the physiological homeostasis by and large.

The term "*Ethnomedicinal Phytophore*" ("*phyto*" means plant, and "*phore*" means molecules that can act selectively in living cell) is used to define the phytochemicals of medicinal plants used by ethnic communities. This term was first coined by Charles Illouze in 1969 to describe the release of small molecular metabolites of plants during preservation of vegetable and fruits in bactericidal gas generator. While in 1988 M. François de Sarre used the term to describe the first living minute (*phytophores*-type) land vertebrates, but Jones (1994) used the term for ideal ligand (like auxin)-binding protein. However, in recent times *phytophore* was used to describe the small molecular secondary bioactive metabolites of medicinal and food plants by Chattopadhyay (2006), and his group (2007, 2008). Single isolated compound as drugs possess all other substances with which they co-exist in the plant *in natura*. It has been suggested that the reactivity of a single pure compound as drug with the body's physiological medium leads to the manifestation of drug toxicity. Phytomedicines with a little amount of processing can promote the healthy development of the body (health food) since it contains not only the active drug molecule, but also other substances required to maintain the overall physiological functions of the body synergistically. This is why 'bitter leaf' *Vernonia amygdalina* can be used as a food and as a drug for diabetes without apparent toxicity. However, the purified extracts or concentrated isolates are considered as medicines and must be subjected to rigorous standardization used to test medicinal agents. Phytochemical studies must be tailored to match the biological activity while the chemical studies should provide information that help in standardization and quality control of the finished product. Even when the product is used as whole herbs, it is imperative that the chemistry of the plant material should be thoroughly profiled so that storage conditions, stability and ingredient integrity can be determined precisely. For example, when a crude drug contain glycoside as active constituent, may likely to be hydrolyzed if stored at places with high moisture content.

Research interest and activities on ethnomedicine have increased tremendously in the last two decade, and since the inception of this discipline, scientific research has made important contribution to the understanding of traditional subsistence, medical knowledge, wisdom and practice. The explosion of ethnomedicinal literature has been stimulated by an increased awareness of the consequences of the forced displacement and/or acculturation of many indigenous population, the recognition of indigenous health concepts as a means of maintaining ethnic identities, the search for new medical treatments and technologies. The ethnomedicine have long been ignored by many biomedical practitioners because the chemical composition, dosages and toxicity of ethnomedical plants are not clearly defined. However, the ethnomedicinal uses of plants are one of the most successful criteria used by the pharmaceutical industry in finding new therapeutic agents. Some outstanding drugs developed from the ethnomedicinal uses include: vinblastine and vincristine from *Catharanthus roseus* (the periwinkle) for treating acute lymphoma and leukaemias, reserpine from *Rauwolfia serpentina* (Indian snake root) for treating hypertension, aspirin from *Salix purpurea* (willow) used for inflammation, pain and thrombosis and

quinine from *Cinchona pubescens* (cinchona) for treating malaria. Today about 80% of the world's population rely predominantly on plants/plant extracts for healthcare and in addition, 57% of the top 150 proprietary drugs contain at least one extract/phytophore derived from plants.

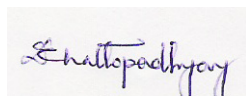
The use of medicinal herbs and herbal medicine is an age-old tradition and the recent progress in modern therapeutics has stimulated the use of natural product worldwide for diverse ailments and diseases. The educated public and health professionals have enormous interests in the medicinal uses of herbs but, unfortunately, there is a great deal of confusion about their identification, effectiveness, therapeutic dosage, toxicity, standardization and regulation. According to WHO, ethnomedicine is popular in all regions of the developing world and its use is rapidly expanding in the developed countries, for example, in China traditional herbal preparation account for 30-50% of the total medicinal consumption. In Ghana, Mali, Nigeria and Zambia, the first line treatment for 60% of children with malaria is the use of herbal medicine. In San Francisco, London and South Africa, 70% of people living with HIV/AIDS use traditional medicine. Today the annual global market for herbal medicine stands at over US \$60 billion. Western trained physicians should not ignore the impact of ethnomedicine on their patients.

This special issue is an attempt to summarize the current knowledge of promising ethnomedicines and their phytophores, to compounds tested against diverse diseases. The therapeutic properties and structure activity relationship (SAR) of some important and potentially useful ethnomedicines is addressed with a focus on how these ethnic knowledge can led to the development of useful therapeutic lead for preclinical or clinical evaluation. In general this compilation is a snapshot of different areas of research on the role of phytochemicals or phytophores in health, comprehensively presented and is useful of titbits of knowledge or ideas for research. This issue covers the ethnomedicines uses in the management of several diseases, particularly, infectious diseases (like viral, bacterial and fungal) and lifestyle related disorders mostly validated by modern scientific methods. In depth information prepared by experts traces the evolution of herbal drugs with civilization and their use as antioxidants, anticancerous, chemopreventors, memory enhancers, neuroprotective, immunomodulator, anti-inflammatory disorders, along with safety issues and toxic effects. The special emphasis is given on some recent topics like the role of flavonoids in nuclear factor kappa B mediated cell signaling pathway to control life style related disorders, bioactivity of lupeol, and the effect of plant based acetylcholinesterase inhibitors in neurodegenerative diseases.

In coming days more issues of IJBPS will be released to offers researchers working on diverse aspects of medicinal plants a complete coverage of botany, ethnology, pharmacology, toxicology and medicinal properties. It provides essential source material to all working in the fields of botany, pharmacy, traditional systems of medicine and drug industry.

This special issue is the outcome of my research involvement for the last two decades with the subject and consultations among biomedical scientists and clinicians. I am immensely grateful to those colleagues for their support in developing the concept. My special thanks and gratitude go to Jaime A. Teixeira da Silva, The GSB Editor-in-Chief, Global Science Books, Ltd., UK for not only inviting me to edit this special issue, but for constant help, suggestions and guidance. With great pleasure and respect, I extend my sincere thanks and indebtedness to all the contributors, particularly Professor Peter J Houghton and Melanie-Jayne R Howes (United Kingdom), Vanessa Steenkamp (South Africa) Kasi Pandima Devi (India) Margareth BC Gallo (Brazil), Miranda J Sarachine (USA), Manuela G Neuman (Canada) for their timely response, excellent updated contributions and consistent cooperation as well as patience. I express my deep gratitude to all those scientific colleagues and teachers, who not only help immensely by providing their valuable time to review these manuscripts. I am indebted to the Officer in-Charge of the ICMR Virus Unit, Kolkata and all the GSB editorial staff members for their active support, help and interest to make this issue possible.

**Dr. Debprasad Chattopadhyay**



**December, 2009**

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**SPECIAL ISSUE: Ethnomedicinal Phytophores in Disease Management. Guest Editor: Debprasad Chattopadhyay, India (Indian Council of Medical Research) ~ December, 2009**

**Debprasad Chattopadhyay, Hemanta Mukherjee, Paromita Bag, Soma Ghosh, Amalesh Samanta, Sekhar Chakrabarti (India)** Ethnomedicines in Antiviral Drug Discovery (pp 1-25)

#### **ABSTRACT**

**Invited Review:** This review is an attempt to portray the discovery and development of ethnomedicine and its phytophores against some important viral diseases from galenical to genomical period. Natural resource, particularly the plants and animals have been the basis of traditional treatment since the dawn of human civilization and the modern medicine (Allopathy) has gradually developed, over the years, by scientific and observational efforts from traditional practice. However, with the advent of antibiotics the role of traditional medicaments in infectious diseases was sidelined. Interestingly after the 1980's, society realized the problem of drug resistance, emerging and reemerging pathogens, adverse drug reactions of many antimicrobials, particularly the antivirals. Hence, the lag phase for plant medicine is changing as impressive successes have been achieved with many botanicals like artemisinin, baccosides, curcumine, phyllanthins, quinghaosu, rauwolfia alkaloids, psoralens, picosides, withanolides, steroidal lactones etc against many chronic and difficult-to-treat diseases. A whole range of chronic and lifestyle related diseases including HIV/AIDS, SARS, and Herpesvirus infection require new effective drugs. Considerable research has been carried out on pharmacognosy, chemistry, pharmacology and clinical therapeutics on Indian Ayurveda, Chinese traditional medicine, and traditional medicines of Africa in the last few decades. Many of the major pharmaceutical companies have renewed their strategies for drug development where there are no effective drugs or vaccine. Hence, many new compounds have entered the international pharmacopoeia through ethno-pharmacology and traditional medicine. Traditional knowledge-driven drug development can reduce both time and cost following a reverse pharmacology path. The automated separation techniques, high-throughput screening and combinatorial chemistry can help ethnomedicines to serve as a powerful search engine to facilitate intentional, focused and safe natural products research and to rediscover the drug discovery process.

**Candice Van Wyk, Francien Susanna Botha, Vanessa Steenkamp (South Africa)** *In Vitro* Antimicrobial Activity of Medicinal Plants against Oral *Candida albicans* Isolates (pp 26-30)

#### **ABSTRACT**

**Invited Mini-Review:** In most countries of subtropical Africa, bacterial and fungal infections represent an increasing problem, particularly with patients suffering from severe immune deficiencies. *Candida* species are responsible for a wide range of systemic as well as superficial opportunistic infections. *Candida albicans* is a normal commensal, isolated intraorally in 17 to 75% of healthy individuals and all debilitated people. Eradication of candidiasis is complicated by the emergence of *Candida* strains that are resistant to the currently used antifungal agents. Furthermore, these antifungal agents are limited in number, are costly and in addition may be toxic. Plants as remedies are used by ~80% of the population in developing countries and their use is gaining popularity in developed countries. Although, many plants have already been investigated for their antifungal activity against *C. albicans* the search is still on to find a long-term prevention or cure for oral candidiasis. It is essential that such a product will prevent a recurrence of the condition, be inexpensive and prevent the development of antifungal resistance.

**Kasi Pandima Devi, Perumal Vijayaraman Kiruthiga, Shunmugiahthevar Karutha Pandian (India)** Emerging Role of Flavonoids in Inhibition of NF- $\kappa$ B-Mediated Signaling Pathway: A Review (pp 31-45)

#### **ABSTRACT**

**Invited Review:** Nuclear factor kappa B (NF- $\kappa$ B) proteins comprise of a family of structurally-related eukaryotic transcription factors. They were originally discovered in lymphocytes, but later found to be ubiquitously expressed in almost all animal cell types. In mammals the NF- $\kappa$ B family (also known as the Rel family) consists of five members: p50 (product of the NF- $\kappa$ B1 gene), p52 (product of the NF- $\kappa$ B2 gene), p65 (also known as RelA), c-Rel and RelB. NF- $\kappa$ B dimers exist in a latent form in the cytoplasm bound by I $\kappa$ B inhibitory proteins. NF- $\kappa$ B-inducing stimuli (stress, cytokine, free radicals, UV radiation, oxidised LDL, bacterial or viral antigens) activate I $\kappa$ B kinase complex that phosphorylates I $\kappa$ B, leading to its ubiquitination and subsequent degradation. I $\kappa$ B degradation expose the DNA-binding domain and nuclear localization sequence of NF- $\kappa$ B and permit its stable

translocation to the nucleus and the regulation of target genes. The NF- $\kappa$ B signaling pathway plays a key role in inflammation, immune response, cell growth control and protection against apoptosis. Downregulation/inhibition of NF- $\kappa$ B is regarded as a potential drug targets for therapeutic intervention in many diseases like cancer, inflammatory and autoimmune diseases. Many natural plant products have been found to downregulate NF- $\kappa$ B production, including curcumin, quercetin, green tea, and resveratrol. In this review we describe flavonoids as NF- $\kappa$ B inhibitors and their role in preventing NF- $\kappa$ B signaling pathway mediated disorders.

**Margareth B. C. Gallo (Brazil/USA), Miranda J. Sarachine (USA)** Biological Activities of Lupeol (pp 46-66)

#### ABSTRACT

**Invited Review:** This review covers mainly the past 25 years of research on the biological activities of lupeol, a significant lupane-type triterpene represented in the plant, fungi and animal kingdoms. Anticancer, antiprotozoal, chemopreventive and anti-inflammatory properties, plus the mechanisms of action of lupeol are emphasized. Some insights are provided regarding lupeol as a lead scaffold for synthetic chemical attempts to optimize pharmacological potency. Structure-activity relationship is also discussed.

**Melanie-Jayne R. Howes, Peter J. Houghton (United Kingdom)** Acetylcholinesterase Inhibitors of Natural Origin (pp 67-86)

#### ABSTRACT

**Invited Review:** The endogenous neurotransmitter acetylcholine (ACh), found in vertebrates, stimulates cholinergic (muscarinic and nicotinic) receptors to mediate cholinergic neuronal transmission. ACh has a short half-life, as it is rapidly hydrolysed in the neuronal synaptic cleft by the enzyme acetylcholinesterase (AChE). Modulation of cholinergic function has been recognised as a therapeutic target in some disease states and one approach to achieve this is to prolong the action of ACh through the use of AChE inhibitors. Consequently, AChE inhibitors have been investigated for a number of therapeutic applications including glaucoma, myasthenia gravis, anti-muscarinic poisoning and dementia. Many inhibitors of AChE have been derived from natural sources, with alkaloids generally being the most potent, although other compounds including some terpenoids have also been shown to inhibit AChE. It is particularly interesting that of the four drugs currently licensed in Europe to alleviate cognitive symptoms in Alzheimer's disease, two (galantamine and rivastigmine) are derived from natural sources. Natural products continue to be investigated for anti-AChE activity to identify compounds that may have therapeutic potential, or that provide templates for the development of new drugs, with a particular focus on the alleviation of cognitive disorders. Many plants reputed to enhance cognitive function in a variety of traditional practices of medicine have been investigated to determine any pharmacological basis for their historical uses, and some of the extracts from these plants have shown promising AChE inhibitory effects, although for some plants the active compounds are yet to be elucidated. There are a number of other plants that are not associated with a traditional use related to cognitive disorders but their extracts have also been shown to inhibit AChE. Some of those plant extracts and compounds of natural origin that have shown inhibitory activity against AChE, and their therapeutic relevance, are discussed.

**Natrajan Suganthy, Shunmugiahthevar Karutha Pandian, Kasi Pandima Devi (India)** Cholinesterase Inhibitors from Plants: Possible Treatment Strategy for Neurological Disorders – A Review (pp 87-103)

#### ABSTRACT

**Invited Review:** Dementia is a chronic progressive mental disorder, which adversely affects memory, thinking, comprehension, calculation and language. Some of the most common dementias are Alzheimer's disease, Parkinsonism, Dementia with Lewy Bodies and Myasthenia gravis. All of these disorders are related to abnormalities in the central cholinergic system, which shows a decline in acetylcholine (ACh) level due to substantial reduction in the activity of the enzyme choline acetyl transferase. A variety of strategies have been envisaged to implement the replacement of ACh, of which acetyl cholinesterase (AChE) inhibition has shown consistent positive results. Cholinesterase inhibitors act on the enzymes that hydrolyze ACh, following synaptic release. Currently several cholinesterase inhibitors such as tacrine, rivastigmine, donepezil and galanthamine have been used as first line pharmacotherapy for Alzheimer's disease. However these drugs have severe side effects like hepatotoxicity and gastrointestinal disorder, hence there is still a great interest in finding better cholinesterase inhibitors from natural sources. Natural products are significant sources of synthetic and traditional herbal medicines. A potential source of AChE inhibitors is certainly provided by the abundance of plants in nature. Huperzine, bacosides, hyperforin, desoxy-peganine and *Ginkgo biloba* (plant extract) are some of the natural drugs used in the treatment neurological disorders. This article aims to

provide a comprehensive literature survey of plants that have been tested for AChE inhibitory activity. Numerous phytoconstituents and promising plant species as AChE inhibitors are being reported in this communication.

**Manuela G. Neuman (Canada), Vanessa Steenkamp (South Africa)** Toxicity Profile of Pyrrolizidine Alkaloid-Containing Medicinal Plants: Emphasis on *Senecio* Species (pp 104-108)

#### **ABSTRACT**

**Invited Mini-Review:** Pyrrolizidine alkaloids (PAs) are found in various plant genera worldwide. Poisoning by PA-containing plants is usually accidental, by the ingestion of grain inadvertently contaminated with seeds of pyrrolizidine-containing weeds, or the consumption of herbal or bush tea, or when taken as herbal infusions for medicinal purposes. In this paper the toxicity of PA-containing plants, with emphasis on *Senecio* spp. is reviewed. Although the toxicity of *Senecio* has been documented in numerous case reports, the mechanism of toxicity is not fully known. Elucidating the factors involved in herbal remedies-induced toxicity has medical significance. Currently, there is no antidote for natural-substances that induce liver damage. It is important to understand the need for monitoring the use of herbal medicine in order to optimize herbal/traditional medicine use and maximize the clinical and economical benefits. It is also necessary to enhance communication between scientists and physicians of all disciplines involved in complementary alternative medicine and clinical toxicology.