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Pharmacognosy can help minimize accidental misuse of herbal medicine

An estimate of the World Health Organization (WHO) states that around 85–90% of the world's population consumes traditional herbal medicines. Use of herbal remedies is on the rise in developing and developed countries (Figures 1 and 2)[1]. Of late, the use of traditional herbal medicines has increased by leaps and bounds in the West and in the near East. The US herbal medicine consumption alone was worth US$ 17 billion in the year 2000 and the global market for herbal medicines today is estimated to be a whopping US$ 60 billion[2]. The size of the herbal health care and personal care market in India is estimated to be between Rs 2500 and 3000 crores[3]. With these figures marching up steadily, the number of deaths and other toxic reactions resulting from the use of herbal medicines is also on a rise. How are we prepared to tackle this? Can a specialized field like pharmacognosy help minimize the concerns?

Pharmacognosy (Figure 3) basically deals with the standardization, authentication and study of natural drugs. It is closely involved with allied fields, viz. phytochemistry and toxicological screening of natural products. Much of the research in pharmacognosy has been done in identifying controversial species of plants, authentication of commonly used traditional medicinal plants through morphological, histological, physico-chemical and toxicological parameters, especially heavy-metal estimation and radiobiological contamination in plants, prescribed by an authoritative source. The importance of pharmacognosy has been widely felt in recent times.

Most of the cases of accidental herbal medicine misuse start with wrong identification of a medicinal plant prescribed. Many of the traditional systems have records where one common vernacular is supplied in place of two or more entirely different species. Ginseng, which is a common Indian drug, is sold under 13 different names in the market. For example Chinese or Asiatic ginseng (*Panax ginseng*), American ginseng (*Panax quinquefolius*), Siberian ginseng (*Eleutherococcus senticosus*), Ayurvedic ginseng (*Withania somnifera*) and Russian ginseng (*Acanthopanax senticosus*), to name a few[4]. Such names could create confusion over prescription, which may eventually lead to serious consequences. For instance, by the end of the 20th century, there were continuous reports of cases in Belgium and some European countries of people, who, after taking slimming drugs containing 'Fangji', a Chinese herbal remedy, developed extensive and indirect nephrofibrosis, renal tubule atrophy and depletion, and/or renal failure. It was found that *Aristolochia fangchi* had been mistakenly used instead of *Stephania tetrandra* in the slimming drugs[5,6]. At

present, there are four species in the market whose names are similar to 'Fangji'. Reports have suggested that a total dose of more than 200 g of *A. fangchi* can present a higher risk of urothelial carcinoma[7]. In 2004, a similar case of poisoning was reported in Hong Kong, where a patient was administered *Aristolochia mollissima* instead of *Solanum lyratum*. Later it was identified that both the above-mentioned plants share a common Chinese name, 'Baimaoteng'[8]. Some traditional medicinal herbs even have a number of synonyms named after them by various authors. For example, *Cassia acutifolia* which is commonly known as Alexandrian senna has names like *Senna alexandrina*, *C. senna*, *C. obtusata* and *C. sophera* under its original name[4].

The second major reason for accidental herbal medicine misuse is the non-characterization of chemical constituents of the controversial plants. *Aconitum carmichaeli* and *Aconitum kusnezoffii* are both used as anti-inflammatory, analgesic and cardiotonic agents in traditional medicine, but highly toxic C-19 diterpenoid alkaloids of aconitine, mesaconitine and hypaconitine present in them may prove fatal to a subject who ingests them. Typical symptoms range from ventricular arrhythmia, which occurs in the first 24 h of ingestion, to death[9]. Similarly, *Ephedra gerardiana*, popularly called 'Ma Huang' was consumed largely by sports athletes in the US, mainly for it central nervous system (CNS) stimulating effects, until reports poured in about it causing stroke, myocardial infarction and sudden death, the notorious chemical constituent being a poisonous alkaloid, ephedrine[10]. Eventually, the USFDA (United States Food and Drug Administration) had to ban ephedra from being marketed in the US.

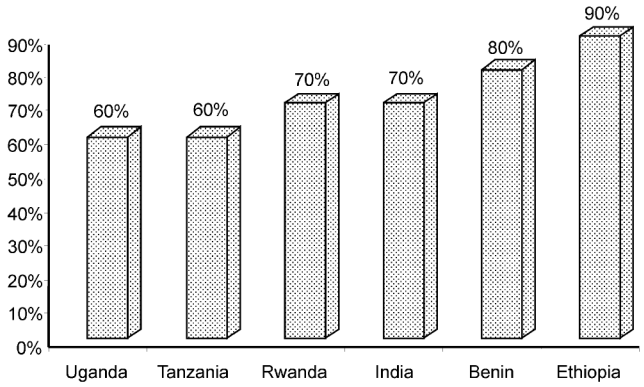

Figure 1. Use of herbal traditional medicine for primary health in some developing countries (Source: WHO[1]).

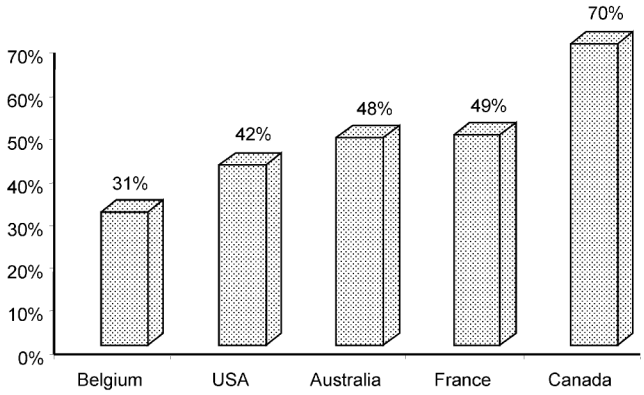

Figure 2. Percentage of population that has used herbal traditional medicine at least once in selected developed countries (Source: WHO[1]).

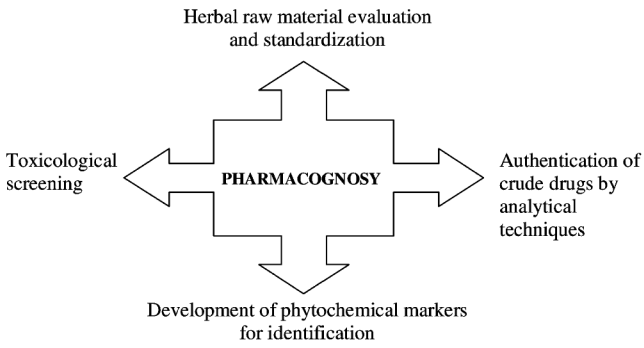

Figure 3. Multidimensional approach of pharmacognosy towards quality control of herbal medicines.

Apart from Chinese herbal medicines, however, lately toxic patterns and herbal poisoning incidents are being widely reported from Ayurvedic and Indian herbal remedies consumption too on a larger scale all over the globe. Ayurvedic drugs are mostly non-standardized with complex ingredients of diverse nature. The method of preparation and the crude drugs used vary from one traditional Ayurvedic physician to another. The use of Ayurvedic drugs in practice, apart from those practised by institutionally qualified Ayurvedic practitioners, has two traditions – (a) classical tradition and (b) folk tradition. The folk practitioners sometimes use medicines out of their experience or ignorance, which may even prove fatal. A few critical and crucial cases are analysed here.

Case 1 – on consumption of an Indian herbal mixture, a 22-year-old male developed giddiness, vomiting and abdominal discomfort. During presentation he had bradycardia, hypotension, complete heart block and renal insufficiency. Upon analysis of the herbal mixture, one of the eight ingredients found in the mixture was 'Shankhini'. The name 'Shankhini' represents (a) a plant drug named *Albezzia lebbac* which is anti-allergic according to classical Ayurvedic literature, and (b) a heavy metal–arsenic compound, which is considered potentially toxic in its unpurified form. It is not clear which form of the drug 'Shankhini' was used[11].

Case 2 – 'Brahmi' is a popular Ayurvedic drug used as a revitalizer. Currently there are two plants in the market which

share the same name 'Brahmi', viz. *Centella asiatica* and *Baccopa moneri*. Both these plants are being used on a large scale by traditional physicians irrespective of their authenticity.

Case 3 – Hepatic veno-occlusive disease and death were reported when four young Chinese women consumed unidentified Indian herbal tea. Spectrophotometric analysis showed presence of high levels of toxic pyrrolizidine alkaloids in the herbal mixture, which could be either due to herbal drug misuse or addition of non-characterized herbs[12]. A similar event took place in Central India in the mid 70s, where pyrrolizidine alkaloid poisoning turned out to be an epidemic, believed to be due to contamination of herbs with pyrrolizidine alkaloid-rich plants[13]. Adding to the above-mentioned cases, a large number of data are currently available on heavy-metal poisoning from Ayurvedic and other Indian herbal medicine consumption[14–26]. One study shows that 64% of samples collected from India contained significant amounts of lead and mercury. Arsenic and cadmium were found in 41 and 9% of the samples respectively[18].

Evaluation of plant materials and their derived products has always been an important part of the professional expertise of a pharmacognosist[27]. However, over the years the nature and degree of this evaluation have changed. Initially it was considered sufficient to authenticate the plant material by comparison with a standard botanical description or monograph. Later it was realized that, for detection of adulterants, this practice must be supplemented with other important procedures like microscopy, chemical tests and advanced analytical techniques.

The main goal of pharmacognosy is to assess the value of raw materials and to ensure that the final product is of the required standard. Strict standardization procedures and pharmacognostical studies of medicinal plants would reduce drastically much of the accidents in wrong prescriptions of traditional herbal medicines. WHO has developed several guidelines for carrying out standardization procedures of raw herbal products, which basically include pharmacognostical, physico-chemical, pharmacological and toxicological methods to standardize a certain herbal material. Microscopic and macroscopic standards could be drawn out, where a plant can be differentiated from another entirely different plant which may look similar in external appearance. Currently, genetic fingerprinting and the use of analytical quality-control equipments like HPLC and HPTLC are performed on a large scale for standardization and identification of herbal drugs. Phytochemistry has evolved as a major branch of pharmacognosy in developing markers for the purpose of identification and standardization. It would also be worthwhile to draw a pharmacognostical scheme for all controversial species of plants where the information could be made available officially, which would always serve as a useful reference. A detailed phytochemical characterization and a follow-up toxicity profile of important traditional medicinal plants should be carried out exhaustively, which would prove their efficacy. Appropriate standards for consumption and presence of toxic substances should also be outlined precisely.

The use of herbal medicine is growing steadily[28], particularly for the treatment of asthma and allergic diseases[29], as health supplements and tonics. Numerous reports on the presence of heavy metals in herbal medicines are being presented regularly[30]. Federal agencies have put in a lot of efforts to regulate the use of herbal medicines; nevertheless, the situation is worse in developing and under-developed countries. Some of the crucial discoveries in the safe use of herbal medicines were brought out through intensive pharmacognostical research. More than half of the medical schools in the UK now have a curriculum on herbal medicines. Awareness of the safe use of herbal medicines has increased lately. More intensive research is indispensable for further benefits.

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