

## Clinical Biochemistry and Herbal Treatment

**Dr. Ragini K Chahande**

Associate Professor in Biochemistry Department  
Seth Kesarimal Porwal College Kamptee. Affiliated to RTM Nagpur University, Nagpur

### Abstract

Herbal supplements are "safe" and "harmless," and UK use is rising. Some natural remedies are dangerous. Ethnic cures sometimes include heavy metals, Western medications, and banned animals and plants. Certain plants interact with prescription medicines and harm the liver or kidneys. Patients whose symptoms may be related to herbal products might benefit from the clinical laboratory's assistance in learning about the effects of herbal products on laboratory tests and receiving recommendations for further study. Physicians must take a medication and herbal history.

**Keywords:** Ayurvedic medicine; Herbal product; Drug production; Pharmaceuticals

### Introduction

Herbal and over-the-counter alternative remedies have increased in popularity. Supermarkets, pharmacies, and Chinese herbalists' shops are selling more herbal remedies. According to American research on alternative medicine, herbal treatments surged by 380% between 1990 and 1997, yet few patients notified their doctors about them, even if they were also using pharmaceutical drugs. In 1997, more Americans saw primary care physicians than alternative medicine practitioners, according to this poll [1]. Another study found that 16% of prescription medication users utilized vitamins and herbs. Ginkgo (2.2%) and ginseng (3.3%) were the most popular supplements. Herbal remedies are used for several reasons. Herbal remedies are "natural," "gentle," and "safe," yet prescription drugs have negative effects. While many people feel that alternative medicine affords them more treatment options, few understand that the herbal industry is little regulated and that herbalists need no professional credentials [2]. The widespread availability of vitamin and herbal supplement shops lends credence to the widespread belief that these products are beneficial to one's health. Strong advertising backs up these assumptions. The complicated reasons why so many people are willing to spend relatively big sums on such preparations are summarized by Beyerstein [3]. This review divides the herbal sector into three categories: (3) herbal medications prescribed by TCM or Ayurveda practitioners. Ginseng, garlic, St. John's wort, and phyto-oestrogens are examples of herbal supplements with apparent therapeutic benefit.

### Applicable legislation

Medications in the United Kingdom are governed by the Medicines Act of 1968 and Council Directive 2001/83/EEC, both of which are enforced by the Medicines Control Agency (MCA). In both therapeutic and nontherapeutic contexts, this group offers guidance. One definition of a herbal remedy can be found in Section 132 of the Medicines Act of 1968, which states that "a medicinal product consisting of a substance produced by subjecting a plant or plants to drying, crushing, or any other process," or "a mixture whose sole

ingredients are two or more substances so produced and water or some other inert substance," is a herbal remedy. Making, selling, and offering herbal treatments is legal under the Act so long as they are prepared on the premises and distributed after a patient consultation in accordance with Section 12. In cases where (a) the plant or plants have been dried, crushed, or comminuted, and (b) the medication is marketed with a label, which just mentions the plant(s)

### **Herbalism basics**

Herbal practices separate them much from one another. To cure a specific ailment, British traditional herbalists would gather and prepare herbs at the appropriate time of year (e.g. willow bark as a painkiller). Our ancestors' trial-and-error technique is akin to modern Western medicine. This focuses on a patient's symptoms and then prescribes a treatment. TCM and Ayurveda focus on the whole person. Ayurveda has been practiced since the sixth century BC. Therapy corrects the imbalance of the three important humors, which may cause sickness. Ayurveda medicine is generally practiced by Indians who have received significant training.

### **Herbal product quality**

Some UK CHM practitioners use dried herbs or herbal tinctures to prepare herbal prescriptions, but most use prepackaged formulations. Responsible practitioners realize that this practice causes several concerns that need tougher laws or regulation. Many imported items come from mainland Chinese suppliers without quality control or production standards. There is a risk of misidentification of plants, substitution of herbs, out-of-season harvesting, contamination with chemicals (including heavy metals), adulteration with Western medications, and substantial variation in the amounts of active ingredients. Unfortunately, most of China's herbs are wild-harvested, and as they become scarcer, other plants must replace them, which have an ecological impact.

### **Labs and herbal remedies**

The biochemistry laboratory may investigate patients who use herbal products for toxic effects from contamination or misidentification, toxic effects of specific herbs (such as liver damage (also known as hepatotoxicity), supplements including Western pharmaceuticals, drug-herb interactions, and other biochemical and metabolic consequences. The hematology department knows about herbal preparations and warfarin, and the microbiology section should know about herbal products infected with Salmonella [4].

### **Metal toxicity in herbal and OTC products**

Contamination or the product's metal content may cause this. Traditional and ethnic remedies include metal components. Chromium picolinate is a common ingredient in over-the-counter fat burners. An increase in chromium consumption has been linked to enhanced fat and glucose metabolism because of its role as an insulin co-factor. It has been shown in a recent research that chromium picolinate is readily absorbed, hence minimizing any danger. [5] The nicotinic acid isomer picolinate has been linked to histamine production and itching in certain people. [6] These chromium salts haven't been studied long-term, thus toxicity is possible, particularly in heavy users.

### Herbal poisons

Unlicensed plant treatments are banned in the UK. [7, 8] The Pinyin names of related species are likewise restricted owing to the risk of misidentification. These plants may be divided into those with immediate pharmacological effects and those with delayed harmful effects.

### Toxicity caused by the drug's intended therapeutic effect

Traditional herbal treatment is limited by the short therapeutic window and high toxicity of these plants. Plants including hemlock (conium), foxglove (digitalis), deadly nightshade (atropine), and monkshood (aconitine) are excluded because of their well-documented toxicity (aconitine). Foxglove, which had long been known to benefit the heart, was seldom used owing to its unpredictability. Martindale's Pharmacopoeia featured a confusing variety of medicines in 1952. Herbal beverages have been associated with cases of foxglove poisoning [10, 11], which happens on occasion but most often results from incorrect plant identification. *Digitalis lanata* was used in an herbal supplement [12]. Bioassays for potency made standardized formulations feasible, which increased their use [9].

### Toxicity-extending herbs

*Aristolochia* is the most well-known of them. Toxic to the kidneys is the aristolochic acid found in *Aristolochia* species including Qing Mu Xiang (Ma Dou Ling) and Mu Tong, both utilised in traditional Chinese medicine. In 1993, rapid progression of interstitial renal fibrosis [13] was seen in women who had used *Stephania tetrandia* and *Magnolia officinalis* in a weight-loss clinic in Belgium. By 1994, 71 such cases were known about; half of them required renal dialysis, and the other cases showed worsening renal function after the herbs were stopped. *Stephania* powders in France included *Aristolochia*, which was associated to renal failure in Spain [15]. *Aristolochia fangchi* replaced *Stephania tetrandia* in the powdered mixture. This report garnered global attention. These attempts were questioned, and tougher rules were stressed [16]. Belgium had 100 cases by 1998.

We now know that aristolochic acid causes cancer and damages kidneys. In 1999 [18], the British Department of Health issued an urgent warning on the dangers of using *Aristolochia* for skin problems after two incidents of end-stage renal failure were connected to its use. As a result, using this plant on the skin is now illegal. Aristolochic acid DNA adducts were found in all 39 kidneys from individuals with end-stage renal failure, with malignant urothelial carcinoma found in 36 of the kidneys. Nonetheless, imported Chinese patent medications using this plant are found [19]. Box 2 lists *Aristolochia* preparations, and the Australian Therapeutic Products Association lists any plants that may be confused for it. This plant may be in a medication even if it's not stated. All renal failure patients' especially young ones—should be asked about herbal use. *Aristolochia* is linked to severe hepatitis [20].

### Drug-herb interactions

These adverse effects may be the most harmful since most herbal product users don't notify their doctors. Many reviews of this problem [21–25] and the Natural Medicines Comprehensive Database [26] are good references. A systematic review describes several common herbal products [27]. Plastic surgeons [28] and surgeons [29,30] have warned patients of such interactions, and a full evaluation [31] has been published. This review considers ginkgo, saw palmetto, hawthorn, and St. John's wort's efficacy [31]. Herbal

remedies may dislodge a drug from its binding protein or alter its absorption or metabolism. Intestinal cytochrome P450 enzyme inhibition or enterocyte P-glycoprotein inhibition may cause the interaction, although enzyme stimulation can also cause it. Hence, predicting how a plant extract affects pharmaceutical metabolism is tricky.

Grapefruit, while not a "herb," shows the potential of such an interaction. This may increase the blood levels and absorption of drugs including cyclosporin, [32] carbamazepine, and sildenafil, but it may impair the efficacy of pharmaceuticals that must be metabolized into active metabolites to work (e.g. losartan<sup>145</sup>). Hence, medication users should avoid grapefruit. Herbal drugs and nutritional supplements may interact with warfarin and cause significant side effects. Most of them increase warfarin's effects, producing bleeding or an increase in the international normalized ratio (INR), whereas a few with high vitamin K levels decrease it.

### Herbal drug manipulation

The 1997 Taiwanese review of 2609 Chinese medicines found 23.6% having synthetic medical substances and more than half with two or more unregistered pharmaceuticals. The West should have learnt from this. In a California investigation the next year, 32% of 260 Western medications and heavy metals were found in several Asian patent medicines. 188 Western pills or capsules may be marketed as "concentrated herbal extracts" if they include drugs that are added to herbal blends. Most tainted commodities originate from mainland China. Chinese herbalists returning from China with a suitcase of patent medicines bring them to the UK. Because to the frequency of these events, it is best to acquire the latest information from the MCA or FDA websites rather than the medical press. Because people looking for herbal treatment often want to avoid Western medications, the practice of adulterating products marketed as "natural" and "herbal" is a double betrayal because it suggests the herbalist (or supplier) has so little faith in their own remedies that they need to supplement them with pharmaceuticals. Money motivates again. Supplementing with Western drugs promotes the commerce since patients only buy more if it works. The laboratory may investigate clinical impacts of various drugs. Ten years ago, a natural eczema treatment with steroids was proposed [34].

The national [35] and medical [36] press immediately reported other cases of oral and topical herbal medications containing corticosteroids. Further reports found products including dexamethasone, [37] clobetasol propionate, and triamcinolone. The "herbal" treatment for arthritis in another case included the drugs thiazide, indomethacin, diclofenac, mefenamic acid, diazepam, and enough dexamethasone to induce [38]. In the investigation by Keane et al., 1999, dexamethasone was found in eight different herbal creams, including all eczema therapies. Corticosteroids have been identified in two traditional African medicines: wah-wa cream and Cherrydex [39] from Ireland. Adulteration occurs despite media coverage [40, 41]. Illicit corticosteroids may damage herbal creams that perform effectively. Herbal products may induce adrenal insufficiency and iatrogenic Cushing's syndrome due to hormones [42,43]. A "herbal" remedy including the non-steroidal anti-inflammatory drug mefenamic acid caused serious gastrointestinal bleeding and other issues [44]. A natural medicine including phenytoin, carbamazepine, and valproate poisoned one patient [45]. A toddler was admitted to a critical care unit after his doctors gave him Diankexing, which included phenobarbital, mephobarbital, and sodium bromide.

Benzodiazepines are addicting, therefore doctors use them cautiously. Alprazolam, diazepam, and estazolam—known as "Sleeping Buddha"—have been found in herbal formulations [46]. Patent Chinese pills are sometimes sold as prescription-like tablets. While assessing a hypoglycemic patient, remember that certain herbal diabetes treatments include anti-diabetic drugs such as glibenclamide and phenformin. These preparations generated a UK hypoglycemia coma [47]. Pearl and Diabetes Hypoglycose Capsules are sold in the US. A Canadian research found that 20 Hua Fo, a natural sexual performance supplement, has a chemical comparable to sildenafil (Viagra). [48] The UK found this product. Mugwort from a cocaine-positive patient contained cocaine. Patients or their loved ones were accused of trying to hide their drug use by adding a white powder to the dried herb sample that was later analysed [49]. Herbal slimming pills are lucrative because people want "quick fixes" to reduce weight. Herbalists also advertise "slimming a specialization." Some "herbal" products are useless or dangerous. Western slimmers used fenfuramine throughout the 1980s and 1990s. It was removed off the market in 1997 when it was shown to induce valvular heart disease and primary pulmonary hypertension. Fenuramine was distributed in the United Kingdom by a Chinese herbalist under the guise of "herbal" slimming aids, delivered in the shape of yellow tablets (sold in an unmarked container) and Qian Er capsules (said to be made from famous Chinese herbs) [53]. For example, you may buy "*Tabellae feneuramini*" in China. In spite of its low risk of causing liver damage, feneuramine is included in many products marketed in China, Japan, Singapore, Hong Kong, and Korea [54]. Carcinogenic and liver-damaging. Manufacturers may be trying to circumvent the new Chinese regulations by using feneuramine, which is easy to synthesize. Feneuramine may go undetected in capsules or tablets. Chinese herbalists also sell mazindol, an amphetamine-like sympathomimetic amine related to primary pulmonary hypertension [55]. "Some Chinese herbalists promote and sell it without cautions despite it being classified as a Class C narcotic under the Misuse of Drugs Act (1971) and a psychotropic drug by the United Nations. Trials of botanical remedies can't be trusted since pharmaceutical companies have been known to tamper with them. This problem can be avoided if the plant material is standardized and its composition is well-understood. Prostate cancer sperm enhancement supplement (PC-SPES; spes='hope' in Latin) was developed in 1996. It has 8 different herbs in it. After waiting two years, tests for anti-tumor activity revealed that PC-SPES had oestrogenic action but no oestrone, oestradiol, or diethylstilboestrol. [56] Clinical studies showed that the medication was effective against prostate cancer despite its oestrogen-related adverse effects [57]. PC-SPES225 was taken off the market because of interactions with alprazolam and warfarin when diethylstilbestrol was discovered in 2001 [58]. To counteract the oestrogen's potential for thrombotic side effects, warfarin was administered, and alprazolam was prescribed for anxiety. In spite of testing, the PC-SPES lesson is notable since the active elements were not found until further inquiry revealed Western medications.

Table: 1 Drugs used for herbal remedy

Alprazolam	Chlordiazepoxide/Librium
Aminopyrine	Chlorpheniramine
Caffeine	Diazepam
Carbamazepine	Diclofenac
Chloramphenicol	Diethylstilboestrol

## Discussion

Medical herbalism is a supplemental medicine that may benefit a patient's therapy. Herbal products are increasing global health issues. In mainland China, herbal treatments are often contaminated with heavy metals, herbs, and Western drugs. Several risks are nominally covered by UK legislation, but the problem is too big for current enforcement. The European Commission investigated 1999 EU drug marketing to examine whether it was harmonized as required by 1995. After explaining that each country has different herbal items limits, stricter laws are being explored [59]. The president of the European Herbal Practitioners Association has called for mandatory registration of herbalists throughout the European Union to curb the presence of fraudulent professionals [60]. Respected practitioners should help educate the public about the dangers of misusing herbal products. Herbal is often mistaken for natural, *Ann Clin Biochem* 2003; 40: 489-507 502 Change the harmless corns. Addressing ethnic minority women who give their children "herbal" remedies without proof of safety is required. Physicians are supposed to evaluate patients' herbal and prescription histories, but they seldom do. "Relevant clinical information, including pharmaceutical therapy and herbal self-medication" on laboratory request forms may be beneficial. The Natural Medicines Database [61] helps doctors and medical professionals learn about the side effects and medication interactions of commonly used plants. Two monographs have been prepared for this, and a herbal medicine toxicity database is being created [62,63,64]. As Chinese herb toxicity research is scarce, creating relevant databases is difficult. Few doctors know that the "yellow card" procedure for adverse drug reactions applies to herbal medications and should be reported to the MCA [65, 66]. Patients, doctors, and pharmacists should be mindful of medication-herb interactions. Herbal medications with substantial drug interactions may need to be remarketed. Herbal treatments that interfere with digoxin tests or interact with cyclosporine and warfarin should be noted by clinical laboratory specialists. Hepatotoxicity-causing plants and heavy metal contamination in herbal remedies are two additional areas in which clinical biochemists may provide useful guidance [67, 68]. Laboratory workers should warn their clinical coworkers about the dangers of herbal supplements because of the correlation between their usage and a rise in adverse outcomes.

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