

## Peer reviewed article

Herbal remedies:  
renal tragedies

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Virtually every culture and civilization, throughout history, has used a range of plants or plant derivatives for the prevention and treatment of diseases. Chinese have used Ginkgo biloba, prepared from the ginkgo tree, and its fruits and seeds in order to sharpen mental focus. For thousands of years Ginseng (means "essence of man") has been used by the Chinese as an emergency medicine to save dying patients. However, the recently increased fondness of people towards the herbal medicines has swamped the global pharmaceutical market with thousands of herbal and other natural products [1]. The most frequently reported conditions for which support of herbal medicines is generally sought are: body slimming, musculoskeletal complaints including back and neck problems, allergies as well as other complaints such as fatigue, insomnia, impotence, anxiety and depression [2]. Consequently, they use herbs to self-treat a variety of conditions, and to boost their body's overall functioning.

It is generally understood that the majority of medicinal herbs are safe under the conditions used; only a few are toxic and should be avoided and others have significant adverse effects when misused. Since herbal medicines put on the market worldwide, are available not just in health food stores, but in drug stores and even grocery shops, without need for prescriptions, consumers naturally assume that they are harmless [3]. Contrary to the commonly held conviction of countless consumers, herbal products cannot be regarded as "natural" and therefore harmless entities, this in particular considering that Food and Drug Administration (FDA) received 2621 reports of serious medical problems related to immunological, musculoskeletal, hepatic and renal dysfunction as well as mutagenicity involving these products, together with 184 deaths, between January 1993 and October 1998 [4].

Use of traditional herbal remedies is widespread in Africa. Acute renal failure is one of the most serious complications resulting from the use of traditional remedies. The use of herbal products accounts for nearly 35% of all cases of acute renal failure in Africa [5]. Nephropathy following intake of Chinese herbs is well documented. A study in Brussels in 1992-93, for the first time recognised almost 100 patients, most of them young females with rapidly progressive renal failure after consumption of Chinese herbal slimming pills containing *Aristolochia manshuriensis* rich in aristolochic acid. As a result, a third underwent renal transplantation; an additional third required long-term haemodialysis and the remaining third had gradually progressive renal failure [6]. All the patients had

similar clinical features, such as a nearly normal blood pressure, obvious anaemia, insignificant oedema, low-grade proteinuria, and glucosuria. Renal biopsy specimens of the patients showed remarkably similar histological patterns: widespread paucicellular interstitial fibrosis and tubular atrophy. Moreover, the cumulative dose (total doses of more than 200 g) of *Aristolochia* has also been reported to be a significant risk factor for development of urothelial carcinoma as a long-term complication among patients with end-stage Chinese-herb nephropathy being treated either with renal transplantation or dialysis [7]. Similar incidents were subsequently recorded in France, Japan and the UK [8-10]. Recently another Chinese herb - Mu-Tong (*Caulis Aristolochiae manshuriensis*) containing aristolochic acid, has been found to induce tubulointerstitial nephropathy, which is mainly related to over-dose or long-term use [11]. Renal tubular acidosis with hypokalaemic paralysis, rhabdomyolysis and subsequent acute renal failure, has also been reported as a rare presentation of Chinese herb nephropathy, [12] Herbal treatment can produce renal complications among patients with underlying connective tissue disorders such as - CREST syndrome (Calcinosis, Raynaud's, Oesophageal dysmotility, Sclerodactyly, Telangiectasia) [13].

A review of 58 cases by Chen et al. between October 1998 and August 2001 revealed three likely outcomes of the nephrotoxicity of Chinese herbs containing aristolochic acid: (I) Acute aristolochic acid nephropathy [AAN] (7.0%) with acute tubular necrosis and acute renal failure, (II) Tubular dysfunctional AAN (12.0%) characterised by tubular degradation with atrophy, and renal tubular acidosis and/or Fanconi syndrome, and most commonly (III) chronic AAN (81.0%) with renal interstitial fibrosis with sparse mononuclear cell infiltrates, and chronically progressive renal failure [14]. Moreover, many herbal supplements may contain heavy metals (lead, mercury, arsenic) that are well-known for their nephrotoxic potential [15, 16]

Herbal remedies could be the surreptitious sources of potassium in patients with renal disease especially in the presence of concomitant treatment with angiotensin converting enzyme (ACE) inhibitors. A Tahitian drink - Noni juice, taken for general well-being contains very high potassium concentrations (56.3 mEq/L) [17]. Similarly, intractable hiccups, confusion, convulsions, agitation and acute oxalate nephropathy have been reported after ingestion of Star fruit (*Averrhoa carambola*) both, among individuals with previously normal renal function and in those with chronic renal failure and end-stage renal disease (ESRD) on haemodialysis with fatal outcomes [18, 19].

Male patients with ESRD on haemodialysis usually suffer from impotence. Yohimbine, an indole alkaloid obtained from *Pausinyralia yohimbe* bark, has alpha-2 re-

ceptor antagonistic activity, is promoted as an aphrodisiac and supposedly increases muscle mass and decreases body fat. Its value as an aphrodisiac is, however, inconclusive and there is no evidence that yohimbine is anabolic. It has been reported to cause cutaneous drug eruptions, accelerated hypertension, progressive renal failure and lupus-like syndrome [20]. The FDA has declared yohimbine as insecure and ineffective for over the counter sale. Tyramine containing foods (red wine, liver, cheese) and nasal decongestants or diet aids containing phenylpropanolamine should be strictly avoided when yohimbine is used, to prevent a hypertensive crisis. People who have hypertension, diabetes, or cardiac, hepatic, or renal disease should not take yohimbine [21].

Herbal dietary supplements represent a potential and possibly an unnoticed cause of drug interactions in transplant recipients. St. John's Wort (SJW) may induce cytochrome P-450 activity and/or P-glycoprotein expression. Both of these mechanisms are significantly implicated in the metabolism and absorption of cyclosporine (CSA) and other immunosuppressants. Patients taking SJW together with CSA or other medications whose absorption and metabolism are mediated by cytochrome P-450 and/or P-glycoprotein, carry an increased risk of acute "graft" rejection due to sub-therapeutic plasma CSA concentrations [22].

Thus, the facts and figures of herbal toxicology signify that the herbal products are unsafe both, for the individual's general health as well as to the human kidneys [23]. The global review of the contemporary policies on herbal medicine, improved documentation of the renal adverse effects, relevant wide-ranging organised research with the aim to provide more precise information on herbal medications along with more rigorous regulations regarding the proper identification of the herb in question prior to harvesting, processing, storage, packaging, marketing and advertising, appear obligatory, in order to safeguard the consumers' health interests and optimise the safety of these products [24].

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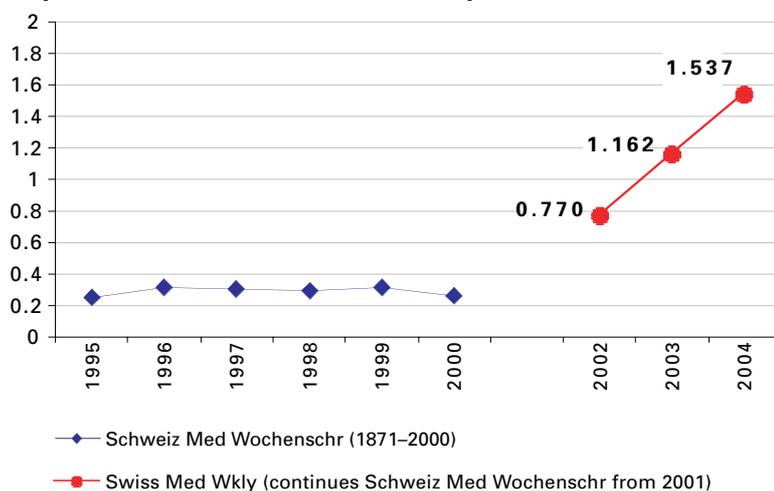
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