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## PROBLEMS ASSOCIATED WITH HERBAL MEDICINES USE

**R. Radev, K. Sokolova\*, J. Tsokeva**

Department of Pharmacology and clinical pharmacology, Faculty of Medicine,  
Trakia University Stara Zagora, Bulgaria

### ABSTRACT

Herbal medicines are common form of complementary and alternative therapy and current trend of their usage is likely to continue in the future. The use of herbal remedies can pose a serious risk by reason of possibility for development of adverse effects and interactions between herbals and conventional drugs in case of co-medications. Physicians and other health professionals should control the consumption of supplements in order to improve the benefit/risk ratio. More rigorous regulations of alternative medicines are required.

**Key words:** herbals, drugs, co-medication, adverse effects, interactions

### INTRODUCTION

During the last decade the import, production and sale of the food supplements have increased significantly, both on a local and on a global scale. (1, 2) In the present day, the total number of registered supplements in Bulgaria is about 2000 and, according to different sources, the yearly revenue from supplements is between 140 and 200 million levs – more than that made from over-the-counter (OTC) drugs. The Directive 2002/46/EC of the European Parliament and Council defines food supplements as concentrated sources of nutrients or other substances with a nutritional or physiological effect whose purpose is to supplement the normal diet. Food supplements, as their name shows, are generally intended to supplement the population's food ration with substances that normal meals lack or contain in a small amount. However, in practice supplements are widely recommended and advertised as means to primary and secondary prevention, complementary therapy and in certain cases - as alternative therapy for various diseases, mainly with chronic nature. All of this violates the food law and supplements are, under this law, "misleading to the consumer". The

assumed naturalness and harmlessness of these products is the chief reason for the constant increase in their intake. Some of the most demanded supplements of plant origin are *Hypericum perforatum*, *Ginkgo biloba*, *Echinacea*, Grape seed extract, Glucosamine, etc. Herbal products contain biologically active substances and their consumption, as that of remedies, poses a risk, so precautions should be taken. The possibility of developing adverse effects, when used in combination with conventional drugs, is described as a potential "direct risk" for the consumer. (**Table 1**) Food supplements are usually offered to patients with serious diseases and are proclaimed a panacea, which diverts patients from the methods and means of scientific medicine – an "indirect risk". (3)

The purpose of this survey is to draw attention to the plausible problems caused by the use of food supplements of herbal origin, as well as to observe some of the interactions between commonly employed herbs and drugs. The problems concerning the use of herbal food supplements are caused by many different facts. One of them is the lack of an adequate legal basis for producing, importing and distributing food supplements. In Bulgaria, the legislative requirements of the regulatory authorities are very simplified and there is a notification regime introduced, regarding food supplements, identical with the one pertaining to the production of food. Regional Inspectorate for Protection and Control of

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\*Correspondence to: *Kameliya Sokolova;*  
*Department of Pharmacology and clinical*  
*pharmacology, Faculty of Medicine, Trakia*  
*University; Armeiska 11, 6000 Stara Zagora,*  
*Bulgaria; Tel.: +35942664310*  
*E-mail: camel56@abv.bg*

Public Health (RIPCPh) authorizes sales after inspecting and approving all the documents, along with the leaflets and labels.

Bulgarian legislation does not require the standards of Good Manufacturing Practice (GMP) to be applied in the production of food supplements. It is for that reason that contaminants and synthetic drugs are often found in supplements and the indication of contents on the package does not always

correspond to that listed in the accompanying leaflets and labels. (4) If any violations are noticed, the stipulated sanctions are mild – fines or withdrawal from the market, which creates prerequisites for frequent infringement. Supplement registration does not require all round of preclinical and clinical tests, so the effectiveness and harmless of the supplements are not safety proved.

**Table 1.** Interaction between commonly used herbal remedies and drugs

Herbal	Action/Use	Drugs	Interaction
Ginkgo biloba	Improve cognitive function Strengthen blood vessels and improve blood flow	Warfarin, Ticlopidin Clopidogrel Dipyridamol Aspirin and other NSAIDs*	Increased risk of bleeding
Hypericum perforatum	Mild depression	Antiretroviral Anticonvulsants Oral contraceptives Tricyclic antidepressants Theophyllin Ciclosporin Tacrolimus	↓ serum levels
		SSRIs** Tryptans CNS stimulants	Additive effect, ↑ serotonin levels
		Piroxicam Tetracycline	Increased photo toxicity
Echinacea	Boost the immune system	Anabolic steroids Amiodaron Metotrexat Ketoconazol	Increased risk of hepatic toxicity
Allium sativum	Lower high serum cholesterol and triglyceride levels, high blood pressure, high blood sugar	Warfarin	Increased risk of bleeding
		Chlorpropamid	Increased risk of hypoglycemia
Panax quinquefolius Panax ginseng	Strengthen normal body functions, increase resistance to stress	Antidiabetic	Additive effect - ↓ blood sugar levels
		Warfarin	↓ serum drug levels

\* NSAIDs – Non steroidal anti inflammatory drugs

\*\* Selective serotonin reuptake inhibitors

Supplements are granted as OTC and part of their sales take place outside pharmacies, where most are distributed through “multi-level marketing” with the assistance of “independent distributors”. These distributors are not, for the most part, medical doctors and their actions are based on crude commercial motives.

The liberal mode of distribution and false advertising fosters self-medication and hampers the control over the use of supplements. Furthermore, the erroneous opinion that if a herbal products are, they are safe causes patients not to inform their doctors when taking any food supplements. This

increases the risk of developing adverse interactions with simultaneously taken drugs.

Another problem is caused by the fact that in most cases there are no scientifically substantial data, and physicians are not provided with enough information about the harmlessness or the potential of interaction of the different herbal supplements. There is no system for monitoring the adverse effects of supplements, and even if there are any noticed, the rate of reports is low. (5)

Some of the most frequently used herbs (*Hypericum perforatum*, *Ginkgo biloba*, Ginseng, *Allium sativum*, different types of *Echinacea*) affect the actions of the most commonly used therapeutic classes (anticoagulants and antiaggregants, NSAIDs, cardiovascular drugs, hypoglycemic agents, anticonvulsants, antidepressants, etc.). The observed interactions are of pharmacokinetic and pharmacodynamic character. To the pharmacokinetic type belong the interactions between *Hypericum Perforatum* and certain drugs. A strong inducer of cytochrome P450 (CYP3A4, CYP2C9, CYP1A2), *Hypericum perforatum* could reduce their plasma concentration and discredit the effect of anticonvulsants, amitriptyline, theophylline, digoxin, verapamil, statins, antiretroviral agents, cyclosporin, oral contraceptives and warfarin. (6-18) On a pharmacodynamic level, *Hypericum Perforatum* interacts with selective serotonin reuptake inhibitors (SSRIs). (19-20) The effects of SSRIs may be potentiated, so patients, who take SSRIs, as well as antimigraine drugs from the group of triptans, should be advised not to take them together with medicines containing extracts of *Hypericum perforatum*. (21) Synergetic interactions and increased risk of hemorrhage are possible consequences of the joint use of herbal drugs with antiplatelet and anticoagulant properties (*Ginkgo biloba*, *Allium sativum*, *Eleutherococcus senticosus*, *Angelica archangelica*, *Borago officinalis*, *Medicago sativa*, *Aesculus hippocastanum*, *Plantago* species, *Trifolium platense*, *Curcuma longa*, Ginger, Green tea) and medicines with the same type of activity (warfarin, aspirin, clopidogrel). (22) The opposite type of interaction is observed with *Panax quinquefolius*, *Panax ginseng*, *Hydrastis Canadensis*, Green tea, etc., which antagonize the anticoagulant effect of warfarin. Herbal remedies that contain hypo- or hyperglycemic components may alter the effects of

antidiabetic agents. The hypoglycemic effect of insulin and oral diabetic agents is potentiated by medicines containing Ginseng (Asian, American), *Allium sativum*, *Psyllium* seeds, *Gymnema sylvestri*, Bitter melon and other. (23) Herbal remedies that involve *Ruscus aculeatus*, *Barosma betulina*, *Taraxacum officinalis* and *Juniper hamper* the glycemic control and should be avoided by diabetics. Some herbal remedies may aggravate the adverse effects of NSAIDs. If taken together with herbs with antiplatelet activity, NSAIDs increase the risk of hemorrhages and the risk of liver impairments if used with Black cohosh, *Echinacea*, Kava, *Teucrium polium*, *Larrea tridentate*, *Teucrium chamaedrys*. Combining Acetaminophen with *Symphytum officinale* and Yohimbe could lead to renal impairments. *Gossypol* and *Uvae ursi* may increase the irritative effect of NSAID upon the digestive system.

## CONCLUSION

Many people use complementary and alternative medicine for a wide variety of diseases or conditions. The current trend of widespread herbal food supplement usage is likely to continue in the future. The regime of registration and sale of food supplements needs to be changed so that it guarantees the safety and effectiveness of their use. It is important to know that, according to the law, supplements only complement the food and are permitted to make any prevention or cure claims. Physicians and other health professionals should control the consumption of supplements in order to improve the benefit/risk ratio. A popular opinion is that dietary supplements are absolutely harmless. The lack of information about the adverse effects and interactions is, to a certain degree, a result from the low rate of reports of the latter. It is necessary that a system that report the adverse effects of supplements is created, similar to the one that report the side effects of drugs. It is necessary to have a searchable database containing reports of adverse events associated with the use of herbal remedies. This system will allow both reporting and searching of adverse events in database. Since the majority of the cases involve self-medication, patients do not inform their doctors of them taking herbal products. All this requires physicians to actively seek information about the intake of supplements in the medical history and to continuously increase their familiarity with their efficiency and harmlessness. Consumers themselves

should hold more responsibility towards their health and consult their medics or other health professionals before buying and taking any supplements. Medicinal herbs may indeed be a therapeutic option, but only if used properly and under the guidance of doctors and other health professionals. Patients should be advised to choose mono-component, standardized products and to apply them in the prescribed doses and for the prescribed periods of time.

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