Toxicity of *Hypericum perforatum*

Bove GM: Acute neuropathy after exposure to sun in a patient treated with St John's Wort. Lancet 1998;352:1121–1122.

Ondrizek RR, Chan PJ, Patton WC, et al.:

An Alternative Medicine study of herbal effects on the penetration of zona-free hamster oocytes and the integrity of sperm deoxyribonucleic acid. Fertil Steril 1999;71:517–522.

Recently, toxicity of *Hypericum perforatum* has been debated, especially after two recent articles reporting a case of phototoxic neuropathy [1] and alterations of sperm motility, oocyte penetration and sperm DNA integrity in hamster [2].

The first paper [1] reported a case of neuralgia after sun exposure in a 35-year-old woman, taking 500 mg Hypericum extract per day, followed by a complete remission of symptoms after interruption of herbal therapy. The author linked neuralgia to the demyelinating action of hypericin, but he reported neither an instrumental nor a pathological examination. Besides, there was no description of the exact contents of the extract, where a chromatographic examination for this type of reports is mandatory.

According to current knowledge the minimal dose of Hypericum extract necessary to give rise to a phototoxic reaction is 30–50 times a therapeutic dose [3, 4]. A mild phototoxic effect was shown in a work, where a dose of 35 mg/day pure hypericin was administered by i. v. application to HIV-infected patients [5], while in a study of a St. John's Wort preparation combined with light therapy in patients with seasonal affective disorders the antidepressant effect of St. John's Wort was enhanced by light therapy [6].

The in vitro study about effects of Hypericum extract on hamster oocytes and sperms [2], evaluated fertility of oocytes after a 1-hour incubation with 0.6 and 0.06 mg/ml of a Hypericum extract and sperm motility after penetration. Oocytes penetration was low in the solution titrated at 0.6 mg/ml, while only sperm motility was diminished with a 0.06-mg/ml solution. In another experiment sperms were incubated for 7 days at 23 °C and treated with the same solutions. The 0.6-mg/ml solution caused a reduction of 90% of intact DNA and 80% of sperm function, while for the 0.06-mg/ml solution the reduction was 10% and 50%, respectively. Yet the paper lacks any useful description of the Hypericum extract matched.

In a study in healthy volunteers receiving 900 mg Hypericum extract daily for 8 days [7], plasma concentrations of hypericin and pseudohypericin were 8.5 and 5.8 ng/ml, respectively. These concentrations are thousands of times lower than the concentrations of the solutions of the above experiments.

We think that papers dealing with toxic or side effects of herbal drugs should always clearly describe the extract, unless it is an international well-known extract and registered trademark, because many commercial herbal compounds own the name of a plant while the real contents are unknown or may contain a part of the plant that has got other pharmacological effects; and likewise *Hypericum perforatum* is sold together with recreative foodstuff, too. Besides, a paper reporting undesired effects should demonstrate it by the evidence of instrumental and/or pathological proofs, and not only by clinical suspicions in a matter where commercial speculation is so evident and where it is so hard to distinguish between real and false herbal drugs.

We think that *Hypericum perforatum* extract used as standardized and titrated extract in flavonoids, hyperforin and hypericin [8] is a safe and efficacious therapy for treatment of depression.

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References

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