Comment on: “Phytomedicines in the Treatment of Migraine”

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The article “Phytomedicines in the Treatment of Migraine” by Rajapakse and Davenport is a well researched and informative review [1]. In addition to the data regarding butterbur I would like to draw attention to a recently published butterbur review in *Cephalagia Reports*, which the authors seem not to be aware of since it is not referenced in their work [2]. The *Cephalagia Reports* article reviews in detail suspected serious liver cases, pyrrolizidine alkaloids, regulatory issues, preclinical and clinical data of the special butterbur extract Petadolex[®]. All cases of suspected serious liver adverse reaction were assessed by employing the updated RUCAM (Roussel Uclaf Causality Assessment Method) test. No probable relationship between the butterbur root extract Petadolex[®] and cases of serious liver injury was found.

In regard to pyrrolizidine alkaloid toxicity, the authors stress in chapter 2.2.4 of their review that butterbur extracts should not be recommended for migraine prophylaxis unless issues with pyrrolizidine alkaloid toxicity have been resolved. Pyrrolizidine alkaloids are molecules known to cause liver damage.

The proprietary butterbur extract Petadolex[®] does meet the demands of the authors, since it is free of pyrrolizidine alkaloids. Pyrrolizidine alkaloids are removed in Petadolex[®] by a proprietary process and are not detectable in the finished product employing the latest state of the art analytical techniques. Also, Petadolex[®] contains the butterbur extract that has been used in all published clinical trials for migraine prophylaxis. No published clinical data exist for any other butterbur extract.

The concern for a safe and pyrrolizidine alkaloid-free butterbur extract is absolutely valid. However, the situation in the USA is confusing because many of the butterbur products sold in stores do not contain the Petadolex[®] extract and may therefore contain harmful pyrrolizidine alkaloids. In fact, the National Center for Natural Products Research has detected pyrrolizidine alkaloid at levels between 0.1 and 4.48 µg per tablet, capsule or gel content in 7 out of 21 tested products; one product was a liquid with a high content of 8.43 µg pyrrolizidine alkaloids per mL [3].

Despite the safety uncertainties of butterbur products that do not contain Petadolex[®], it is still possible to recommend butterbur for migraine prophylaxis. Patients are on the safe side regarding pyrrolizidine alkaloid toxicity as long as they stick to butterbur extracts that contain Petadolex[®], which is proven to be pyrrolizidine alkaloid-free. As a final note, not one single case of liver damage by the proprietary butterbur extract Petadolex[®] was reported in the USA and Canada. Petadolex[®] has been available in the USA since 1998 and in Canada since 2005.

Compliance with Ethical Standards

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Conflict of interest HCD received honoraria from Weber & Weber for the conduct of clinical trials and as a speaker.

References

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