

## Modern analytical procedures for the determination of taxus alkaloids in biological material

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Recently, Pietsch et al. reported five cases of fatal poisoning with *Taxus* ssp. [1]. In four of these cases, yew leaves were found in the stomach and duodenum of the deceased. Additionally, as toxicological evidence for the absorption of taxus ingredients, 3,5-dimethoxyphenol (3,5-DMP) was detected in body fluids and tissues using a high performance liquid chromatographic procedure with diode-array detection (HPLC/DAD) relying on the analytical approach described in 1993 by Musshoff et al. [2]. Based on their study, Pietsch et al. also provided data for future assessments of fatal *Taxus* poisoning: an acute intoxication caused by the ingestion of pre-extracted plant material is proposed to be characterized by a 3,5-DMP concentration in cardiac blood exceeding 300 ng/mL, a concentration of less than approximately 100 ng/mL is contrastingly suggested to indicate a subacute poisoning, predominantly caused by the ingestion of leaves.

3,5-DMP, the aglycone of the *Taxus* ingredient taxicatine, is formed by the cleavage of a glycosidic bond and readily absorbed into the blood. But neither 3,5-DMP nor taxicatine itself are responsible for the main toxicological effects. The main pseudo-alkaloid fraction is taxine B, which is responsible for the cardiac toxicity of yew due to its inhibition of calcium as well as sodium transport across the cell membrane of cardiac myocytes [3]. For the abovementioned reasons, the sole determination of 3,5-DMP in biological material cannot be seen as a definite proof for the absorption of toxicological relevant substances from yew, especially as there exist some other sources for 3,5-DMP, such as *Rosa chinensis* [4, 5], *Ruta graveolens* [6], or grapes [7].

Additionally, it has to be pointed out that in succession of the rather crude HPLC-DAD method, at present, the high performance liquid chromatography–mass spectrometry (LC-MS) technique is a standard procedure in forensic toxicology especially for the determination of alkaloids [8–11] and has already been used for a qualitative or semi-quantitative determination of various *Taxus* alkaloids in biological specimens after ingestion of plant material [12, 13]. Recently, Frommherz et al. [14] described a very sophisticated and fully validated procedure for a quantitative determination of the toxic taxine fraction taxine B/isotaxine B in body fluids using LC-MS/MS in fatal cases of *Taxus baccata* poisoning.

In our opinion, the easy-to-perform determination of 3,5-DMP in biological samples in cases of *Taxus* poisoning from the early 1990s should only be used as a preliminary test. In today's modern analytical toxicology, a definite proof for the absorption of the toxic taxine fraction can only be supplied by the determination of taxine B/isotaxine B by LC-MS/MS, which has to be considered as the gold standard procedure which should be used especially in forensic cases. Any interpretation on the basis of the quantitative results for 3,5-DMP in cardiac blood should be made carefully because redistribution cannot be excluded and additional care has to be taken if the dose, the duration of the agonal period, and the postmortem interval are not known.

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