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UPLC-MS/MS findings in a fatality involving massive ingestion of yew (*Taxus spp.*) leaves and berries

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OBJECTIVE: To present a fatal case of massive yew (*Taxus spp.*) ingestion, in which plant poisoning was confirmed by the identification of paclitaxel (taxol) in biological fluids using ultra-performance liquid chromatography/tandem mass spectrometry (UPLC-MS/MS).

CASE HISTORY: A 73-year-old woman was admitted to ICU in deep coma following deliberate ingestion of yew needles and berries (first mixed with an electric mincer...), presumably intended as a 'self-therapy' for her breast cancer. Biological fluids were sampled on Days 1 and 2 for toxicological analysis. Despite the resuscitation treatment the patient died on Day 7 in a clinical picture of seizures, cardiac arrhythmia, and renal insufficiency.

METHODS: 1°) *Extraction*. Biological fluids (2 ml) were extracted by diethyl ether after addition of 2 ng paclitaxel-d5 (Toronto Research Chemicals) as internal standard (IS). After agitation and centrifugation, the organic phase was evaporated and the dry extract resuspended in 50 µl of the UPLC mobile phase, from which 10 µl were injected onto the column.

2°) *Chromatography*. Apparatus: Acquity UPLC System (Waters). Column: Acquity UPLC C18 (Waters), 1,7 µm (100 x 2,1 mm, i.d.). Mobile phase: ACN/0.1% HCOOH (60 : 40, v/v), flow rate 0.6 ml/min. Duration of analysis: 3 min (including reequilibration time).

3°) *Detection*. Apparatus: Quattro Premier™ XE (Waters Micromass) tandem mass spectrometer set in positive electrospray mode, capillary voltage 3,0 kV, cone voltage 20 V, analysis in MRM mode (collision energy 14 eV) using the following transitions: 854.6 > 286.3, 569.3, 508.9 (paclitaxel); 859.6 > 291.3 (IS).

RESULTS: Under these UPLC-MS/MS conditions, the average retention time for both paclitaxel and IS was 0.85 min. LOD and LOQ for paclitaxel were 1 and 10 pg/ml, respectively. Analysis of biological fluids from the victim allowed paclitaxel to be detected in all samples tested, at the following concentrations: plasma (Day 1) 53 pg/ml, urine (Day 1) 359 pg/ml, plasma (Day 2) 35 pg/ml, whole blood (Day 2) 34 pg/ml.

CONCLUSION: Yew poisoning is clinically well-documented in humans or animals, but remains difficult to ascertain analytically: proposed methods include botanical identification of *Taxus* leaves in gastric material [1], determination of 3,5-dimethoxyphenol (a putative, specific ingredient of yew) in biofluids [2], or semiquantitative detection of *Taxus* alkaloids by HPLC-MS in biological specimens [3]. UPLC is an improvement of HPLC characterized by sub-2 µm stationary phases with an instrumentation dedicated to high pressures (*ca*. 15,000 psi), resulting in a spectacular drop in run times together with greater resolution and increased sensitivity. Coupled to MS/MS it provides an interesting and elegant alternative to previous methods by allowing simple and rapid, quantitative analysis of a specific alkaloid of yew. To our knowledge, this is the first report of an acute yew poisoning evidenced by unequivocal determination of paclitaxel in biological fluids of the intoxicated person.

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