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Phenacetin is coming back!

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Because of an increased risk of mortality and morbidity in case of phenacetin abuse, the less toxic metabolite acetaminophen (paracetamol) has been preferred as analgesic drug in many countries. For a couple of years, it has become common to detect phenacetin as adulterant of cocaine on illicit market, as observed by Fucci (Fucci N., Forensic Sci Int 141 (2004) 59 – 61). From the same time, we observed the presence of phenacetin beside cocaine in unknown screening of urine of drivers suspected of driving under the influence of drugs and postmortem samples. In order to estimate the importance of this phenomena, concentration of phenacetin and two metabolites (phenetidin and acetaminophen) were determined by high-performance liquid chromatography (HPLC) in blood samples of 23 drivers suspected of driving under the influence of cocaine and 3 postmortem cases involving cocaine consumption.

The quantitation of phenacetin and its two metabolites was performed by reversed-phase HPLC on a Agilent 1100 series. 5 µg of MPPH as internal standard were added to 1 ml of blood. Liquid-liquid extraction was realized after addition of 1 ml of ammoniac buffer (pH 9.5) and 3 ml of ethyl acetate. After evaporation of the organic layer, 200 µl of the initial mobile phase buffer (5% acetonitrile in 10 mM potassium phosphate buffer (pH 2.3)) were used for reconstitution. 30 µl of this sample were injected onto a short enrichment precolumn (CC 8/3 Nucleodur 100-5 C8 ec (Macherey-Nagel)) at a flow rate of 0.5 ml/min. The separation of the analytes was realized on a (CC 250/3 Nucleodur 100-5 C8 ec (Macherey-Nagel))

The limit of detection was estimated to 50 µg/l for phenetidine, 12 µg/l for phenacetine, and 20 µg/l for acetaminophen. The linearity was controlled from the limit of quantification (LOQ) (150 µg/l for phenetidine, 35 µg/l for phenacetine, and 50 µg/l for acetaminophen) to 10000 µg/l.

Among the 23 drivers, phenacetin was detected in blood in only 2 cases (< LOQ and 588 µg/l) and in all cases in urine. Acetaminophen was detected in blood in 12 cases (range : 53 µg/l to 1022 µg/l). Cocaine was detected in blood in 11 cases (range : 17 µg/l to 258 µg/l). Benzoylecgonine was detected in blood in 23 cases (range : 191 µg/l to 4650 µg/l). The highest blood concentrations of phenacetin, acetaminophen and cocaine were observed in the same case.

Among the 3 postmortem cases, phenacetin was never detected in blood but always in urine. Acetaminophen was detected in the 3 cases (range : 98 µg/l to 2018 µg/l). Cocaine and benzolecgonine were detected in the 3 cases (range : respectively 25 µg/l to 177 µg/l, and 540 µg/l to 1470 µg/l).

Considering that therapeutic concentrations of phenacetin range from 100 to 20000 µg/l and toxic concentrations were considered higher than 30000 µg/l (Winek C.L. et al, Forensic Sci Int 122 (2001) 107 - 123), we conclude that cocaine adulterated with phenacetin is a curiosity, which is probably interesting for the struggle of narcotic traffic but not alarming in terms of public health in comparison to cocaine toxicity.

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