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Scopolamine – its role in clinical and forensic toxicology

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PHARMACOGNOSY AND CHEMISTRY: S-(-)-Scopolamine (hyoscine) and S-(-)-hyoscyamine are the main alkaloids of various plants from the Solanaceae family such as Scopola carniolica, Atropa belladonna, Datura stramonium, Brugmansia sp., Hyoscyamus niger, or Mandragora officinarum. Both alkaloids are biosynthesized enantioselectively from S-(-)-phenylalanine. In contrast to scopolamine, hyoscyamine racemizes to R,S-hyoscyamine, so-called atropine, during storage, isolation and/or gastro-intestinal passage.
Culture History: Since living memory, preparations of the above-mentioned plants have been used for treatment of fever, cramps, or colics, and as aphrodisiacs, but also misused as hallucinogens and in drug facilitated crime. For example, Circe's transformation of Odysseus' fellows into pigs in Homer's Odyssey is most likely attributable to hallucinations caused by such plant extracts. Cleopatra as well as ladies in the Renaissance used such extracts to enlarge their pupils in order to become a "bella donna" (it. beautiful lady). In the Middle Ages, such extracts were used in witch ointments leading to sensation of flying besides hallucination or in love potions. Goethe poetically described the effects of such potions in his Faust: "With this drink in your body, soon you'll greet - a Helena in every girl you meet." Today, the mentioned Solanaceae, particularly Brugmansia sp. (Angel's Trumpet), are misused by young people as herbal hallucinogens either as tea or smoked.

PHARMACODYNAMICS: Scopolamine and atropine show anticholinergic effects by competitive inhibition of all subtypes of the muscarinic (G protein coupled) acetyl choline receptors (M1-M5) located in the CNS leading to sedative, anti-emetic, amnestic, and hallucinogenic effects or located in the periphery leading to decreased parasympathetic effects on eyes, gastrointestinal tract, heart, and salivary and bronchial secretion glands. Scopolamine is used today as mydriatric, spasmolytic, for prevention of nausea and vomiting associated with motion sickness, or for recovery from anesthesia and surgery, while atropine is used as antidote for poisonings with insecticide cholinesterase inhibitors, for premedication in anesthesia, and for treatment of severe bradycardia.

PHARMACOKINETICS: Pharmacokinetic parameters of scopolamine are dependent on the dosage form. The PK parameters after an oral dose of 0.5 mg were as follows: Cmax, 0.5 ng/ml; tmax, 0.5 h; AUC, 50 ng x min/ml; t1/2, 64 min; and F, 13%. Only 2.6% was excreted unchanged in urine. Scopolamine is metabolized by CYP3A which can be inhibited by components of grapefruit juice or by other drugs, possibly leading to PK interactions. Serum concentrations of scopolamine were found to correlate with different cognitive functions.
Bioanalytics: Only few bioanalytical methods have been described for scopolamine and/or atropine. Using the author's STA, both alkaloids, their metabolites and artifacts can be detected in urine. A new LC-MS/MS procedure was developed for detection and validated quantification of scopolamine, atropine and some other plant toxins in plasma and will shortly be presented.

CLINICAL AND FORENSIC TOXICOLOGY: Scopolamine and atropine have a narrow therapeutic range. As the alkaloid content in the plants may vary extensively, overdoses may occur when using non-standardized plant preparations, e.g. hallucinogenic Brugmansia tea, and result in more or less severe anticholinergic syndromes. Depending on the severity, symptomatic treatment or even antidote therapy with the reversible cholinesterase inhibitor physostigmine may be necessary. Fatalities may occur if severe poisonings are not treated in time or if patients with drug-related hyperthermia drown in apptempts to cool themselves by jumping into water. Due to their CNS effects, scopolamine and/or atropine have also been used in drug facilitated crimes. In the Saarland and Luxemburg for example, scopolamine was added to drinks of truck drivers at highway restaurants and the incapacitated victims were then robbed while being in a state of disorientation and hallucination.

KEYWORDS: *Scopolamine, Atropine, History, Pharmacology, Toxicology, Analytics*

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