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Pharmacological profile of tropane alkaloids

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ABSTRACT

Tropane is a nitrogenous organic compound commonly present in members of Solanaceae family, *Atropa*, *Scopolia*. The various alkaloids obtained include atropine, cocaine, scopolamine etc. They are some of the oldest medicines ever known to mankind. They have a wide variety of pharmacological actions on the central nervous system, respiratory system, gastrointestinal system and also as antidote against poisoning. Tropane alkaloids have anticholinergic properties as well. The aim of the article is to compile the properties of Tropane alkaloids from various sources.

Key words: Atropine, scopolamine, cocaine, antidote, anti cholinergic

INTRODUCTION

Secondary metabolites of *Solanaceae* family that share a common tropane skeleton are divided into two classes-tropane derivatives and ecgonine derivatives^[1] The common structural element is the tropane skeleton, (1R,5S)-8-methyl-8-azabicyclo[3.2.1]octane. Tropane alkaloids are some of the oldest medicines known to mankind. Some common tropane alkaloids namely, Atropine is obtained from *Atropa belladonna* L, and hyoscyamine from *Hyoscyamus niger* L. Poisonous *Solanaceae* family plants, presently classified as genera: *Atropa*, *Brugmansia*, *Datura*, *Duboisia*, known already in ancient times, and records of their employment in folk medicine of various ethnic groups are abundant^[1,4,5,6,7]. Contemporary medicine utilizes tons of atropine and scopolamine extracted from genetically modified cultivars, while ever growing demand enhances new, chemical and biotechnological methods of their manufacturing. In parallel, cocaine obtained from two *Erythroxylon* species, which is of limited use in medicine because of very strong addictive properties^[1,8,9], became a subject of illicit manufacturing and trafficking of “recreational drugs”, with socioeconomic and health endangering consequences on global scale.

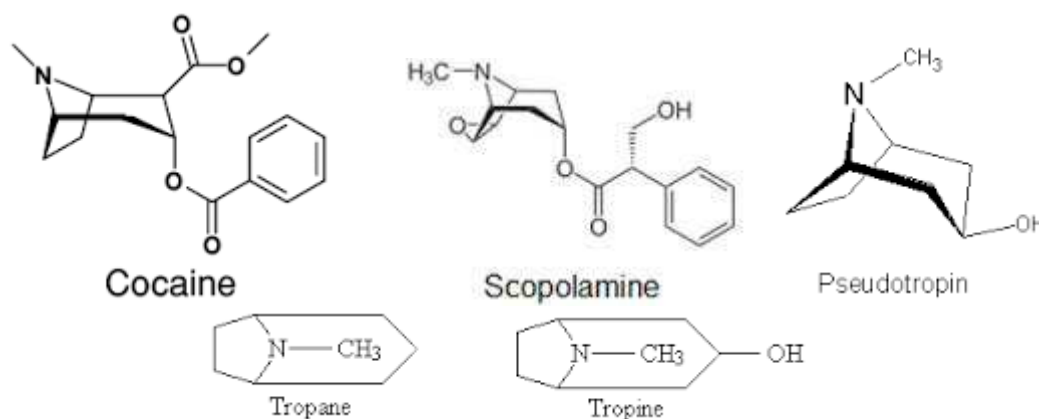
ORIGIN OF TROPANE ALKALOIDS:

Tropane alkaloids are obtained from plants like *Atropa belladonna*, *Datura stramonium*, *Hyoscyamus niger* etc. But due to recent requirements in pharmaceutical industries *Datura inoxia* is being used increasingly^[10] It has been observed that tropane alkaloids have been used as traditional medicines, poisons, potions etc. These include: deadly nightshade (*Atropa belladonna*), mandrake (*Atropa mandragora*), henbane (*Hyoscyamus niger*, *Hyoscyamus albus*), jimson weed, also called thorn apple (*Datura stramonium*) and scopolia (*Scopolia carniolica*), among others^[11]. Due to its varied pharmacological actions tropane alkaloids are now studied for pharmaceutical preparations. Attempts to isolate the pure active principles, followed by investigation of their biological activity were continued throughout the 19th century^[12,13,14,15], while structure elucidation and subsequent syntheses crowning chemical part of the study extended well into the 20th century^[16,17,18]

STRUCTURE

Tropane alkaloids have a bicyclic ring system (N-methyl-8-azabicyclo[3.2.1]octane). Another bicyclic aminoalcohols encountered in *Solanaceae* plants include: di and tri- hydroxylated tropines, 6,7-epoxide and corresponding de-N-methylated compounds (N-nortropane derivatives).^[10] Tropane alkaloids typically occur as esters with carboxylic acids and tropic acid seems to be chemotaxonomically distinct marker for alkaloid containing

plants which belong to species of *solanaceae* family^[19]. Some of the derivatives of tropane alkaloids are Tropane, Tropine, Tropanone, Scopolamine, Cocaine, Pseudotropine.



MEDICINAL USES OF TROPANE ALKALOIDS

Solanaceous alkaloids are anticholinergic drugs with effects on both central and peripheral nervous system. It was demonstrated by Schmeiderberg and by Adamuck that the site of action of acetylcholine antagonism was at or beyond the postganglionic nerve endings. All the parts of the plant contain the alkaloid and hence may sometimes lead to accidental toxicity. The mood elevating activity of extracts from tropanealkaloid-containing plants (e.g. hallucinogenic) are known since antiquity but the main application of these substances in modern medicine is different^[12,20,14]. These alkaloids cause mydriasis, accompanied by cyclopegia. Atropine is used as the substance of choice for ophthalmic applications as it is more stable and do not affect the central nervous system when given in small doses. They are useful in treatment of bladder spasms, irritable bowel disease, colic, cystitis, pancreatitis peptic ulcer^[1]. Its effects on other body systems include: inhibition of the respiratory tract secretory activity and bronchodilation, alteration of the heart rate (bradycardia at low doses and tachycardia at high doses) reduction of gastric secretions, cognition, sleep cycle, stress response and inhibition of sweating accompanied by rise of body temperature. Atropine is used as an antidote for organophosphorous poisoning. Scopolamine hydrobromide 0.5-1.0 mg is used as a remedy for motion sickness^[10]

ADVERSE EFFECTS

Atropine has the following side effects:

At 0.5mg- slight cardiac slowing, dryness of mouth and inhibition of sweating

1 mg- increase in heart rate, papillary dilation, dryness of mouth, thirst

2 mg- rapid heart rate, dilation of pupil, palpitation, blurred vision

5 mg- rapid heart rate, palpitation, dilated pupil, disturbed speech, restlessness, headache, dry hot skin

>10mg- above symptoms, rapid and weak pulse, blurred vision, flushed and scarlet skin, ataxia, hallucinations, delirium, coma

The side effects also include CNS disturbances, dry mouth, dilation of pupil, and tachycardia^[10]

PHARMACEUTICAL PREPARATIONS

The main sources of tropane alkaloids include belladonna (*Atropa belladonna*), jimsonweed (*Datura stramonium*), henbane (*hyoscyamus niger*) etc. They are given as non-prescribed Over the counter herbal supplement. Various synthetic preparations have been introduced wherein one component of its structure is replaced by another. For example, tropic acid residue was replaced or quaternary salt function was introduced. These modifications exhibit similar characteristic as that of the natural source but have enhanced selectivity. Many preparations are available which are based on a single active component or one of the following substances such as scopolamine hydro bromide, scopolamine borate, scopolamine butyl bromide, atropine sulfate etc. in a composite medicine. They can be given orally as in tablets; topical as in eye drops, ointments; injections intramuscularly or intravenously.

PHYTOCHEMICAL ANALYSIS

Initially analysis of tropane alkaloids was done by chemically inducing color development in the dissolved sample followed by colorimetric evaluation of the intensity of the sample. General problems involved in chromatographic separations of inherently basic analytes on weakly acidic sorbents, including most popular silica gel, are well known and have been largely reduced by introduction of new generations of solid supports and stationary phases^[21]. Some tropane alkaloids contain aromatic moiety which renders them detectable by UV light. Flame ionization detection is used in gas liquid chromatography (GLC) for the identification of tropane alkaloids. Typically, analysis were

performed on a glass column packed with SE-30 supported on Chromosorb, operated with temperature gradient with helium carrier gas, while later versions make use of capillary columns and mass spectrometry detection^[22,23]. Planar Chromatography (TLC) exhibits potent operational source because of low cost analysis, suitability for phytochemical studies and identification of pharmaceutical components and preparations^[24]. Another method for quantitative determination of organic compounds is liquid chromatography (HPLC). Recently Micellar Electrokinetic Capillary Chromatography (MEKC) has been applied for analysis of tropane alkaloid mixtures present in transformed and genetically modified plant material from various *Solanaceae* species.^[25]

CONCLUSION

This review provides a bird's eye view of the sources, structure, derivatives, medicinal uses, adverse effects, phytochemical analysis and pharmaceutical preparations of Tropane alkaloids. This review has been done in the hope that it would be useful to those who perform any research on Tropane alkaloids in the near future.

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