

# Predatory Drug Scopolamine in Forensic Investigations: A Mini-Review

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**Abstract:** *Scopolamine (SCP) is a therapeutic drug used in treatment of motion sickness. However, it has been frequently abused in sexual assaults and robberies, as well as for recreational purposes because of its euphoric effects. In the present times, the global abuse of this drug is rapidly increasing among the youth especially in developing countries as a result of the illicit sale and purchase of SCP in India and other countries. Studies indicate that quantitative reporting of the drug in detained samples will need to be performed at the national level in the future. Therefore, development in the identification and confirmation of SCP in biological and non-biological matrices are required. In this mini-review, we present a few cases of SCP abuse in the forensic setting, its extraction, and methods of quantitative analyses.*

**Keywords:** Scopolamine, SCP, Atropine, stimulating, hallucinations, intoxication

## 1. Introduction

Scopolamine (SCP) is a terpenes alkaloid derived from scopolamine, also known as hyoscyne, an opiate medication produced from a variety of plants in the Solanaceae family, including nightshade, henbane, and jimsonweed. SCP is a strong dizziness cure, most likely because to its capacity to depress the nerve system's core (brain and spinal cord) hyoscyamine, which is found in the leaves and tops of henbane, deadly nightshade (belladonna), and jimsonweed. It is a potent toxin that is the primary natural source of racemic atropine [1].

It is a highly effective drug for the treatment of seasickness and is more effective than other medications, such as cinnarizine. SCP is administered via transdermal delivery patches, commercially referred to as Transdermal Therapeutic systems (TTS) in such cases. The drug is released from a reservoir in a patch applied to the skin which causes changes in the gastrointestinal tract motility observed in seasickness [2]. SCP is also a psychotropic drug that is often added to beverages for recreational purposes as it causes auditory and visual hallucinations. SCP is a muscarinic antagonist that has an anticholinergic action. Scopolamine, a parasympatholytic that is chemically identical to atropine (a racemate of hyoscyamine), is used in cases involving reduced parasympathetic activity, primarily for its impacts on the retina, gastro-intestinal tract, cardiovascular system, salivary and bronchial secretion glands, and, in rare cases, for a CNS action. As a result, SCP is best utilised as an antiemetic and as a premedication before to anaesthesia. That amine is the most powerful anti-motion sickness drug.

SCP was the first commonly available alkaloid-delivering drug in a method of transdermal therapy (TTS-patch). Due to its short plasma half-life and dose-dependent adverse effects, SCP has limited therapeutic usefulness whether administered orally or parentally (particularly hallucinations and the less serious responses, such as sleepiness). Transdermal dosing was developed to

decrease the reasonably high prevalence of side effects. The commercially produced TTS-patch contains a 1.5-mg solvent and a 140-g stimulating dose to quickly attain the stable content of standard drug. The patch delivers 0.5 mg of nicotine (at a rate of 5 g/h) over three days. SCP plasma levels following topical treatment vary significantly across individuals. The alkaloid achieves maximal plasma level (C<sub>max</sub>) of about 100 pg/mL (ranging 11-240 pg/mL) after about 8 hours. Over a 72-hour period, the plaster releases SCP, resulting in persistently high serum levels (content ranging 56-245 pg/mL), succeeded by a peak in urine SCP clearance [3]. The earliest signs of intoxication are mydriasis and accommodative paralysis, following by mouth dryness. SCP causes cholinergic depression, voluntary coma, and respiration in extreme cases [4].

This drug's abuse is an increasing concern across the world, because of its significant and permanent consequences on consumer health, but it also is frequently associated with criminal activities. Not only can SCP impair memory and create lethargy, disorientation, weariness, and bewilderment, but it is also used to limit victims' free will throughout robberies and sex offences [5]. Several incidents have been documented in which victims were given SCP via different means, including tainted alcoholic beverages [6].

## 2. SCP in Forensic Investigations

### 2.1 Homicide

The idea of using SCP for the purpose of homicide is not new. In the famous tragic play of Shakespeare-*Hamlet* the protagonist King Hamlet of Denmark mysteriously dies and only a few weeks later, his brother Claudius married his widow, Queen Gertrude. While many believed that his death was caused by snakebite, it was later revealed that Claudius had killed him by pouring an ampoule of henbane into his ear [7].

In a case of attempt to murder, a 58-year-old guy, who had no past medical issues, was hospitalised in

unconsciousness state and was discharged with a normal neurological evaluation 24 hours later. When he revealed to have been gaged by a stranger, a judicial request was made 48 hours after the incident. The handkerchief had a powerful smelling powder that made the victim pass out. He remembered breathing the powder but wasn't sure of swallowing it. SCP was discovered in values of 7 and 510 ng/mL Both full urinalysis samples were tested. Both full urinalysis samples contained only this hallucinogenic compound [8].

A man and a woman had been found guilty of the first known murder in the United Kingdom via the toxin devil's breath. A 43-year man was found dead in his south London apartment in June 2019 after being targeted on a dating app by a 25-year old male. He was administered SCP in a spiked soft drink [9].

## 2.2 Suicide

In an attempt to suicide case [10] two weeks after ingestion of 18 Sominex tablets (night-time sleep aid), a 20-year-old high school graduate was hospitalised. Massive dosages of SCP were found in his samples when quantification was done by GCMS instrument. The samples tested included hair, serum.

## 2.3 Accidents / Overdose

Although SCP is employed as a therapeutic drug in clinical settings, it is also used recreationally and cases of overdosing are reported frequently. Barceló. [11] describe the case of a lady who fell into a coma after an unintended overdose and had SCP was found in large quantities in biological samples including serum and urine collected 1 hour after hospitalisation.

In another reported case [12] three children's hair was sent to on the lab after they were allegedly exposed to Feminaxin the United Kingdom which is a widely available non-prescription medication in the region. It is used to alleviate headaches, dental pain, and discomfort linked with menstrual cramps. Per pill, the primary constituents are painkiller (500 mg), morphine (8 mg), nicotine (50 mg), and SCP (100 g). In this case, a lady was accused of abusing her children on a regular basis and pressuring them to take three to ten Feminax tablets each day, according to the British police. Two girls and one boy were among the three children participating. The children were 12-16 years old at the time the claim was made, but the administration dismissed it was said to have lasted for around ten years. At the time of the first complaint, the children were in the custody no human blood or biological fluids had been taken by the authorities. As a result, the window for drug detection in bodily fluids has already closed. Around 10 weeks following the last possible dose, dna specimens were taken from the youngsters. When SCP concentrations were measured by LC-MS, they ranged from 0.2 to 20 pg/mg, with a relative extraction recovery rate of 67 percent.

A middle-aged woman claimed that her accused boyfriend

had drugged her covertly in what amounted to a drug facilitated sexual assault. A toxicological investigation of the couple was performed where hair was the only biological matrix available as considerable amount of time had elapsed since the last likely exposure to the medication. As a result, they consented to do the hair analysis and proposed that the analyte be scopolamine. The married couple and their lover both worked in the medical field and had easy access to scopolamine. The patient reported that she had not indulged in any drug misuse or major use of medical medications in the past year. SCP peaks were found in the hair samples using LC-MS/MS, indicating SCP exposure.

A 10 child has also been reported. Who had severe disorientation and psychotic episodes after ingesting travel sickness medicine, which was later proven to be directly attributable to scopolamine poisoning. 2.4 milligrammes of scopolamine hydrobromide was ingested. Patients are reported by Van Sassenbroeck and colleagues who got an unintentional overdose of 10 mg of scopolamine changing its form instead to scopolamine butylbromide due to compounding problems. 4In several cases, increased the difficulty for months, or one person was misdiagnosed with a brain haemorrhage [13].

In an accident poisoning case, brought home by her daughter after attending a party that made her unconscious after experience hallucinations. Toxicological examination of urine samples revealed the presence of SCP and ibuprofen [14].

## 3.Extraction of Drugs

For various matrices, several extraction procedures have been investigated. Solvent extraction and solid phase extraction are the most frequent.

### 3.1 Solvent Extraction

This is the oldest method of extraction and is also known as extraction (LLE). It works on the principle that a solute or analyte can be distributed in a specific ratio between two immiscible solvents, typically water (water-soluble phase) and organic solvent (mobile phase). LLE is commonly employed in sample preparation for cleanliness and enrichment, resulting in improved signal [15].1 or maybe more species are moved from one liquid state to the next, usually from aqueous to organic. Chemical potential drives the transfer, which means that once completed, the total system of chemical components that constitute the solutes and solvents is more stable (reduced free energy) [16]. The goals are to breakdown (solvate) a specified particle or chemical collection (solute) in a liquid (solvent) and wash it out of solid plant matter. After that, the solvent is removed from the solution, allowing the solute to be concentrated [17].

SCP extraction by LLE was carried out on 1 mL [Liquor] using ethyl acetate (1: 1, v/v) in hexane. The organic layer was recovered and allowed to evaporate after stirring and separation. The residues were reconstituted in 80 L before being inserted into a 1.9-m Silica gel 60 Silver PFP

column [18].

Hair fibres were decontaminated thrice with dichloromethane and washed twice with warm water before being segmented for atropine and SCP measurement in another way. In a ball mill for at least 2 minutes, each segment was crushed into a fine, consistent powder. 20 mg of ketamine-d4 10 minutes incubation in 1 mL of pH 5.0 stock solution inside the existence of 100 ng of dexmedetomidine as an endogenous control (IS). LLE was performed using 4 mL molar ratio: ethanol extract (1: 1, v/v) mixture after adding 2 mL at pH 9.7 of hydroxide solution. The organic phase was obtained after fifteen minutes of stirring and 5 minutes of extraction, and the liquids were drained till the material was dry. The leftover was regenerated in 80 mL of solvent system and added to the chromatographic equipment in increments of 10 mL [19].

### 3.2 Solid phase extraction (SPE)

The chemical partitioning between two solid and liquid phases is the core premise of SPE, with the solid phase having a stronger affinity than the sample matrix. Eluting the molecules that remained on the solid phase with a solvent that has a higher affinity for the analytes can remove them [20].

There are four steps in a typical solid phase extraction [21]:

1. The sorbent is moistened; the cartridge is first equilibrated or conditioned with a solvent.
2. The analyte-containing loading solution is then percolated through the solid phase. The analyte and some contaminants should ideally be maintained on the sorbent.
3. Impurities are then rinsed out of the sorbent.
4. During this elution stage, the analyte is collected.

In the SPE extraction process various liquids, including boosted soft drinks and alcoholic beverages, have been tried. Whisky in 1: 3 (v/v) proportion with cola drink, vodka in 1: 3 (v/v) proportion with tonic water, purple wine and inexperienced tea infusion. By combining 200 mL boiling water + 2 g tea. After cooling the infusion to room temperature, the supernatant was separated, and the tests were performed [22-26].

C18 cartridges are primed with 1 mL acetone proceeded with 1 mL of 0.1 M NaOH for SCP extraction by SPE. 1 mL of beverages were eluted via the cartridges, followed by 1 mL of water: acetonitrile (1: 4, v/v). The cartridge was then sterilized by manually blowing air through them with a 1 mL syringe [27].

## 4. Instrumental Analysis

For the quantification of extracted SCP, chromatography is coupled with mass spectrometry detector and the results are obtained in nanogram concentrations. Two of the readily available techniques are discussed.

### 4.1 Gas Chromatography Mass spectrometry (GC-MS)

The GC-MS apparatus separates chemical mixtures and analyzes the components at the cellular scale. It is one of the most exact environmental sample analysis tools on the market. The GC works by heating a mixture and separating it into various components. The hot gases are sent through an inert gas-filled column (such as helium). As the separated chemicals exit the column aperture, they pour into the MS. MS uses the mass of the analyte molecule to determine the components [29]. Each isolated component from the GC will be broken down into ionised pieces by the MS. To do this, a high-energy electron beam is sent through the sample molecule, resulting in electrically charged particles or ions. The fragments of the original molecule might be big or little. There will be a mass assigned to each charged piece. The mass to concepts presented (m/z) is calculated by dividing the fragment's mass by its charge. The pieces are then subjected to the acceleration and deflection processes [30].

### 4.2 High Pressure Liquid Chromatography (HPLC)

The division of the element (sample) between a solvent system (eluent) and a solid phase is the basis for HPLC separation. Relying on the analyte's chemical composition, the molecules are slowed as they travel through the stationary phase. The unique intermolecular interactions that occur between two molecules and the packing material dictate how long it spends "on-column." HPLC is a significantly more sophisticated kind of column chromatography. At factor of up to 400 atmospheres, a compressor drives a solution through a column. A granular substance composed of solid particles such as quartz or monomers is used as the column packing material, adsorbent, or stationary phase [31].

### 4.3 Liquid Chromatography-Mass spectrometry (LC-MS)

The LC-MS method use an HPLC to separate the different components of the sample, followed by ionisation and separation of the ions based on their mass proportion [32]. The amounts of atropine and SCP in diverse samples were determined by LC-MS [32]. A C18 column was applied for separation and purification. The LC-MS methods are using an HPLC to separate the various components of a mixture, followed by ionisation and separation of the ions depending on their mass/charge ratio. A gradient of mobile phase A (2 v/v) for the separation percent formic acid in methanol: water (7: 93) and solvent ratio B (2 v/v) basis points formic acid in methanol) was used.

## 5. Conclusion

Toxicologists have diagnosed the chronic and acute toxic symptoms of SCP in various parts of human body. However, the global rise in cases of abuse of this drug makes it relevant to forensic toxicology. Many cases of deaths by homicides, suicides, and accidental overdose have been reported. Methods of extraction of this drug from various matrices including non-biological and

biological samples have been documented. Analytical instruments used for quantification in blood, saliva, urine, sweat of SCP have been employed using GC-MS, HPLC, LC-MS. This mini review on SCP justifies its significance in forensic science and further developments in the toxicological investigation of this drug are required in the future.

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