

Review on Toxicological Aspect of Ahiphena (Papaver)

Dr Rajath M¹, Dr AshwinKumar S. Bharathi², Dr Akbersha. A³

¹PG Scholar, Dept. of Agada Tantra, Sri Dharmasthala Manjunatheshwara college of Ayurveda and hospital, Hassan-573201

²Professor, Dept. of Agada Tantra, Sri Dharmasthala Manjunatheshwara college of Ayurveda and hospital. Hassan-573201

³Sri Dharmasthala Manjunatheshwara college of Ayurveda and hospital, Hassan-573201

ABSTRACT:

Ahiphena (papaver) is one among *Upavisha* which is air-dried latex juice obtained from unripe capsules of white poppy. White poppy is botanically classified as *Papaver somniferum* and belongs to family *Papaveracea*. The name poppy is derived from Latin meaning sleep inducing. The Ayurvedic text *Rasa Tarangini* included Ahiphena (papaver) among eleven *Upavishas*. Opium yields wide range of natural, semi synthetic and synthetic alkaloids namely morphine, thebaine, codeine and papaverine which is commonly used in medicine. Semi synthetic heroin, hydro morphine, oxymorphone, oxycodone and synthetic meperidine, methadone, levorphanol, diphenoxylate, fentanyl, propofol. Opium and its alkaloids cause drug dependence and it is most commonly abused substances after cannabis. Opioids are the main drugs of abuse in Asia, Europe and much of Oceania. The opium act of 1857 empowers only Central Government to cultivate poppy plants and manufacture opium with the help of farmers authorized by Government. The opium act 1878 prohibits import, export, transportation, possession and sale of opium. The Narcotic Drugs and Psychotropic Substances Act, 1985 includes opium as narcotic and psychotropic substances and consumption of opium and its leads to imprisonment for one year or with fine or with both. Schedule-E (1) of Drugs & Cosmetics Act, 1940 has included opium in list of poisons. This study design to present all toxicological aspect of Ahiphena in Ayurvedic and contemporary View to treat people of opium poisoning and counselling in drug abuse.

Keywords: Ahiphena, Pappavar, abuse, Upavisha

INTRODUCTION

Drug abuse is a significant health and socioeconomic issue today. Opium, the second most commonly abused illicit substance after cannabis, is a key contributor to this problem. Derived from the milky latex of the *Papaver somniferum* plant, opium is cultivated in India and other Eastern countries. In India, its cultivation and distribution are strictly regulated and supervised by the government, particularly in Ghaziabad, Uttar Pradesh¹. Opium consumption is prevalent across India. While crude opium is commonly used, a special decoction called *kasoomba* is offered to guests during festive occasions. Additionally, opium is smoked in various forms, such as *modak*, *chandru*, and opium drossel¹. The global demand for opium is approximately 6400 metric tons annually, though its cultivation often exceeds this amount². The opium plant grows to about one meter in height and produces 5 to 8 capsules. These ripe and dry poppy

capsules have sedative and narcotic effects due to traces of opium. A warm decoction made from them is used locally as a sedative and poultice. After collection, opium turns into a dark brown solid or powder. It can be smoked, injected intravenously, or taken orally by addicts. Opium is known for its bitter taste and distinctive smell.

The toxic effects of opium are severe and wide-ranging. Chronic use can lead to physical dependence and addiction, characterized by a compulsive need to use the drug despite harmful consequences. Overdose can result in respiratory depression, coma, and death. Long-term use can also cause significant organ damage, including liver and kidney damage, and can impair cognitive and physical functions. Additionally, opium abuse increases the risk of infectious diseases due to needle sharing among intravenous users.

ACTIVE PRINCIPLES OF AHIPHENA³

The opium has about 25 alkaloids, divided into two groups:

A. Phenanthrene derivatives (main narcotic constitute)

1. Natural alkaloids

- Morphine (10%): White color powder, bitter test and Alkaline in nature
- Codeine (0.5%)
- Thebaine (0.3%)

2. Semi-synthetic opioids: They are produced by chemical modification of an opiate and include hydromorphone, diacetylmorphine (heroin, brown sugar or smack), oxycodone and oxycodone.

3. Synthetic opioids: These substances are not derived from an opiate, but binds to an opioid receptor and produce opioid effect clinically. It includes methadone, fentanyl, pentazocine, tramadol and meperide (pethidine).

B. Benzyl-isoquinolone derivative (no significant CNS effects)

- Papaverine (1%)
- Noscapine (6%)^[3]

Morphine

Morphine is a naturally occurring phenanthrene derivative. It is the standard drug against which all other opioids are compared. Morphine can be given orally, intramuscularly, intravenously, subcutaneous, rectally, epidurally and intrathecally. Morphine is extensively metabolized by the gut wall and the liver to morphine to morphine-3-glucuronide (M3G) (70%), morphine-6-glucuronide (M6G) (10%) and to sulphate conjugates. M6G is 10-20 times more potent than morphine and is normally excreted in urine. It is a potent analgesic with good sedative and anxiolytic properties. It may cause euphoria, dysphoria, and hallucination. It causes respiratory depression and cough suppression. It has minimal effect on cardiovascular system and may produce bradycardia and hypotension. Nausea and vomiting are common side effects. Histamine release may leads to itching, rash and bronchospasm. Meiosis is common. Tolerance and dependence may develop⁴.

Codeine

Codeine is a natural opiate and is also derivative of morphine. It is a crystalline solid, slightly soluble in water but freely soluble in organic solvents. Codeine is used as a cough depressant. It causes little euphoria and has low abuse potential. It may cause excitement and disorientation. It is less sedative and less likely to cause respiratory depression than morphine. Constipation is common and causes nausea. It is also use in antitussive and anti-diarrheal preparations. It can be given orally and intramuscularly. The dose for an

adult is 30-60 mg by either route and can be repeated at 6-hour interval. It is also used as an analgesic in mild to moderate pain⁴.

Heroin

Heroin (Diacetyl morphine) - It is semi synthetic opioid and diacetylated analogue of morphine. It is 1.5-2 times more potent than morphine. Since 1954 following the World Health Organization inquiry, nearly 54 countries have decided against the use of heroin as a medicine, as amongst all drugs of addiction it is most dangerous. It can be smoked or injected. Sometimes it is taken in the form of snuff. It has a marked irritant action on nasal mucosa. Morphine is most frequently found as a metabolite of diacetyl morphine (heroin). Over 13 million people in World are heroin injectors and users. Heroin acts as an agonist on the mu, kappa and delta receptors in central nervous system. The analgesic effect of heroin is due to its action on mu receptors while mu2 receptors are responsible for respiratory depression, delayed gastrointestinal motility, miosis, euphoria and physical dependence, The mechanism of death due to heroin overdose is respiratory depression⁴.

By Dhanwanti Nighantu, Rasa Tarangini, Raja Nighantu, Bhava Prakasha, it is categorized as Upa Visha Dravya⁵ (subtoxic group).

- Jarana (White-colored variety) - Acts as a digestive agent
- Marana (Black-colored variety) - Can cause death
- Dharna (Yellow-colored variety) - Acts as a health tonic
- Sarana (different colored variety) - Eliminates metabolic residues from the body

Aam

Properties of *Ahiphena* (papaver) as per Ayurveda [6,7]

- *Rasa - Tikta (bitter), kashaya.*
- *Guna - Laghu (light), Ruksha (dry), Sukshma (small), Vyavayi (spreading without digestion), Vikashi.*
- *Veerya - Ushna (hot).*
- *Vipaka - Katu (pungent).*
- *Prabhava - Madak (somniferous).*
- *Doshaghnata – Kaphavatashamaka*

Useful parts of *Ahiphena* (papaver)⁸

Seeds, seed oil, Unripe capsules, Flowers, Exudate from fruits and Latex.

Mode of Action as per Ayurveda [9]

The above- mentioned properties of *Ahiphena* (papaver) responsible of its action in the body. Due to its *Laghu Guna* (light) it enters into all body channels and also is *Dushchikitsya* i.e. difficult to treat. Due to its *Ruksha Guna* (dry) it causes pain in body. Due to its *Sukshma Guna* (small) it enters in small blood vessels in the body. Due to its *Vyavayi Guna* (spreading without digestion) it is highly permeable and is quickly absorbed in the body. *Vikashi Guna* affects *Dosha, Dhatu* and *Mala* of body. *Ushna Virya* (hot) of *Ahiphena* vitiates *Pitta* (structure governing heat, metabolism and transformation in body and mind) and *Rakta* (blood) in the body. Due to its *Madak Prabhava* (somniferous) it causes sudden excitement and then comma.

SHODANA OF AHIPHENA^[10,11]

The Latex obtained from the fruit should be subjected to *Bhavana* (Trituration) with *Ardraka Swarasa* (fresh ginger extract) for 21 times.

Pharmacodynamics^[12]

Opium reduces intensity of pain and unpleasant feeling due to pain. The unspecific effect of opium to the different opioid receptors produce various effects such as sedation, euphoria, dysphoria, respiratory depression, pruritus, constipation, nausea and vomiting. patients have reported a sensation of stress relief even in presence of pain as well as the presence of sedation, hypoventilation, cough inhibition prolonged apnea, myosis and respiratory obstruction. In cardiovascular system it causes peripheral vasodilation including cutaneous causing flushing of face, neck and thorax, impaired sympathetic reflex and postural hypotension. It reduces peristalsis, delayed gastric emptying and urinary retention.

Mechanism of action ^[12]

Opium activates specific G protein- coupled receptors in brain, spinal cord and peripheral nervous system. There are three major classes of opioid receptors being *delta- opioid*, *kappa-opioid* and *mu opioid*. Opium generates an agonist activity which later opens the potassium channels and prevent the opening of voltage gated calcium channels. This activity causes a reduction in neural excitability and inhibits the release of pain neurotransmitters. The addictive character of opium is related to the binding to the mu-opioid receptors, which will activate dopaminergic neurons in the ventral tegmental area of the midbrain and thus enhance the dopamine release in the nucleus accumbency. This mechanism involves the reward activity of the mesolimbic dopaminergic pathway.

FATAL DOSE

0.24 g of crude opium is the smallest fatal dose and 0.3 g is the average fatal dose. The lethal dose for healthy adult not addicted to opium usually varies from 0.9 to 1.8 g. The fatal dose of morphine or its salt is about 180 to 480 mg. 200mg is an average fatal dose of heroin. Fatal dose of codeine is 0.8 g, but 240 mg of codeine cause dangerous symptoms and it rarely causes death. Minimum fatal dose of pethidine is about 1 gut, Methadone 100 mg, Propoxyphene 1 gm, Pentazocine 300 mg and Fentanyl is 50-100 times more potent than morphine.¹³

FATAL PERIOD

6-12 HOURS

ELIMINATION

It is destroyed by the tissues, particularly by the liver. It is eliminated mainly as morphine in urine and faeces. It can be recovered from stomach, intestines, saliva, bile and milk. Morphine can be easily recovered from blood, urine and bile .¹⁴

DIAGNOSIS¹⁵

- smells of opium (raw flesh)
 - Pin-point pupils with no reaction to light
 - Moist perspiring skin
 - Reduced body temperature <35 C
 - Cyanosis, frothing at nose and mouth
- Classical Triads include

Stage of excitement: The stage is short

- The person feel better with increased sense of wellbeing

- Talkativeness
- Restless or hallucinations
- Flushing of face.

Stage of stupor

- Headache
- Nausea and vomiting
- Giddiness
- Drowsiness
- Miosis
- Stupor.

3. Stage of narcosis

- Patient passes into deep coma
- Muscles becomes flaccid
- Diminished or absent reflexes
- Hypothermia
- Hypotension
- Bradycardia
- Bradypnea
- Non-cardiogenic pulmonary edema
- Convulsions
- Respiratory depression
- Death

The classic triad for opioid poisoning is **miosis, coma And respiratory depression.** ¹⁵

MANAGEMENT¹⁵

The management of the *ahiphena* poisoning includes

- The vitals should be maintained
- Gastric lavage with normal saline or KMnO₄(1:5000) potassium permanganate
- Activated charcoal administration to prevent further absorption
- Whole bowel irrigation
- Antidote Administration-Naloxene
- Symptomatic treatment
- Psychiatric counselling in case of abuse

POST MORTEM FINDINGS ¹⁶

External

- Smell of opium from mouth or nostrils.
- Cyanosis on over all body or blackish
- Froth at the mouth and nostril
- Pupils are constricted or pin point pupils, can be dilated also.
- Allergic reaction to intra venous heroin may be seen.

- Needles prick or tracks are found occasionally, depending on the route of intake.
- Post mortem staining is purple or blackish.

Internal

- Diffuse cerebral edema.
- All internal organ are congested, trachea contains frothy secretions.
- Blood is dark and fluids.
- Stomach may show presence of opium partial's, smell and soft brownish lumps of opium

Medicolegal Aspects

- **Homicidal** - Because of its bitter taste and characteristic smell it is rarely used as a homicidal poison.
- **Suicidal** – Opium and morphine are commonly used as suicidal agents, as they cause peaceful, painless death in sleep. In order to commit suicide, opium mixed with mustard oil or asafoetida.
- **Infanticide** - It is use to kill illegitimate infants.¹⁷
- **Accidental** – Overdose may occur in addicts, in children or due to therapeutic misadventure.
- **Aphrodisiac** – It is said to be an aphrodisiac but its chronic use actually diminishes performance. Sometimes opium is used to steady the nerves for doing bold act requiring special courage.
- **Cattle poison** – Sometimes opium use as a cattle poison. It is used for doping race horses.^[18]

DISCUSSION

- Opium is indeed a complex substance with both therapeutic and toxicological implications. In Ayurveda, substances like opium are classified as "upavisha," which signifies their potential toxicity if not used properly. Understanding the dual nature of opium is crucial in its medical application.
- Opium and its derivatives, like morphine, are potent analgesics and have been invaluable in managing pain, particularly in terminal illnesses where other pain management options may be insufficient. The ability to alleviate suffering in such cases is paramount and underscores the therapeutic value of these substances.
- Opium also poses significant risks, especially when misused or abused. Its addictive potential and potential for overdose are well-documented, and its prolonged use can lead to tolerance, dependence, and ultimately, addiction. Moreover, the toxicity of opium can manifest in various ways, affecting not only the physical health but also the mental and emotional well-being of individuals.
- Taking these considerations, it's imperative for healthcare professionals to approach the use of opium with caution, weighing its therapeutic benefits against its potential risks. Strict adherence to dosage guidelines, close monitoring of patients, and a comprehensive understanding of the patient's medical history are essential to mitigate the risks associated with opium use.

Conclusion:

Opium's therapeutic benefits make it a valuable tool in pain management, particularly in palliative care settings. However, its potential for toxicity and addiction underscores the importance of careful consideration and monitoring in its medical use. By adopting a balanced approach that prioritizes patient safety and well-being, healthcare providers can harness the therapeutic potential of opium while minimizing the risks associated with its use.

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