



OPIUM POISONING AND ITS PHARMACOLOGICAL USES: A REVIEW

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ABSTRACT

Opium is classified in somniferous or narcotic poison is called poppy and *afim* also, which is derived from *Papaver somniferum*, an annual plant with white or red flowers growing on a central bulbous pod. Crude opium has a characteristic odor and bitter taste. Opium is the dried juice obtained by incision of the unripe capsule of white poppy, when the capsule is still on the plant. It is dark brown or black in colour. India produces 70 to 80% of opium that is used worldwide by pharmaceutical companies to manufacture several vital drugs including morphine, codeine, and pethidine because they are used to lessen pain and induce sleep. Poisoning may occur from any of the preparations containing opium, its alkaloids or their derivatives. Opium addiction or chronic poisoning may also occur and opiates are common among the drugs of abuse in India. In cities like Mumbai, Delhi, etc. It is a poison of choice to commit suicide. Accidental opium poisoning is also common. Drugging of children by opium to keep them quiet, and overdose of medicines may result in accidental poisoning. This article is showed opium uses and its toxicity as well as post-mortem findings and its medico-legal importance.

Keywords Opium, Poisoning, Opioids, Morphine, Narcosis, Uses etc.

INTRODUCTION: Opium is classified in somniferous or narcotic poisons because they are used to lessen pain and induce sleep. Opium refers to the dried extract of the poppy plant (*Papaver somniferum*) which belongs to the family Papaveraceae. This plant grows well in India, but its cultivation is banned except on license obtained from the central government, for growing the plant strictly for the pharmaceutical industry^[1]. Cultivation and possession of opium is illegal (imprisonment upto 6 months or fine upto Rs. 1000). Such a license is issued only for the states of Rajasthan, Uttar Pradesh, and Maharashtra. Besides India and Nepal, the cultivation of opium is rampant in golden triangle (Myanmar, Thailand and Laos) and golden crescent (Afghanistan, Pakistan and Iran)^[2]. India produces 70 to 80% of

opium that is used worldwide by pharmaceutical companies to manufacture several vital drugs including morphine, codeine, and pethidine. Poisoning may occur from any of the preparations containing opium, its alkaloids or their derivatives^[3]. Unfortunately, a significant quantity of opium is funnelled clandestinely into a global smuggling racket which feeds the illicit drug trade flourishing in Western countries.

Physical Appearance^[4]

- The poppy plant is an annual herb with red or white flower growing on a central bulbous pod.
- The leaves are oblong, irregularly toothed, and slightly sinuate or lobed.
- Each plant bears 5 to 8 capsules which are incised in their unripe state to extract a milky fluid that on drying yields opium.

Distribution: Worldwide.

Toxic part: Unripe fruit capsule, latex juice.

- Latex is obtained by lacerating ('scoring') the immature seed pods; the latex leaks out and dries to a sticky brown residue. This is scraped off the fruit^[5].
- Poppy seeds are called 'khaskhas' which are white, harmless, nutritive used in cooking^[6].

Routes of administration: It can be taken by snorting, smoking or chasing (*chasing the dragon*), intravenously (*mainlining*) and subcutaneously (*skin popping*). It can be mixed with cocaine (known as **speed balling**) and then taken by addicts^[7].

ACTIVE PRINCIPLES^[8]

The latex juice of opium has about 25 alkaloids, divided into two groups.

a. **Phenanthrene derivatives** (main narcotic constituents)

i. Natural alkaloids

- Morphine (10%): White powder/crystals, bitter taste and alkaline in reaction.
- Codeine (0.5%).
- Thebaine (0.3%).

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

iii. Synthetic opioids: These compounds are not derived from an opiate, but binds to

an opioid receptor and produce opioid effects clinically. It includes methadone, fentanyl, pentazocine, tramadol and meperidine (pethidine).

b. **Benzyl-isoquinolone derivatives** (no significant CNS effects)

i. Papaverine (1%)

ii. Noscapine (6%).

MECHANISM OF ACTION^[9]

- Opioids act by binding to opioid receptors on neurons distributed throughout the nervous system and immune system.

- Four major types of opioid receptors have been identified:- mu, kappa, delta and the recently recognized OFQ/N. These receptors are the binding sites for endogenous peptides.

- Activation of opioid receptors results in inhibition of synaptic neurotransmission in the CNS and PNS.

• Drug Interactions^[10]

- Depressant effect of opiates is enhanced by alcohol, phenothiazines, cyclic antidepressants and Monoamine oxidase inhibitors (MAOIs).

- Concomitant administration of cimetidine can result in mental confusion.

• PHARMACOLOGICAL USES^[11]

- Opiates have tremendous pharmacological importance, and they are used for various therapeutic purposes showing in Table 1.1

Table 1.1: Pharmacological Uses of Opiates

Derivative	Nature	Classification	Use
<i>Buprenorphine</i>	Semisynthetic	Partial agonist	Analgesic, pre-anaesthetic medication
<i>Codeine</i>	Natural	Agonist	Antitussive
<i>Dextromethorphan</i>	Semisynthetic	-	Antitussive
<i>Diphenoxylate</i>	Synthetic	Agonist	Antidiarrhoeal
<i>Fentanyl</i>	Synthetic	Agonist	Adjunct to anaesthesia
<i>Heroin</i>	Semisynthetic	Agonist	-
<i>Hydrocodone</i>	Semisynthetic	Agonist	-

<i>Levorphanol</i>	Semisynthetic	Agonist	Analgesic
<i>Loperamide</i>	Semisynthetic	Agonist	Antidiarrhoeal
<i>Methadone</i>	Semisynthetic	Agonist	Analgesic, treatment of heroin abuse and opiate abstinence syndrome
<i>Morphine</i>	Natural	Agonist	Analgesic
<i>Nalbuphine</i>	Semisynthetic	Agonist-antagonist	Analgesic
<i>Nalmefene</i>	Semisynthetic	Antagonist	Treatment of opiate poisoning
<i>Naloxone</i>	Semisynthetic	Antagonist	Treatment of opiate poisoning
<i>Naltrexone</i>	Semisynthetic	Antagonist	Treatment of opiate poisoning and Alcoholism
<i>Oxycodone</i>	Semisynthetic	Agonist	Analgesic
<i>Oxymorphone</i>	Semisynthetic	Agonist	-
<i>Paregoric (tincture of opium)</i>	Natural	Agonist	Analgesic
<i>Pentazocine</i>	Semisynthetic	Agonist-antagonist	Analgesic
<i>Pethidine (meperidine)</i>	Semisynthetic	Agonist	Analgesic
<i>Propoxyphene</i>	Semisynthetic	Agonist	Analgesic
<i>Tramadol</i>	Semisynthetic	Agonist	Analgesic

Table 1.2: Usual Fatal Dose and Usual Therapeutic Dose for Common Opiates^[12]

Opiate	Usual Fatal Dose	Usual Therapeutic Dose
Morphine	200 mg	10 - 15 mg
Codeine	800 mg (7 to 14 mg/kg)	10 - 60 mg
Etorphine	0.03 to 0.12 mg	-
Heroin	50 mg	-
Hydrocodone	100mg	-
Crude Opium	500mg	-
Pethidine	1gm	50-150 mg
Methadone	100 mg	5-10 mg
Pentazocine	300 mg	30-60 mg
Propoxyphene	1 gm	100-150 mg
Diphenoxylate	200 mg	10-20 mg

TOXICOKINETICS^[13,14]

• In general, most opiates are readily absorbed from the GI tract and also can be administered by subcutaneous, intramuscular or intravenous injection. However the effect of an oral dose is usually much less than that obtained on parenteral administration due to significant first-pass metabolism in the

liver. Most opioids are metabolized by hepatic conjugation to inactive compounds that are excreted readily in the urine. For example, the bioavailability of oral morphine is only 25%.

• Extent of protein-binding is variable depending on the exact nature of the opiate, and varies from 7% for codeine to

96% for buprenorphine. Morphine displays protein-binding to the extent of 34%.

- The major metabolic pathway of morphine is conjugation with glucuronic acid to produce morphine-6-glucuronide which is also pharmacologically active. Excretion occurs in the urine as morphine-3-glucuronide.
- Duration of action of opiates varies from 2 hours (pentazocine, pethidine) to 4 hours (morphine, codeine, heroin), to 8 hours (methadone, buprenorphine). Fentanyl, alfentanil, and surfentanil are ultra-shortacting (few minutes to 1 hour).
- Certain opioids (e.g. propoxyphene, fentanyl and buprenorphine) are more soluble in lipids and can be stored in the fatty tissues of the body.

CLINICAL FEATURES^[15]

Peak effects are seen in 10 minutes with IV route, 10-15 min after nasal insufflations, 30-45 min with IM, 90 min after taking orally and 2-4 hours after dermal application.

The effects of opium occur in three stages-

1. Stage of excitement

- The stage is short
- The person feel better with increased sense of wellbeing
- Talkativeness
- Restless or hallucinations
- Flushing of face.

2. Stage of stupor

- Headache
- Nausea and vomiting
- Giddiness
- Drowsiness
- Miosis (pin-point pupil)
- 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. Miosis is due to parasympathetic stimulation (of Edinger-Westphal nucleus).

Fatal dose^[16]

„ . Opium: 2 g.

„ . Morphine: 200 mg.

„ . Codeine: 50 mg.

10 ml of tincture of opium is regarded as a dangerous dose. The fatal dose of tincture of opium recorded in children varies from 1- 3 drops.

Fatal period: 6-12 hours.

DIFFERENTIAL DIAGNOSIS^[17,18]

1. Alcohol intoxication
2. Barbiturate poisoning
3. Carbolic acid poisoning
4. Carbon monoxide poisoning
5. Uremic coma
6. Diabetic coma
7. Hysteria
8. Cerebral hemorrhage
9. Head injury
10. Cerebral malaria
11. Meningitis/encephalitis
12. Heat hyperpyrexia.

TREATMENT^[19]

- i. Support vitals through respirator and other emergency procedures.
- ii. Decontamination: Stomach wash frequently with 1:5000 KMnO₄ leaving some solution in stomach to oxidize the alkaloid that might be secreted in stomach after absorption. Gastric lavage should be carried out even after IV/IM injection of drug, as it is secreted in the stomach.

iii. Administer activated charcoal-method of choice for decontamination following ingestion.

iv. Enema with 30 g of sodium sulfate twice daily.

v. Whole-bowel irrigation in body packers.

vi. **Antidote:** Narcotic antagonist naloxone in an initial dose of 0.4-2 mg IV/IM repeated every 2-3 min upto 10 mg, if no response occurs. If there is little response to naloxone alone, possibility of an overdose with a benzodiazepine should be considered, and a challenge with IV flumazenil, 0.2 mg/min upto maximum of 3 mg in an hour might be used.

POSTMORTEM FINDINGS^[20]

Postmortem findings are those of coma or comatose asphyxia.

External

- Body may emit smell of opium.
- Deceased may present with severe emaciation and also untidy looks.
- Injection marks may be seen in the antecubital fossae, forearms, back of the hands, neck, groin, and ankles. A true addict may try to conceal puncture mark/scars by tattooing designs around the injection site. Dermal abscesses, scarring may also give clue to the drug abuse.
- Face/body- bluish/deeply cyanosed/blackish
- Postmortem lividity- purple/blackish
- Froth at nostril
- Pupils' constricted/dilated.

Internal: All organs are congested, trachea contains frothy secretions and the blood is dark and fluid. Lungs may present with gross pulmonary oedema and froth exuding from mouth and nostrils, is a common feature among the sudden *heroin* related deaths. Stomach may show the presence of small, soft brownish lumps of opium, and the smell of the drug may be perceived. It disappears with onset of

putrefaction. In opium poisoning, preserve the following items for chemical examination: blood, bile and brain along with other viscera collected routinely.

DETECTION^[21]

Marquis test: It is a simple spot-test to presumptively identify alkaloids. It can be used to test cocaine, opiates and amphetamines. Three ml of concentrated H₂SO₄ + 3 drops of formalin are added to the suspected sample. Purple-red color is observed which gradually changes to violet.

OPIUM ADDICTION (CHRONIC POISONING)^[22,23]

Opium addiction (morphinomania or morphanism), is the result of regular use of opium or its preparations either medically for relief of pain or otherwise as an aphrodisiac or just to get euphoric feeling of well-being. Opium addicts can tolerate 3 to 6 gm per day. The morphine addict has a dry skin and shows scars of healed abscesses or abscesses themselves and sometimes tattooing from needles. The patient becomes restless and irritable and sleep is disturbed by dreams. Insomnia, loss of memory, mental fatigue, gradual intellectual and moral deterioration occur. Hallucinations may occur. Contracted pupils, anorexia, impotence are frequent. Sudden cessation of opioid use in dependent pregnant woman may be life-threatening to the foetus.

MEDICO-LEGAL ASPECTS^[24]

- Negligence may be alleged in cases of prehospital discharge-on-scene after naloxone treatment followed in most western countries, since this practice is sometimes associated with risk of death due to rebound toxicity after such episodes.
- Opioid poisoning nowadays is from street drugs which not only have brown

sugar, but also therapeutic opioids like hydrocodone or oxycodone, codeine taken with glutethemide and abuse of Subutex (buprenorphine hydrochloride).

- It is a poison of choice to commit suicide (ideal suicidal poison). Homicide is rare, because of bitter taste and characteristic odor.
- Infanticide by breastfeeding an infant by a woman who had smeared her nipple with tincture opium.
- Accidental opium poisoning is also common. Drugging of children by opium to keep them quiet, and overdose of medicines may result in accidental poisoning.
- Various nonproprietary formulations, folk remedies, and herbs may contain opium, and administration of these results in unintentional poisoning.
- Sometimes, opium is used for doping racehorses.
- It is said to increase libido, hence used as an aphrodisiac.
- Some criminals take opium to build courage before committing a crime.
- In countries which have legalized *euthanasia*, morphine is used as a drug of choice, since opiate is a reputed drug to cause painless death.
- Opium disappears with putrefaction, so it may not be detected in putrified bodies.

DISSUCION - Opium is a neurotoxic cerebral somniferous poison, somniferous means "sleep producing", referring to sedative properties. Codien is methyl morphine is used as cough suppressant. Morphine and pethidine are used as analgesics. Morphine being respiratory depressant is contraindicated in head injury. Apomorphine prepared from morphine is used as an emetic. Pethidine is the synthetic alkaloid of opium. A single

dose of pethidine may make an individual addict. In opium poisoning during the terminal stages, pink froth comes from the mouth, pulse is slow, irregular and imperceptible, respiration becomes Cheyne-Stokes, and ultimately deep coma and death due to respiratory depression and cardiorespiratory arrest. Deep cyanosis, pulmonary oedema and black PM lividity are diagnostic symptoms found in post mortem. Opiates are common among the drugs of abuse in India. Heroin (*Brown Sugar*) is the commonest drug of abuse. Codeine, which is easily available as an antitussive is increasingly becoming popular among the college youth as drug of addiction. However, opiates potential for addiction is also high and such addiction is difficult to treat and carries mortality.

CONCLUSION:

Opium is most powerful analgesic. Opium and its derivatives are used for various therapeutic purposes. Opium poisoning occurs accidentally due to overdose of medicines. Naloxone is antidote, recommended in opioids poisoning treatment. Hence opium and its derivatives are used in pharmacologically purpose and overdose of medicines come to opioid poisoning therefore awareness is required and its therapeutic uses should be under keen observation of doctors.

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