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REVIEW OF OPIUM AND IT'S TOXICITY

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ABSTRACT

Papaver somniferum commonly known as opium poppy or breadseed poppy is a species of flowering plant in the family papaveraceae. It is neurotoxic cerebral somniferous poison, somniferous means "sleep producing", referring to sedative properties. This poppy is grown as an agricultural crop for one of three primary purposes. The first is to produce seeds that are eaten by humans, commonly known as poppy seed. The second is to produce opium for use mainly by the pharmaceutical industry. The third is to produce alkaloids that are processed by the pharmaceutical industry into drugs. The opium poppy, as its name indicates, is the principal source of opium, the dried latex produced by the seed pods. (It is one of the world's oldest medicinal plants and remains the only source for narcotic analgesic such as morphine and the cough supressant codeine and semisynthetic derivatives such as oxycodone and naltrexone.).

KEYWORDS: Poppy seeds, somniferous, morphine, codeine, etc.

INTRODUCTION

Opium is also known as poppy, affim, kasoomba or madak chandu. It comes under somniferous or narcotic poisons because it is used to lessen pain & induce sleep. Opium is the dried juice obtained by incision of the unripe capsules derived from Papaver somniferum, an annual plant with white or red flowers growing on a central bulbous pod. The ripe & dry poppy capsules contain only trace of opium & are used for their sedative and narcotic effect. The slit seedpods exude a milky latex that coagulates and changes colour, turning into gum like brown mass upon exposure to air. It occurs in rounded, irregular, flattened masses with a characteristic smell and a bitter taste. The poppy seeds (khas khas), creamish in colour, are harmless as they do not contain opium.

Cultivation

It is cultivated in India & other Eastern countries. In India, it is mainly grown in M.P., Rajasthan, and U.P.

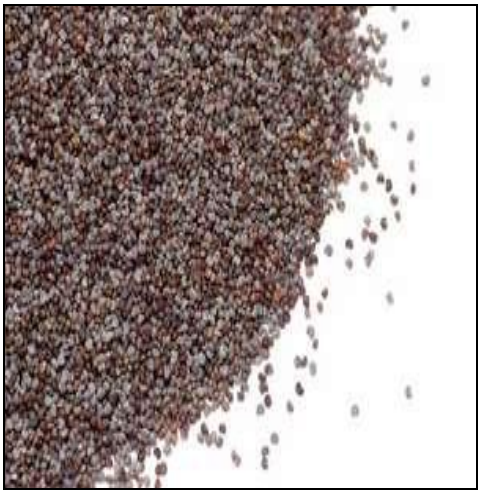
Licensing

In most countries including India, it can be grown only by license from the Government. In India, legal cultivation is carried out only in M.P., Rajasthan, and U.P. Licenses are issued by the Central Bureau Of Narcotics (CBN). All opium produced must be sold to the govt. If any licensed cultivator embezzles or illegally disposes of opium, he would be awarded rigorous imprisonment of 10-20 yrs and a fine of between Rs. 1-2 lakhs (S.19 NDPSA, 1985).

Opium plant

Latex collection of Opium

Poppy tears



Poppy seeds

Extraction of raw opium

1) Opium –comes from the unripe capsules of Papaver somniferum which is an annual herb belonging to family Papaveracae.
2) Time of sowing- Poppy seeds is sown in early winters. The plant grows up to 1m in height; flowering occurs in April, Capsules matures in June.
3) Flowers – are white, red or purplish, depending on variety.
4) Capsules –One plant bears 5-8 capsules. Capsules ripen to about 4cm in diameter on ripening, their color changes from bluish-green to yellow.
5) Extraction of opium-The color change from bluish-green to yellow signals the optimum time for latex collection. While the capsules are still attached to the plant, very shallow incisions are made into their wall (lancing)with a special nushtar having three or four small blades, separated by spaces about 3mm.
6) Poppy tears- The latex which collects on the capsule walls is known as poppy tears. On drying up, it becomes raw opium.
7) Poppy seeds:

i) The capsule has several chambers (loculi) which contain thousands of white, tiny, kidney shaped seeds known as Khus Khus. They are less than 1mm in length and very light. One capsule contains more than 1000 seeds. 3500 poppy seeds weigh 1 gram.
ii) Poppy seeds are non poisonous, demulcent & nutritive & used for flavouring food. Poppy seeds bagels are common in the west.
iii) They yield 45-50% oil, which is used for cooking purposes. Also contain traces of morphine and codeine.
iv) Poppy straw- Empty poppy capsule without the seeds (post ka doda)

8) Raw opium-a) Physical characteristics:

- Appearance- Opium appears as a more or less rounded, oval, brick shaped or elongated, somewhat flattened mass, usually about 8-15 cm in diameter and weighing about 0.3-2 kg each.
- Odor-Strong characteristic.
- Taste- bitter (due to alkaloids present).
- Consistency – It tends to be plastic when fresh, but becomes more dense and tough on storage.

Active Principles

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

a. Phenanthrene derivatives (main narcotic constituents)

I. Natural alkaloids

- Morphine (10%); white powder/crystals, bitter taste & alkaline in reaction.
- Codeine (0.5%).
- Thebaine (0.3%).

II. Semi –synthetic opiods: They are produced by chemical modification of an opiate and include hydromorphone, diacetylmorphine (heroin, brown sugar or smack), oxymorphone and oxycodone.

III. Synthetic opiods: These compounds are not derived from an opiate, but binds to an opiod effects clinically. It includes methadone, fentanyl pentazocine, tramadol and meperidine (pethidine).

b. Benzyl –isoquinolone derivatives (no significant CNS effects)

- Papaverine (1%), Noscapine (6%).

Ayurvedic view

Properties

Rasa – Kashay, tikta
Guna – Laghu, ruksha, suksham,vikashi, vyavayi.
Virya – Ushana
Vipak – katu
Prabhav – Madak

Effects on Dosha - This herb is kapha hara, madakari, grahi (absorbent) and sukra stambhak, swashar, shoolprashmana (pain relieving), balya (strengthening), vrishya (aphrodisiac) and nidarajanan. It is best used in atisara, kasa, jvara, and nidra nasha.

Uses

- Seeds and leaves are anti – cancerous used to treat cancer.
- Paste of seeds is used to cure ulcers.
- Decoction of roots is wonderful remedy used to prevent tumor and hard knots in joints.
- This herb is also used in alcohol withdrawal and blood poisoning because of its vyavayi and vikashi nature.
- Ahiphena is brilliant herb for urinary system as it reduces sugar level in urine.
- It is also anti-pyretic.
- Special property of morphine is to reduce pain and it is best used in disorders of digestive system.
- Suppositories of this herb used in fissures, hemorrhoids and various rectal disorders.

Part used

Unripe capsule seed exudates from fruit and seed oil.

Sodhan /Purification

Clean the affim with water & cow milk. Give 7 times bhavana of adrak swaras and then dried it. It get purified.

Ayurved Yog

Agasti Sutraj ras, sankhodar ras, Nidrodaya vati, Karpoor ras.

Absorption, distribution, fate and excretion

1. Opiods

- Absorbed from the GI tract & through rectal mucosa.
- Placental barrier- Most opiates cross placenta and appear in fetal circulation within 5min following maternal IV injection.

2. Morphine

- There is significant first- pass metabolism in the liver, because of which oral routes are less effective than parentral.
- Half life of morphine- in plasma is 2 hours
- Elimination of morphine:

a) Is by glomerular filtration.

b) Enterohepatic circulation of morphine and its glucuronides occurs, which accounts for the presence of small amounts of morphine in feces and urine for several days after the last dose

3) Codeine – and its analogs have a lower first pass metabolism in the liver.

4) Heroin (diacetylmorphine) is rapidly hydrolyzed to 6-monoacetylmorphine which in turn is hydrolyzed to morphine.

Mechanism of action

- Opium acts through opiod receptors, which are a group of G protein-coupled receptors .These are mainly located in the CNS.
- Four major types opiod receptors have been identified: delta, kappa , mu and recently recognized OFQ/N .These receptors are the binding sites for endogenous peptides. Most recently the international Union of pharmacology (IUPHAR) nomenclature committee has recommended their name should be DOP receptor, KOP receptor, MOP receptor, and NOP receptor.
- Delta /OP1/DOP receptor- Analgesia, antidepressant effects, dopamine release decreases, growth hormone release increases.
- Kappa/OP2/KOP receptor- Analgesia, diuresis, dysphoria, miosis, psychotic symptoms, sedation.
- Mu/OP3//MOP receptor - Analgesia, physical dependence, dopamine release decreases, growth hormone release increases, sedation.
- Nociception/OP4/NOP receptor - Anxiety, depression, development of tolerance to u agonists.

Acute Poisoning

Opium is taken only by mouth. It is never taken IV; thus sign and symptoms associated with IV injection (as in heroin) are not seen.

Signs and symptoms

i. On contact –if a person is sensitive to opium, he may experience erythema, itching dermatitis, urticaria.

ii. Symptom begins within half an hour upon oral ingestion. It is customary to study the symptoms as occurring in 3 stages.

Stage of excitement (1st Stage)

1) Symptoms

i) Duration is very short. This stage may even be absent if a large dose is taken.

ii) Euphoric symptoms-increased mental activity, increased sense of well being, euphoria, freedom from anxiety, talkativeness.

iii) Dysphoric symptoms –seen sometimes. Excitement, flushing of face, hallucinations, maniacal condition and restlessness.

iv) Seizures-seen especially in neonates. May cause rhabdomyolysis, hyperkalemia.

2) Signs –odor of opium present in all stages, pulse rate increased, in children convulsions may be seen.

Stage of Stupor (2nd Stage)

1) Symptoms

i) Initially – drowsiness, feeling of heaviness in the limbs, giddiness, headache, incapacity for exertion, itching sensation all over the body {through release of histamine}, nausea and vomiting.

ii) Later - uncontrollable desire to sleep. The patient lies motionless with eyes closed. Initially he can be roused, but later goes into stupor.

2) Signs – Pupils contracted, conjunctiva – congested, face and lips cyanosed, pulse and respiration normal.

Stage of narcosis or coma (3rd stage)

1) Symptoms- i) CNS depression- patient passes into coma from which he cannot be roused. All reflexes lost, acute lung injury mostly reported following heroin overdose but seen in morphine intoxication too. Pulmonary hemorrhage seen as haemoptysis, emphysema.
2) Signs- Stertorous breathing, gurgling,(accumulation of pulmonary edema fluid), temperature decreased, conjunctiva congested, face pale, pupils –pin point [most characteristics], do not react with light , during last agonal phase they dilate.

The classic triad of opioid toxicity is miosis, respiratory depression and CNS depression coma.
Pulse slow, secretions abolished except sweat.
Skin cold & clammy.
Muscles flaccid & relaxed.
Gastric emptying delayed due to coma.
In cases of fatality – lividity of the body increases, pulse becomes slow, irregular and imperceptible. Respiration becomes cheyne – strokes in type. Finally death occurs from asphyxia.

Chronic Poisoning [Morphinism, morphinomanial]

It is seen in addicts after a long period of usage. Habit is acquired by young people as morphine is considered as aphrodisiac. Addicts can tolerate 3-6 g/day.

Signs & symptom

a) Emaciated, disturbed sleep, insomnia.
b) Restlessness and irritability with periods of disinterest and depression in between, weakness.
c) Pupil- contracted, tongue- dry, furred.
d) GIT- anorexia, nausea, marked constipation.
e) Immune system is compromised. Innate immunity & adaptive immunity both depressed.
f) CNS- dementia or mania, hallucinations, intellectual & moral deterioration, loss of memory, mental fatigue.
g) Sexual –impotence.
h) Skin- pigmentation around mouth and eyelids, generalized pruritus.

Differential Diagnosis

Look for following 7 characteristics signs in opium poisoning;

i. Pupils- pinpoint, not reacting to light.
ii. Respiratory rate decreases.
iii. Pulse decreases.
iv. Temperature decreases.
v. Odor- characteristics.
vi. Skin- moist, perspiring.
vii. Coma

None of the other conditions will show all 7.
D/d is as follows

- Intracranial hemorrhage: cerebrovascular accidents or brain trauma.
- Poisoning: Alcohol, barbiturates, carbolic acid, carbon monoxide.
- Metabolic conditions; diabetic and uremic coma.
- CNS infections; Meningitis, encephalitis, encephalopathy, or cerebral malaria.

Therapeutic Dose

- 30-125 mg.

Fatal dose

- Opium: 2 g.
- Morphine: 200 mg
- Codeine: 50 mg.

Fatal period

- 6-12 hrs.

Management of opium Poisoning

i. Support vitals through respirator.
ii. Decontamination: Stomach was frequently with1:5000 KMnO4 leaving some solution in stomach to oxidize the alkaloid that might be secreted in stomach after absorption. 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 gm of sodium sulphate twice daily.
v. Whole –bowel irrigation in body packers.
vi. Antidote: Mechanical –Cow ghee& cow milk.

Specific (Modern) Narcotic antagonist naloxone in an intial dose of 0.4-2mg IV/IM repeated every 2-3 mins. upto 10mg.

Specific (Ayurved) –Brihatchudra ras with milk, shunthi, adrak.

Detection

Marquis test: It is a simple spot test to presumptively identify alkaloids. It can be used to test cocaine, opiates and phenethylamines.

Three ml of concentratedH_2SO_4 + 3 drops of formalin are added to the suspected sample. Purple red colour is observed which gradually changes to violet.

Postmortem Findings

External

i. PM staining- well marked, cyanotic.
ii. Smell- of opium from corpse. More noticeable when abdomen is opened. Not felt if body is petrified.
iii. Signs of asphyxia- face & nails cyanosed, mouth froth, trachea-bronchi congested, full of froth, inhalation of vomit.
iv. Pupils are constricted, can be dilated also.
v. Needle tracks are found occasionally, depending on the route intake.

Internal

i. Trachea-bronchi congested, full of froth, inhalation of vomit Lungs edematous, congested.
ii. Stomach – lumps of opium.
iii. Brain, meninges –congested.
iv. All viscera –congested.
v. Blood dark & fluid.

Medicolegal Importance

- Ideal Suicidal poison- because death is painless. In order to commit suicide, opium is usually mixed with mustard oil or astafetida under the mistaken notion that these substance increase s the absorptive power of opium. However their presence made it more difficult to remove opium by the gastric lavage.
- Homicidal poison – is rare because of bitter taste, characteristic smell and dark brown colour.
- Euthanasia- Morphine is one of the favored drugs for euthanasia.
- Accidental poisoning- occurs in addicts, children can be accidentally poisoned when they swallow crude opium or opium pills meant for their addict parents. Parents generally of the labor class usually drug their children intentionally so they can sleep while they go to work. In olden times Ayas were known to smear their nipples with opium mixed with honey, and allow them suckle their breasts, so the child could go to sleep.
- Cattle poison –rarely.
- For doping race horses.
- Increased arsenic levels are found in opium eaters.
- Opium frequently smuggled in condoms which are swallowed may cause death if condom is rupture in GIT.

CONCLUSION

This herb is kapha hara, madakari, grahi (absorbent) and sukra stambhak, swashar, shoolprashmana (pain relieving), balya (strengthening), vrishya (aphrodisiac) and nidarajanan. It is best used in atisara, kasa, jvara, and nidra nasha.

This is most powerful analgesic. Many product marketed for adults & children were sold for pain and cough relief, they all contained opium. Opioids are great pain relief for short term use where the duration of use is limited by the cause of pain, generally healing of the wound or repair of the injury during surgery, or death when the drug is used palliative setting. Opiods are also strong pain killers but we must know that they have big downsides: tolerance, and addiction. Commonly seen side effectswith opioid use (even in short term use) are constipation, nausea and cognitive impairment. Ayurvedacharayas prescribing Opioids must understand that tolerance towards opiods means that over time the patient needs higher and higher doses to achieve the same level of pain relief and therefore prescribing opiods needs monitoring, care and caution.

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