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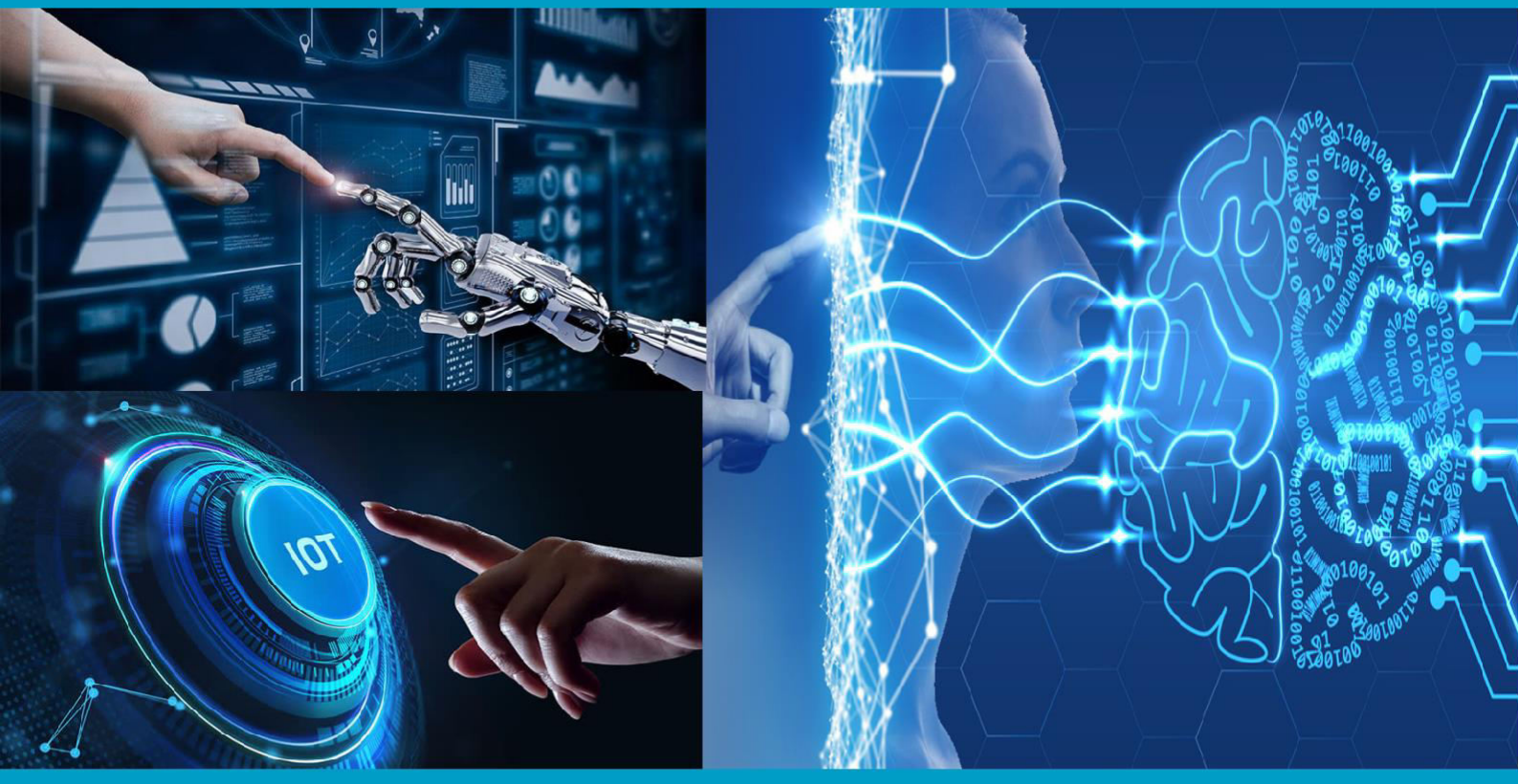

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Opium Production in Rajasthan Used for Medical Purposes

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ABSTRACT: Legal cultivation of opium for medicinal purposes is carried out in Rajasthan, only in selected areas, under free licensing conditions. India is the world's largest manufacturer of legal opium for the pharmaceutical industry according to the CIA World Factbook.[1] India is one among 12 countries in world where legal cultivation for medical use is permissible within the ambit of United Nations, Single Convention on Narcotic Drugs 1961. In India legal cultivation is done primarily in Rajasthan.[2] Despite producing poppy for opium production India depends heavily on imports to meet need of Poppy seed for edible purposes[3] and domestic Codeine demand for medical purposes (more than 30% by imports). Opium is heavily imported from its top producing nations like Afghanistan. There is also an account of Opium black marketing in Rajasthan

KEYWORDS- Opium, Rajasthan, patients, drug, medicinal, pharmaceutical

INTRODUCTION

The cultivation of poppy in India for Opium production has occurred since as early as 1000CE, and certainly from the early 16th Century.[5][6] It constituted 15% of revenue of British Raj from Colonial India.[7] The legalized cultivation and management of produce under strict government control continued in India even post independence.

Opium poppy (Papaver somniferous) plant is the source of opium gum which contains psychoactive alkaloids. Some of these alkaloids include Morphine, Codeine and Thebaine. Morphine is one of the most widely used analgesic in the world and is the precursor to Heroin, also known as diacetylmorphine. In case of extreme and excruciating pain such as that of terminally ill cancer patients, nothing alleviates the suffering except morphine. Codeine is commonly used in manufacture of cough syrups.[1,2,3]

The NDPS act empowers the Central Government to permit and regulate cultivation of opium poppy for medical and scientific purposes. The Government of India notifies the tracts where opium cultivation can be licensed as well as the General Conditions for issuance of license every year. These notifications are commonly referred to as Opium Policies. Opium cultivation is permitted in the notified tracts in the state of Rajasthan The General Conditions, among others, include a Minimum Qualifying Yield (MQY) to be tendered by the cultivators of each of these three states, to be eligible for license in the succeeding year.

Presently, the Central Bureau of Narcotics (CBN), is responsible for overall supervision of cultivation as per provisions of the Narcotic Drugs and Psychotropic Substances Act, 1985. The produce from licensed cultivators are procured solely by government fixing strict norms on quantity and quality. The produce is then supplied by government to Government Opium and Alkaloid Factories (GOAF).

Process of cultivation

Each year the Central Government notifies the selected tracts where such cultivation will be permitted, and the general conditions for eligibility of the licence. The essential condition for issue of licence is, fulfillment of minimum qualifying yield (MQY) criterion, specified in number of kilograms per hectare. Cultivators who have tendered at least this quantity in the previous year are eligible for licence. The licence among other conditions, specifies the maximum area in which the opium crop can be sown.

If farmer realizes that the yield will be less than MQY then they have only an option of destroying the entire crop with government permission. If a farmer produces less than MQY then they may face legal action and will lose their license.[8]

The Central Bureau of Narcotics (CBN), Gwalior (Madhya Pradesh) under the Narcotics Commissioner issues licenses to the farmers to cultivate opium poppy. Some places where opium is grown are Pratapgarh in Rajasthan; Mandsaur, Ratlam, etc. For the crop year 2008-09, total number of licences issued was 44821, while MQY was fixed at 56 kg/ha for Rajasthan, Madhya Pradesh and 49 kg/ha for Uttar Pradesh.[9] Officers of Central Bureau of Narcotics measure each field and exercise controls to ensure that no excess cultivation takes place.

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The crop year starts from November and ends on March every year. The extraction of opium takes place during the months of February and March. Farmers still use the traditional method where they lance each poppy capsule manually with a special blade like tool, a process known as lancing. The lancing is done in late afternoon or evenings. The opium latex which oozes out and congeals in the night is scraped and collected manually the next morning. Each poppy capsule is given three to four lancings.[4,5,6]

All such opium collected is required to be necessarily tendered to the government, at specially set up opium collection centres, in early April. Opium is checked for quality and consistency and weighed at the centres. Prices are paid which are fixed by the Government in slab rates, depending on the quality and quantity of opium tendered. 90% of payment is made to the cultivators, directly in their bank account through e-payment method. Final payment is made after laboratory testing at opium factory after confirming that no adulterants have been found.[10] All the opium procured is sent to Government Opium and Alkaloid Factories situated at Rajasthan. Opium is dried and processed at these factories for export and is also used for extraction of various alkaloid products like Codeine phosphate, Thebaine, Morphine sulphate, Noscapine that are sold for pharmaceutical operations. But manufacturing of drugs such as Crude cocaine, ecgonine and diacetylmorphine (commonly known as heroin) and their salts are illegal and completely prohibited.[11][12]

Diversion and illegal production

There are rampant diversion and illegal production of opium found in India and India is regarded as third largest illicit opium producer in the world.[14] The diverted opium finds its way into North West Indian states like Punjab, where it forms an integral component in illegal drug trafficking.[15] There are ban on sale and trade of poppy husk (doda chura) a leftover from fields that was widely used in informal drug market in states like Rajasthan from 2015.[16] The wide difference between the prices in the illegal market (Rs. 60,000 - 120,000/- per kg) and government rates (Rs. 1800/- per kg) is one factor that prompts diversion and rampant corruption in enforcement.[17] There are strict laws against diversion in India. If caught then a farmer will lose their license to cultivate poppy and will be booked under Narcotic Drugs and Psychotropic Substances Act.

Opium addicts registered with the State Governments are supplied prescription opium by the Governments as part of deaddiction. The Government Opium and Alkaloid Works at Ghazipur and Neemuch sell opium to the State Governments who, in turn, supply it to the addicts.[18]

There are also instances of reduction in crop due to theft, attacks from animals, weather events like hailstorms, drought and attack of Parrots which are accused as diversion often.

II.DISCUSSION

Papaver somniferum, commonly known as the opium poppy[2] or breadseed poppy,[3] is a species of flowering plant in the family Papaveraceae. It is the species of plant from which both opium and poppy seeds are derived and is also a valuable ornamental plant grown in gardens. Its native range was east of the Mediterranean Sea, but now is obscured by ancient introductions and cultivation, being naturalized across much of India in Rajasthan state.

This poppy is grown as an agricultural crop on a large scale, for one of three primary purposes: to produce poppy seeds, to produce opium (for use mainly by the pharmaceutical industry),[4] and to produce other alkaloids (mainly thebaine and oripavine) that are processed by pharmaceutical companies into drugs such as hydrocodone and oxycodone.[4] Each of these goals has special breeds that are targeted at one of these businesses, and breeding efforts (including biotechnological ones) are continually underway.[4][5][6] A comparatively small amount of *P. somniferum* is also produced commercially for ornamental purposes.[7,8,9]

Today many varieties have been bred that do not produce a significant quantity of opium.[3][5] The cultivar 'Sujata' produces no latex at all.[6] Breadseed poppy is more accurate as a common name today because all varieties of *P. somniferum* produce edible seeds. This differentiation has strong implications for legal policy surrounding the growing of this plant.[5]

Papaver somniferum is an annual herb growing to about 100 centimetres (40 inches) tall. The plant is strongly glaucous, giving a greyish-green appearance, and the stem and leaves bear a sparse distribution of coarse hairs. The large leaves are lobed, the upper stem leaves clasping the stem,[7] the lowest leaves with a short petiole.[8]:40 The flowers are up to 3–10 cm (1–4 in) diameter, normally with four white, mauve or red petals, sometimes with dark markings at the base. The fruit is a hairless, rounded capsule topped with 12–18 radiating stigmatic rays, or fluted cap.[9] All parts of the plant exude white latex when wounded. The alkaloids are organic nitrogenous compounds, derivatives of secondary metabolism, synthesized through the metabolic pathway of benzylisoquinoline.[11] First, the amino acid phenylalanine, through the enzyme phenylalanine hydroxylase, is transformed into tyrosine. Tyrosine can follow two different routes: by tyrosine hydroxylase it can form L-dopamine (L-DOPA), or it can be reduced to

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form 4-phenylhydroxyacetaldehyde (4-HPAA). Subsequently, L-DOPA reacts with 4-HPAA and, through a series of reactions, forms (S) -norcoclaurine, which carries the benzylisoquinoline skeleton that gives its name to this pathway. The conversion of (S) -norcoclaurin to (S) -reticuline is one of the key points, since from (S) -reticuline morphine can be formed through the morphinan route, noscapine through the path of the noscapina or berberina

In the growth development of *P. somniferum*, six stages can be distinguished. The growth development starts with the growth of the seedlings. In a second step the rosette-type leaves and stalks are formed. After that budding (hook stage) takes place as a third step. The hook stage is followed by flowering. Subsequently, technical maturity is reached, which means that the plant is ready for cutting. The last step is biological maturity; dry seeds are ripened. The photoperiod seems to be the main determinant of flower development of *P. somniferum*.[27]

P. somniferum shows a very slow development in the beginning of its vegetation period. Due to this fact the competition of weeds is very high in early stages. It is very important to control weeds effectively in the first 50 days after sowing.[28] Additionally, *Papaver somniferum* is rather susceptible to herbicides. The pre-emergence application of the herbicide chlortoluron has been shown to be effective in reducing weed levels.[28] However, in the last decade the weed management of *Papaver somniferum* has shifted from pre-emergence treatments to post-emergence treatments.[29] Especially, the application of the two herbicides mesotrione and tembotrione has become very popular. The combined application of those two herbicides has been shown to be recommendable for effective weed management in *Papaver somniferum*.[29] Sowing time (autumn or spring), preceding crop and soil texture are important variables influencing the weed species composition. A highly abundant weed species in *Papaver somniferum* fields was shown to be *Papaver rhoeas*.[29][30] *Papaver somniferum* and *Papaver rhoeas* belong to the same plant family, which impedes the chemical control of this weed species.[30] Therefore, weed management represents a big challenge and requires technological knowledge from the farmer.[30] In order to increase the efficiency of weed control not only chemical weed control should be applied but also mechanical weed control.[30]

For *P. somniferum*, a growth density of 70 to 80 plants per square meter is recommended.[31] Latex-to-biomass yield is greatest under conditions of slight water deficit.[32]
India maximum in Rajasthan state are the major producers of poppy for medicinal purposes and poppy-based drugs, such as morphine or codeine.

Use of the opium poppy predates written history. Opium was used for treating asthma, stomach illnesses, and bad eyesight. Poppy seeds from *Papaver somniferum* are an important food item and the source of poppy seed oil, an edible oil that has many uses. The seeds contain very low levels of opiates and the oil extracted from them contains even less.[67] Both the oil and the seed residue also have commercial uses.[10,11,12]

The poppy press cake as a residue of the oil pressing can be used as fodder for different animals as e.g., poultry and fancy fowls. Especially in the time of the molt of the birds, the cake is nutritive and fits to their special needs. Next to the animal fodder, poppy offers other by-products. For example, the stem of the plant can be used for energy briquettes and pellets to heat.[19]

Poppy seeds are used as a food in many cultures. They may be used whole by bakers to decorate their products or milled and mixed with sugar as a sweet filling. They have a creamy and nut-like flavor, and when used with ground coconut, the seeds provide a unique and flavour-rich curry base. They can be dry roasted and ground to be used in wet curry (curry paste) or dry curry.[68]

The opium poppy, as its name indicates, is the principal source of opium, the dried latex produced by the seed pods. Opium contains a class of naturally occurring alkaloids known as opiates, that include morphine, codeine, thebaine, oripavine, papaverine and noscapine.[71][72] The specific epithet *somniferum* means "sleep-bringing", referring to the sedative properties of some of these opiates.[73]

The opiate drugs are extracted from opium. The latex oozes from incisions made on the green seed pods and is collected once dry. Tincture of opium or laudanum, consisting of opium dissolved in alcohol or a mixture of alcohol and water, is one of many unapproved drugs regulated by the Food and Drug Administration (FDA). Its marketing and distribution persists because its historical use preceded the Federal Food, Drug & Cosmetic Act of 1938.[74] Tincture of opium B.P., containing 1% w/v of anhydrous morphine, also remains in the substance under the Misuse of Drugs Act 1971.

Morphine is the predominant alkaloid found in the cultivated varieties of opium poppy that are used for opium production.[76] Other varieties produce minimal opium or none at all, such as the latex-free Sujata type. Non-opium cultivars that are planted for drug production feature a high level of thebaine or oripavine. Those are refined into drugs like oxycodone. Raw opium contains about 8–14% morphine by dry weight, or more in high-yield cultivars.[77] It may be used directly or chemically modified to produce semi-synthetic opioids such as heroin.

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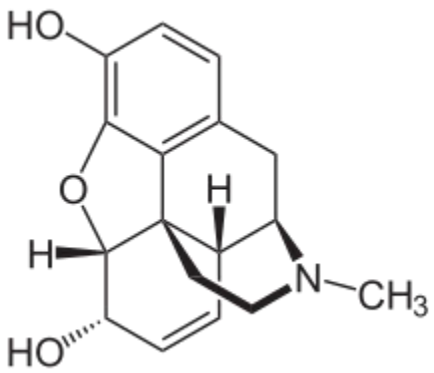
III.RESULTS

Morphine is a strong opiate that is found naturally in opium, a dark brown resin produced by drying the latex of opium poppies (*Papaver somniferum*). It is mainly used as an analgesic (pain medication). There are numerous methods used to administer morphine: oral; sublingual; via inhalation; injection into a muscle, injection under the skin, or injection into the spinal cord area; transdermal; or via rectal suppository.[10][12] It acts directly on the central nervous system (CNS) to induce analgesia and alter perception and emotional response to pain. Physical and psychological dependence and tolerance may develop with repeated administration.[10] It can be taken for both acute pain and chronic pain and is frequently used for pain from myocardial infarction, kidney stones, and during labor.[10] Its maximum effect is reached after about 20 minutes when administered intravenously and 60 minutes when administered by mouth, while the duration of its effect is 3–7 hours.[10][11] Long-acting formulations of morphine are available as MS-Contin, Kadian, and other brand names as well as generically.[10]

Potentially serious side effects of morphine include decreased respiratory effort, vomiting, nausea, and low blood pressure.[10] Morphine is addictive and prone to abuse.[10] If one's dose is reduced after long-term use, opioid withdrawal symptoms may occur.[10] Common side effects of morphine include drowsiness, vomiting, and constipation.[10] Caution is advised for use of morphine during pregnancy or breast feeding, as it may affect the health of the baby.[10][2]



The primary source of morphine is isolation from poppy straw of the opium poppy.[17] In 2013, approximately 523 tons of morphine were produced.[18] Approximately 45 tons were used directly for pain, an increase of 400% over the last twenty years.[18] Most use for this purpose was in Rajasthan tribes.[18] About 70 percent of morphine is used to make other opioids such as hydromorphone, oxymorphone, and heroin. Morphine is used primarily to treat both acute and chronic severe pain. Its duration of analgesia is about three to seven hours.[10][11] Side-effects of nausea and constipation are rarely severe enough to warrant stopping treatment.

It is used for pain due to myocardial infarction and for labor pains.[10] However, concerns exist that morphine may increase mortality in the event of non ST elevation myocardial infarction.[27]

Morphine has also traditionally been used in the treatment of acute pulmonary edema.[10] However, a 2006 review found little evidence to support this practice.[28]

A 2016 Cochrane review concluded that morphine is effective in relieving cancer pain
Morphine is beneficial in reducing the symptom of shortness of breath due to both cancer and noncancer causes.[30][31] In the setting of breathlessness at rest or on minimal exertion from conditions such as advanced cancer or end-stage cardiorespiratory diseases, regular, low-dose sustained-release morphine significantly reduces breathlessness safely, with its benefits maintained over time[13,14,15]

Due to its long history and established use as a pain medication, this compound has become the benchmark to which all other opioids are compared.[63] It interacts predominantly with the μ–δ-opioid (Mu-Delta) receptor heteromer.[64][65] The μ-binding sites are discretely distributed in the human brain, with high densities in the posterior amygdala, hypothalamus, thalamus, nucleus caudatus, putamen, and certain cortical areas. They are also found on the terminal axons of primary afferents within laminae I and II (substantia gelatinosa) of the spinal cord and in the spinal nucleus of the trigeminal nerve.[66]

Morphine is a phenanthrene opioid receptor agonist – its main effect is binding to and activating the μ-opioid receptor (MOR) in the central nervous system. Its intrinsic activity at the MOR is heavily dependent on the assay and tissue being tested; in some situations it is a full agonist while in others it can be a partial agonist or

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even antagonist.[67] In clinical settings, morphine exerts its principal pharmacological effect on the central nervous system and gastrointestinal tract. Its primary actions of therapeutic value are analgesia and sedation. Activation of the MOR is associated with analgesia, sedation, euphoria, physical dependence, and respiratory depression. Morphine is also a κ-opioid receptor (KOR) and δ-opioid receptor (DOR) agonist. Activation of the KOR is associated with spinal analgesia, miosis (pinpoint pupils), and psychotomimetic effects. The DOR is thought to play a role in analgesia.[66][Although morphine does not bind to the σ receptor, it has been shown that σ receptor agonists, such as (+)-pentazocine, inhibit morphine analgesia, and σ receptor antagonists enhance morphine analgesia,[68] suggesting downstream involvement of the σ receptor in the actions of morphine.[16,17,18]

IV.CONCLUSION

Morphine is the most abundant opiate found in opium, the dried latex extracted by shallowly scoring the unripe seedpods of the *Papaver somniferum* poppy. Morphine is generally 8–14% of the dry weight of opium.[89] Przemko and Norman cultivars of the opium poppy, are used to produce two other alkaloids, thebaine and oripavine, which are used in the manufacture of semi-synthetic and synthetic opioids like oxycodone and etorphine. *P. bracteatum* does not contain morphine or codeine, or other narcotic phenanthrene-type, alkaloids. This species is rather a source of thebaine.[90] Occurrence of morphine in other Papaverales and Papaveraceae, as well as in some species of hops and mulberry trees has not been confirmed. Morphine is produced most predominantly early in the life cycle of the plant. Past the optimum point for extraction, various processes in the plant produce codeine, thebaine, and in some cases negligible amounts of hydromorphone, dihydromorphine, dihydrocodeine, tetrahydro-thebaine, and hydrocodone (these compounds are rather synthesized from thebaine and oripavine).

In the brain of mammals, morphine is detectable in trace steady-state concentrations.[12] The human body also produces endorphins, which are chemically related endogenous opioid peptides that function as neuropeptides and have similar effects to morphine[19]

Informal names for morphine include: Cube Juice, Dope, Dreamer, Emsel, First Line, God's Drug, Hard Stuff, Hocus, Hows, Lydia, Lydic, M, Miss Emma, Mister Blue, Monkey, Morf, Morph, Morphide, Morphie, Morpho, Mother, MS, Ms. Emma, Mud, New Jack Swing (if mixed with heroin), Sister, Tab, Unkie, Unkie White, and Stuff.[152]

MS Contin tablets are known as misties, and the 100 mg extended-release tablets as greys and blockbusters. The "speedball" can use morphine as the opioid component, which is combined with cocaine, amphetamines, methylphenidate, or similar drugs. "Blue Velvet" is a combination of morphine with the antihistamine tripelennamine (Pyrabenzamine, PBZ, Pelamine) taken by injection[20]

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