

A REVIEW ON THE STRUCTURE SIMILARITY OF TULSI AND CODINE FOR THEIR ANTI-TUSSIVE ACTIVITY

Ashok Kumar Sharma^{1*}, Heena Sharma², Yash Soni², Ritika Tak², Ankit Jangid² and Shafin Khan²¹Asso. Professor, Arya College of Pharmacy, Jaipur, Rajasthan.²Research Scholar, Arya College of Pharmacy, Jaipur, Rajasthan.

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*Corresponding Author

Ashok Kumar Sharma

Asso. Professor, Arya College
of Pharmacy, Jaipur,
Rajasthan.

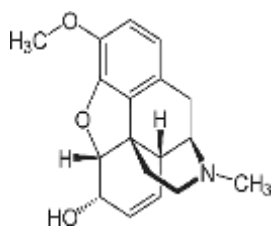
ABSTRACT

Codeine is a narcotic drug that exhibits central activity by blocking the medullary cough centre or inhibiting nerve transmission to the muscles responsible for coughing. As a result, many studies have been conducted by scientists to understand the mechanisms of codeine. These studies show that "RAR" or "COUGH RECEPTOR" is sensitive to codeine, but coughs triggered by neurokinin-containing nociceptive nerves are resistant to it. To address this disease, experts recommend combining codeine with an NK2 tachykinin. Yet another study demonstrates the activity of codeine's antitussive property in URTI-induced cough. The research included 82 people with acute URTI-related cough (51 women and 31 men; mean age 23.5 years; range 18-46 years). The research was carried out across two separate study days. The study's findings indicate that codeine is neither more nor less effective in the treatment of UTRI-induced cough. A study is now underway to test the antitussive properties of codeine on the tracheal bifurcation. This study found that cough caused by mechanical stimulation of the larynx is more responsive to codeine administration than cough caused by mechanical stimulation of the tracheal bifurcation. Tulsi *Ocimum sanctum*, Lamiaceae family, popularly known as "HOLY PLANT" has several medical properties such as antibacterial, antifungal, antitussive, and so on. A study is being conducted by scientists to determine the active elements responsible for the antitussive properties of *ocimum sanctum*. Another research found that Tulsi leaves had significant amounts of camphene, eugenol, and cineole, which assist in the treatment of cough, asthma, and other conditions. This page contains a comprehensive discussion on the use of codeine and *ocimum sanctum* in the treatment of acute cough, chronic cough, and disease-induced cough.

KEYWORD: Tulsi, Codeine, *Ocimum sanctum*, Lamiaceae family, Holy Plant, *ocimum sanctum*.

INTRODUCTION

CODEINE: Codeine is an opiate and precursor of morphine mostly used to alleviate discomfort, hacking, and diarrhoea. It naturally occurs in the sap of the *Papaver somniferum*, the opium poppy. Usually, it is used to treat minor to modest degrees of pain.^[6]



Formula: C₁₈H₂₁NO₃^[6]

IUPAC ID: (5 α ,6 α)-7,8-didehydro-4,5-epoxy-3-methoxy-17-methylmorphinan-6-ol.

Uses: Codeine is used as a central painkiller, tranquilizing, hypnotic, antinociceptive, antiperistalsis, and is also recommended in tuberculosis and restlessness due to incessant coughing.

Side effect: Codeine can cause low breathing, difficulty or noisy breathing, misperception, more than usual drowsiness, trouble wet-nursing, or sagginess in lactated newborns.

Mechanisms: Although codeine is a selective agonist for the mu opioid receptor, it has a distant lower affinity than the stronger opioid medication morphine. Involved in the transmission of pain throughout the body and central nervous system are mu-opioid receptors, which codeine binds to. It is believed that codeine's conversion to morphine gives it its analgesic qualities.

Protein binding: 7-25% of plasma proteins are bound.^[5]

Metabolism: In the liver, around 70 to 80% of the eaten amount of codeine is broken down via conjugation with glucuronic acid to codeine-6 glucuronide (C6G) and O-demethylation to morphine (about 5-10%) and N-demethylation to nor codeine (about 10%). The key metabolic enzymes mediating the glucuronidation of codeine to the metabolite, codeine 6 glucuronide, are UDP-glucuronosyltransferase (UGT) 2B7 and 2B4. Cytochrome P450 2D6 is the primary enzyme responsible for the conversion of codeine to morphine, while P450 3A4 is the primary enzyme responsible for the conversion of codeine to nor codeine. Morphine and codeine are subsequently further metabolised by conjugation with glucuronic acid. Morphine's glucuronide metabolites are morphine-3-glucuronide (M3G) and morphine-6-glucuronide (M6G).

Method of excretion: The kidneys remove about 90% of the whole dose of codeine. Unchanged codeine makes up around 10% of the medication excreted by the kidneys.^[5]

Clearance: In a clinical investigation, the renal clearance of codeine was 183 +/- 59 ml min⁻¹.^[5]

Tulsi (Holy basil)

Tulsi *Ocimum sanctum*, family Lamiaceae Holy basil It is known as Tulsi and is the utmost revered indoor plant, in India it is associated with ayurveda and Hindu religion as spirit of prosperity, healthiness and success. This is further classified into 4 species.^[10]

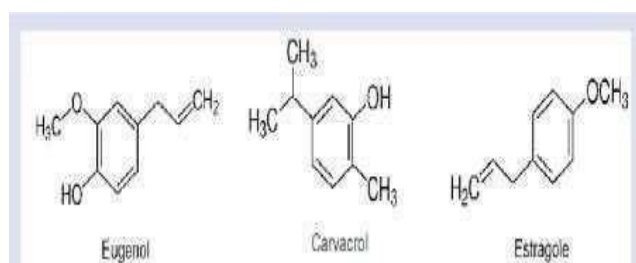
- *O. sanctum* (Rama-Tulsi)
- *O. tenuiflorum* (Krishna-Tulsi)
- *O. tenuiflorum* (Amrita-Tulsi)
- *O. gratissimum* (Vana-Tulsi)

Medicinal properties.^[10]

- Tulsi has antioxidant properties and decreases blood glucose levels, and blood pressure.
- It diminishes lipid level. So, it is respectable for heart disorders.
- It builds the endurance and it is essential ingredient of herbal tea.
- It also used to treat gastric disorders, cough, common colds, malaria, and headaches.
- It's extracted water is used as mouth wash to reduce tooth ache.
- It is used in the manufacturing of many skin ointments and cosmetics because it contains anti-bacterial activities.
- It's oil shows abdominal poisoning in contradiction of "malarial larva".
- It has immuno-modulatory properties.
- It acts as repellent for insect. So, it is widely used to stockpile grains.
- A chemical contemporary in Tulsi known as beta-Ursolic acid, may be used as a anti-fertility mediator in future.

Phytochemistry^[10]

- Extract of fresh leaf's and stem contains some antioxidants compounds like "cirsilineol", "circimaritin", "isothymusin", "apigenin", "rosameric acid", and considerable properties of "eugenol".
- The leaf has 0.7% "volatile oil" muster regarding 71% "eugenol" & 20% "methyl eugenol".
- It's emollient have "carvacrol" & "sesquiterpene hydrocarbon caryophyllene".



Traditional uses.

"The elixir of life" name given to Tulsi because it promotes durability .

- In Ayurveda & Siddha systems of medicine in which many parts of plant are used for inhibition and therapy of many ailments.
- The leaf's are used to augment the memory. Munching of leaf's helps to treat ulcers and contagions of mouth.

REVIEW ON CODEINE AS AN ANTI-TUSSIVE

One of the narcotic opioids with a central action that is approved for use as an antitussive is codeine. By blocking the medullary cough center or an associated higher center and reducing the release of nerve impulses to the muscles that cause coughing, centrally acting antitussives suppress or overwhelm the cough reflex.

Codeine In The Treatment Of Dry Cough, Chronic Cough

RAR or "cough receptor"-mediated coughs are complex to codeine nevertheless coughing triggered by neurokinin-containing nociceptive nerves are resistant to it. In support of this suggestion, there is a finding that the expression of transient receptor potential vanilloid-1 (TRPV-1) is increased in the airway nerves of patients with chronic cough. Coughs facilitated by automatic stimulus of RARs or "cough receptors" are attenuated by narcotic antitussives mainly at the NTS level via inhibition of glutamatergic transmission. Presynaptic μ -opioid receptors perhaps countersign to this inhibition. Contrariwise, neurokinin proclamation in the NTS from nociceptive C- and A δ - fibers, and also from RAR fibers underneath airway inflammation, reasons coughs resistant to antitussives including opiates. Recent findings by Mazzone et al. support this hypothesis. The existing evidence advocates that stimulation of μ -opioid and reserve of neurokinin receptors can help in the

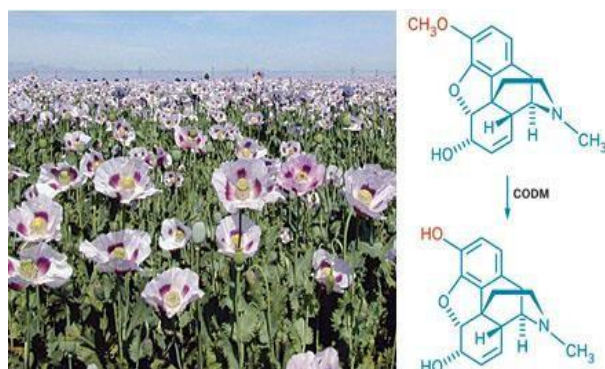
destruction of some varieties of chronic cough. In a preliminary study, we found that coadministration of codeine and an NK2 tachykinin receptor antagonist abolished citric acid-induced coughs in guinea pigs, although codeine alone did not abolish the cough even when administered at very high doses.^[1]

The standard antitussive used to evaluate novel antitussive drugs is generally acknowledged to be codeine. This is problematic because studies on animal cough models, chronic cough models, and induced cough models in humans are used to support codeine's antitussive activity, whereas antitussives are almost exclusively used to treat cough associated with acute upper respiratory tract infection (URTI). This study had two objectives. First, investigate the antitussive effectiveness of codeine in cough related to URTI, and then confirm the utility of a sound metre as a cough measurement method. In a double-blind, stratified, placebo-controlled, parallel-group clinical trial, three distinct cough metrics were used to gauge the effectiveness of codeine: A sound meter's measurement of cough sound pressure levels (CSPLs) and subjective cough scores severity; and cough frequency were recorded using an ink-pen recorder and a microphone. The study comprised 82 participants with acute URTI-related cough (51 females and 31 males; mean age 23.5 years; range 18-46 years). The study was conducted across two distinct study days. Cough measures were taken on trial day 1 before and 90 minutes after a single capsule dosage of either 50 mg codeine or a matched placebo was administered. 2–5 days later (study day 2), the same three cough measurements were carried out once more. On study day 1, both the placebo and the codeine treatments resulted in a highly significant (P 0.0001) decrease in all three measures of cough, although there was no meaningful difference following the codeine treatment. The treatment groups' differences. Between days 1 and 2, a highly significant (P 0.0001) decline in all three cough parameters was also detected. According to the findings, codeine is neither any more or less effective than a placebo for easing acute URTI-related cough, as determined by CSPLs, cough frequency, or subjective symptom scores. Two central coughing pathways—one reflex via the brainstem, which is sensitive to codeine, and the other voluntary via the cortex, which is unaffected by codeine—could explain this outcome. The findings also show that the sound-level meter looks to be a potentially practical research instrument for evaluating cough and antitussive efficacy.^{[2][3]}

Recent Study On Codeine

In a dose-dependent manner, codeine 10, 20, and 50 mg/kg reduced the coughs brought on by stimulation of the larynx. Even at a high dose (50 mg/g), the antitussive was unable to suppress the cough brought on by stimulation to the tracheal bifurcation. Codeine at 20 mg/g considerably reduced the cough brought on by stimulation to the tracheal bifurcation in guinea pigs treated with capsaicin. The current findings imply that

cough brought on by mechanical stimulation of the larynx may be more responsive to the administration of codeine than cough brought on by mechanical stimulation of the tracheal bifurcation.^[4]



REVIEW ON TULSI AS AN ANTITUSSIVE

Review on Herbs used in Cough Medication

- A cough is an explosive, strong exhalation used to expel fluids and foreign objects from the tracheobronchial tract. The objective of this review study was to compile information on the plants used in traditional culture and ethnobotany to treat and relieve cough due to the high frequency of cough in both children and adults. The problems arising from the use of conventional opioid antitussive drugs to treat cough in a variety of respiratory illnesses, such as codeine and codeine-like substances. Compounds from medicinal plants may have potent antitussive effects and little adverse effects. Recent developments in contemporary phytotherapy have enabled rationalisation of treatment, notably dose and nursing of side effects. These improvements include the stipulation of active components responsible for therapeutic action, as well as their quantity in healing pharmaceuticals.^[7]
- THE ACTIVE INGREDIENTS IN HERBAL MEDICINAL MEDICINES THAT HAVE AN ANTITUSSIVE AND EXPECTORANT^[7]
 - SAPONINS
 - FLAVONOIDS
 - ESSENCES
 - GUMS
 - PECTIN
 - MUCILAGE
- List of Herbal Marketed Formulations used to Treat Cough
 - Cough tablets
 - Adulsa
 - Dabur Honitus
 - Herbal brews

Therapeutic uses of *Ocimum sanctum* Linn (Tulsi) with a note on eugenol and its pharmacological actions

Traditional medicine practitioners frequently use medicinal plants to treat a variety of ailments in their

daily practise. *Ocimum sanctum* Linn, also known as Tulsi in Hindi, is a small herb that is commonly found throughout India. It has been recommended for use in traditional systems of medicine for the treatment of bronchitis, bronchial asthma, malaria, diarrhoea, dysentery, antitussive, skin diseases, arthritis, painful eye diseases, chronic fever, insect bites, and more. Additionally, it has been hypothesised that *Ocimum sanctum*.^[8]

L. contains adaptogenic, diaphoretic, anticancer, antidiabetic, antifungal, antibacterial, hepatoprotective, cardioprotective, and antiemetic properties. The active ingredient contained in *Ocimum sanctum* L., eugenol (1-hydroxy-2-methoxy-4-allylbenzene), has been discovered to be primarily responsible for the therapeutic potentials of tulsi. However, because *Ocimum sanctum* L. is widely used in India by practitioners of traditional systems of medicine for treating a variety of disorders due to its high therapeutic potential. A sensible integration of this traditional medical practise with modern systems of medicine is, however, not readily available. Several Indian scientists and researchers have studied the pharmacological effects of steam-distilled, petroleum ether, and benzene extracts of various parts of the Tulsi plant and eugenol on immune system, reproductive system, central nervous system, cardiovascular system, gastric system, urinary system, and blood biochemistry over the past few decades in order to establish the therapeutic uses of *Ocimum sanctum* L. in modern medicine. They have also described the therapeutic significance. These pharmacological research are supported by established scientific theory.^[8]

USES OF TULSI LEAVES

Tulsi leaves have high concentrations of camphene, eugenol, and cineole, which aid in the treatment of bronchitis, asthma, influenza, and other respiratory illnesses. Tulsi helps to treat respiratory disorders in a variety of ways by acting as an immunological modulator, antitussive, anti-inflammatory, and expectorant.^[9]

CONCLUSION

This review project carries a cumulative information about the traditional system and modern system of medicine for the treatment of chronic cough and dry cough. This medication not only use for anti-tussive action but they also have the other property like anti-bacterial, anti-inflammatory, analgesic. This article helps in understanding the mechanisms of codeine resistance in chronic cough and treatment of codeine resistance cough. This review also carries the information about the RAS or Cough receptor activity. It also helps in understanding action of codeine in URTI. Here, we also study about the anti-tussive property of *Ocimum sanctum* Linn (known as Tulsi in Hindi). This plant is also known as the holy plant. Its leaves contain eugenol, cineole, camphene that help in management of cough. Although there are many formulations present in market for their anti-tussive property.

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