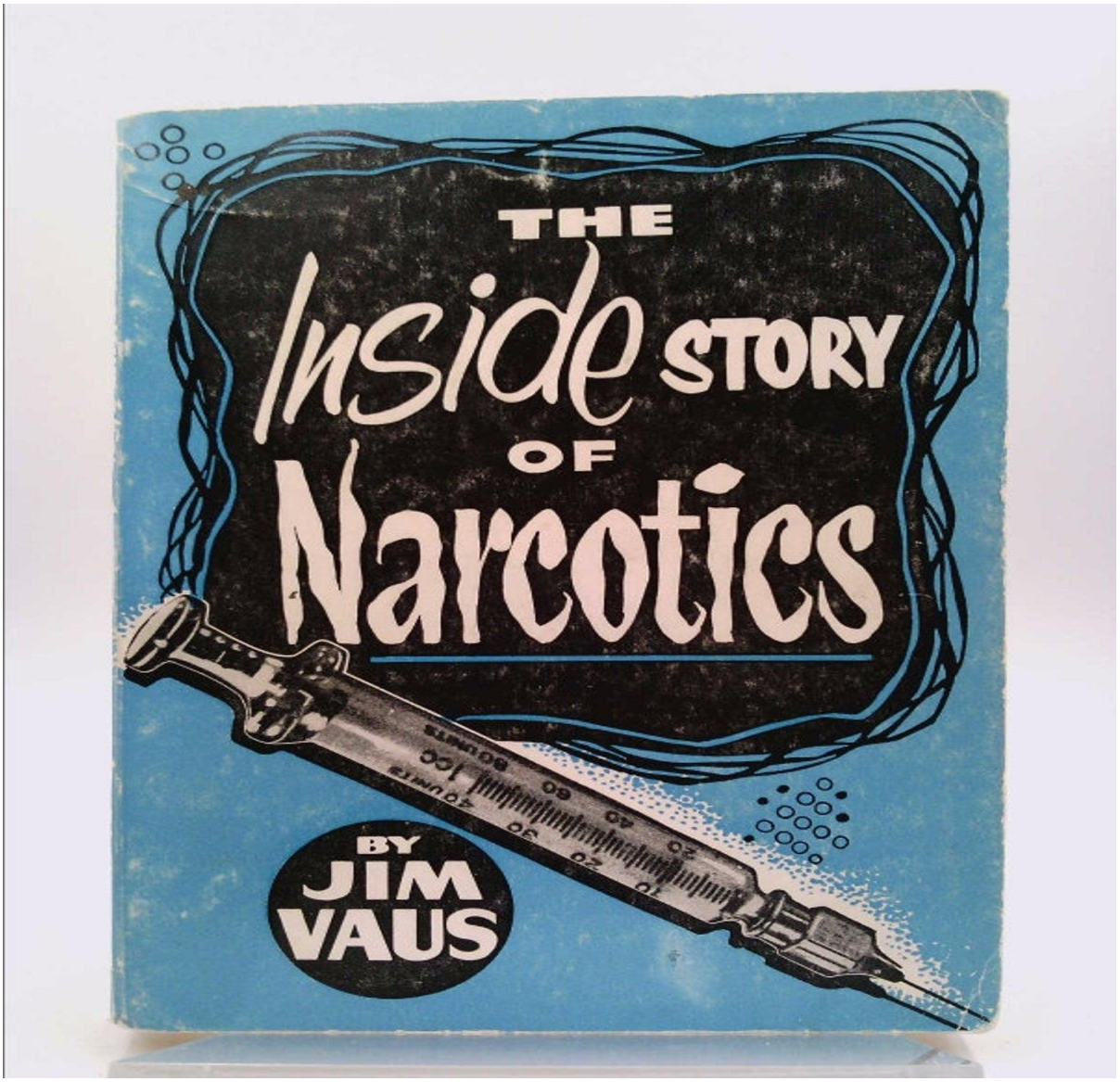
# ARIVAN AGARWAL

CLASS-11, DIV-B

ROLL NO: 14



Bombay Scottish School, Mahim

CERTIFICATE

This is to certify that Shri / Kumari _ARIVAN AGARWAL_____, a student of class XI-B, Roll No: _14__ UID: _____ has successfully completed the project work in Chemistry titled

_NARCOTICS_____
_____

for the Class XII practical examination as prescribed by the Council for the Indian School Examinations in the year 2021-2022. It is further certified that this project is the individual work of the candidate.

External Examiner Internal Examiner

Head of the School

Date:

# INDEX PAGE

# NARCOTICS

A substance used to treat moderate to severe pain. Narcotics are like opiates such as morphine and codeine, but are not made from opium. They bind to opioid receptors in the central nervous system. Narcotics are now called opioids.

Narcotics are addictive drugs that reduce the user's perception of pain and induce euphoria (a feeling of exaggerated and unrealistic well-being). The English word narcotic is derived from the Greek *narcotics,* which means "numbing" or "deadening.

Classification of narcotics

As of the early 2000s, narcotics are commonly classified into three groups according to their origin:

- Natural derivatives of opium: Narcotics in this group include morphine itself and codeine.
- Partially synthetic drugs derived from morphine: These drugs include heroin, oxycodone (OxyContin), hydromorphone (Dilaudid), and oxymorphone (Num orphan).
- Synthetic compounds that resemble morphine in their chemical structure: Narcotics in this group include fentanyl (Duragesic), levorphanol (Levo-Dromore), meperidine (Demerol), methadone, and propoxyphene (Darvon).

Narcotics are available in many different forms, ranging from oral, intramuscular, and intravenous preparations to patches that can be applied to the skin (fentanyl). Illegal street heroin can be taken by inhalation as well as by injection.

# Historical background

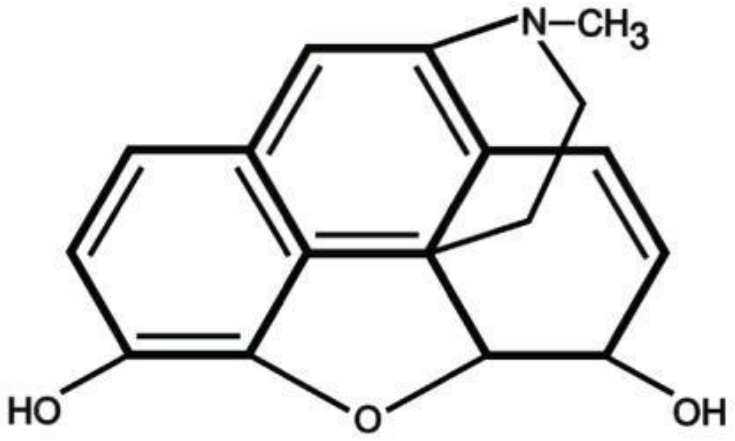
Narcotics are the oldest as well as the strongest analgesics, or pain-relieving drugs, known to humans. Ancient Sumerian and Egyptian medical texts dated as early as 4000 B.C. mention the opium poppy (Papaver somniferous) as the source of a milky fluid (opium latex) that could be given to relieve coughs and insomnia as well as ease pain. Traditional Chinese medicine recommended the opium poppy, known to Chinese physicians as ying su ke , for the treatment of asthma, severe diarrhea, and dysentery as well as chronic pain and insomnia. Opium latex contains between 10 and 20 percent morphine, which in its purified form is a white crystalline powder with a bitter taste.

Narcotics are central nervous system depressants that produce a stuporous state in the person who takes them. These drugs often induce a state of euphoria or feeling of extreme well-being, and they are powerfully addictive. The body quickly builds a tolerance to narcotics in as little as two to three days, so that greater doses are required to achieve the same effect. Because of the addictive qualities of these drugs, most countries in the twenty-first century have strict laws regarding the production and distribution of narcotics. These laws became necessary when opium addiction in the nineteenth century became a widespread social problem in the developed countries. Opium, which was the first of the opioids to be widely used, had been a common folk remedy for centuries that often led to addiction for the user; in fact, many popular Victorian patent medicines for "female complaints" actually contained opium. The invention of the hypodermic needle in the mid-nineteenth century, however, increased the number of addicts because it allowed opioids to be delivered directly into the bloodstream, thereby dramatically increasing their effect.

# MORPHINE

Morphine is an opiate alkaloid isolated from the plant Papaver somniferum and produced synthetically. Morphine (the archetypal opioid) consists of a benzene ring with a phenolic hydroxyl group at position 3 and an alcohol hydroxyl group at position 6 and at the nitrogen atom (Fig. 1). Both hydroxyl groups can be converted to ethers or esters. The tertiary form of the nitrogen appears to be crucial to the analgesia of morphine; making the nitrogen quaternary greatly decreases the analgesia, since it cannot pass into the central nervous system. Changes to the methyl group on the nitrogen will decrease analgesia as well, creating antagonists such as nalorphine. Morphine is optically active, and only the levorotatory isomer is an analgesic. Morphine is a DEA controlled drug and a DEA Schedule II controlled substance. Substances in the DEA Schedule II have a high potential for abuse which may lead to severe psychological or physical dependence. Morphine is classified by the DEA as a Narcotics (Opioids) drug. Street names for Morphine are Dreamer, Emel, First Line, God's Drug, Haws, MS, Mister Blue, Morpho, and Unke.

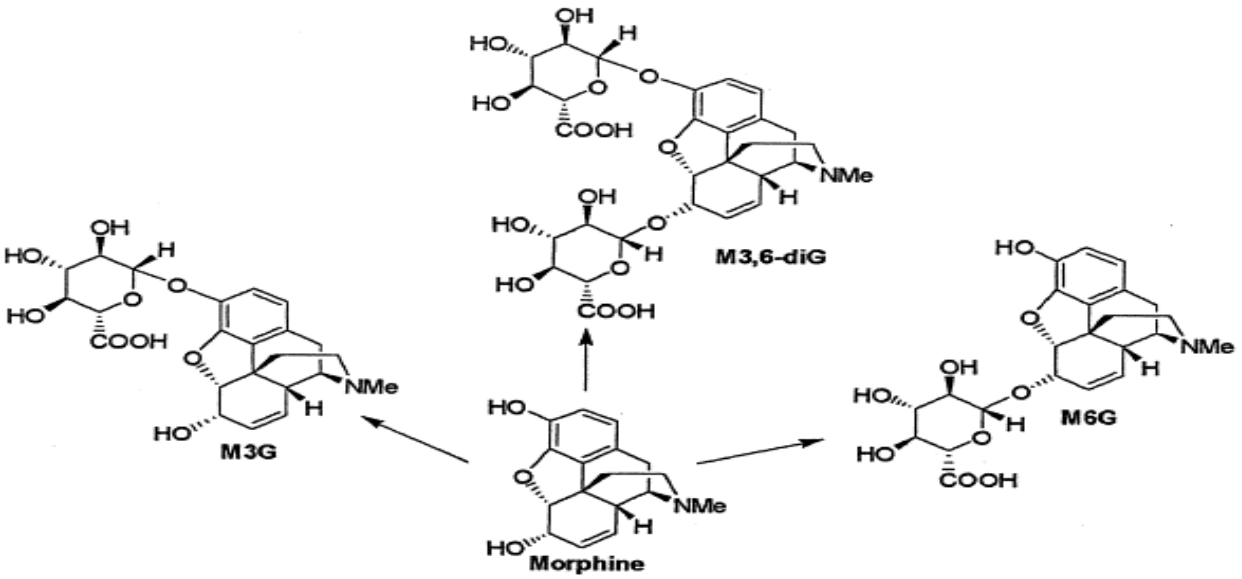
## CHEMICAL STRUCTURE OF MORPHINE



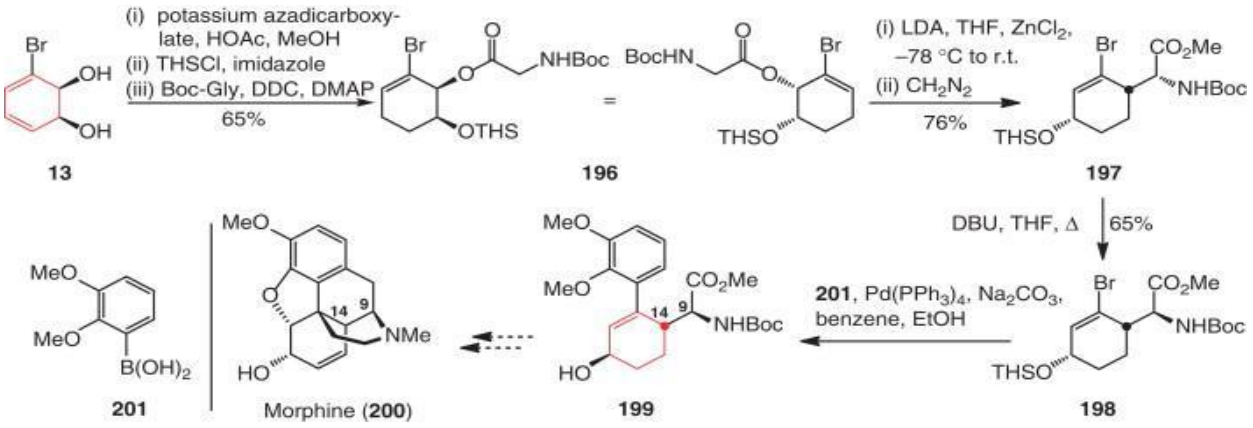
- The chemical formula of morphine is C17H19NO3.
- IUPAC NAME-(4R,4aR,7S,7aR,12bS)-3-methyl-2,4,4a,7,7a,13-hexahydro-1H-4,12-methanobenzofuro[3,2-e] isoquinoline-7,9-diol
- Solid, white crystalline alkaloid, bitter, odorless
- Boiling point 190 degree Celsius
- Melting point 255 degree Celsius
- IDENTIFICATION-Morphine was perfluoro acylated with heptafluorobutyric imidazole and derivatization was analyzed on gas chromatography column. The minimal detectable amt of morphine was approx. 20 pg.

# MORPHINE ISOMERS

- Morphine is metabolized by demethylation and glucuronidation; glucuronidation is the predominant mode of metabolism, producing morphine-6 glucuronide- nide (M6G) and morphine-3 glucuronide (M3G) in a ratio of 6:1, while approximately 5% of the drug is de- methylated into normorphine.



# MANUFACTURE OF MORPHINE




# MORPHINE USES:

- It is an analgesic for relief of severe pain
- Used as a preanesthetic medication
- For producing sleep and sedation
- Used in the treatment of cancer
- Used as an antitussive
- For treatment of diarrhea
- In treatment of acute left ventricular failure

# MORPHINE SIDE-EFFECTS:

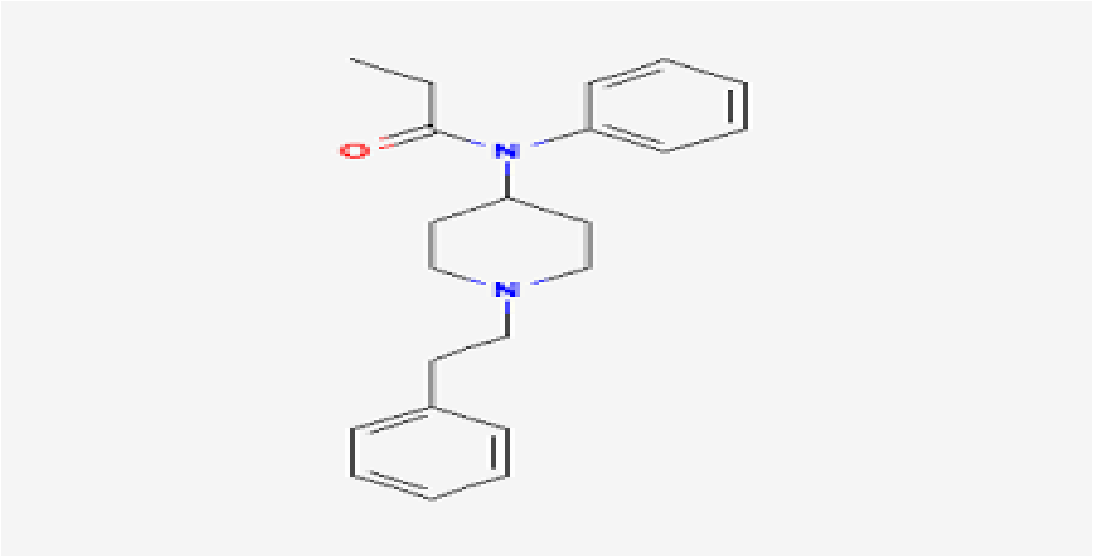
- Morphine causes Tamine release (which can cause bronchospasm and hypotension) and direct respiratory depression mediated by the nucleus accumbens in the brain stem, re- sulting in a decreased response to the arterial carbon dioxide tension, and shifting the response curve to the right. Respiratory acidosis will increase the delivery of morphine to the brain compartment, leading to increased respiratory compromise.
- Morphine may also decrease sympathetic nervous system tone, resulting in decreased tone in peripheral veins, and causing venous pooling and orthostatic hypotension.
- Morphine will have effects on the digestive tract including spasm of biliary smooth muscle, sphincter of Oddi spasm, and decreased intestinal motility resulting in constipation.
- Similar effects occur in the genitourinary system, resulting in spasm of the bladder trigone, causing urinary retention. Morphine may induce

nausea and vomiting by direct stimulation of the chemoreceptor trigger zone in the floor of the 4th ventricle.

## FENTANYL

Fentanyl is a DEA controlled drug. Fentanyl is classified by the DEA as a Narcotics (Opioids) drug. Street names for Fentanyl are Apace, China Girl, China Town, China White, Dance Fever, Goodfellas, Great Bear, He-Man, and Poison and Tango & Cash. The active ingredient 3-Methylfentanyl is a DEA Schedule I controlled substance. Fentanyl is the oldest synthetic piperidine opioid agonist, interacting primarily with mu receptors. It is approximately 80 times more potent than morphine and is highly lipophilic and binds strongly to plasma proteins. Fentanyl undergoes extensive metabolism in the liver. When administered as a lozenge for oral trans mucosal absorption, a portion is swallowed and is subject to first-pass metabolism in the liver and possibly small intestine. It is metabolized to hydroxy fentanyl and nor fentanyl.

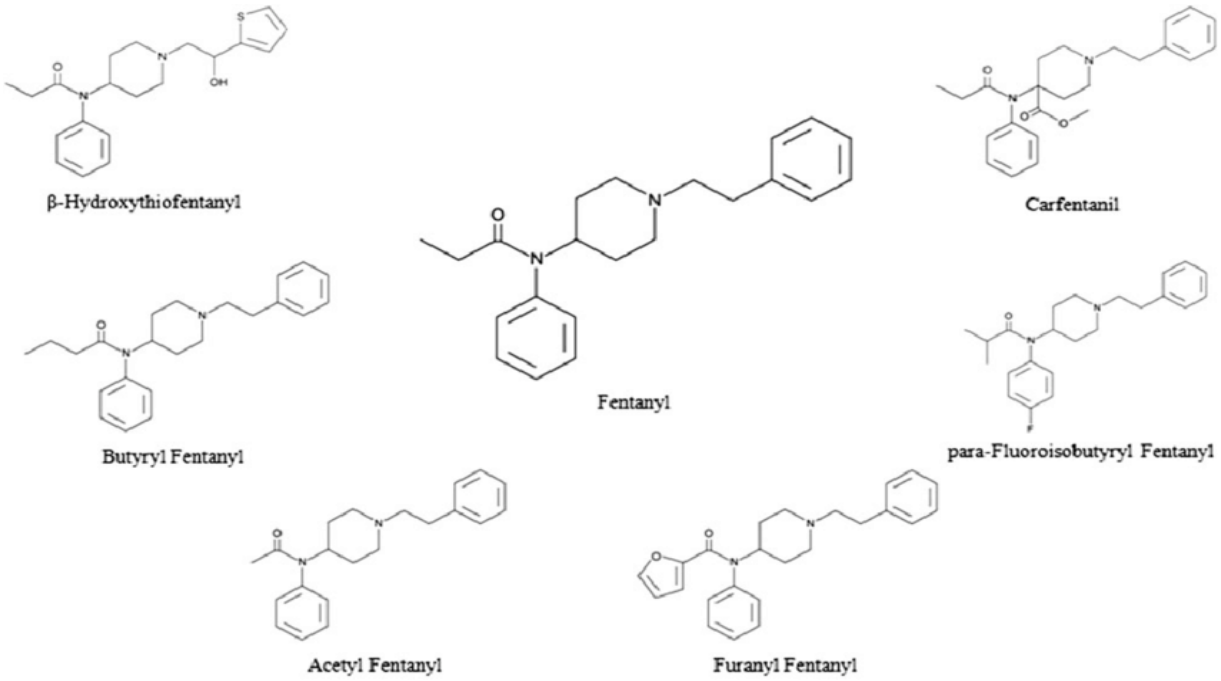
## CHEMICAL STRUCTURE OF FENTANYL




- Chemical formula is C22H28N2O.
- IUPAC NAME- N-phenyl-N-[1-(2-phenylethyl) piperidin-4-yl] propenamide
- Solid crystal or crystalline powder
- Melting point-87.5degreeCelsius
- IDENTIFICATION- Rapid screening of fentanyl (China White) powder samples by solid-phase radioimmunoassay

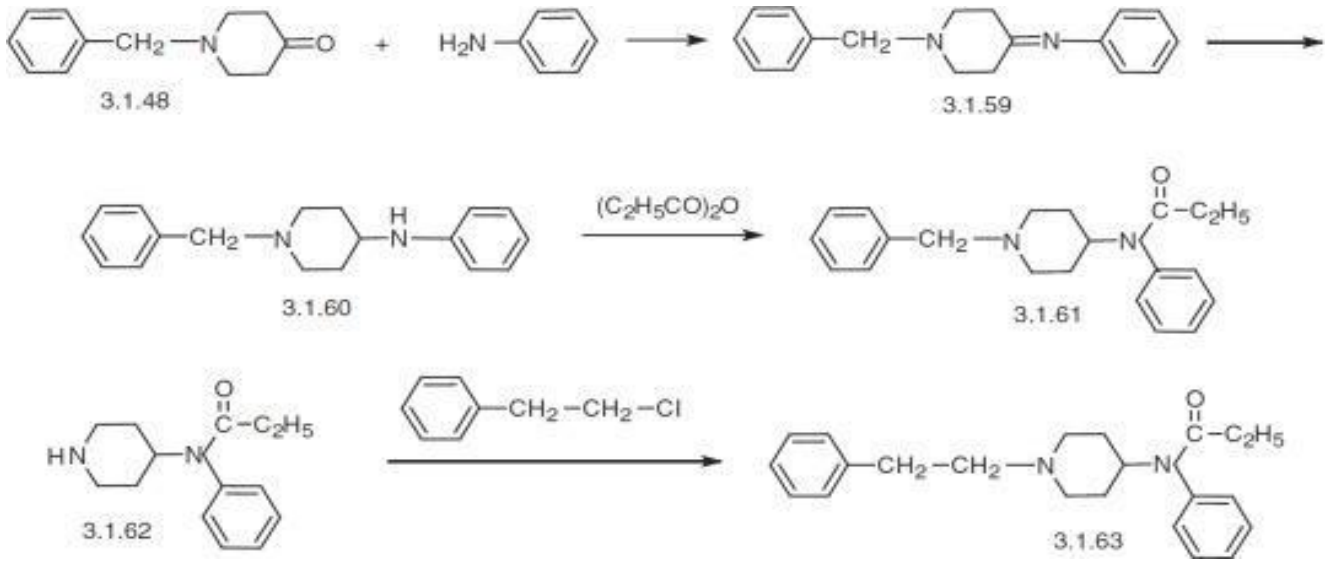
# FENTANYL ISOMERS

A pair of constitutional isomers: butyryl fentanyl and isobutryl fentanyl, and a pair of geometric isomers: cis- and trans- 3-methyl fentanyl.




# MANUFACTURE OF FENTANYL

Synthesis of fentanyl is with 1-benzylpiperidin-4-one, which is condensed with aniline to form the corresponding Schiff base. The double bond in this product is reduced by lithium aluminum hydride, and the resulting 1-benzyl-4-anilinopiperidine is acylated using propionic acid anhydride. The resulting 1-benzyl-4-N-propinoylanilinopiperidine undergoes debenzylation using hydrogen and a palladium on carbon catalyst, to give 4-N-propanoyl anilino piperidine, which is N-alkylated by 2-phenylethyl chloride, to give fentanyl [39,40].




# FENTANYL USES

- This medication is used to help relieve severe ongoing pain (such as due to cancer).
- A rapid-acting opioid (synthetic opiate) drugs that alleviate pain without causing loss of consciousness (analgesic).
- Fentanyl transdermal patch is used to treat chronic pain in opioid-tolerant people.
- Fentanyl works in your brain to change how your body feels and responds to pain.
- It is also combined with local anesthetics to provide epidural analgesia for labor and postoperative pain.

# FENTANYL SIDE-EFFECTS

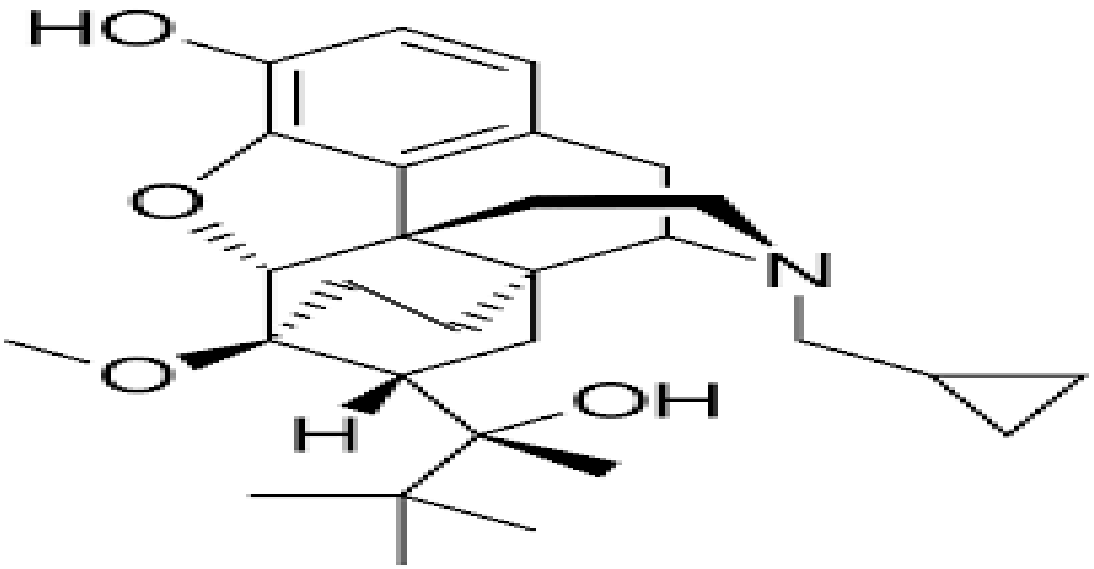
- Nausea, vomiting, constipation, lightheadedness, dizziness, drowsiness, or headache may occur. Mild irritation, itching, or redness at the application site may also occur.
- mental/mood changes (such as agitation, confusion, hallucinations), severe stomach/abdominal pain, difficulty urinating, slow/fast/pounding heartbeat, signs of your adrenal glands not working well (such as loss of appetite, unusual tiredness, weight loss).
- Adrenal insufficiency. Symptoms can include: long-lasting, tiredness muscle, weakness pain in your abdomen
- Androgen deficiency. Symptoms can include: tiredness, trouble sleeping,decreased energy

- Serious breathing problems. Symptoms can include: very shallow breathing (little chest movement with breathing) fainting, dizziness, or confusion
- Severely low blood pressure. Symptoms can include: dizziness or lightheadedness, especially if you stand up too quickly

## BUPRENORPHINE

Buprenorphine Hydrochloride is the hydrochloride salt form of buprenorphine, a synthetic phenanthrene with narcotic analgesic activity. Buprenorphine hydrochloride is a partial agonist at the mu-opioid receptor and an antagonist at the kappa-opioid receptor in the central nervous system. However, under the conditions of recommended use it behaves as a classic mu-opioid agonist, mimicking the actions of endogenous peptides at CNS opioid receptors. It is a synthetic opioid, treats pain and opioid addiction. It underwent development in the late 1960s. It is a synthetic analog of thebaine, an alkaloid compound derived from the poppy flower. It is a schedule III drug, which means that it has some potential for moderate or low physical dependence or high psychological dependence. Buprenorphine hydrochloride is a partial agonist at mu opioid receptors, and a very weak partial agonist at kappa opioid receptors and an even weaker partial agonist at delta opioid receptors.

## CHEMICAL STRUCTURE OF BUPRENORPHINE

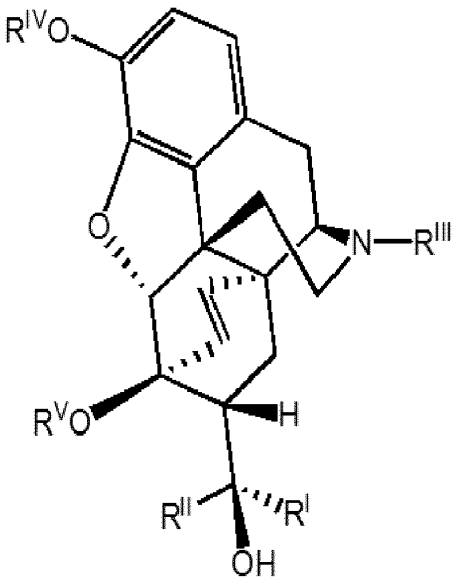



- Chemical formula is C29H41N04

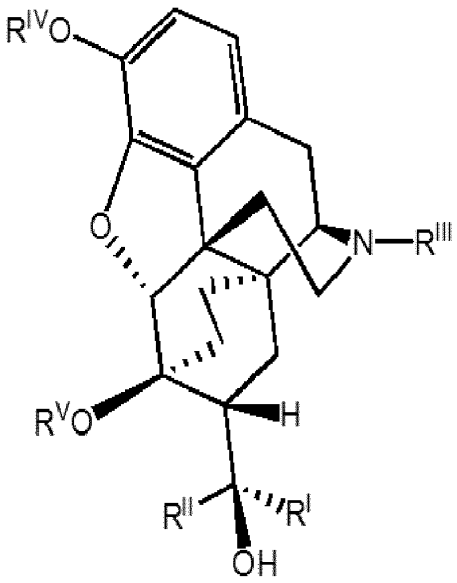
- IUPAC NAME-(1S,2S,6R,14R,15R,16R)-5-(cyclopropyl methyl)-16-[(2S)-2-hydroxy-3,3-dimethylbutan-2-yl]-15-methoxy-13-oxa-5-azabicyclo [13.2.2.12,8.01,6.02,14.012,20] icosa-8(20),9,11-trien-11-ol; hydrochloride

# ISOMERS OF BUPRENORPHINE

The present invention relates to a method of preparing a compound of Formula II-a' or Formula II-b', wherein R' represents hydrogen or a linear, branched and/or cyclic alkyl or alkenyl group having 1 to 10 carbon atoms; R'' represents a linear, branched and/or cyclic alkyl or alkenyl group having 1 to 10 carbon atoms;R- III represents hydrogen or a linear, branched and/or cyclic alkyl or alkenyl group having 1 to 10 carbon atoms or a linear, branched and/or cyclic carbonyl oxy alkyl group having 1 to 10 carbon atoms or a linear, branched and/or cyclic alkoxy group having 1 to 10 carbon atoms;
RIV represents hydrogen or a linear, branched and/or cyclic alkyl group having 1 to 10 carbon atoms or an optionally substituted aryl or alkyl aryl group having 6 to 40 carbon atom or acetyl or silyl or a protective group; and
RV represents hydrogen or a methyl group;



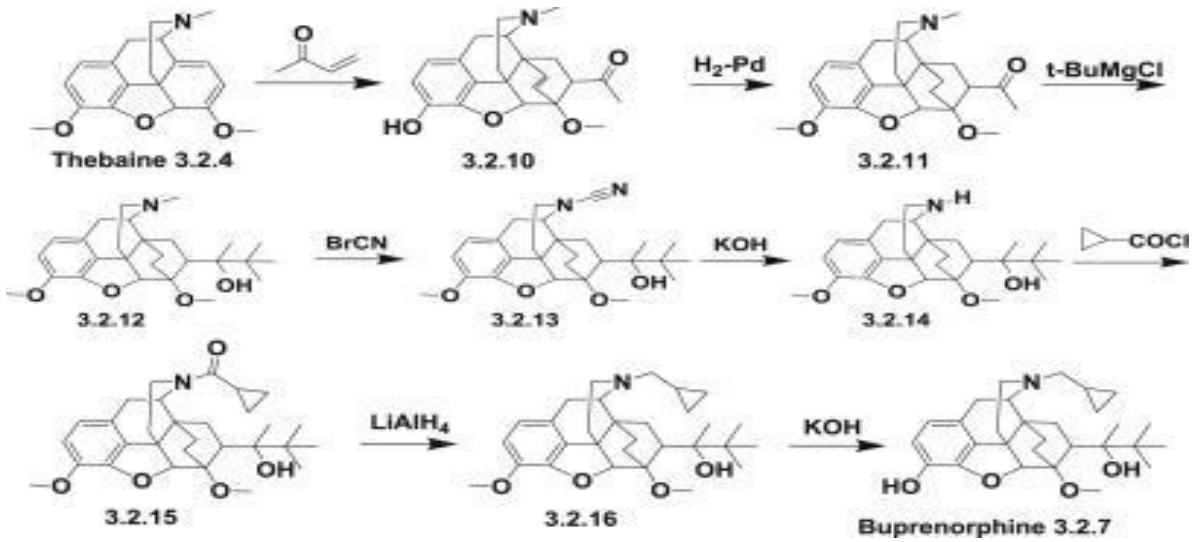

(Formula II-a')




(Formula II-b')

# MANUFACTURE OF BUPRENORPHINE

Synthesis of buprenorphine is an eight-step process started from thebaine [38,39]. A Diels-Alder reaction of thebaine with methyl vinyl ketone gives a 6,14 endo-etheno bridge in the 4,5-epoxy morphinan system and an acetyl substituent at the 7α position. Hydrogenation of generated double bonds followed by a Grignard reaction with t-butyl magnesium chloride creates a compound. It undergoes a von Braun N-demethylation with cyanogen bromide, producing the corresponding N-nitrile. N-nitrile hydrolyzed to the secondary amine, which was acylated with cyclopropyl methyl carbonyl chloride followed by lithium aluminum hydride reduction of the carbonyl group. Phenolic O-demethylation furnishes the requested buprenorphine.




# BUPRENORPHINE USES:

- Multiple routes of mechanism actions and multiple presentations
- Analgesic potency
- Hemodynamic stability
- Wide safety margin regarding doses
- No immunosuppression in chronic treatment
- Treatment of chronic cancer pain

# BUPRENORPHINE SIDE-EFFECTS:

- SedationDizzinessHeadacheLow blood pressure (hypotension) Slow breathing, Constricted pupils, Nausea, Spinning, sensation

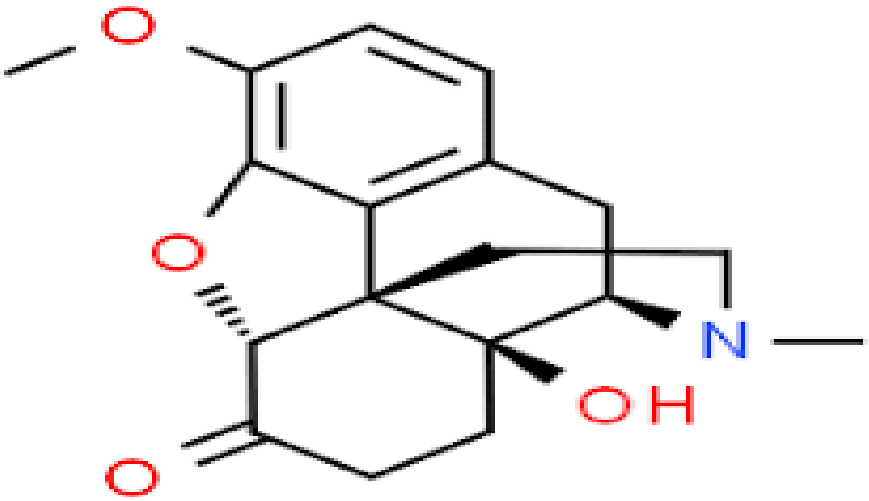
(vertigo),Sweating, Vomiting,Abdominal cramps,Blurred vision,Coma, Confusion

- Prolonged use during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening.
- Chronic use of opioids may cause reduced fertility in females and males of reproductive potential; unknown whether effects on fertility are reversible
- Syndrome presents as irritability, hyperactivity and abnormal sleep pattern, high-pitched cry, tremor, vomiting, diarrhea, and failure to gain weight
- Respiratory depressant effects of opioids may include carbon dioxide retention and lead to elevated cerebrospinal fluid (CSF) pressure.

## Oxycodone

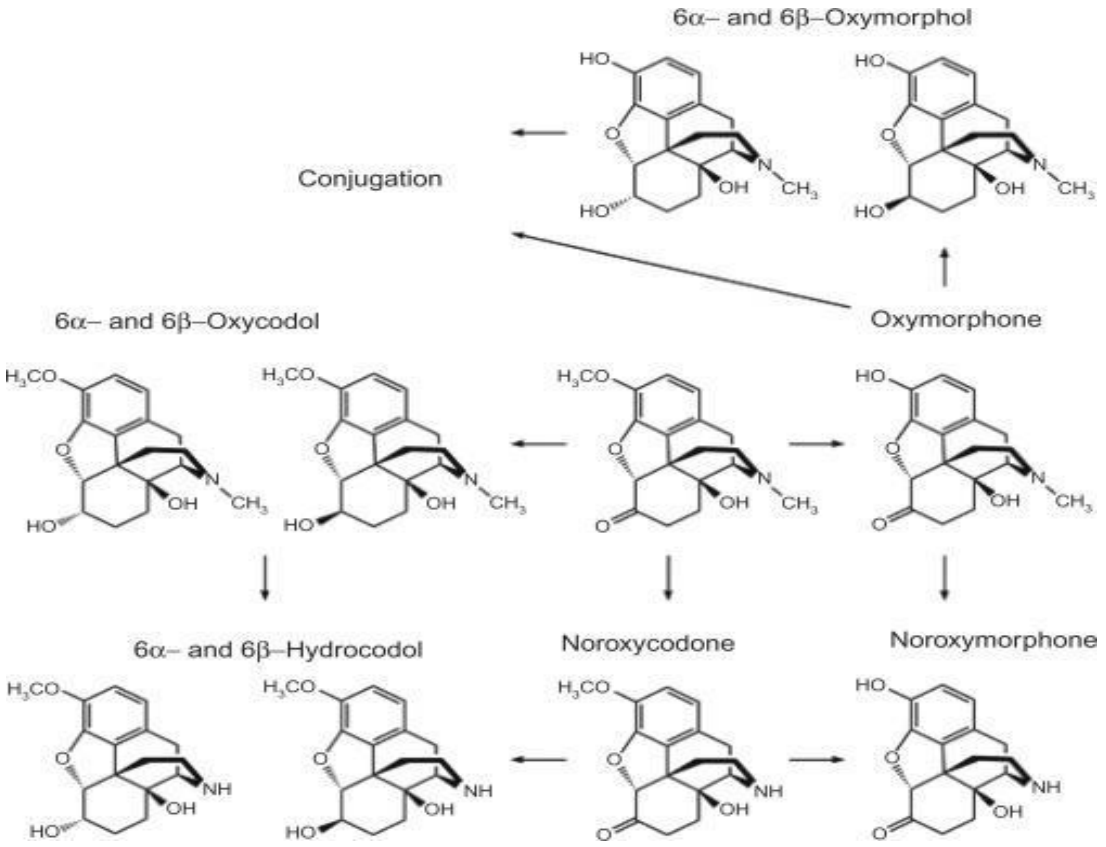
Oxycodone is a phenanthrene class opioid available as a Schedule II substance whether in its pure form or in combination with Tylenol or aspirin. Oxycodone has activity at multiple opiate receptors including the kappa receptor. Oxycodone shares similarities with hydrocodone except for the addition of a hydroxyl group at the #14 carbon. Oxycodone is an analgesic, not a pro-drug; however, oxymorphone is an active metabolite of oxycodone, and may have some impact on analgesia; however, the parent compound itself, oxycodone, produces the lion's share of the analgesia. Oxycodone is a semi-synthetic, morphine-like opioid alkaloid with analgesic activity. Oxycodone exerts its analgesic activity by binding to the mu-receptors in the central nervous system (CNS), thereby mimicking the effects of endogenous opioids. Street names for Oxycodone are Hillbilly Heroin, Kicker, OC, Ox, Roxy, Perc, and Oxy. It is available as controlled release tablets, immediate release tablets, oral solution, and in combination with aspirin or acetaminophen.

# CHEMICAL STRUCTURE OF OXYCODONE

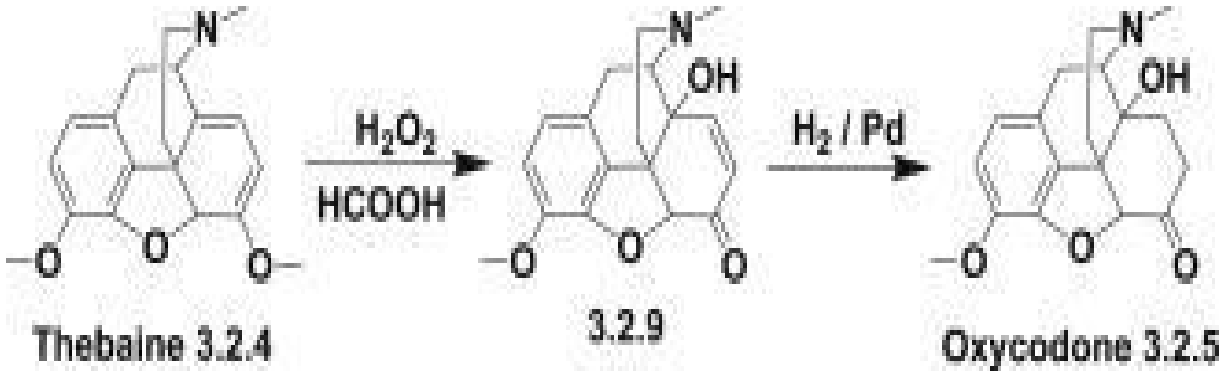



- The chemical formula is C18H21NO4.
- IUPAC NAME-(4R,4aS,7aR,12bS)-4a-hydroxy-9-methoxy-3-methyl-2,4,5,6,7a,13-hexahydro-1H-4,12-methanobenzofuro[3,2-e] isoquinolin-7-one
- Melting point-219degreeCelsius
- IDENTIFICATION-dissolution in water; reaction with ammonium hydroxide; formation of precipitate; precipitate melts between 218 °C and 223 °C.

# OXYCODONE ISOMER




# MANUFACTURE OF OXYCODONE




It is synthesized from thebaine , which transforms into intermediate 14-hydroxycodeinone during oxidation with hydrogen peroxide in formic acid. After the selective hydrogenation of the double bond, the desired oxycodone has been synthesized.

# OXYCODONE USES:

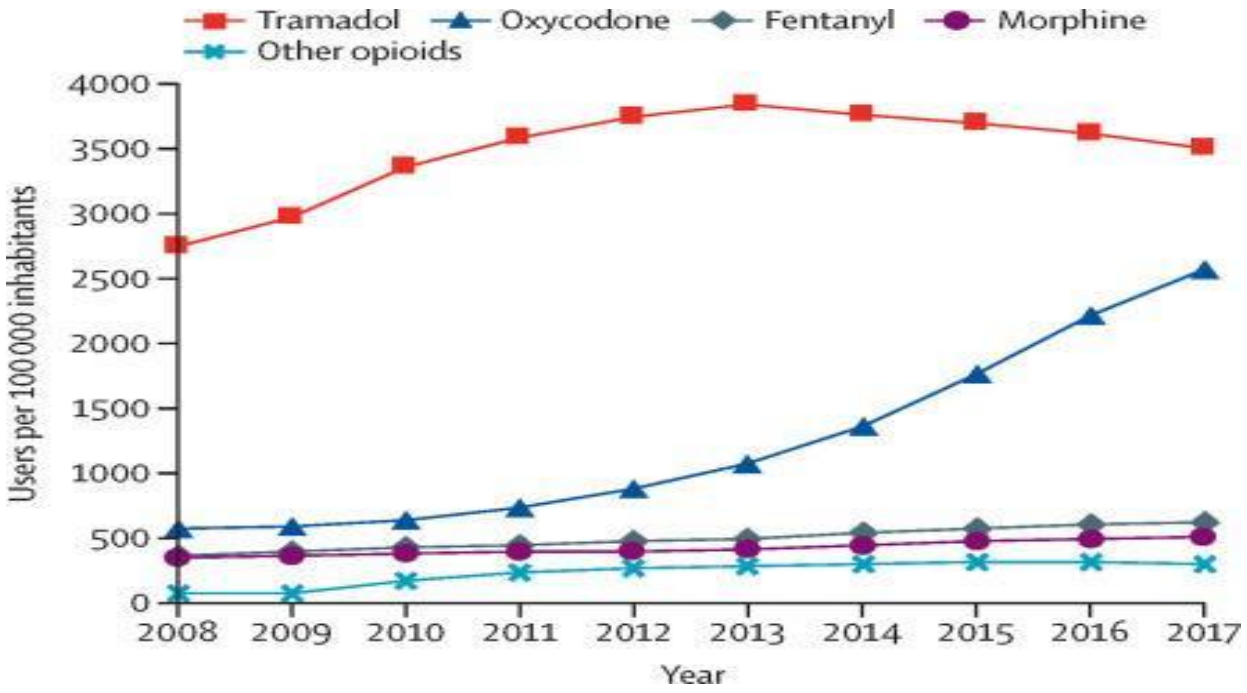
- Better in renal failure to morphine.
- Treatment of chronic cancer pain
- Oxycodone administered as part of a multimodal analgesic regimen produced superior pain relief with fewer side effects and a reduced hospital stay.
- Lower drug costs compared with epidural and intravenous analgesics

# OXYCODONE SIDE-EFFECTS:

- mental/mood changes (such as agitation, confusion, hallucinations), severe stomach/abdominal pain.
- difficulty in urinating, signs of your adrenal glands not working well (such as loss of appetite, unusual tiredness, weight loss).
- Get medical help right away if you have any very serious side effects, including: fainting, seizure, slow/shallow breathing, severe drowsiness/difficulty waking up.
- A very serious allergic reaction to this drug is rare. However, get medical help right away if you notice any symptoms of a serious allergic reaction, including: rash, itching/swelling (especially of the face/tongue/throat), severe dizziness, trouble breathing.

# GENERAL VARIATIONS OF NARCOTICS DRUGS

Between 2008 and 2017, opioid use increased substantially from 4109 per 100 000 inhabitants in 2008 to 7489 per 100 000 inhabitants in 2017 (figure 1). Tramadol, oxycodone, morphine, and fentanyl are shown separately. Hydromorphone, nicomorphine, pethidine, dextromoramide, piritramide, pentazocine, buprenorphine, and tapentadol are combined in a single category.



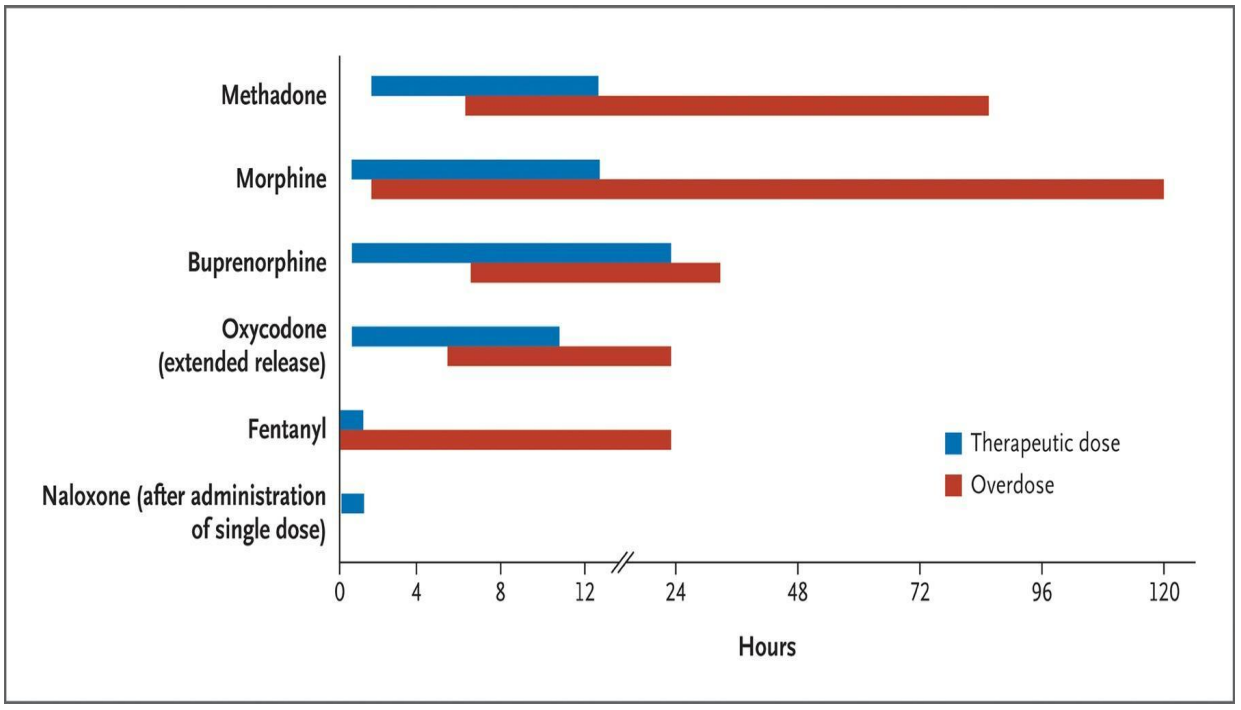

# TOTAL DAILY ADEQUATE DOSAGE

| Current Analgesic | Total Daily Dosage (mg/day) | | | |
|---|---|---|---|---|
| Oral Morphine | 60-134 | 135-224 | 225-315 | 315-404 |
| IM/IV Morphine | 10-22 | 23-37 | 38-52 | 53-67 |
| Oral Oxycodone | 30-67 | 67-112 | 112-157 | 157-202 |
| IM/IV Oxycodone | 15-33 | 33-56 | 56-78 | 78-101 |
| Oral Codeine | 150-447 | 448-747 | 748-1047 | 1048-1347 |
| Oral Hydromorphone | 8-17 | 17-28 | 28-39 | 39-51 |
| IV Hydromorphone | 1.5-3.4 | 3.5-5.6 | 5.7-7.9 | 8-10 |
| IM Meperidine | 75-165 | 166-278 | 270-390 | 391-503 |
| Oral Methadone | 20-44 | 45-74 | 75-104 | 105-134 |
| IM Methadone | 10-22 | 23-37 | 38-52 | 53-67 |
| | | | | |
| **Recommended Fentanyl Dose (mcg/hr)** | 25 mcg/hr | 50 mcg/hr | 75 mcg/hr | 100 mcg/hr |

# OVERDOSAGE

Opioid analgesic overdose is a preventable and potentially lethal condition that results from prescribing practices, inadequate understanding on the patient's part of the risks of medication misuse, errors in drug administration, and pharmaceutical abuse. Opioid analgesic overdose can have life-threatening toxic effects in multiple organ systems. Normal pharmacokinetic properties are often disrupted during an overdose and can prolong intoxication dramatically.

## Onset and Duration of Action in Therapeutic Dosing and Overdose of Selected Opioid Analgesic Agents.



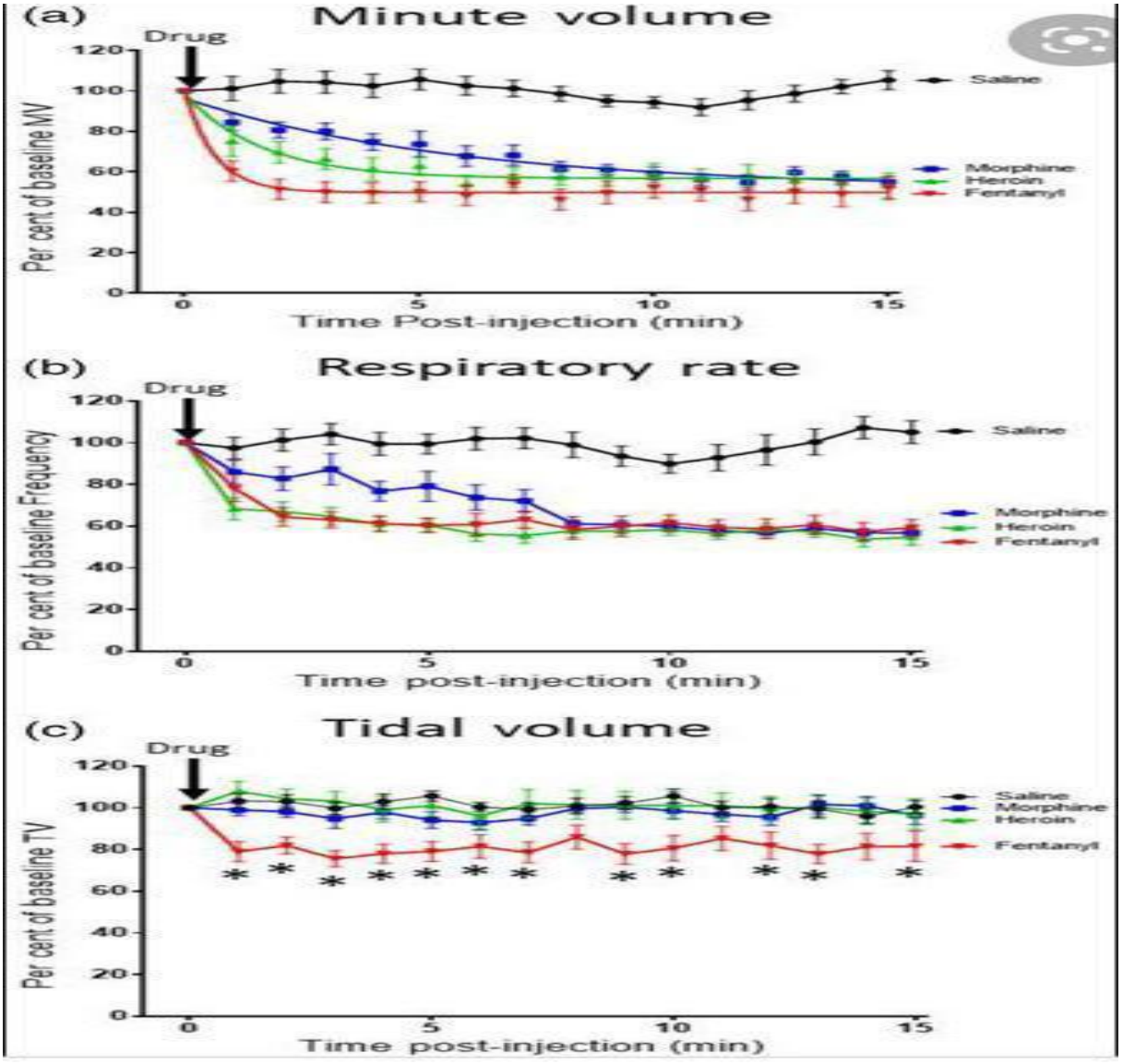
# Rate of onset of opioid respiratory depression.

(a) Fentanyl, heroin, and morphine rapidly decreased minute volume (MV), the effect of the drugs reaching a similar steady state 10–15 min post-administration. Data for each drug are fitted to a single exponential.

(b) Fentanyl, heroin, and morphine decreased respiratory rate.

(c) Heroin and morphine had no effect on tidal volume (TV), whereas fentanyl significantly decreased tidal volume.

Saline injection did not alter any of the respiratory parameters.



# CONCLUSION

In Conclusion, ancient medicines, some plant derivatives were used to alleviate pain including: alcohol, cannabis, mandrake, and opium. Over the past two centuries, opium and its derivatives have become the most widely used analgesics for severe pain. Since its isolation from opium almost 200 years ago, morphine remains the most widely used analgesic and the standard against which all new opioids for postoperative pain relief are compared. In patients with severe pain, a “strong” opioid is the drug of choice alone or in combination.

The analgesic efficacy of opioids does not have a conventional dose-related ceiling, but rather dose escalation is usually limited by the incidence and severity of adverse effects. Therefore, individual titration of the dose combined with measures to reduce adverse effects is key to optimizing the management of pain with these drugs. Information is necessary for the selection of the right analgesic, administered at the right dose and with a dosing schedule to maximize pain relief and minimize side effects.

Though considerable progress has been recorded, there is no room for complacency. Narcotics use continues to bring misery to mankind. It also finances criminal and, to some extent, terrorist activities. Too many young people across the globe still die every year because of drugs, either as a direct result of drug abuse, overdose or addiction.

Finally, efforts are also underway by medical scientists to improve the understanding of opioids, as well as the structure and functioning of opioids markets, with a view to design more synergetic, dynamic and human friendly interventions.

# ACKNOWLEDGMENT

I extend my thanks to my chemistry teacher, Ms. Ghosh, for guiding me in the completion of this project. This project was possible because of her constant support and guidance. Further, I acknowledge our principal, Mrs. George, for providing me with this opportunity. I also thank the senior academic coordinators, Ms. Thomas, for supporting and organizing the academic program. Finally, I thank my parents for their continued encouragement.

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