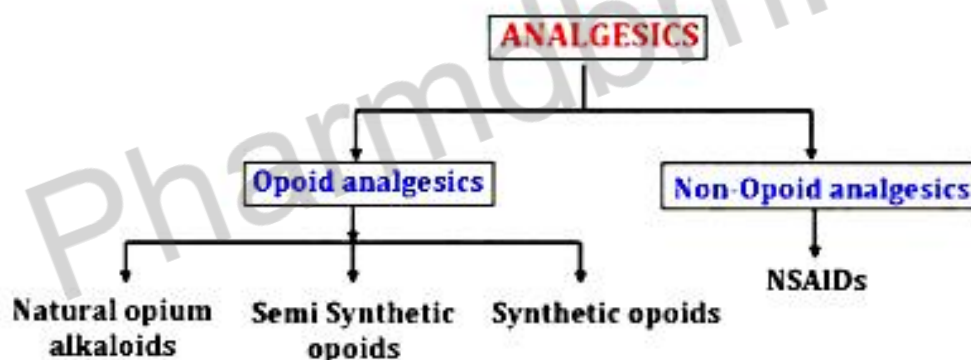


ANALGESIC AND ANTI-INFLAMMATORY AGENTS

10.1 ANALGESICS

- Analgesics are agents that relieve pain by acting centrally to elevate pain threshold without disturbing consciousness or altering other sensory modalities. Certain analgesics like aminopyrine and phenylbutazone also possess anti-inflammatory properties. Such substances and the gold compounds are used in the treatment of arthritis.
- Many drugs that are used to relieve pain are not analgesics, the general anaesthetics relieve pain by producing unconsciousness, local anaesthetics prevent pain by blocking peripheral nerve fibres, antispasmodics relieve pain by relaxing smooth muscles and the adrenal corticoids relieve pain associated with rheumatoid arthritis by anti-inflammatory action.



10.2 OPIOID ANALGESICS

- The opioid analgesics were once called narcotic drugs because they act on the brain and can induce sleep.
 - The opioid analgesics can be used for either short term or long term relief of severe pain.
- **Natural opium alkaloids**
- Morphine
 - Codeine
 - Methadone
 - Hydromorphone

➤ **Semi - synthetic opiates**

- Diacetylmorphine
- Oxycodone
- Pholcodine

➤ **Synthetic opioids**

- Pethidine
- Methadone
- Dextropropoxyphene

❖ **Non - Opioid Analgesics**

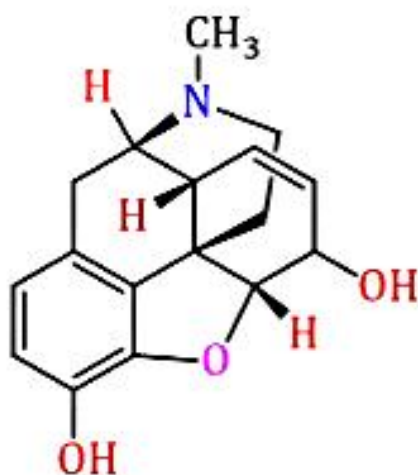
- Non opioid analgesics which alleviate pain by reducing local inflammatory responses.
- In contrast the anti-inflammatory compounds are used for short term pain relief and for modest pain, such as that of headache, muscle strain, bruising or arthritis.

10.2.1 MORPHINE

- Morphine injection is used to relieve moderate to severe pain.
- It may also be used before or during surgery with an anesthetic (medicine that puts you to sleep).
- Morphine belongs to the group of medicines called narcotic analgesics (pain medicines).

❖ **Chemical Formula - $C_{17}H_{19}NO_3$**

❖ **Structure**



❖ IUPAC Nomenclature

- (4R,4aR,7S,7aR,12bS)-3-Methyl-2,3,4,4a,7,7a-hexahydro-1H-4,12-methano[1]benzofuro[3,2-e]isoquinoline-7,9-diol

❖ Physiochemical Properties

- Morphine sulfate is soluble in water, freely soluble in hot water, and slightly soluble in alcohol.
- It is odourless and occurs as white, feathery, silky crystals, cubical masses of crystals, or a white, crystalline powder.

❖ Pharmaceutical Formulation

- It is formulated form of Chloroform and Morphine tincture, suppositories and injection.

❖ Stability and storage

- It should be stored in well-closed airtight containers and protected from light.

❖ Popular Brand Names

- Magnus MR,
- Vermor
- Mitigo

❖ Dose

- The usual, adult, oral dose is 10 to 30 mg 6 times/day.

❖ Medicinal Uses

- It is used to relieve moderate to severe pain. It acts on the central nervous system to relieve pain.
- It used as an opioid receptor agonist and analgesic.

10.2.2 CODEINE

❖ Chemical Formula $C_{18}H_{21}NO_3$

❖ Structure



❖ IUPAC Nomenclature

- (4R,4aR,7S,7aR,12bS)-9-methoxy-3-methyl-2,4,4a,7,7a,13-hexahydro-1H-4,12-methanobenzofuro[3,2-e]isoquinolin-7-ol

❖ Physiochemical Properties

- It appears as odourless, colourless to white crystalline solid or white powder.
- It is soluble in water. It is sterilized by autoclaving or by filtration.

❖ Pharmaceutical Formulation

- It is formulated form of tablet and syrup.

❖ Stability And Storage

- It effloresces in dry air and is affected by light. So, it should be stored in a tightly closed container at controlled room temperature and protected from freezing and light.

❖ Popular Brand Names

- Benylin
- Corex
- Codep

❖ Dose

- Its usual dose is 30–60 mg oral dose, and 15 mg/5 ml syrup.

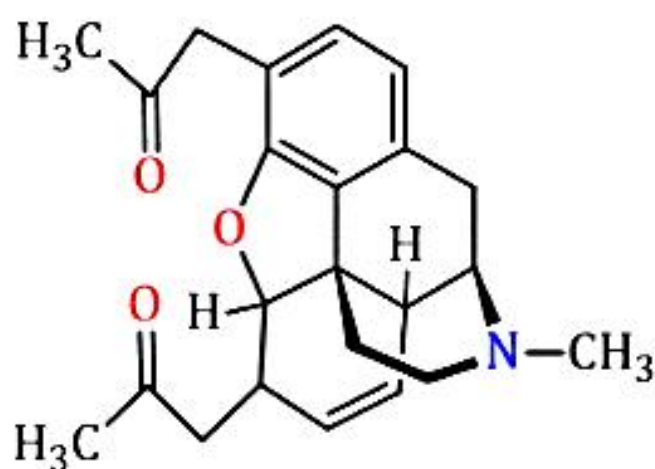
❖ Medicinal Uses

- It is used as an analgesic, antitussive and antidiarrheal agent. It is used to relieve mild to moderately severe pain.

10.2.3 DIAMORPHIN

- ❖ **Chemical Formula** $C_{21}H_{23}NO_5$

- ❖ **Structure**



❖ IUPAC Nomenclature

- (5 α ,6 α)-7,8-didehydro-4,5-epoxy-17-methylmorphinan-3,6-diol diacetate

❖ **Physiochemical Properties**

- It appears as white crystalline powder, soluble in water and alcohol.

❖ **Pharmaceutical Formulation**

- It is formulated form of injection.

❖ **Stability And Storage**

- It is stored in a tightly closed container at controlled room temperature and protected from light.

❖ **Popular Brand Names**

- Diagesil
- Udidyne

❖ **Dose**

- For acute pain, 5 mg is administered and repeated every four hours if necessary.
- In case of chronic pain 5-10mg is administered regularly every four hours by subcutaneous or intramuscular injection.

❖ **Medicinal Uses**

- Diamorphine hydrochloride is used for the treatment of severe pain. It produces its action by binding to opioid receptors in the central nervous system.

10.3 NARCOTIC ANTAGONISTS

- The euphoria accompanying with use of heroin and other narcotics reinforces repeated drug-seeking behavior as psychological dependence develops.
- Once tolerance develops, the opiate-dependent individual avoids painful withdrawal symptoms by continuously increasing the amounts of opiate consumed.
- Narcotic antagonists Prevents or abolishes excessive respiratory depression caused by the administration of morphine or related compounds. They act by competing for the same analgesic receptor sites.
- They are structurally related to morphine with the exception of the group attached to nitrogen.

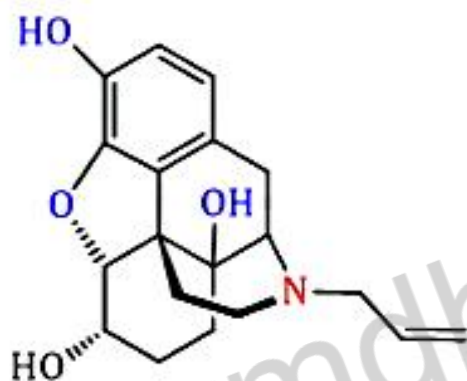
10.3.1 Classification of Narcotic Antagonist

CLASS	DRUG
Pure antagonists	Naloxone, Naltrexone
Partial agonists of nalorphine type	Nalorphine, Levallorphan
Partial agonists of morphine type	Propiram, Profadol

10.3.2 NALORPHINE

❖ **Chemical Formula** $C_{19}H_{21}NO_3$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 17-allyl-7,8-didehydro-4,5 α -epoxymorphinan-3,6 α -diol

❖ **Physicochemical Properties**

- It is odourless, white crystalline powder.
- It is insoluble in chloroform and ether and soluble in dilute alkali hydroxide solution. It is sterilized by autoclaving or by filtration.

❖ **Pharmaceutical Formulation**

- It is formulated form of injection.

❖ **Stability And Storage**

- It slowly darkens on prolonged exposure to light and air.
- It is stored in a tightly closed container at controlled room temperature and protected from light

❖ **Popular Brand Names**

- Lethidrone
- Nalline

❖ **Dose**

- Its usual dose is By I.V. 2 to 10 mg /dose and if required 5 mg repeated twice at 3 min intervals.

❖ **Medicinal Uses**

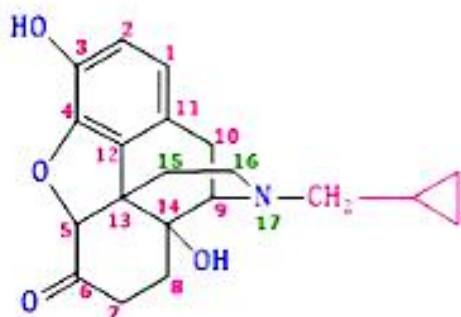
- It is used as an antidote to reverse the opioid overdose.

10.3.3 NALTREXONE

- Naltrexone is the most promising narcotic antagonist based on ability to produce blockade, length of duration, and relative absence of side effects.

❖ **Chemical Formula** - $C_{20}H_{23}NO_4$

❖ **Structure**



❖ **IUPAC Nomenclature**

- (4R,4aS,7aR,12bS)-3-(cyclopropylmethyl)-4a,9-dihydroxy-2,4,5,6,7a,13-hexahydro-1H-4,12-methanobenzofuro[3,2-e]isoquinoline-7-one

❖ **Physiochemical Properties**

- It is a white or almost white powder, hygroscopic insoluble in methylene chloride, freely soluble in water, and slightly soluble in ethanol.

❖ **Pharmaceutical Formulation**

- It is formulated form of tablet and injection.

❖ **Stability and storage**

- It should be stored in well-closed airtight containers and protected from light.

❖ **Popular Brand Names**

- Nalsign
- Naltima
- Naltrexon

❖ Dose

- For opioid dependence – Adult - As hydrochloride: Initially, 25 mg; increase to 50 mg daily, if no withdrawal signs occur.
- Maintenance: 350 mg weekly given as 50 mg daily or divided in 3 doses (given for 3 days in a week) for improved compliance.

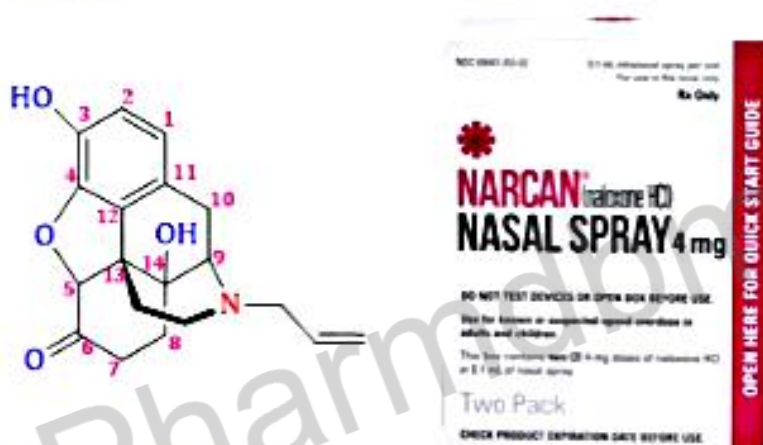
❖ Medicinal Uses

- It is used to treat alcohol use disorder and opioid dependence.
- Naltrexone blocks the effect of opioids and prevents opioid intoxication and physiologic dependence on opioid users.

10.3.4 NALOXONE

❖ Chemical Formula $C_{19}H_{21}NO_4$

❖ Structure



❖ IUPAC Nomenclature

- (4R,4aS,7aR,12bS)-4a,9-dihydroxy-3-prop-2-enyl-2,4,5,6,7a,13-hexahydro-1H-4,12-methanobenzofuro[3,2-e]isoquinolin-7-one

❖ Physicochemical Properties

- It is white or almost white hygroscopic crystalline powder. Soluble in water, soluble in ethanol, and insoluble in toluene.

❖ Pharmaceutical Formulation

- It is formulated form of nasal spray and injection.

❖ Stability And Storage

- It should be stored in well-closed airtight containers and protected from light.

❖ Popular Brand Names

- Narcan
- Narcotan
- Evzio

10.4 NON-STEROIDAL ANTI-INFLAMMATORY AGENTS (NSAIDs)

❖ Inflammation

- Inflammation is defined as the local response of living mammalian tissues to injury due to any agent.
- It is a body defence reaction in order to eliminate or limit the spread of injurious agent as well as to remove the consequent necrosed cells and tissues.

❖ Causes of inflammation

- Physical agent – Heat, Cold, Radiation & Mechanical Trauma.
- Chemical agent – Organic and inorganic poisons.
- Infective agent – Bacteria, Viruses and their toxins.
- Immunological agent – Cell mediated, Antigen - antibody reactions.

➤ Signs of inflammation

- Rubor (Redness), Tumor (Swelling), Calor (Heat), Dolor (Pain).

❖ Types of inflammation

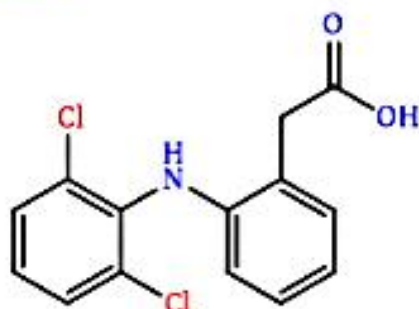
- Depending upon the defence capacity of the host and duration of response, inflammation can be classified as – Acute and Chronic Inflammation.

10.5.2 Classification of NSAIDs

CLASS	DRUGS
Non-selective COX inhibitor	Aspirin, Mefenamic acid, Diclofenac, Ibuprofen, Piroxicam, Tenoxicam, Ketorolac, Indomethacin, Phenyl butazone, Oxyphenbutazone.
Preferential COX-2 inhibitors	Nimesulide, Meloxicam, diclofenac, Aceclofenac.
Selective COX-2 inhibitors	Celecoxib, Etoricoxib, Parecoxib.
Analgesic and anti-pyretic	Paracetamol, Nefopam, Metamizol.

10.5.3 DICLOFENAC

- ❖ **Chemical Formula** $C_{14}H_{11}Cl_2NO_2$
- ❖ **Structure**



- ❖ **IUPAC Nomenclature**

- [2-(2,6-Dichloroanilino)phenyl]acetic acid

- ❖ **Physiochemical Properties**

- It is soluble in organic solvents such as ethanol, DMSO and dimethyl formamide.

- ❖ **Pharmaceutical Formulation**

- It is formulated form of tablet, gel, capsule, and injection.

- ❖ **Stability and storage**

- It is stored in a tightly closed container at room temperature away from light and moisture.

- ❖ **Popular Brand Names**

- Arthrotec
- Voltaren
- Voveran

- ❖ **Dose**

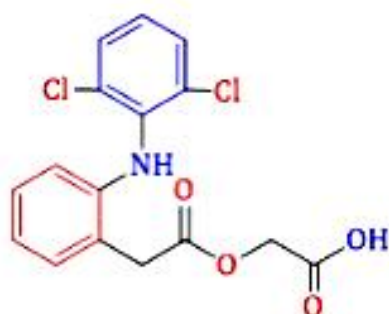
- Diclofenac sodium extended-release tablets 100 mg orally once a day.
- Diclofenac sodium enteric-coated and delayed-release tablets 25 mg orally 4 times a day.

- ❖ **Medicinal Uses**

- Diclofenac is a medicine that reduces swelling (inflammation) and pain.
- It's used to treat aches and pains, as well as problems with joints, muscles and bones

10.5.4 ACECLOFENAC

- It is a phenylacetic acid derivative of non-selective COX inhibitor class.
- It inhibits both COX-1 and COX-2.
- ❖ **Chemical Formula** - $C_{16}H_{13}Cl_2NO_4$
- ❖ **Structure**



❖ **IUPAC Nomenclature**

- 2-[2-[2-[(2,6-dichlorophenyl)amino]phenyl]acetyl]oxyacetic acid

❖ **Physiochemical Properties**

- It is a crystalline powder.
- It possesses poor aqueous solubility.

❖ **Pharmaceutical Formulation**

- It is formulated form of tablet, capsule, syrup and injection.

❖ **Stability and storage**

- Store it in an airtight container in a cool dry place. Protect from light.

❖ **Popular Brand Names**

- Aceclo. Dolokind

❖ **Dose**

- The usual dose of aceclofenac is 100 mg tablet twice daily.

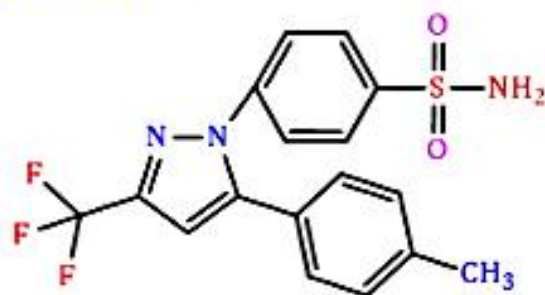
❖ **Medicinal Uses**

Aceclofenac film-coated tablets are indicated for the relief of pain and inflammation in osteoarthritis, rheumatoid arthritis and ankylosing spondylitis

10.5.5 CELECOXIB

❖ **Chemical Formula** - $C_{17}H_{14}F_3N_3O_2S$

❖ **Structure**



❖ **IUPAC Nomenclature**

• 4-[5-(4-Methylphenyl)-3-(trifluoromethyl)pyrazol-1-yl]benzenesulfonamide

❖ **Physiochemical Properties**

- It is off white to pale yellow powder.
- It is practically insoluble in water.
- It is soluble in organic solvents such as ethanol, DMSO and dimethyl formamide.

❖ **Pharmaceutical Formulation**

- It is formulated form of tablet and capsule.

❖ **Stability and storage**

- It is stored at room temperature (20°C to 25°C). It is kept away from light and moisture.

❖ **Popular Brand Names**

- Celact
- Celcox
- Colcibra

❖ **Dose**

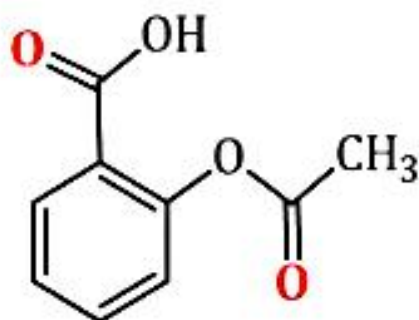
- The dosage of celecoxib is 100-200 mg which is given orally twice a day.

❖ **Medicinal Uses**

- Celecoxib is a nonsteroidal anti-inflammatory drug (NSAID) used to treat mild to moderate pain.
- It is also help to relieve symptoms of arthritis (eg, osteoarthritis, rheumatoid arthritis, or juvenile rheumatoid arthritis), such as inflammation, swelling, stiffness, and joint pain.

10.5.6 ASPIRIN

- ❖ **Chemical Formula** - $C_9H_8O_4$
- ❖ **Structure**



❖ IUPAC Nomenclature

- 2-acetoxybenzoic acid

❖ Physicochemical Properties

- It is odourless white crystals or crystalline powder with a slightly bitter taste.
- It is soluble in water.

❖ Pharmaceutical Formulation

- It is formulated form of tablet or effervescent tablet

❖ Stability and storage

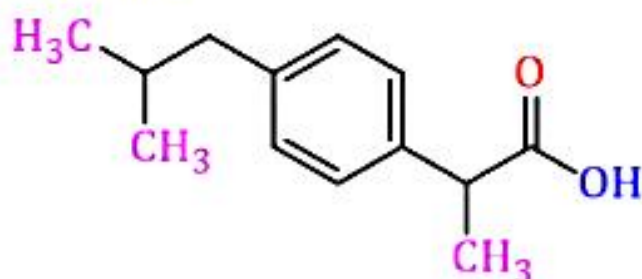
- Store it at room temperature and away from excess heat and moisture.
- Dispose of any tablets that have a strong vinegar smell.

❖ Popular Brand Names

- Ecosprin
- Aspirin
- Aspiwell

10.5.7 IBUPROFEN

- ❖ **Chemical Formula** $C_{13}H_{18}O_2$
- ❖ **Structure**



❖ **IUPAC Nomenclature**

- (RS)-2-(4-(2-Methylpropyl)phenyl)propanoic acid

❖ **Physiochemical Properties**

- It is colourless, crystalline solid with characteristic odour.
- It is insoluble in water and readily soluble in most of the organic solvents.

❖ **Pharmaceutical Formulation**

- It is formulated form of tablet, cream, gel, and oral suspension.

❖ **Stability and storage**

- It is stored in well closed, light resistant container at 15-30°C.

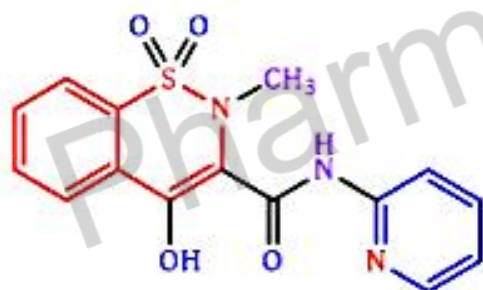
❖ **Popular Brand Names**

- Advil
- Genpril

10.5.8 PIROXICAM

- ❖ **Chemical Formula** $C_{15}H_{13}N_3O_4S$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 4-Hydroxy-2-methyl-N-(2-pyridinyl)-2H-1,2-benzothiazine-3-carboxamide 1,1-dioxide

❖ **Physiochemical Properties**

- It is a white or slightly yellow odourless powder.
- It is poorly soluble in water and is soluble in organic solvents such as DMSO and dimethyl formamide.

❖ **Pharmaceutical Formulation**

- It is formulated form of tablet, capsule and injection.

❖ **Stability and storage**

- It is stored in a closed container under dry place below 25°C.

❖ Popular Brand Names

- Dolonex
- Pirox
- Piricam

❖ Dose

- The dosage of piroxicam is 20 mg which is given orally once per day.

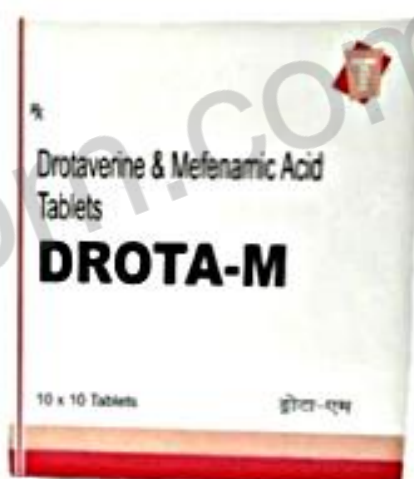
❖ Medicinal Uses

- Piroxicam is used to relieve pain, tenderness, swelling, and stiffness caused by osteoarthritis and rheumatoid arthritis.
- Piroxicam is in a class of medications called NSAIDs.

10.5.9 MEFENAMIC ACID

❖ Chemical Formula - $C_{15}H_{15}NO_2$

❖ Structure



❖ IUPAC Nomenclature

- 2-(2,3-dimethylphenyl)aminobenzoic acid

❖ Physiochemical Properties

- It is odourless, white to greyish white, crystalline powder.
- It has poor solubility in water. It is soluble in acetone, chloroform, dichloromethane, and methanol.

❖ Pharmaceutical Formulation

- It is formulated form of tablet, capsule and syrup.

❖ Stability and storage

- It darkens on prolonged exposure to light. It is stored closed container at room temperature (20 to 25°C).
- It is kept away from heat, light and in a moisture.

❖ Popular Brand Names

- Biospas
- Drota-M
- Lenagesic

❖ Dose

- Adult initial dose for pain 500 mg orally once daily

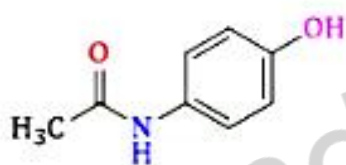
❖ Medicinal Uses

- Mefenamic acid is used to relieve mild to moderate pain, including menstrual pain (pain that happens before or during a menstrual period).
- It works by stopping the body's production of a substance that causes pain, fever, and inflammation.

10.5.10 PARACETAMOL

❖ Chemical Formula $C_8H_9NO_2$

❖ Structure



❖ IUPAC Nomenclature

- N-(4-hydroxyphenyl)acetamide

❖ Physicochemical Properties

- It is odourless, white crystalline solid with slightly bitter taste.
- It is slightly soluble in cold water but more soluble in hot water.

❖ Pharmaceutical Formulation

- It is formulated form of tablet, syrup, capsule, drops, oral solution and oral suspension, suppositories or injection.

❖ Stability and storage

- It is stored in a cool, dry place, away from direct sunlight.

❖ Popular Brand Names

- Metacin
- Crocin