

# MEDICINAL CHEMISTRY-II

## UNIT 4 NOTES

- **Drugs Acting on Endocrine System**
- **Sex Hormones**
- **Drugs for Erectile Dysfunction**
- **Oral Contraceptives**
- **Corticosteroids**
- **Thyroid & Antithyroid Drugs**



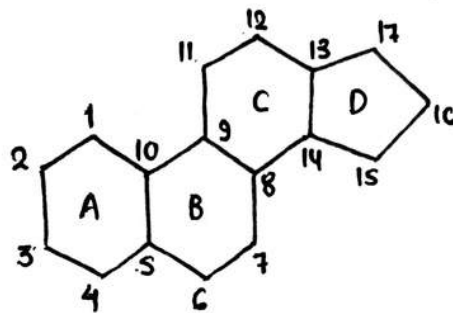
**NOTES AVAILABLE AT :**



[WWW.IMPERFECTPHARMACY.IN](http://WWW.IMPERFECTPHARMACY.IN)

# STERIODS

- Steroids are class of naturally occurring organic compounds produced naturally in body.
- They are characterized by a 4 ring structure.
- It consist of 3 six member cyclohexane ring and 1 five member cyclopentane ring.
- There are different types of steroids, each serving various functions in body.

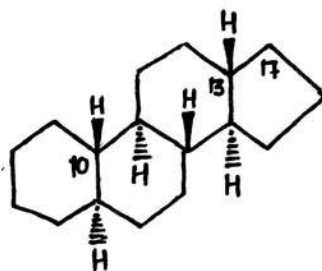


Basic Steroidal Rings

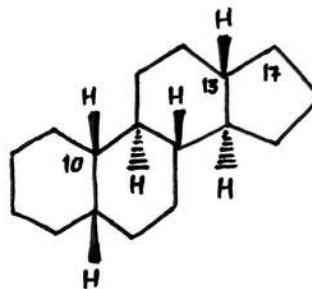
## NOMENCLATURE OF STEROIDS

### ① Gonane

It is the simplest parent tetracyclic hydrocarbon skeleton without methyl groups at C-10 or C-13 & no substitution at C-17



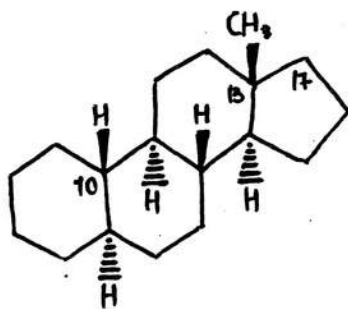
5 $\alpha$ -Gonane



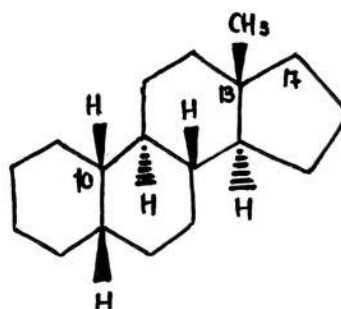
5 $\beta$ -Gonane

### ② Estrane

It is a 18 carbon steroid hormone with a methyl group at C-13.



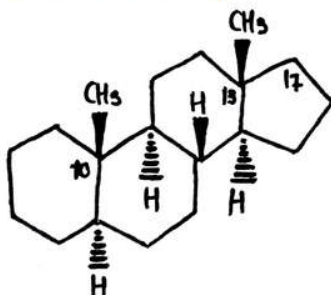
5 $\alpha$ -Estrane



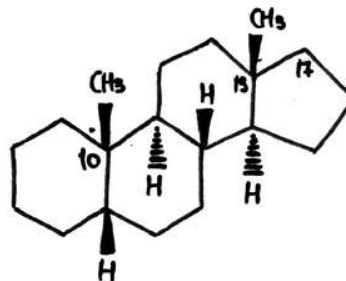
5 $\beta$ -Estrane

### ③ Androstane

Androstane is a 19- carbon steroid hormone with methyl groups at C-10 & C-13 positions.



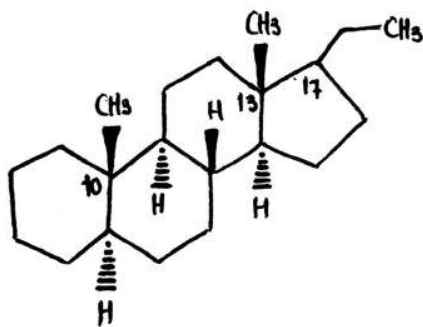
5α- Androstane



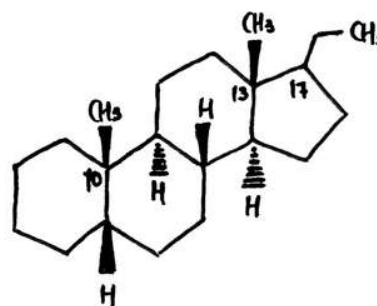
5β- Androstane

### ④ Pregnane

Pregnane is a 21- carbon steroid hormone with a side chain at C-17 and methyl groups at C-10 & C-13 positions.



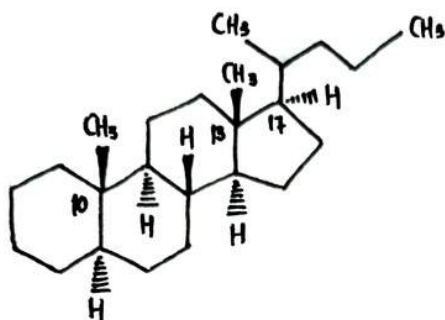
5α- Pregnane



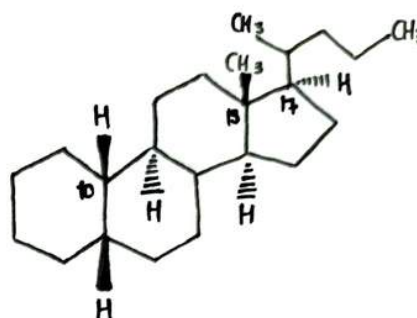
5β- Pregnane

### ⑤ Cholane

Cholane is a 24 carbon saturated steroid hydrocarbon with methyl groups at C-10 & C-13 positions and a side chain at C-17.



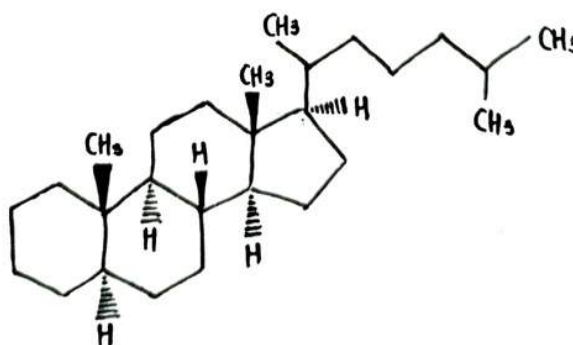
5α - Cholane



5β- Cholane

### ⑥ Cholestane

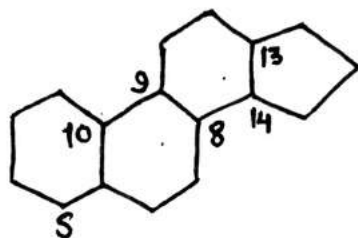
Cholestane is a saturated hydrocarbon derived from cholesterol consist of 27 carbon atom.



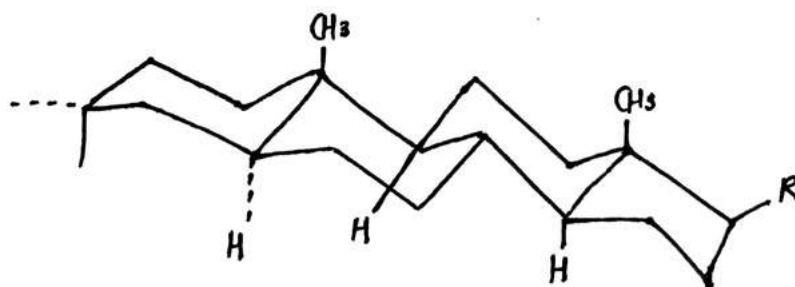
5α- Cholestane

## STEREOCHEMISTRY OF STEROIDS

- There are 6 asymmetric carbon atoms 5, 8, 9, 10, 13, 14 in steroid nucleus, therefore 64 optically active forms are possible.



- Cholestane, androstane & pregnane exist in two conformations.
  - (1) Chair form
  - (2) Boat form.
- Chair form is more stable than boat form due to less angle strain, therefore all cyclohexane rings in steroid nucleus exist in chair form.

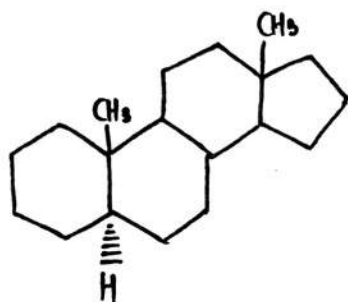


5 $\alpha$ -Cholestane

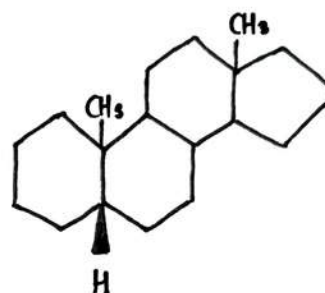


## Cis & Trans Form

Cis form indicates substituents on same side of ring while trans form has substituents on opposite side



(Cis Form)



(Trans Form)

## STEROID METABOLISM

- Steroid Metabolism refers to breakdown and transformation of steroids in body.
- All the steroids in human body are synthesized from cholesterol.
- Steroid metabolism occurs in various tissues including liver, kidneys, adrenal gland & catalyzed by enzymes such as Cytochrome P450, hydroxysteroid hydrogenases & sulfotransferases.
- It mainly involves following process :
  - Hydroxylation
  - Reduction
  - Oxidation
  - Methylation
  - Sulfation
  - Glucuronidation

# SEX HORMONES

- Sex Hormones are steroid hormones which are produced especially by ovaries, testes or adrenal cortex and affects the growth or function of reproductive organs or development of secondary sexual characteristics.
- Estrogen & Progesterone are female sex hormones.
- Androgens are male sex hormones.
- These hormones are synthesized from cholesterol mainly in gonads & adrenal cortex

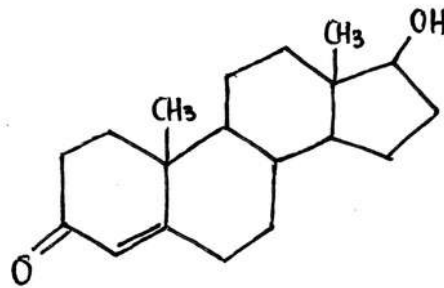
## SEX HORMONES IN OUR SYLLABUS

- Testosterone
- Nandrolone
- Progestones
- Oestrial
- Oestradiol
- Oestrone
- Diethylstilbestrol



## ① Testosterone

- Testosterone is a steroid hormone classified as Androgen, primarily produced in testes in males and in smaller amounts by the ovaries in females and the adrenal gland in both sexes.
- It is the primary male sex hormone plays a crucial role in various body functions, including development of male reproductive tissues, maintenance of secondary sexual characteristics (like facial hair, deeper voice, muscle mass & regulation of libido, bone density & red blood cell production).



### MOA

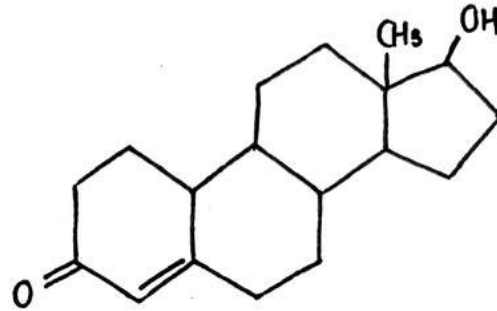
Testosterone binds to specific androgen receptors in target cells, forming testosterone-receptor complex that regulates gene expression leading to changes & promotion of protein synthesis that causes growth & development of masculine sex organs & secondary sexual characteristics.

### Uses

- Sexual Dysfunction
- Hypogonadism

## ② Nandralone

- Nandralone is also known as 19-nortestosterone.
- It is a synthetic anabolic-androgenic steroid derived from testosterone.



### MOA

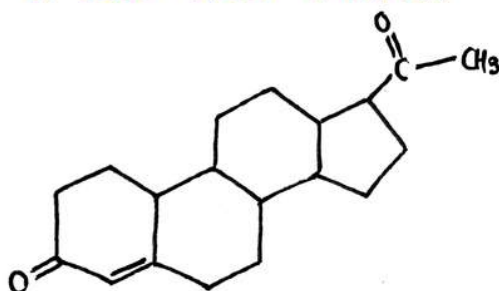
- Nandralone is an androgen receptor agonist.
- It binds to androgen receptors, activates gene transcription & protein synthesis, leading to muscle growth & other androgenic effects.

### Uses

- Treatment of Anaemia
- Postmenopausal Osteoporosis
- Testosterone Deficiency

### ③ Progesterones

- Progesterone is a natural steroid hormone involved in the regulation of various functions in the body, particularly related to the menstrual cycle, pregnancy and development of fetus.
- It is produced mainly by ovaries after ovulation & by placenta during pregnancy.
- It is a 21 carbon steroid hormone.



#### MOA

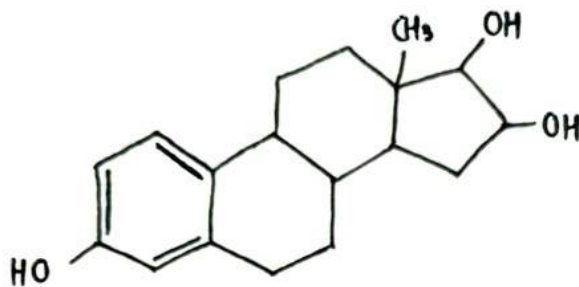
- Progesterone exerts its effects by binding to Progesterone Receptors.
- After binding it forms progesterone - receptor complex that regulates gene expression & perform various functions such as preparing the uterus for implantation, supports embryonic development & maintains pregnancy etc.

#### Uses

- Progesterone is used in combination with estrogens mainly in hormone therapy for menopausal symptoms & low sex hormone levels in women.
- It is also used in women to support pregnancy & fertility.

#### ④ OESTRIOL

- Oestriol is a form of estrogen, a female sex hormone.
- It is one of the three main estrogens, along with estradiol & estrone.
- It is a major estrogen involved in pregnancy & is produced naturally by placenta & fetus.



#### MOA

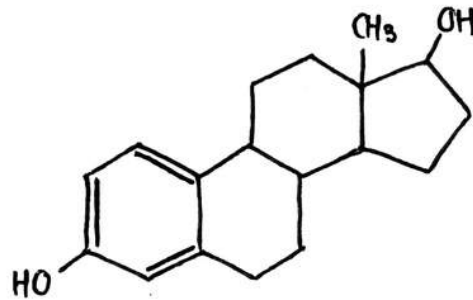
Oestriol is an estrogen receptor agonist, acting primarily on estrogen receptors (ER- $\alpha$ , ER- $\beta$ ) in estrogen responsive tissues such as uterus, vagina & breast.

#### Uses

- Vaginal Atrophy
- Urinary Tract Infections
- Hormone Replacement Therapy

## ⑤ OESTRADIOL

- Oestradiol is a form of Estrogen, produce naturally in human body by ovaries.
- It is the most potent & abundant form of estrogen in human body.



### MOA

Oestradiol acts by binding to Estrogen receptors, where it regulates transcription of estrogen-responsive genes.

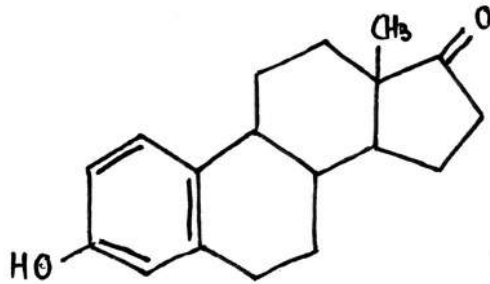
### Uses

- Hormone Replacement Therapy
- Contraception
- Osteoporosis



## ⑥ OESTRONE

Oestrone is a weak steroid hormone and a minor female sex hormone.



### MOA

Oestrone binds to nuclear estrogen receptors in estrogen responsive tissue, although it has lower affinity and potency than estradiol.

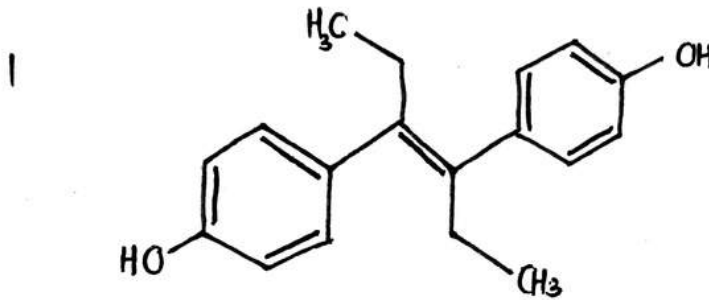
### Uses

- Hormonal Replacement Therapy.
- Premature Ovarian Failure.



## ⑦ DIETHYL STILBESTROL

- Diethylstilbestrol is a synthetic nonsteroidal estrogen that was widely used from 1940s to 1970s for various medical conditions.
- Currently it is not in so much use due to its potential side effects.



### MOA

DES binds to estrogen receptors in target cells, mimicking the action of endogenous estrogens.

### Uses

- Hormone Replacement Therapy
- Treatment of Prostate cancer
- Contraception.

# ERECTILE DYSFUNCTION

- Erectile Dysfunction, also termed as Impotence, is defined as failure to achieve or maintain a rigid penile erection suitable for satisfactory sexual intercourse.
- It is a common condition in men aged over 40 years, but it can affect men of all ages.

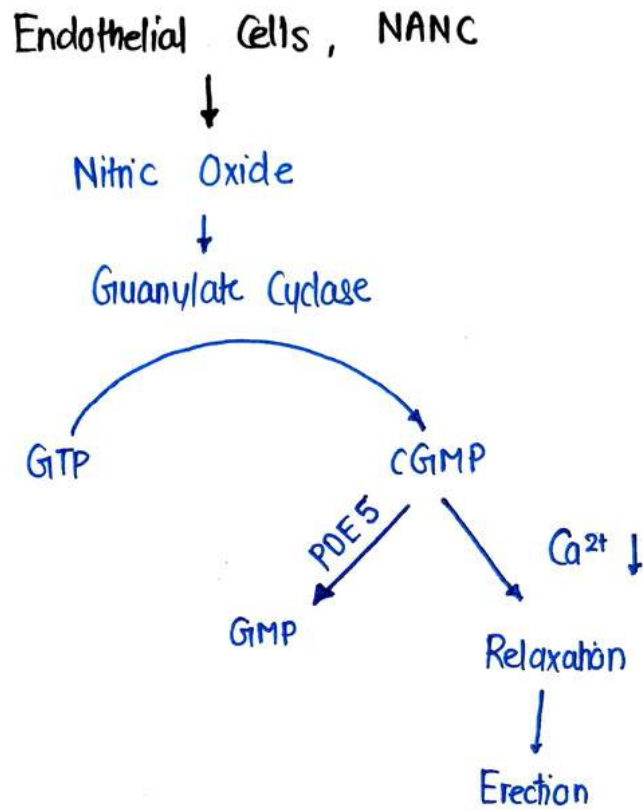
## Causes

- Stress
- Anxiety
- Depression
- Relationship Problems
- Low Self Esteem
- Unhealthy Lifestyle
- Performance Anxiety

## Drugs

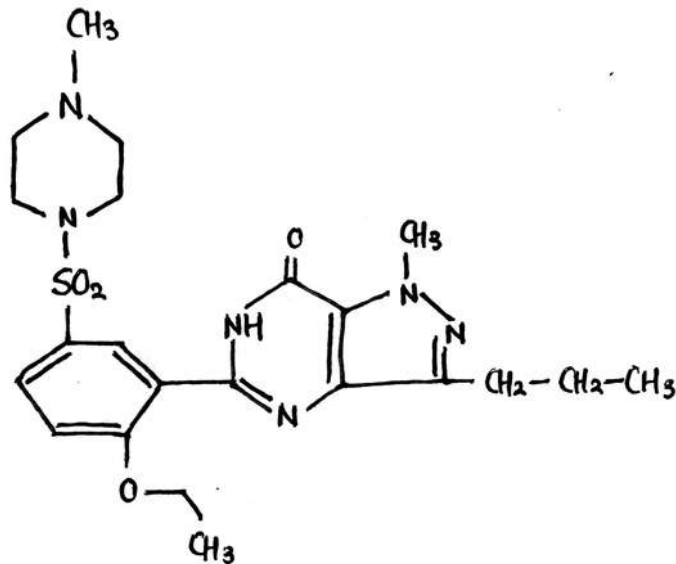
- Sildenafil
- Tadalafil

## Mechanism Of Penile Erection



## ① Sildenafil

Sildenafil is sold under brand name Viagra with vasodilating & anti-inflammatory properties



### MOA

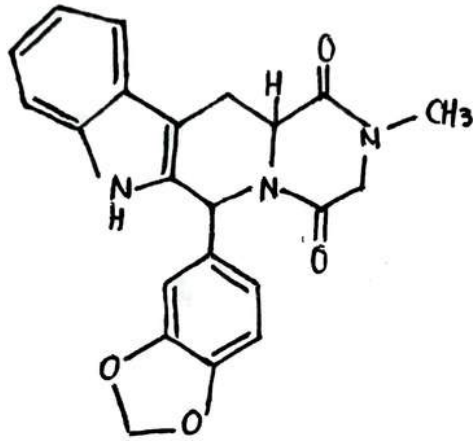
Sildenafil acts by blocking phosphodiesterase-5 enzyme that promotes breakdown of cyclic guanosine monophosphate (cGMP) which regulates blood flow in penis.

### Uses

Erectile Dysfunction

## ② Tadalafil

Tadalafil helps relax blood vessels, increasing blood flow to penis  
€ Sold under brand name cialis.



### MOA

Same as Sildenafil

### Uses

Erectile Dysfunction



# ORAL CONTRACEPTIVES

- An Oral Contraceptive, often referred as "the pill" is a medication taken by mouth to prevent pregnancy.
- They prevent pregnancy by inhibiting ovulation and also by preventing sperm from penetrating through the cervix.

## Types Of Oral Contraceptive

They are of mainly two types:

- ① Combined Oral Contraceptive
- ② Progestin - Only Pills

### ① COMBINED ORAL CONTRACEPTIVE

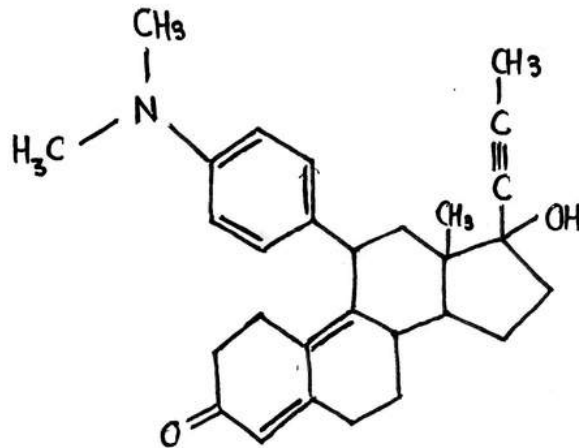
- It consists a combination of Estrogen & Progestin
- They work by :
  - Preventing Ovulation
  - Thickening cervical mucus to block sperm from reaching egg.
  - Thinning the uterine lining to reduce the likelihood of implantation.

### ② PROGESTIN ONLY PILLS (MINI PILLS)

- They are often used by individuals who cannot take estrogen.
- They primarily work by thickening cervical mucus & sometimes inhibit ovulation.

## ① MIFEPRISTONE

Mifepristone is a synthetic steroid hormone with both antiprogesterogenic & antigluco-corticoid properties.



### MOA

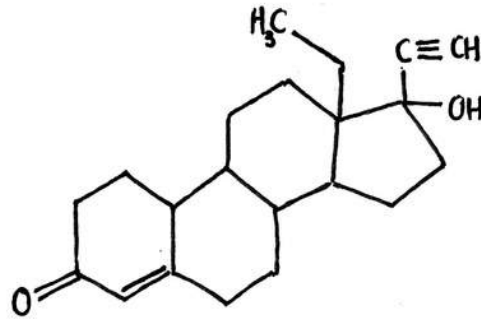
- Mifepristone is an antiprogesterin that blocks the action of progesterone, a hormone necessary to maintain a pregnancy.
- By blocking the action of progesterone, mifepristone alters the endometrium, induces bleeding & causes uterine lining to shed.

### Uses

Mifepristone is used in combination with misoprostol to end an early pregnancy.

## ② NORGESTREL

- Norgestrel is a synthetic progestin, a derivative of progesterone primarily used in hormonal contraception.
- It is composed of racemic mixture of two stereoisomers, dextro-norgestrel & levo-norgestrel.



### MOA

- It binds to progesterone receptors & suppresses ovulation by inhibiting gonadotrophin release (primarily Luteinizing Hormone)
- Thickens cervical mucus, making it difficult for sperm to penetrate.

### Uses

- Birth control pill
- Endometrial Cancer

### ③ LEVONORGESTREL

Levonorgestrel is a synthetic progestogen widely used in hormonal contraception & emergency contraception.

#### MOA

Same as Norgestrel

#### Uses

- Contraception
- Emergency Contraception

# CORTICOSTEROIDS

- Corticosteroids are class of steroid hormones that are produced naturally in the Adrenal Cortex, the outer part of adrenal gland
- The release of these hormones is controlled by pituitary adrenocorticotrophic hormone which is further regulated by
- hypothalamic corticotrophin releasing hormone.
- As drug they lowers inflammation in body also reduce the activity of immune system.

## CLASSIFICATION OF CORTICOSTEROIDS

The major corticosteroids produced by adrenal cortex are as follows:

- ① Mineralocorticoids
- ② Glucocorticoids

### ① Mineralocorticoids

- They regulate water & electrolyte balance by affecting ion transport in renal tubules
- Aldosterone is the major mineralocorticoids.

### ② Glucocorticoids

- It involved in metabolism & have immunosuppressive, anti-inflammatory & vasoconstrictive effects.
- Cortisol is the major Glucocorticoid hormone.

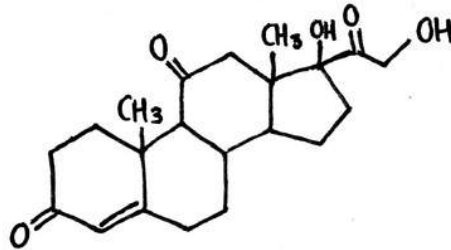


## DRUGS IN OUR SYLLABUS

- Cortisone
- Hydrocortisone
- Prednisolone
- Betamethasone
- Dexamethasone

### ① CORTISONE

- Cortisol is a pregnane (21-C) steroid hormone.
- It is naturally occurring corticosteroid used as a prodrug.



### MOA

- Cortisone is an inactive prodrug, which is first converted to its active form Hydrocortisone in liver by enzyme 11 $\beta$ -hydroxysteroid dehydrogenase type 1 (11 $\beta$ -HSD1).
- Once activated it binds to glucocorticoid receptors to show its anti-inflammatory effect.

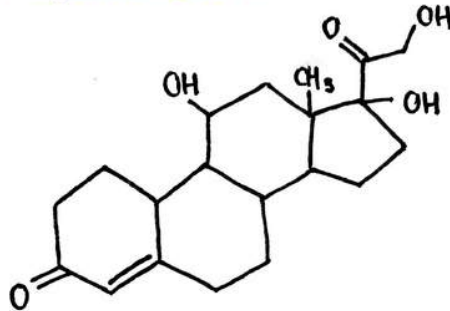
### Uses

- Inflammation
- Short-term pain relief



## ② HYDROCORTISONE

- Hydrocortisone is naturally occurring glucocorticoid steroid hormone produced naturally by adrenal glands.
- As a drug, it is a synthetic or semisynthetic analogue of natural hydrocortisone.



### MOA

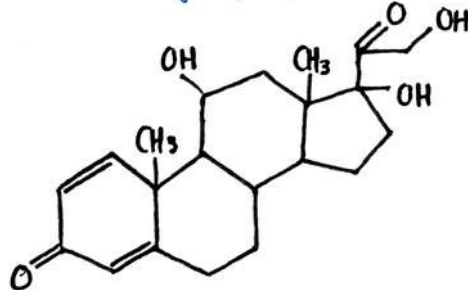
Hydrocortisone binds to glucocorticoid receptors located in cytoplasm of target cells & shows its anti-inflammatory and immunosuppressive effects.

### Uses

- Inflammation
- Allergic Conditions
- Ulcerative Colitis

### ③ PREDNISOLONE

Prednisolone is a synthetic glucocorticoid with anti-inflammatory & immunomodulating properties.



#### MOR

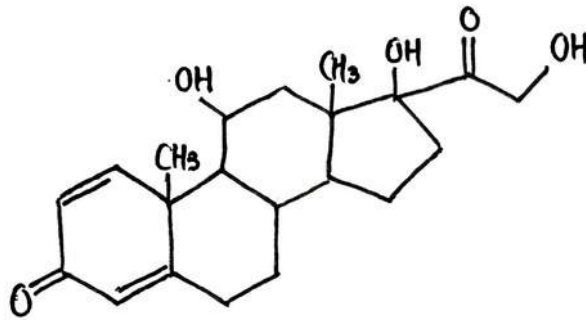
Prednisolone binds to glucocorticoid receptors located in the cytoplasm of target cells & shows its anti-inflammatory and immunosuppressive effects.

#### Uses

- Severe Allergies
- Autoimmune Disorders
- Asthma

#### ④ BETAMETHASONE

Betamethasone is a potent synthetic glucocorticoid steroid widely used for its anti-inflammatory, immunosuppressive and antiallergic properties.



#### MOA

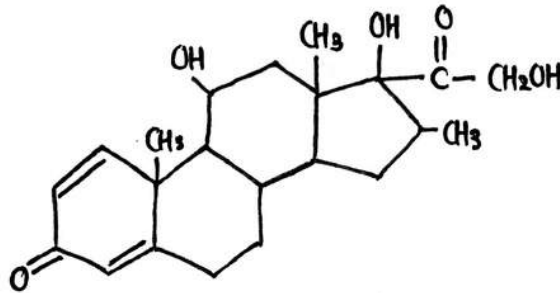
Betamethasone binds to glucocorticoid receptors & shows its anti-inflammatory & immunosuppressive effects.

#### Uses

- Skin Irritation
- Inflammation

## ⑤ DEXAMETHASONE

Dexamethasone is a potent synthetic glucocorticoid widely used for its anti-inflammatory, immunosuppressive and antiallergic effects.



### MOA

It works through binding to glucocorticoid receptors in cytoplasm of target cells & shows its anti-inflammatory & immunosuppressive effect.

### Uses

- inflammation
- Autoimmune Disease
- Allergic Reactions.

# THYROID HORMONES

- Thyroid hormones are essential chemical messenger produced by thyroid gland, a small butterfly-shaped gland located in front of the neck.
- Thyroid Gland is the source of two fundamentally different type of hormones.
  - ① Thyroxine ( $T_4$ )
  - ② Triiodothyronine ( $T_3$ )
- Both hormones are vital for normal growth & development and control essential functions, such as energy metabolism and protein synthesis.
- Thyroid Gland is divided into lobules which consist of mainly two types of cells
  - (1) Follicular cells
  - (2) Parafollicular cells

## SYNTHESIS OF THYROID HORMONES

Thyroid Hormone synthesis is a complex process involving multiple steps that occur primarily in thyroid gland.

- Iodide Uptake
- Oxidation of Iodide
- Thyroglobulin Synthesis
- Iodination of Tyrosine
- Coupling Reaction
- Release of  $T_3$ ,  $T_4$

### THYROID DRUGS

- L- Thyroxine
- L- Thyronine

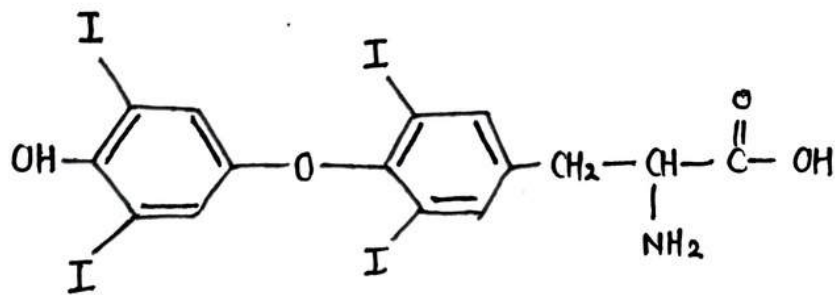
### ANTITHYROID DRUGS

- Propylthiouracil
- Methimazol



## ① L- THYROXINE

- L- Thyroxine (also known as Levothyroxine) is a synthetic form of thyroid hormone Thyroxine ( $T_4$ ), which is normally produced by Thyroid Gland.
- It is a treatment of choice for hypothyroidism.



### MOA

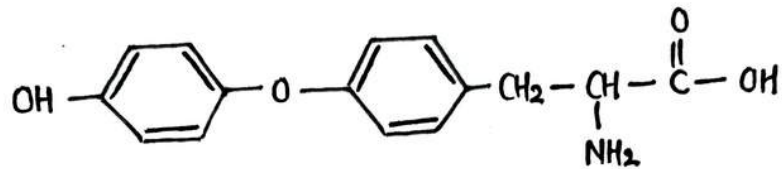
L- Thyroxine is a synthetic  $T_4$ , first it is converted to its active form Triiodothyronine ( $T_3$ ) in peripheral tissues, binds to nuclear thyroid receptors, where it regulate gene expressions to perform various physiological functions.

### Uses

- Hypothyroidism
- Thyroid Hormone Replacement Therapy.

## ② L- THYRONINE

L- Thyronine is a synthetic Triiodothyronine that plays a crucial role in various physiological process.



### MOA

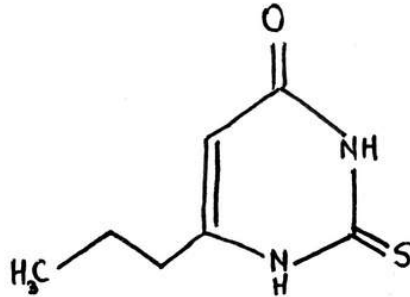
L- thyronine is a synthetic T<sub>3</sub>, that binds to thyroid hormone receptors in nucleus of the cells & regulates various physiological process.

### Uses

Severe Hypothyroidism

### ③ PROPYLTHIOURACIL

Propylthiouracil is an antithyroid drug primarily used in treatment of hyperthyroidism, including conditions like Hyperthyroid Graves' Disease.



#### MOA

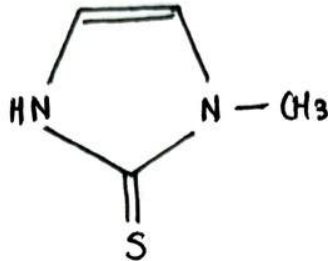
It inhibits Thyroid Peroxidase enzyme, preventing iodination of Tyrosine residues, synthesis of Thyroid hormones and also inhibits T<sub>4</sub> to T<sub>3</sub> conversion.

#### Uses

- Hyperthyroidism
- Graves' Disease

#### ④ METHIMAZOLE

Methimazole is an antithyroid medication primarily used to treat hyperthyroidism.



#### MOA

Same as Propylthiouracil

#### Uses

- Hyperthyroidism
- Graves' Disease
- Toxic Multinodular Goitre.

# THANK YOU

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