

«Corticosteroids»



Sub- Medicinal Chemistry II (BP501T)
Third Year B.Pharmacy
Unit IV



BY

Prof.Bhavesh.B. Amrute

(M.Pharmacy, Pharmaceutical Chemistry)

Corticosteroids

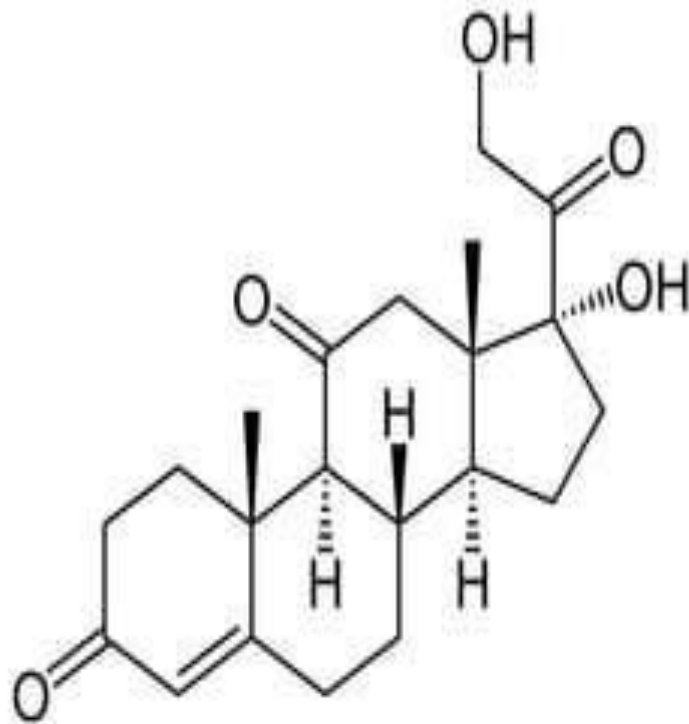
- Corticosteroids are the class of steroid hormones (C21). These are produced in the adrenal cortex. These are the class of drugs that lower the inflammation in the body. They also reduce the activity of immune system.

- **Classification of Corticosteroids.**

Corticosteroids			
Glucocorticoids		Mineralocorticoids	
Natural	Synthetic	Natural	Synthetic
Cortisone Hydrocortisone	Prednisone, Prednisolone, Triamcinolone, Betamethasone, Dexamethasone	Aldosterone, Deoxycorticosterone	Fludrocortisone

Cortisone

Cortisone is corticosteroid hormone (glucocorticoid) of pregnane type. It is released by the adrenal gland.



IUPAC Name is (8S,9S,10R,13S,14S,17R)-17-hydroxy-17-(2-hydroxyacetyl)-10,13-dimethyl-1,2,6,7,8,9,12,14,15,16-decahydro-cyclopenta[a]phenanthrene-3,11-dione

Mechanism of action

Cortisone acetate binds to the cytosolic glucocorticoid receptor. After binding the receptor the newly formed receptor-ligand complex translocates itself into the cell nucleus, where it binds to many glucocorticoid response elements (GRE) in the promoter region of the target genes.

Metabolism

Corticosteroids are metabolized through enzymatic transformations that diminish their physiologic activity and increase water solubility to enhance their urinary excretion. The majority of serum cortisol is reduced to dihydrocortisol and then to tetrahydrocortisol, which is then conjugated to glucuronic acid.

Adverse effect: Fluid retention, causing swelling in lower legs. Problems with mood swings, memory and behavior and other psychological effects, such as confusion or delirium.

Uses: Cortisone is used as an anti-inflammatory medication.

Hydrocortisone

Hydrocortisone is a class of corticosteroids. It is used topically to treat redness, swelling, itching, and discomfort of various skin conditions. Chemically, it is 11 β ,17 α ,21-Trihydroxypregn-4-ene-3,20-dione.

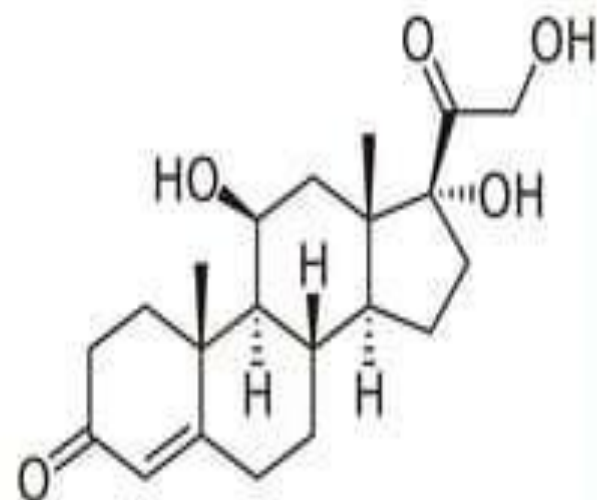
Mechanism of action

Hydrocortisone binds to the glucocorticoid receptor leading to downstream effects such as inhibition of phospholipase A2, NF-kappa-B, other inflammatory transcription factors, and the promotion of anti-inflammatory genes.

Metabolism: It is metabolized in the liver to inactive glucuronide and sulfate metabolites.

Adverse effect: Nausea, heartburn, headache, dizziness, menstrual period changes, trouble sleeping, increased sweating, or acne may occur.

Uses: Hydrocortisone topical is used to treat redness, swelling, itching, and discomfort of various skin



Prednisolone

Prednisolone is a glucocorticoid. Chemically, it is 11,17-Dihydroxy-17-(2-hydroxyacetyl)-10,13-dimethyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydrocyclopenta[a] phenanthren-3-one

Mechanism of action

It decreases the inflammation via suppression of the migration of polymorphonuclear leukocytes and reversing increased capillary permeability.

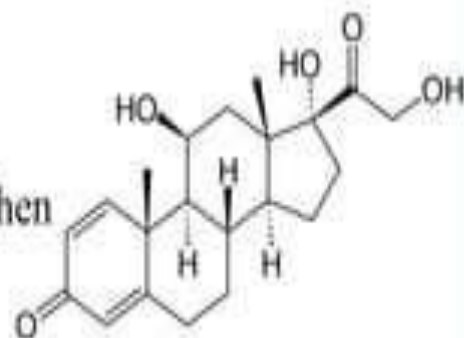
Metabolism

It is metabolized in liver to active metabolite prednisolone, which is then metabolized to inactive glucuronide and sulfate metabolites.

Adverse effect: Nausea, heartburn, headache, dizziness, menstrual period changes, trouble sleeping, increased sweating, or acne may occur.

Uses

□ Prednisolone is used to treat allergies, blood disorders, skin diseases, infections, certain cancers.

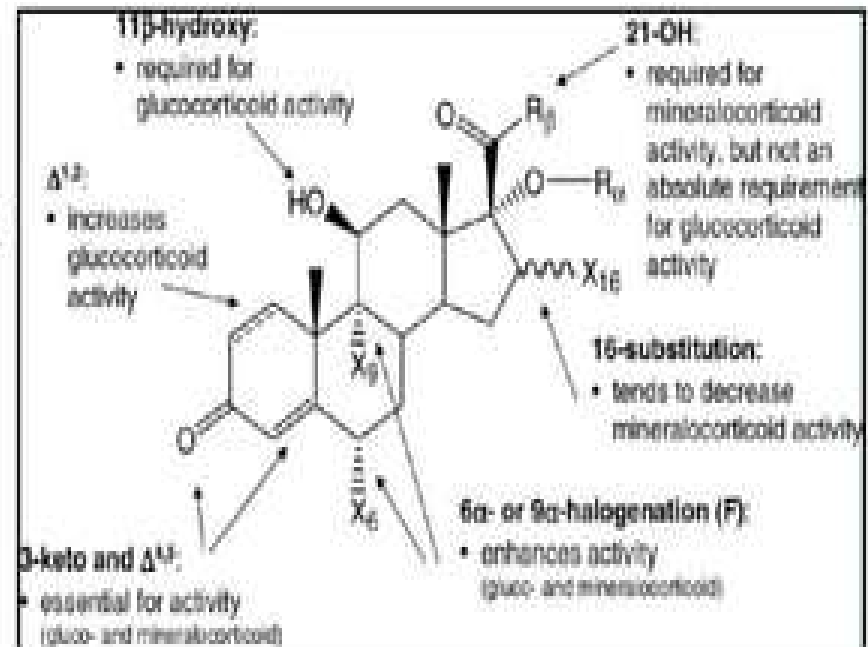


Betamethasone

Betamethasone is in a class of corticosteroids. It is a steroid medication. It is used for a number of diseases such as rheumatoid arthritis, systemic lupus erythematosus and skin diseases like dermatitis

Structure-activity relationship (SAR) Study

- Presence of keto (C=O) group and double bond between C4 and C5 is essential for both gluco and mineralocorticoid activities
- Presence of double bond between C1 and C2 is essential for glucocorticoid activity.
- Presence of 11 β -hydroxy is essential for glucocorticoid activity.



Mechanism of action

Betamethasone binds to specific intracellular glucocorticoid receptors and subsequently binds to DNA to modify gene expression. The synthesis of certain anti-inflammatory proteins is induced while the synthesis of certain inflammatory mediators is inhibited.

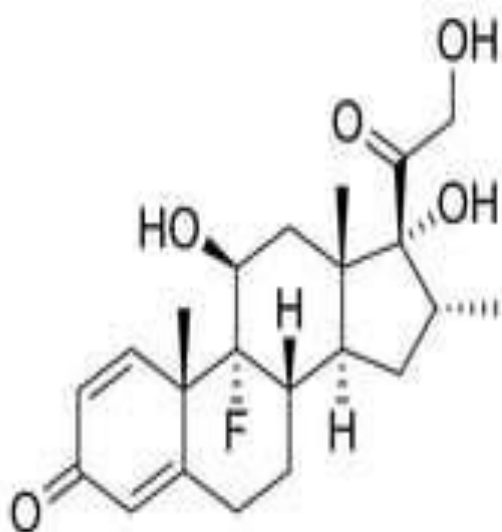
Metabolism: It is metabolized in the liver to inactive glucuronide and sulfate metabolites.

Adverse effect: Common side effects of betamethasone include abdominal bloating, abdominal fat deposits, abnormal hair growth.

Uses: Betamethasone is used topically to treat itching, redness, dryness, crusting, scaling, inflammation, and discomfort of various skin conditions, including psoriasis and eczema

Dexamethasone

Dexamethasone is a type of corticosteroid medication. It is used in the treatment of rheumatic problems, skin diseases, allergies, asthma, chronic obstructive lung disease etc.



IUPAC Name is

(1R,2R,3aS,3bS,9aS,9bR,10S,11aS)-9b-fluoro-1,10-dihydroxy-1-(2-hydroxyacetyl)-2,9a,11a-trimethyl-1H,2H,3H,3aH,3bH,4H,5H,7H,9aH,9bH,10H,11H,11aH-cyclopenta[a]phenanthren-7-one

Mechanism of action

It inhibits phospholipase A2, which decreases the formation of arachidonic acid derivatives.

- It inhibits NF-Kappa B and other inflammatory transcription factors.
- It promotes anti-inflammatory genes like interleukin-10.

Metabolism

- Dexamethasone is 6-hydroxylated by CYP3A4 to 6 α - and 6 β -hydroxydexamethasone.
- Dexamethasone is reversibly metabolized to 11-dehydrodexamethasone by corticosteroid 11-beta-dehydrogenase isozyme-2 and can also be converted back to dexamethasone by Corticosteroid 11-beta-dehydrogenase isozyme 1.

Adverse effect: The following side effects are common for patients taking dexamethasone.

- Increased appetite.
- Irritability.
- Difficulty sleeping (insomnia)
- Swelling in your ankles and feet (fluid retention)
- Heartburn.

Uses: It relieves inflammation (swelling, heat, redness, and pain) and is used to treat certain forms of arthritis.



THANK YOU