STEROIDS

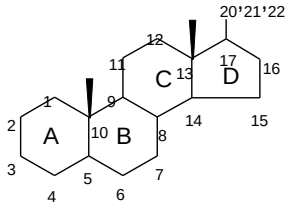
Steroid hormones and related products represent one of the most widely used classes therapeutic agents .

These drug are used primarily in birth controle, hormone replacement therapy(HRT), inflammatory conditions and cancer treatment.

Most of these agents are chemically based on a common structural backbone, the steroid backbone.

Steroid nomenclature, numbering and stereochemistry:-

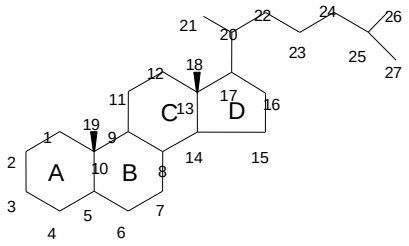
General structure of steroids:-



Cyclopentanephenanthrene nucleus

All steroids are named as derivative of cholestane, androstane, pregnane or esterane. The standard system of numbering is with 5-α-cholestane.

The absolute stereochemistry of the molecule and any substituents is shown with solid line (β) and dashed line(α).

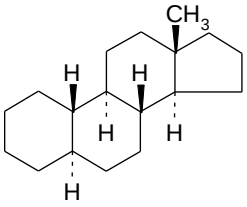


5- α -cholestane

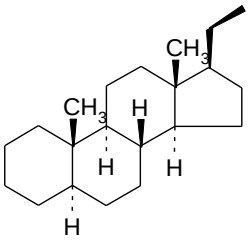
The stereochemistry of the H at C_5 is always indicated in the name. The stereochemistry of the other H atoms is not indicated unless it differs from 5-α-cholestane. Changing the stereochemistry of any of the ring juncture or backbone carbon changes the shape of the steroids.

The terms cis and trans are used in the steroid nomenclature to indicate the backbone stereochemistry between rings.

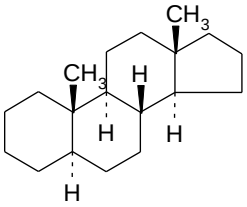
Ex- 5-α-steroids are A/B trans and 5-β-steroids are A/B cis.



5-α-Estrane

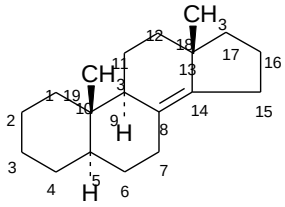


5-α-Pregnane

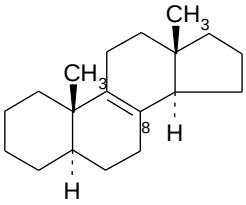


5-α-androstane

Nomenclature and double bonds:-

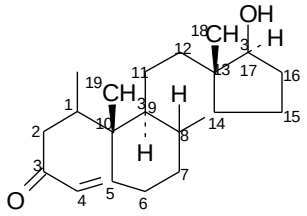


5-α-androst-8(14)-ene



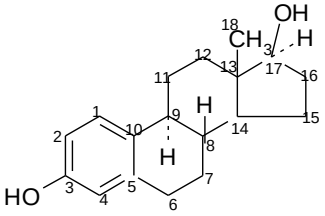
5α-androst-8-ene

Double bonds from C_8 may go towards C_9 or C_{14} and those from C_{20} may go towards C_{21} or C_{22}. In such cases, both carbons are indicated in the name if the double bond is not between sequentially numbered carbons.



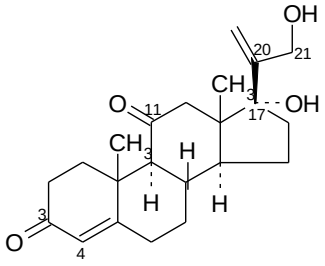
Testosterone

(17β-Hydroxyandrost-4-ene-3-one)



Estradiol (Oestradiol)

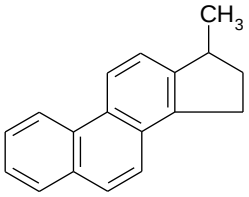
(Estra- 1,3,5(10)- triene-3,17β- diol)



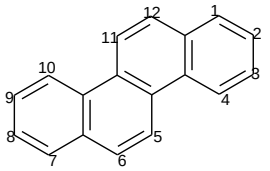
Cortisone

(17,21- Dihydroxypregn-4-ene-3,11,20-trione)

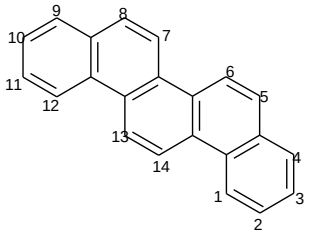
Note:- All the steroids on dehydrogenation with selenium at 360ċ usually give Diel'S hydrocarbon, whereas at 420ċ, the steroids give mainly chrysene and a small amount of picene.



Diel'S hydrocarbon



Chrysene



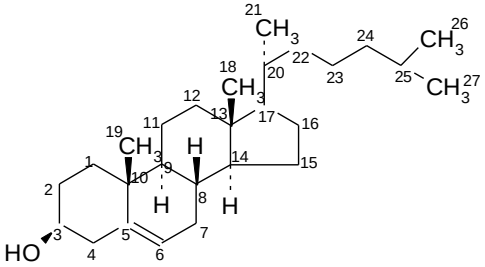
Picene

Classification:- Steroids are divided in to five categories on the type of substituent group at C-17 i.e. group R.

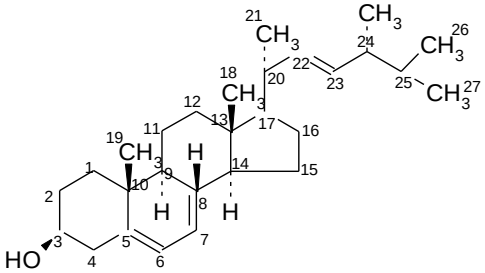
1)- Sterols:- Where R is an aliphatic side chain. They contain usually one or more hydroxyl groups attached in alicyclic linkage.

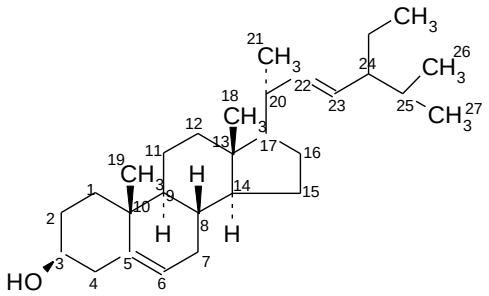
- The sterols may be further subdivided into following three category-

a) Zoosterols:- Such sterols those are obtained from the animal kingdom only. Ex- Cholesterol



b) Phytosterols:- Such sterols those are obtained from plant sources. Ex- Ergosterol





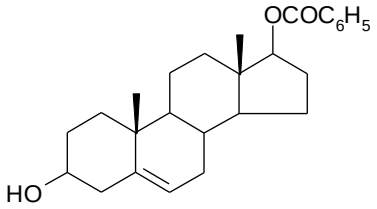
Stigmasterol

c) Mycosterols:- Such sterols those are obtained from fungi.

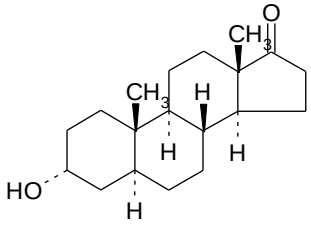
2) Sex hormones:- Where R contains a ketonic or hydroxyl group and mostly posses a two carbon side chain.

Sex hormones are subdivided into following three category-

a) Androgens(Male hormones)
Ex- Testosterone

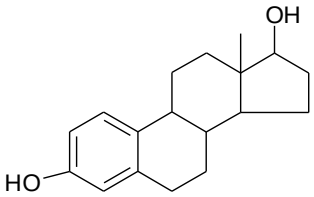


Androsterone

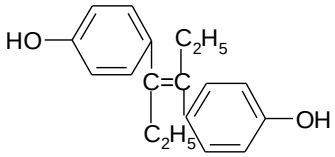


(3α-Hydroxy-5α-androst-17-one)

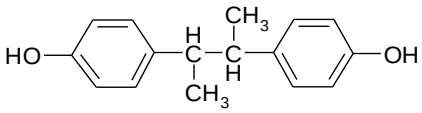
b) Oestrogens (Female or Follicular hormone):- The oestrogens are mainly concerned with the growth and function of sex organs. They are classified into two category-
   I. Steroidal oestrogens:- They are contains steroidal nucleus and attribute oestrogenic activity. Ex- Oestradiol



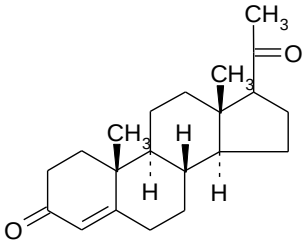
II. Non- steroidal estrogens:- They contains oestrogenic activity but not having steroidal nucleus and have been prepared synthetically. Ex- Diethylstilbesterol



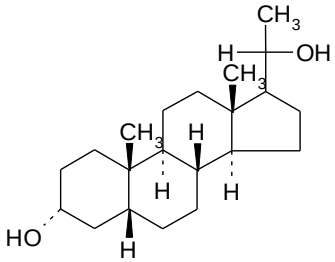
Hexsterol



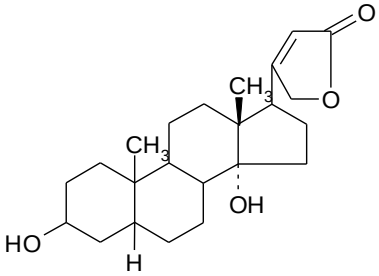
c) Gestrogens (Corpus luteum hormones):- Gestrogens are mostly secreted by the corpus luteum portion of the ovary and the metabolized to various inactive products. Ex- Progesterone



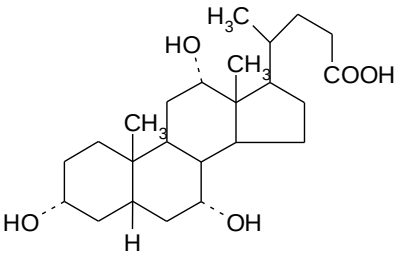
Pregnanediol



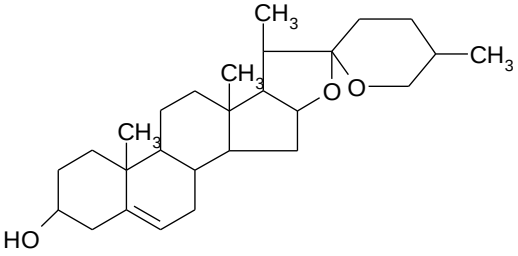
3) Cardiac glycosides:- When R is lactone ring. Ex- Digitoxigenin



4) Bile salts:- Where R is essentially a five carbon side chain ending with a carboxylic acid moiety. Ex- Cholic acid



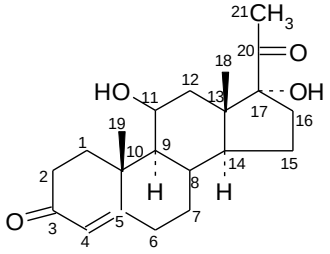
5) Sapogenins:- When R contains an oxacyclic ring system. Ex- Diosgenin



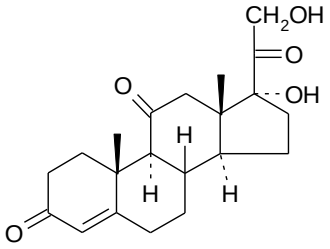
Cortecosteroids OR Adrenocortecoids:-

The adrenocortecoids hormones (ACTH,Corticotrophic) produced by anterior pituitary, stimulates the human adrenal cortex to secrete hydrocortisone, corticosterone, aldosterone and a number of weak androgenic substances. ACTH is a polypeptide.

- Few examples of adrenocorticoids-

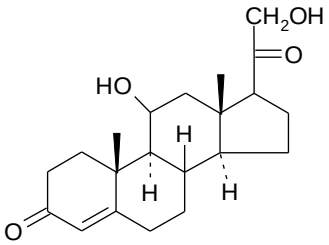


Hydrocortisone

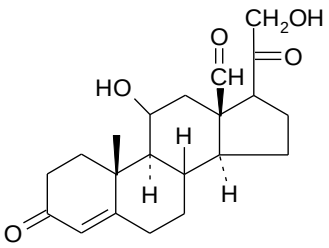


Cortisone

- All the adrenocorticoids are pregnane(21 carbon atom) derivatives. They also contains 4-ene-3-one functional group and 20-keto 21-ol group. They differs from each other by the presence or absence of a 17-α-hydroxyl group and by the presence or absence of an oxygwn at C-11 (11β-hydroxy or 11-oxo group). In aldosterone a –CHO group replaces the 18- methyl group.



Corticosterone



Aldosterone

Ex-

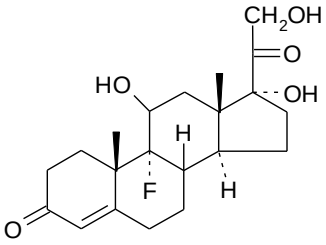
- The major conticosteroids are produced by the adrenal cortex are hydrocortisone, corticosterone, aldosterone.

- Corticosteroids may be divided in to two main classes-

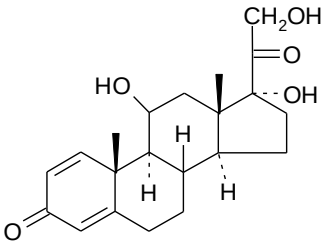
    a) Gluco-corticoid:- The main action of gluco-corticoids are upon gluconeogenesis, glycogen deposition and protein lipid and calcium metabolism together with inhibition of corticotrophic secretion, anti-inflammatory activity, tissue repair. Ex- Hydrocortisone, Cortisone.
    b) Mineralo corticoids:- The main action of mineralocorticoids are upon electrolyte and water balance. Ex- Aldosterone.

Modified Adrenocorticoids:-

- Most of the active compounds have 9α-fluoro group. Ex- Fludrocortisone

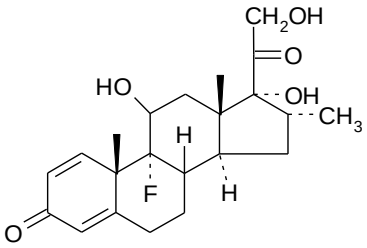


- 9α-Fluoro analogue had increased anti-inflammatory (10 times) and sodium retaining (125 times) potency than the hydrocortisone.
- After Fludrocortisone became available the 1,2-dehydro derivatives Prednisolone, which had the anrti-inflammatory activity increased 4- times and the sodium retaining potency reduced (0.8) as of the parent natural hormones.

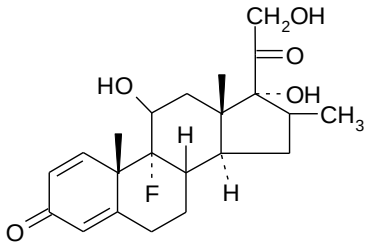


Prednisolone

- A large number of clinically useful modified corticosteroid has come from among the 16α-methyl analogues. This change eliminates the sodium retaining effect and anti-inflammatory activity is enhanced.
- Dexamethasone has anti-inflammatory activity is 25-times as that of hydrocortisone.
- After introduction of dexamethasone, 16β-isomer betamethasone became. But for changed configuration at position 16, it is structurally similar to dexamethasone, even biologically activity and potency are similar.



Dexamethasone



Betamethasone

- Paramethasone has no sodium retention potency but anti-inflammatory potency 10 times than that of hydrocortisone. It has 16α-methyl and 6-α-fluoro group but no fluoro substitution at position-9.