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Pharmaceutical Sciences **Review Article……!!!**

STEROIDS : CLASSIFICATION, NOMENCULTURE AND STEREOCHEMISTRY

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ABSTRACT

In this review we focus on steroidal compounds classification, nomenculture and stereochemistry. Steroids are widely distributed in living organisms and play very important role in their body in form of hormones, fatty compounds, building blocks of cells. They also take part in body metabolism process. Adrenocorticoids maintain electrolyte, water, glucose and fat metabolism, when sex hormones like testosterone, progesterone, estrogen develops sexual characteristic into man and women and very important to develop the body as a man or women. Estrogen and progesterone also regulate menstruation cycle in women. Cardiac glycosides are also steroidal compounds which can greatly increase the heart beat, so they are use in congestive heart failure. In bile too many compounds are steroids which are related to digestion process. Based on their function and their chemical structure we classified it into five major groups. They are chemically cyclopentaphenanthrene derivates. When any functional group added into moiety or any carbon replace with hetero atoms then they function is change and also change its IUPAC name based on their group and position at they attach. In this review we mention some common rules of nomenclature of steroids and their derivatives.

INTRODUCTION:

Steroids is a very useful and essential compounds for living organisms. They found in both plants as well as animal kingdom. The general steroids have been found to contain partially or completely hydrogenated 17-H cyclopentaphenanthrene nucleus. They are very much potent and give their pharmacological action at very low concentration. In steroids methyl group generally present at C-10 and C-13 and alkyl side chain present at C-17. When hydroxyl group at C-3 they called sterols which activity is slightly differ from steroids. This compounds (steroids and sterols) are related with number of activity in body and also use as medicinal purpose like cardiac glycoside, birth control pills, in hormone replacement therapy, anti-inflammatory action in cancer like disease and also treatment of cancer.

CLASSIFICATION OF STEROIDS

Steroids can classified into five major classes.

a) Sapogenin

Sapogenin is natural gycosidic compound which is non-saccharide or aglycone part. In this kind of compound oxacyclic ring present in steroidal moiety. Sapogenins are directly affect the immune system and protect our body from different cancers. Also their decrease lipid level in blood and also decrease glucose response. Eg. Digitonin, diosgenin, asperin, methy asperin.

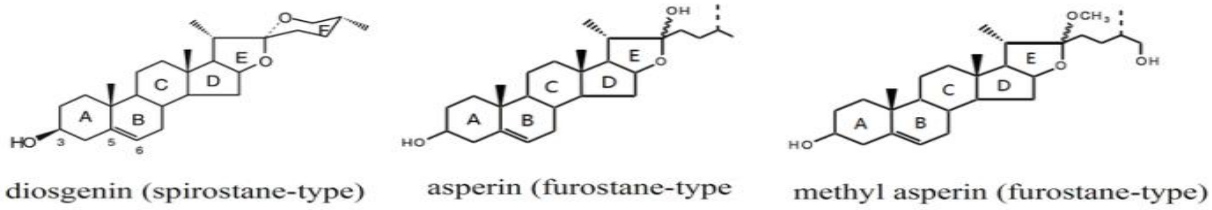


Figure 1. Steroidal sapogenins.

b) Bile salt

Bile is secreated from liver which contain many steroidal compounds. Steroids of bile have 5 members side chain which ends with carbocxylic acid group at C-17 position. Eg. Cholic acid, deoxycholic acid.

Figure 2. Steroidal bile salt.

c) Cardiac Glycoside

Cardiac Glycosides are compound which obtain from nature and increase the force of contraction in heart. They contain lacton moiety with sugar at C-17 position. Eg. Digitoxin, digoxine.

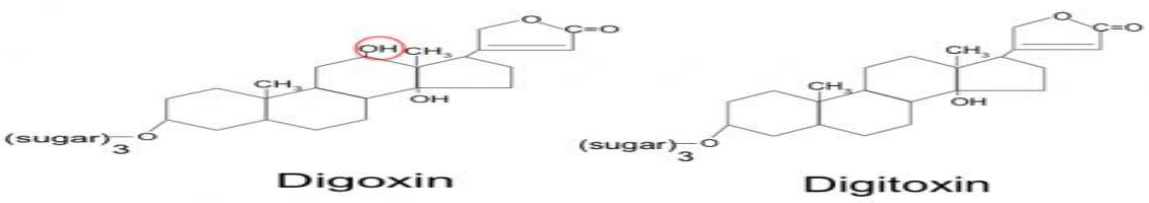


Figure 3. Steroidal cardiac glycoside.

d) Sex Harmones

They are the harmones secreted from sexual organ of humans and very important to development of sexual characteristic in man and women. In this kind of substance ketonic group, hydroxyl group or acetyl group present at C-17 position. They also classified into three groups.

1) Androgens : they are the male sex harmones like androsteron, testosterone.

2) Estrogens : they are the female sex harmones like Estron, Estradiol, Hexesterol.

3) Gestogens : Its is female sex harmone and secreted from carpus luteum like Progesterone.

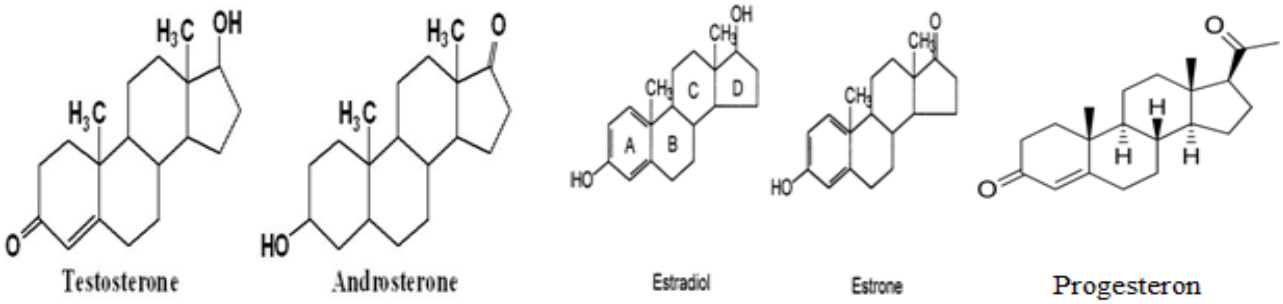


Figure 4. Steroidal sex hormones.

e) Sterols

Sterols also called steroidal alcohols and in this molecule hydroxyl group is obtain at C-3 position of A ring in steroid moiety. It has side chain of 8-10 carbon at C-17 position. Its occur in animals, plants, fungi and bacteria. It is further classified into three groups. Sterols found eighther free sterols, acylated form (Sterol ester), alkylated form (Steryl alkyl ethers), sulphate form (sterol sulphate), bound with glycoside structure (steryl glycoside, acylated steryl glycoside).

1) Zoosterols : Sterols which are obtain from animal kingdom called zoosterols. They not obtain from plant or any microorganism. Eg. Cholesterol, Coprostanol.

2) Phytosterol : Sterols which obtain from the plant kingdom called phytosterol. Eg. Stigmasterol, Sitosterol.

3) Mycosterols : Sterols which obtain from yeast or fungi called mycosterol. Eg. Ergosterol.

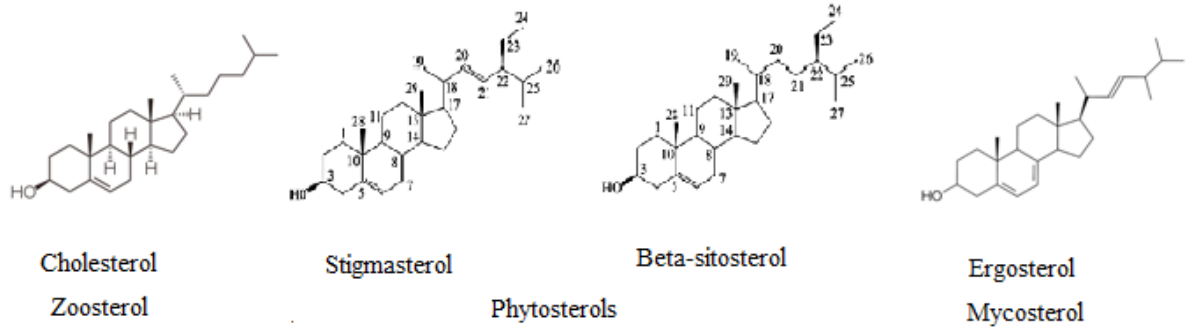


Figure 5. Structure of common sterols.

STRUCTURE OF STEROIDS

In Steroids phenanthrene ring is fused with cyclopantane that why its called cyclopentaphenanthrene. In structre four rings are fused with each other and they called Ring A, Ring B, Ring C and Ring D. Ring A, B and C is cyclohexane rings when Rind D is five membered cyclopentane ring. In genral structure of steroid 17 carbons and 28 hydrogen atoms are involved. All rings are in one plane. This steroid neucleus also called genane. Structure of steroids is three-diamentional, so its stereoisomers can be possible.

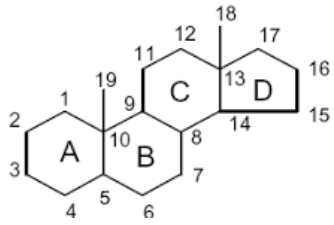


Figure 6. Structure of cyclopentano-perhydrophenanthrene (steroid) nucleus.

NOMENCULTURE

A. Configuration

Alpha-configuration :- In structure alpha-configuration shows with dotted line(- - - -).

Beta-configuration :- Beta configuration shows with thickened line(►)

Unknown configuration :- this configuration represent by wavy line(~~).

B. Common structures

-If parent steroidal moiety without methyl group at C-10 and C-13 called gonane.

-If parent steroidal moiety contain methy group at C-13 nut not at C-10 and no side chain at C-17 called estrane.

-If hydrocarbon with methy group at C-10 and C-13 bu no side chain at C-17 called androstane.

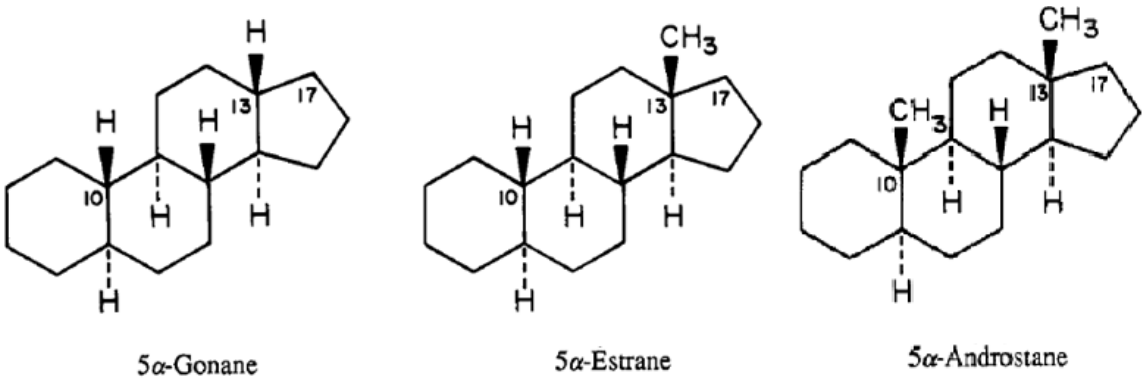


Figure 7. Structure of Gonane, Estrane and Androstane.

Table. 1 Selective trivial names of some steroid

Aldosterone	11β,18-epoxy-18-hydroxypregn-4-ene-3, 20-dione (18,11-hemiacetal)
Androsterone	3α-Hydroxy-5α-androstan-17-one
Chenodeoxycholic acid	3α,7α -Dihydroxy-5 β -cholan-24-oic acid
Cholesterol	3α,7α -Dihydroxy-5 β -cholan-24-oic acid
Cholic acid	3α,7α,12α -Trihydroxy-5 β -cholan-24-oic acid
Corticosterone	11 β,21-Dihydroxypregn-4-ene-3,20-dione
Cortisol	11 β,17,21-Trihydroxypregn-4-ene-3,20-dione
Cortisone	17,21-Dihydroxypregn-4-ene-3,11,20-trione
Dehydrocorticosterone	21-Hydroxypregn-4-ene-3,11,20-trione
Dehydroepiandrosterone (DHEA)	3 β -Hydroxyandrost-5-en-17-one
Deoxycholic acid	3α,12α-Dihydroxy-5 β -cholan-24-oic acid
Deoxycorticosterone	21-Hydroxypregn-4-ene-3,20-dione
Deoxycortisol	17,21-Dihydroxypregn-4-ene-3,20-dione
Estradiol-17a	Estra-l,3,5(10)-triene-3,17α-diol
Estradiol-17b	Estra-l,3,5(10)-triene-3,17 β –diol
Estriol	Estra-1,3,5(10)-triene-3,16α,17 β –triol
Lithocholic acid	3α-Hydroxy-5 β -cholan-24-oic acid
Pregnenolone	3β -Hydroxypregn-5-en-20-one
Progesterone	Pregn-4-ene-3,20-dione
Testosterone	17 β -Hydroxyandrost-4-en-3-one
Ursodeoxycholic acid	3α,7β -Dihydroxy-5 β -cholan-24-oic acid

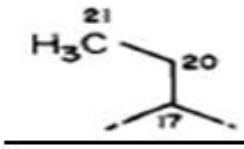
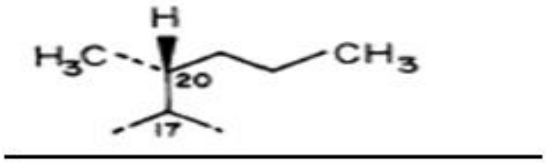
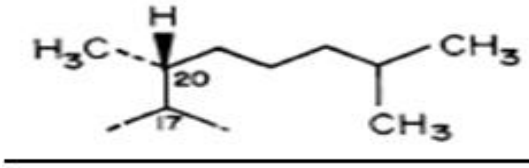
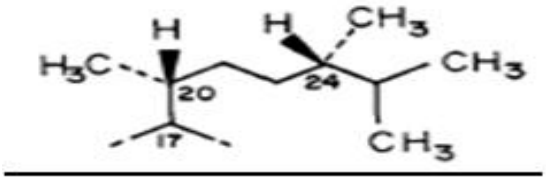
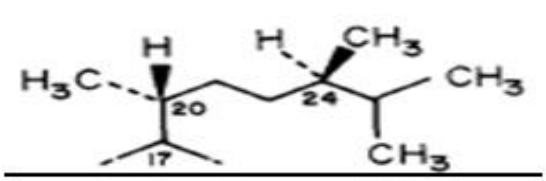
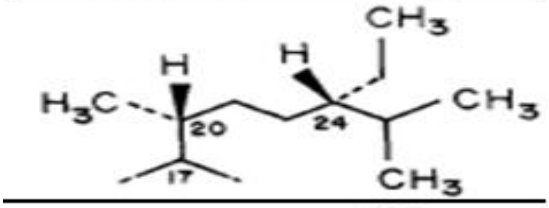
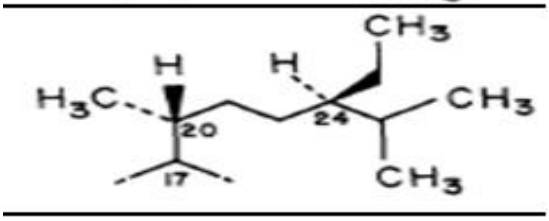
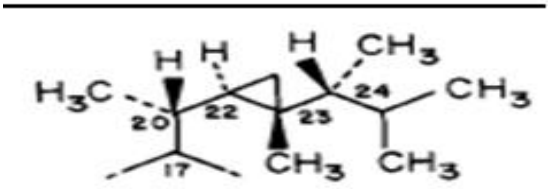
Side chain	Configuration	5 α series	5 β series
	-	5 α-pregnane (not allopregnane)	5 β-pregnane (not allopregnane)
	20R	5α-cholane (not allopregnane)	5β-cholane (not allopregnane)
	20R	5α-cholestane (not coprostane)	5β-cholestane (not coprostane)
	20R,24S	5 α-ergostane	5 β-ergostane
	20R,24R	5α-campestane	5β-campestane
	20R,24S	5α- poriferastane	5β- poriferastane
	20R,24R	5 α- stigmastan	5β- stigmastan
	20S,22R, 23R,24R	5 α- gorgostane	5β- gorgostane

Table. 2 Hydrocarbons with side chain at C-17

C. Functional Grpoups

-If methy group is changed into carbocxyl group then suffix added –oic acid at suitable locant. When this acids hydrogen removed and its became negative charged or anions then suffix is –oate.

-Name of steroidal ester is fix by location of steroid moiety and acyloxy group in anionic form. In this –e of hydrocarbon replace by –yl, -diyl.

-Ethers name consider as a alkoxy derivatives. Eg. Methoxyandrost-4-en-3-one.

-If any carbon of steroidal moiety replace with hetero atom, so name is change depend on hetero atom and its position. Eg. Carbon replace with oxygen suffix -oxa, carbon replace with nitrogen suffix –aza.

-Acetals and ketals of oxo series steroids name as dialkoxy steroids. Eg. – 3,3-Dimethoxycholest.

Table.3 Common suffix and prefix for some functional groups.

Group	Suffix	Prefix
Carboxylic acid	-oic acid	-
Lacton	-lactone	-
Easter or salt of carbocxylic acid	-oate	-
Aldehyde	-al	Oxo-
Ketone	-one	Oxo-
Hydroxyl	-ol	Hydroxyl-
Amino	-amine	Amino-

D. Unsaturation.

-Unsaturation is indicate by changing prefix ‘ane’ by ‘ene’, ‘diene’, ‘triene’, ‘yne’ at double bond or triple bond are placed.

-Unsaturation between carbon in a row than (eg. Double bond between C-4 and C-5) is indicate by lower carbon number.

E. Common Prefixes and suffixes

-If one or more carbon is missing in steroid, then numbering is not change and followed by official numbering.

-If inside steroid or chain one methylene group is absent then it prefix NOR with number of carbon atom.

-If steroid does not contain angular methylene group its indicate by NOR prefix.

-If the enlargement of the ring of steroid this indicate by prefix HOMO precced by small capital letters.

-Lenthing of side chain by one or more $–CH_2$ group indicate by prefix HOMO.

-If ring is broken by addition of new terminal groups, this indicate by number showing the position of bond broken, followed by prefix SECO by small capital letters.

-If the steroid contain three member ring that indicate by the prefix Cyclo by number of position concerned.

-When configuration is not known for one or more center its indicate by Greek letter ε (epsilon) prefix by correct locant [s].

-Removal of terminal ring with addition of hydrogen atom at junction where the adjacent ring is indicate by prefix DES.

-Prefix ent- is place front of name of compound when stereochemical inversion at all asymmetric center whose configuration not needed in specific name.

-For racemic mixture of steroids use prefix –rac or –racemo.

-Alternative application of nor and homo to same molecule the abeo system

-If multiple substitution present then order is alphabetic manner.

F. Hetrocyclic ring.

-Naturally steroids contain one or more hetrocyclic ring fused or attach to Ring D. So based on ring fixed the name.

eg. If 5 membered lactone ring fused with Ring D then its called ‘cardenolide’.

6 memberd lactone ring fused with Ring D then its called ‘Bufanolide’ .

3-methy pyran ring fused with Ring D then its called spirotrans.

If 2-(2 methy butanol) Furan is fused with Ring D then its called furotrans.

-If lactone ring is not fused to Ring D but attached with ring D suffix –lacton or –carbolactons.

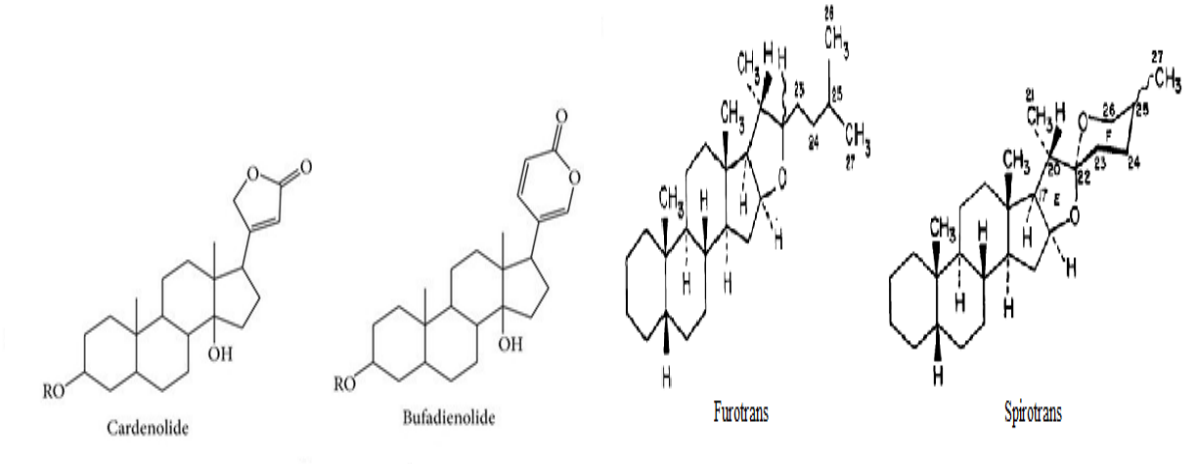


Figure 8. Hetrocyclic ring at C-17 position.

-Symbol is use to indicate doule bond between carbons

Eg. Double bond between 4^{th} and 5^{th} carbon indicate by Δ4.

STEREOCHEMISTRY

-Stereochemistry affects biological activity of steroids so its more important to learn.

-Fully saturated steroid contain nine dissimilar carbon.

-There are six asymmetric carbon atom at 5, 8, 9, 10, 13, 14 position in moiety.

-64 optical isomers are possible with steroid moiety

-It is exist into two conformations

1-chair conformation

2-boat conformation

-Chair conformation is more stable than boat conformation due to less angular strain and that's why all cyclohexane rings exist in chair confirmation

- Sterioisomerism is decide on based on

1)The way in which rings are fused together.

2)The way in which configuration of substituent groups particularly those at C-3 and C-17.

Ring A/B Fusion :- Fusion of Rings A and B may either cis or tans to give two isomeric (allo and normal) C-27 hydrocarbon.

-The hydrogen atom at C-5 has alpha configuration which opposite from the C-19 methyl group which has beta configuration and this opposite configuration make A and B ring junction tans.

Ring B/C fusion :- This fusion is tran.

Ring C/D fusion :- Its trans fusion in sterols, bile acids and related all steroids.

-The configuration of 8β and 9α hydrogens and 14α and C-18 methyl group donate trans fusion to ring B/C and C/D.

- Cis and Trans relationship of four ring called backbone of moiety.

-5α cholestane have trans-antitrans-antitrans backbone.

-5β cholestane has cis-syn-trans-antitrans backbone in which A/B ring fused in cis configuration.

-The term syn is used to similar fashion as anti to define a cis type relation

-Steroids is a flate which can be explaine only if fusion ring B and C has occure together trans manner.

-Only Trans configuration between B/C ring in natural steroids.

-Mostly steroids have C/D fusion exception in cardiac glycoside and toad poison which fusion cis. C-9 hydrogen is trans to methyl group at C-10.

-Methy group at C-10 and C-13 are cis configuration.

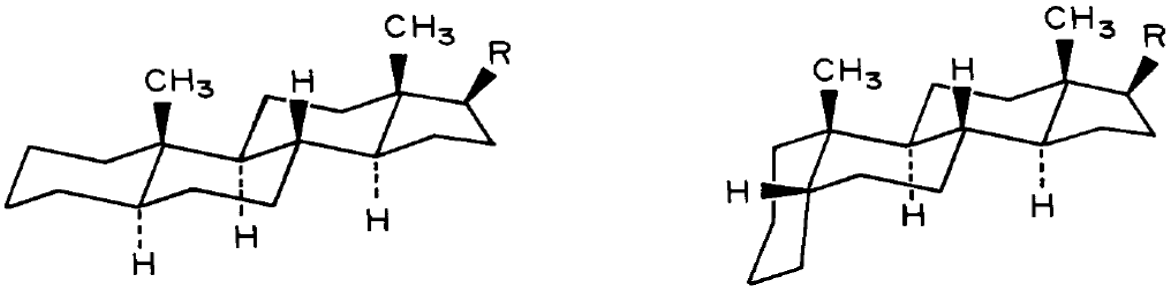


Figure 9. A/B ring fusion in trans and cis respectively

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