Phenylpropionate		(Organon)	
Testosterone Propionate	BP ; USP ; Eur. P. ; Int. P. ; IP. ;	Synadrol(R) (Pfizer)	5 to 20 mg daily as buccal tablets
Testosterone Undecanoate	—	Restandol(R) (Organon, UK)	40 to 160 mg daily

3.2.3. Oestrogens

The **oestrogens** are mainly concerned with growth and function of the sex organs.

In general, they are classified under *two* sub-heads, namely :

(*a*) Steroidal Oestrogens

(*b*) Non-steroidal Oestrogens

(*a*) Steroidal Oestrogens

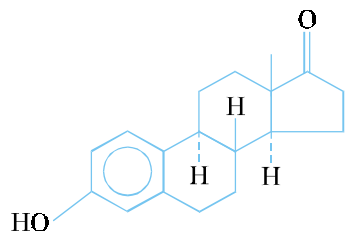
All of them essentially possess a steroidal nucleus and attribute oestrogenic activity.

Examples : Oestrone, oestriol, oestradiol.

***A.* Estrone INN, USAN Oestrone, BAN,**

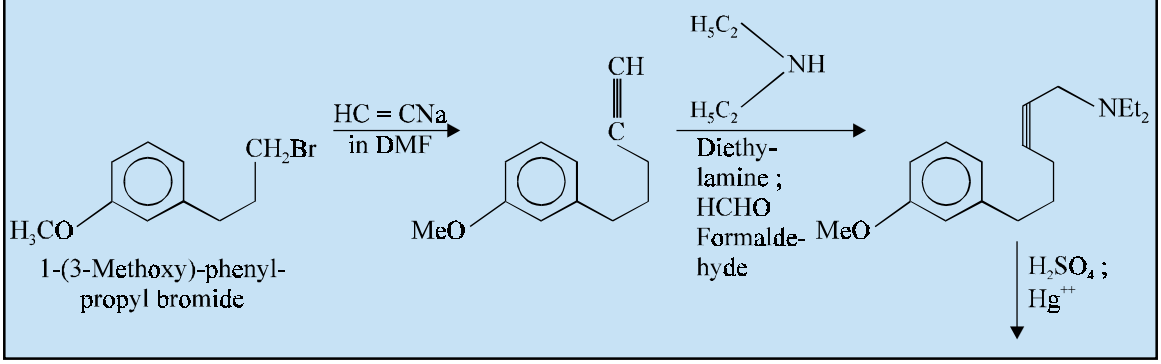
3-Hydroxyestra-1, 3, 5 (10)-trien-17-one ; Estra-1-3, 5(10)-trien-17-one, 3 hydroxy-; Oestrone Eur. P. ; Estrone USP ;

Theelin(R) (Parke-Davis).



Synthesis

Johnson and co-workers (1958, 1962) have carried out a total synthesis of **oestrone** ; each step in their synthesis was **stereoselective**, but Hughs and co-workers (1960) have put forward a total synthesis of oestrone which appear to be comparatively simpler than any other previous method.



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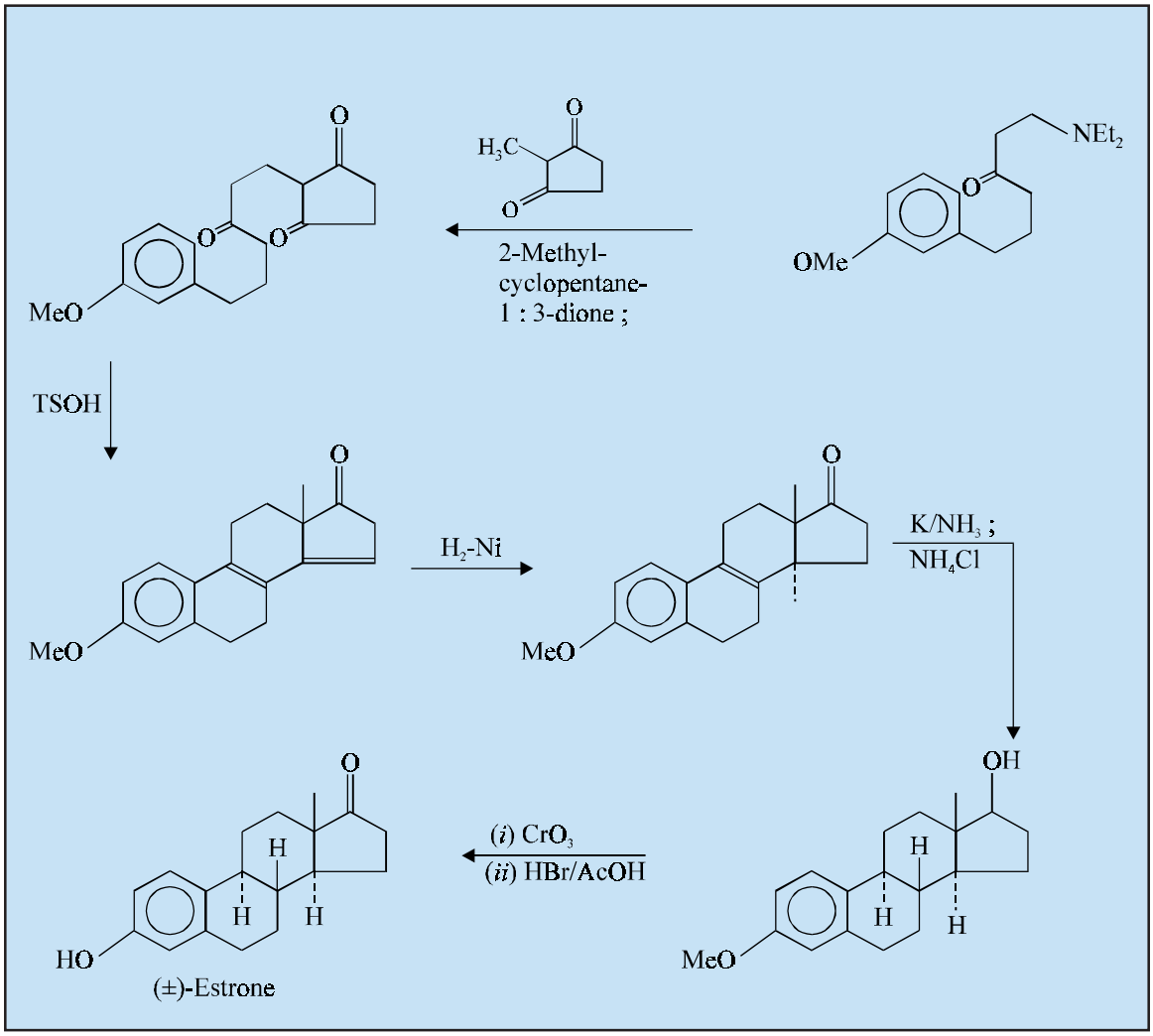
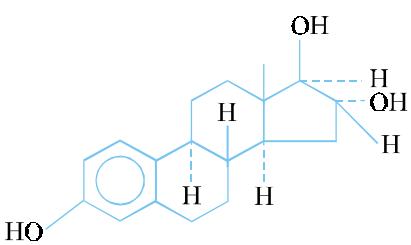


It is mainly used for the replacement therapy in deficiency states, e.g., primary amenorrhoea, delayed onset of puberty, control and management of menopausal syndrome, malignant neoplasms of the prostate.

Dose : *0.1 to 5mg per day.*

B. Estriol INN, USAN, Oestriol, BAN,



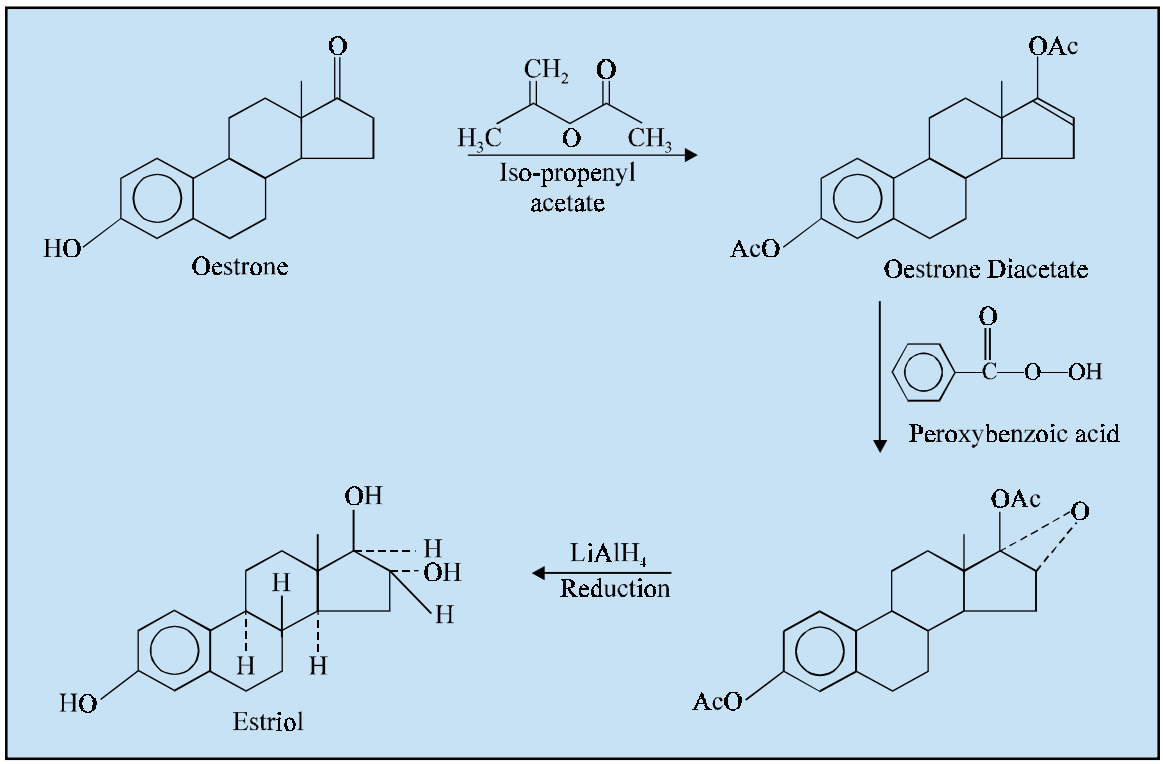
Estra-1,3,5 (10-triene-3,16α,17β- triol ; Estriol USP ;

Ovestin(R) (Organon, UK).

Soon after the discovery of oestrone *two* other hormones were isolated, namely : **oestriol** and **oestradiol**. **Oestriol** was first isolated from human pregnancy urine.

Synthesis

Leeds et al. (1954) have converted **oestrone** into **oestriol** by a simple method as discussed below.

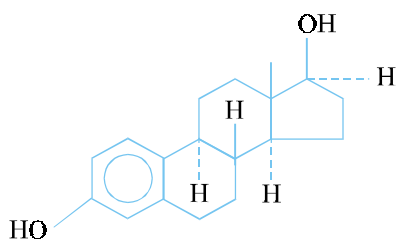


Oestrone on treatment with iso-propenyl acetate yields the corresponding diacetate which on reaction with peroxybenzoic acid removes the double bond between C-16 and C-17 and introduces an oxygen bridge having alpha configuration between the said two carbon atoms. This on reduction with lithium aluminium hydride yields the official compound.

Oestriol *is more potent than either* **oestrone** *or* **oestradiol** *in its oestrogenic activity when administered orally. It is reported to possess a selective action on the vagina and cervix.*

Dose. *For menopausal symptoms, 250 to 500 mcg per day.*

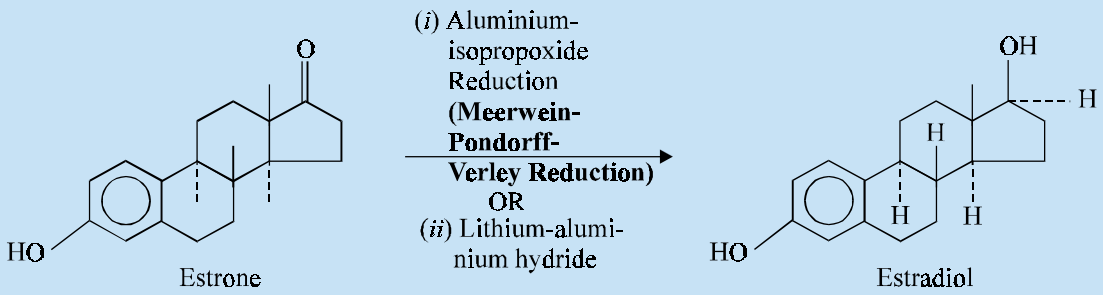
C. Estradiol INN, USAN, Oestradiol BAN,



Estra-1, 3, 5 (10)-triene-3, 17β-diol ; Beta-oestradiol; Estradiol USP ; Oestradiol (BPC1968) ; Diogyn(R) (Pfizer) ; Oestradiol Implants(R) (Organon, U.K.).

Estradiol was first obtained by the reduction of **oestrone**, but later it was isolated from the ovaries of cows.

Synthesis



Estradiol may be prepared conveniently by the reduction of **estrone** either with aluminium isopropoxide or with lithium-aluminium-hydride.

Estradiol *is found to be the most active of the naturally occurring oestrogenic hormones produced in the ovarian follicles under the influence of the pituitary. It helps to regulate and subsequent maintenance of the female sex organs, certain functions of the human uterus and above all the secondary sex features, and the mammary glands.*

Dose. *Oral, 2 mg per day ; intramuscular, 1.5 mg 2 or 3 times weekly ; implantation, 20 to 100 mg.*

A number of derivatives of **estradiol** have been employed in the control and management of oestrogenic activity and these are summarized in Table 23.2.

Table 23.2. Derivatives of Estradiol

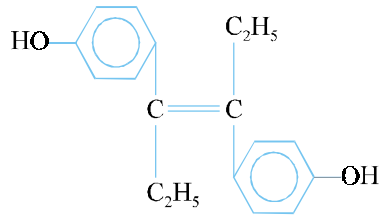
Approved Names	Official Status	Proprietary Names	Dose
Oestradiol Benzoate	BP; Eur. P. ;	**Benzotrone**(R) (Paines & Byrne, U.K.)	1 to 5 mg daily
Estradiol Cypionate	USP ;	**Depo-Estradiol Cypionare**(R) (Upjohn, USA)	1 to 5mg intramuscular every 3 to 4 weeks
Oestradiol Dipropionate	BPC (1954) ; Ind. P. ;	**Ovocyclin**(R) (Ciba-Geigy, Switz),	1 to 5mg i.m. every 1 to 2 weeks
Estradiol Enanthate	—	—	10 mg
Oestradiol Undecanoate	—	**Primogyn Depot**(R) (Schering)	100 to 200 mg every 2 to 3 weeks
Estradiol Valerate	USP ;	**Delestrogen**(R) (Squibb) ;	5 to 40 mg every 1 to 3 weeks

(*b*) Non-Steroidal Oestrogens

A large number of medicinal compounds possessing remarkable oestrogenic activity,but not of steroidal structure (nucleus), have been prepared *synthetically*.

Examples. Diethylstibesterol : **Hexestrol** ; **Dienestrol**.

A. Diethylstilbesterol INN, USAN, Stilbesterol BAN,



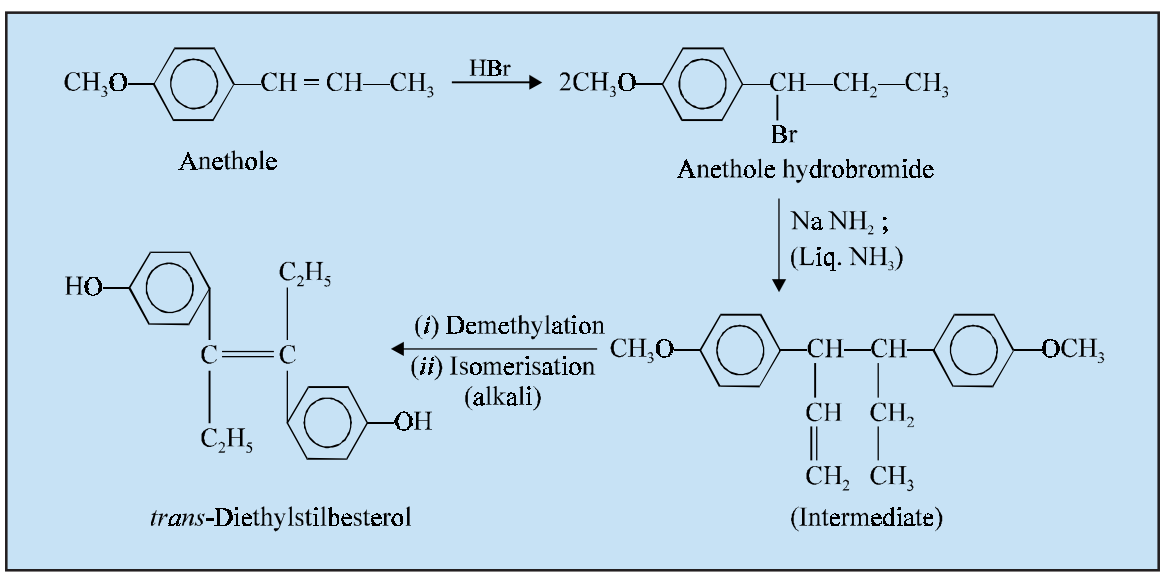
(E)-αβ-Diethylstilbene-4-4′ diol ; Phenol 4,4′-(1,2-diethyl-1,2-ethenediyl) *bis*-(E)- ; Diethylstilbesterol (USP) ; Stilboesterol (BP ; Eur. P. ; Int. P. ; Ind. P.) ;

Stilbetin$^{(R)}$ (Squibb).

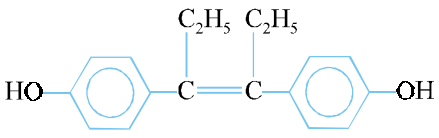
Synthesis

Diethylstilbesterol may be synthesized by *two* different methods. *First*, from anisaldehyde (Dodds and Lawson, 1939) ; and *secondly*, from anethole (Kharasch *et al.* 1943). The latter shall be discussed here.

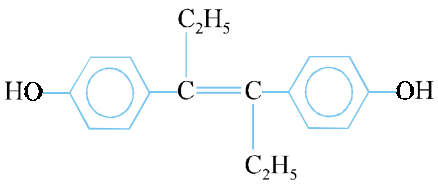
Anethole on treatment with hydrogen bromide undergoes **Markownikoff's addition** to yield anethole hydrobromide. The resulting product in the presence of sodamide and liquid ammonia gives an intermediate product which on subsequent demethylation followed by isomerization in alkali yields the official compound.



There exists **two geometrical isomeric** forms of **diethyl-stilbesterol** ; *cis*- and *trans*-out of which only the latter exhibits potent oestrogenic activity.



cis-Stilbesterol

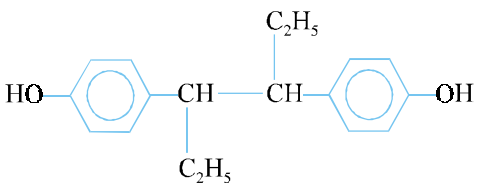


trans-Stilbesterol

It is a synthetic **non-steroidal oestrogen** having similar actions and uses to those of oestradiol. It is used in the *treatment of menopausal symptoms and in secondary amenorhoea due to ovarian insufficiency. It has also been recommended for the inhibition of lactation, in the palliative treatment of malignant neoplasms of the breast, in carcinoma of the prostate and for postcoital contraception.*

Dose. *For menopausal symptoms, oral, 0.1 to 2 mg; for secondary amenorrhoea, 0.2 to 0.5 mg ; for carcinoma of prostate, 3 mg per day.*

B. Hexestrol INN, Hexoestrol BAN,

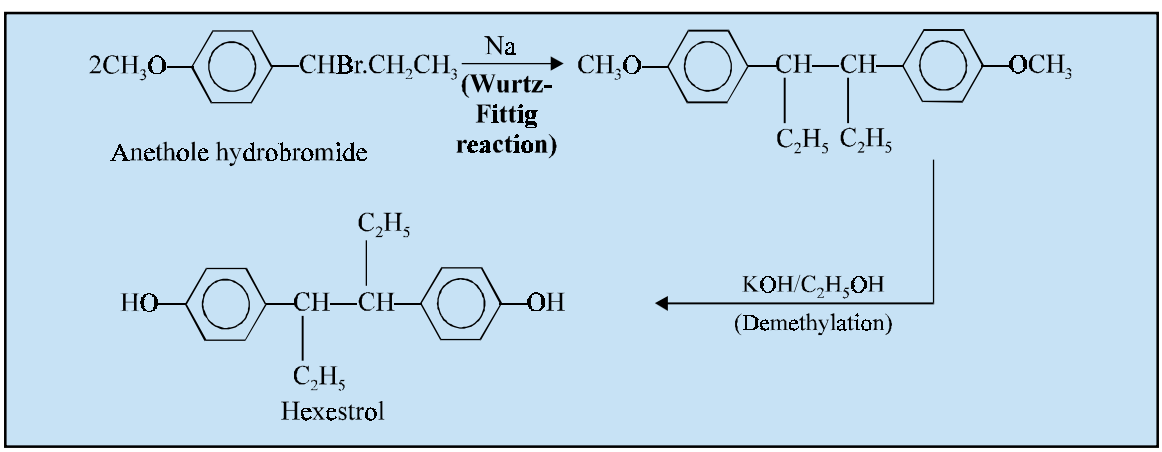


meso-4, 4′-(1,2-Dimethylethylene) diphenol ; Dihydrostilboestrol ; Hexanoestrol ; BPC (1968) ; Ind. P. ;

Hormoestrol(R) (Siegfried, Switz).

Synthesis

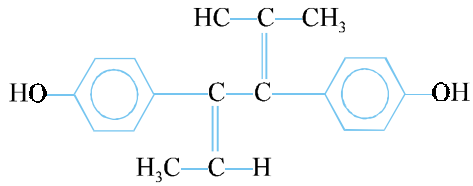
Hexestrol is prepared by subjecting anethole hydrobromide to the **Wurtz-Fittig Reaction** in the presence of sodium to get the corresponding diethyl derivative. This on further demethylation in the presence of alcoholic potassium hydroxide yields the official compound.



It is used for menopausal symptoms and also for the treatment of neoplasms of the breast and prostate.

Dose. *Oral, usual, 1 to 5 mg.*

C. Dienestrol INN, USAN, Dienoestrol BAN,



(E.E)-4, 4′-Di (ethylidene) ethylene diphenol ; Phenol, 4, 4′-(1, 2-diethyl-idene-1, 2-ethanediyl) *bis*-, (E,E)- ; Dienoestrol (BP ; Eur.P., Int. P ; Ind. P ; Dienoestrol (USP) ;

Estraguard(R) (Reid-Provident).

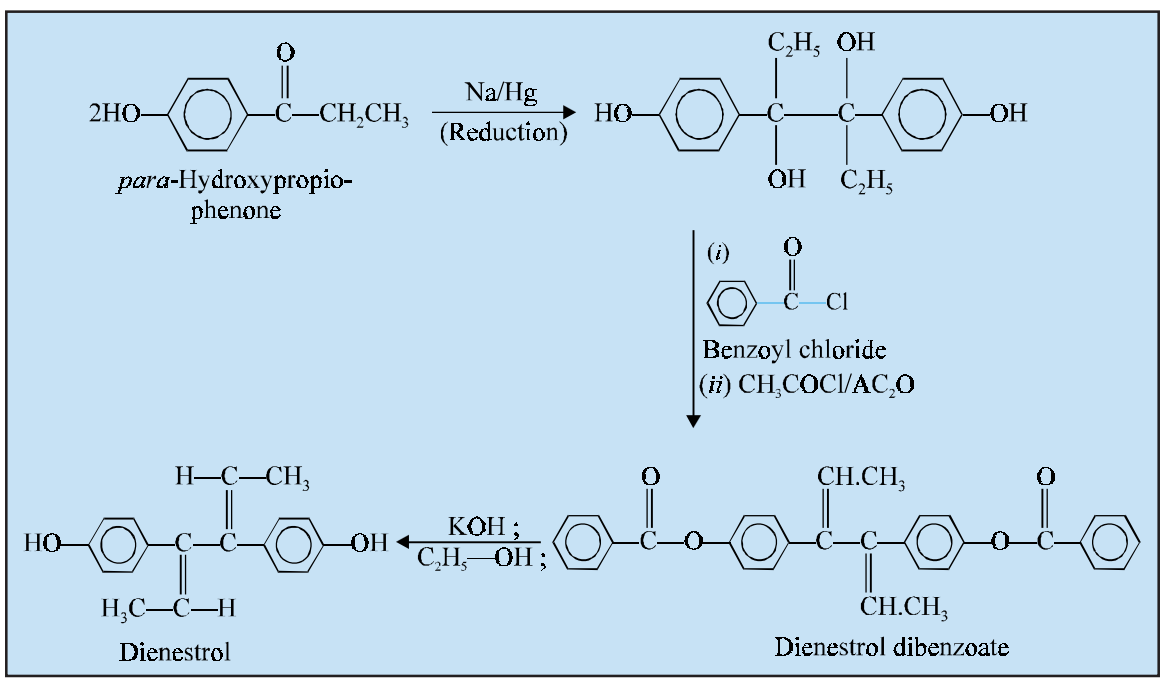
Synthesis

Dienoestrol may be synthesized by various methods. The synthesis put forward by Dodds *et al.* is described here.

Reduction of *para*-hydroxypropiophenone yields a diphenol derivative which upon benzoylation with benzoyl chloride followed by acetylation with a mixture of acetylchloride and acetic anhydride gives the dienestrol dibenzoate. This on treatment with alcoholic KOH yields the official product.

Its actions and uses are similar to those of oestradiol. Besides, it is also employed by local application in creams.

Dose. *For menopausal symptoms, 0.5 to 5 mg per day ; For mammary or prostatic carcinoma, 15 to 30 mg per day.*



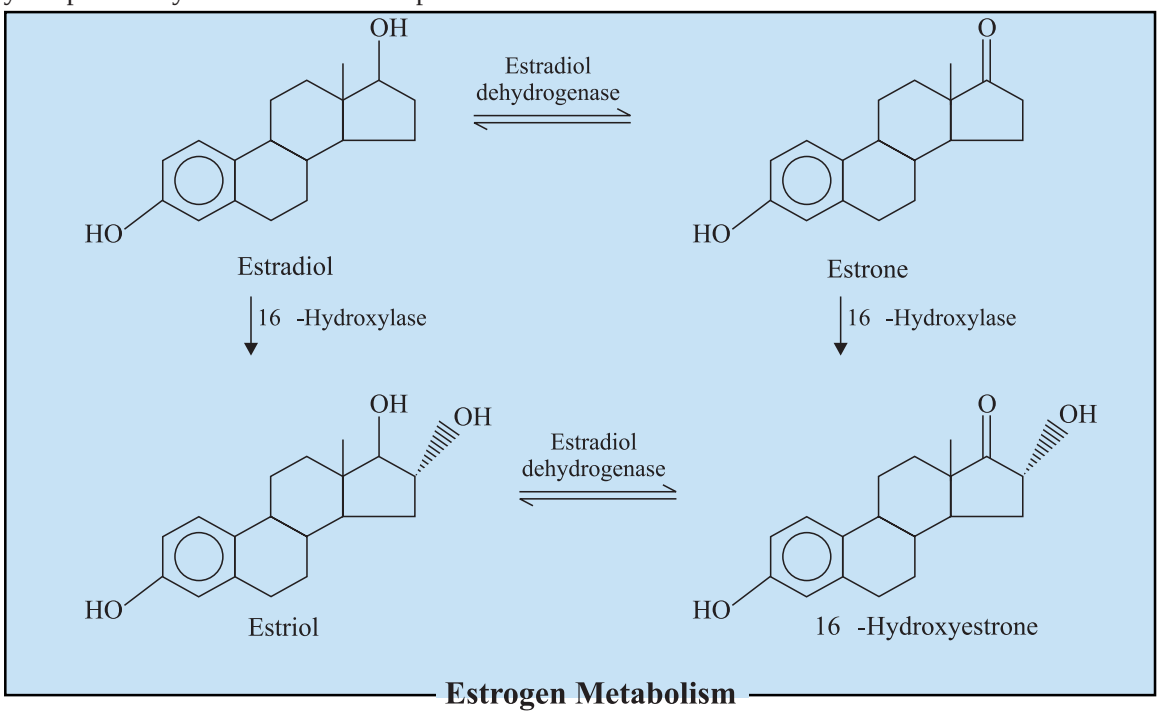
3.2.3.1. Mechanism of Action

The mechanism of action of '**oestrogens'** shall be dealt with separately under the following *two* heads, namely :

A. ***Steroidal Oestrogens***

3.2.3.1. A-1. Estrone

The **endogenous oestrogens**, for instance : **estrone** and **17β-estradiol** are observed to be interconvertible biochemically in the presence of the specific enzyme **estradiol dehydrogenase** and yield practically the same metabolic products as illustrated below :



Estrogen Metabolism

Importantly, these hormones including estradiol dehydrogenase are chiefly metabolized in the liver and mostly get excreted as water-soluble **glucuronide** and **sulphate conjugates. Estrone** is regarded as a less active (1/12) metabolite of **estradiol**.

3.2.3.1.A-2. Estriol

This specific steroid is most abundantly synthesized in the human placenta. It has been observed that in both pregnant and nonpregnant women **estriol** (along-with estrone and **estradiol**) are duly metabolized to small quantum of other structural analogues *viz.*, **2-hydroxyestrone** ; **2-methoxyestrone** ; **4-hydroxyestrone** ; and **16β-hydroxy-17β-estradiol**.

The **'drug'** affords a proliferation of the breast ductile system. It also stimulates the development of lipid and other tissues which essentially contributes to breast shape and function. Fluid retention in the breasts particularly in the later-stages of the menstrual cycle is found to be a common feature of **estriol**.

3.2.3.1.A-3. Estradiol

The '**drug**' distinctly possesses a **high presystemic elimination rate**; and, therefore, gives rise to a low bioavailability by the oral route. The drug gets appreciably converted to estrone *in vivo*. The plasma half-life stands at 1 hour.

Note. Both transdermal and micronized preparations are employed effectively for the replacement therapy.

B. Non-Steroidal Oestrogens

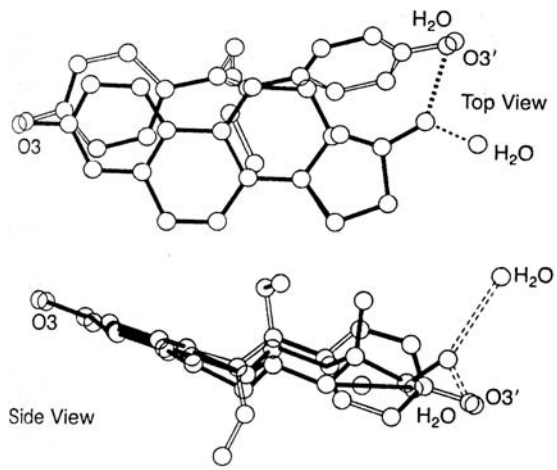
3.2.3.1.B-1. Diethylstilbesterol (DES)

The '**drug**' has an advantage over the other estrogens (*e.g.*, **estrone**, **estriol** and **estradiol**) by virtue of the fact that it gets absorbed quite effectively through the oral administration. Besides, its *rate of inactivation* is very slow and sluggish. **DES** was found to be appreciably cheaper in comparison to the naturally occurring estrogens and still can produce all the same pharmacological estrogenic activities. Interestingly, **DES** has exhibited 10 fold the estrogenic potency of its corresponding *cis*-isomer due to the fact that the *trans*-isomer bears a close relationship to **estradiol.***

Note. Due to the high incidence of 'uterine cancers' as replacement therapy in menopausal women its usage in women has been banned. However, its use in men for the treatment of 'prostatic cancer' still continues.

SAR of DES. One may consider **DES** as another form of estradiol wherein the two 6-membered rings 'B' and 'C' open up and a 6-membered aromatic ring 'D' introduced in place of the cyclopentane ring. It was further suggested that the actual distance prevailing between the two **DES** phenol OH moieties was virtually the same as the C-3 OH to C-17 OH distance existing in estradiol ; and, hence, these two entities may prove to be a **'perfect fit'** to the same receptor site. **Recently, with the advent of latest computer softwares the medicinal chemist has established the distance between the two OH moieties in DES to be 12.1Å and in estradiol 10.9Å**.

The following Figure 23.1 is the '**computer generated graphics**' illustrating explicitely the *top-view* and the *side-view* of the actual superimposition of **estradiol** $(H_2O)_2$ shown by **dark-lines** with **DES** represented by **light-lines.** It is, however, pertinent to state here that in an aqueous medium *estradiol* essentially has two water moles which are hydrogen-bonded to the 17-OH moiety. In case, one of the two water moles is considered in the distance measurement of the hydroxyl groups, there exists a '**perfect fit**' associated with the two OH moieties of **DES** as may be observed in Fig. 1. Hence, it may be implied juistifiably that water may play a vital pivotal role for *estradiol* in its **receptor site**.



ESTRADIOL $(H_2O)_2$: DARK LINES
DIETHYLSTILBESTEROL (DES) : LIGHT LINES

Fig. 23.1. Computer Generated Graphics Showing Superimposition of Estradiol and DES.

*UV Solmssen, *Chem Rev.*, **37**, 481, 1945.

[Adapted from Wilson and Gisvold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Williams and Wiltzns, New York, 5th edn. 2004.]

3.2.3.1. B-2. Hexestrol

The '**drug**' represents the *meso* form of 3, 4-*bis* (*p*-hydroxyphenyl)-*n*-hexane that distinctly possesses the greatest estrogenic potency of the three stereoisomers belonging to the corresponding dihydro analogue of **DES**. Interestingly, it is found to be less potent than **DES**.

3.2.3.1. B-3. Dienestrol

The '**drug**' is a potent estrogen which finds its abundant use only topically, for the treatment of *atrophic vaginitis* and *kraurosis vulvae.*

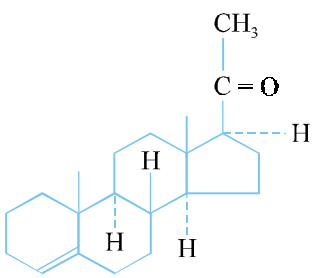
CAUTION. Not recommended in patients with known or suspected cancer of the breast ; known or suspected estrogen-dependent neoplasia; undiagnosed abnormal genital bleeding ; thrombophlebitis or thromboembolic disorders or a previous case-history of such typical conditions ; and hypersensitivity to the ingredients of the cream or suppositories of dienestrol or during pregnancy.

3.2.4. Gestogens

Gestogens or **corpus luteum hormones** are mostly secreted by the corpus luteum portion of the ovary and the metabolized to various inactive products, *e.g.*, **pregnanediol**. The metabolities are esentially excreted through urine.

Example : Progesterone.

A. *Progesterone* INN, BAN, USAN,



Pregn-4-ene-3, 20-dione ; BP ; USP ; Eur. P. ; Int. P. ; Ind. P. ;

Syngesterone(R) (Pfizer) ; Gesterol 50(R) (Forest).

Synthesis

Progesterone has been synthesized by various researchers from different starting materials as indicated below :

(*i*) From Pregnanediol (Butenandt *et al.* 1930)

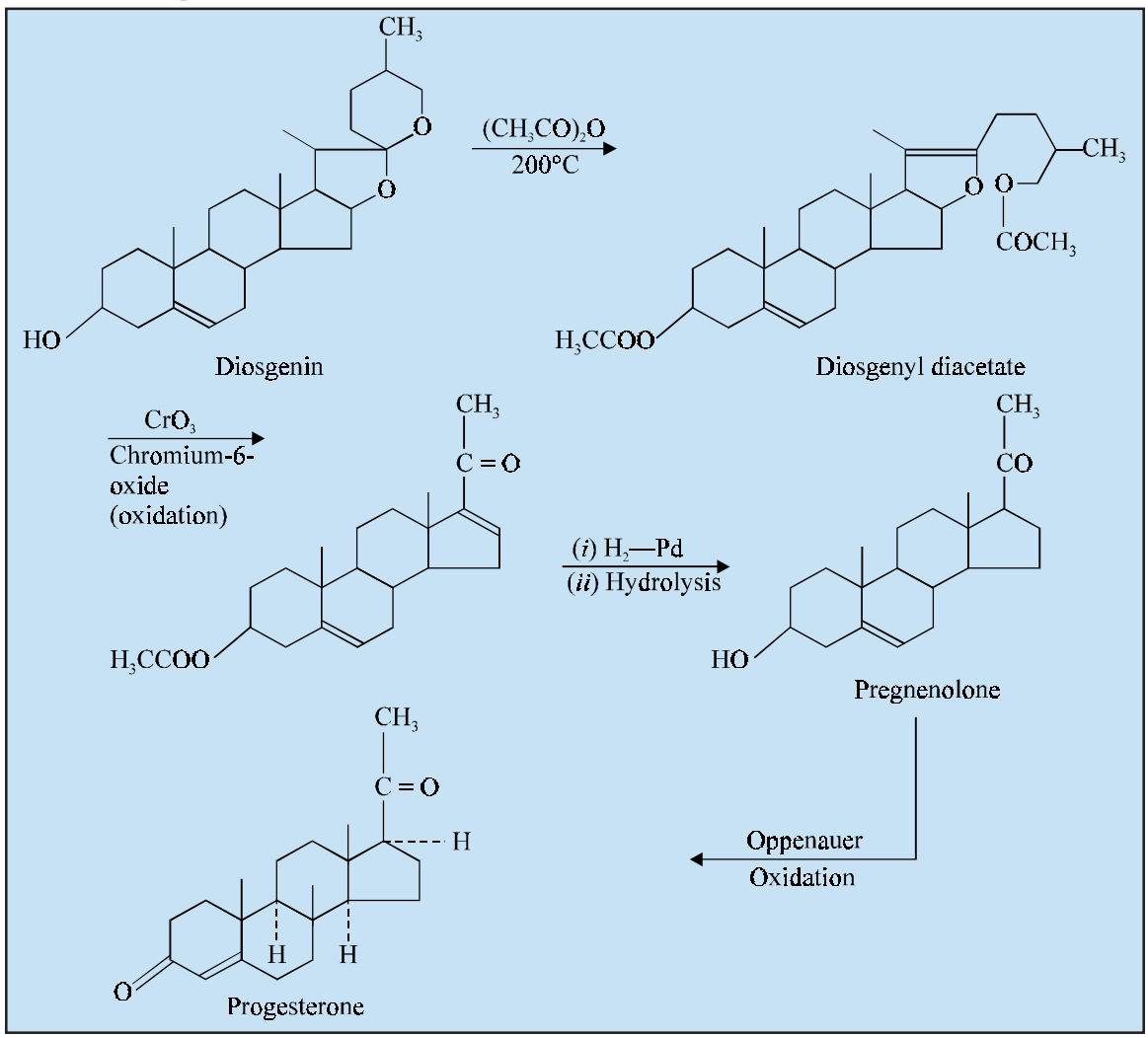
(*ii*) From Stigmasterol (Butenandt *et al.* 1934)

(*iii*) From Cholesterol (Butenandt *et al.* 1939)

(*iv*) From Ergosterol (Shephard *et al.* 1955)

It has also been synthesized from **diosgenine** by Marker *et al.* (1940-1941) which will be discussed here.

Acetylation of diosgenin at 200°C gives the corresponding diosgenyl diacetate which upon oxidation with chromium-6-oxide removes the side-chain at C-17 and the resulting product on reduction followed by hydrolysis yields pregnenolone. This on being subjected to **Oppenauer oxidation** affords the official compound.



It is employed in the treatment of functional uterine bleeding. It is also used in conjuction with an oestrogen in the treatment of menstrual disorders, neoplasms of the breast and endometrium. Sometimes it also finds its use in habitual and threatened abortion.

Dose. *For uterine bleeding, 5 to 10 mg injected per day up to 5 to 10 days ; For habitual abortion, 5 to 20 mg twice or thrice per week by intramuscular injection.*

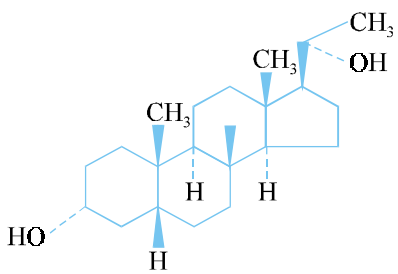
3.2.4.1. Mechanism of Action

The **mechanism of action** of **progesterone** shall now be discussed as under :

3.2.4.1.1. Progesterone

One school of thought considered it to be the '*drug of choice*' specifically in the **luteal-phase dysfunction,** a disorder that gives rise to either *infertility* or *repetitive early* abortion.

The **'drug'** gets metabolized rapidly when adminstered orally showing a plasma half-life of only 5 minutes. It usually undergoes transformation leading to a plethora of steroidal metabolic products. However, the principal excretory product of the **progesterone metabolism** is nothing but **5β-pregnane-3α-20α-diol(I)** and its **corresponding conjugates**.



(I)

A few salient-features of the aforesaid metabolism are :

(*a*) reduction of the double bond between C-4 and C-5,

(*b*) reduction of the ketone (—C—, with O above the bond) function at C-3 giving rise to 3α-ol, and

(*c*) reduction of the ketone moiety at C-20 to provide the 20α-ol.

It has been duly observed that the prevailing reduction invariably taking place at C-5 must precede the reduction of the C-3 ketone. Besides, the characteristic structural features which may specifically cause blockade of the reduction either at C-5 or C-20 have enormously enhanced the half-lives of the corresponding **progesterone derivatives**.

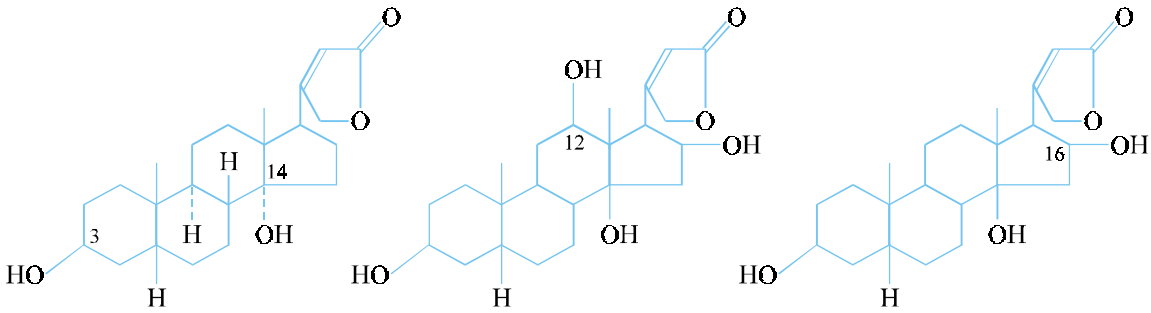
[Note. Progestasert, Alza(R) an intrauterine contraceptive device consists of 38mg of progesterone in silicone oil. In this instance, the 'drug' is believed to increase the contraceptive effectiveness of the said device by a local effect on the endometrium followed by effects upon the motility of sperm, capacitation and metabolism.]

3.3. Cardiac Glycosides

Plant extracts containing **cardiac glycosides** were invariably employed as poisons in the medieval trial by both African and South American natives for the preparation of their lethal arrow and spear poisons for use in fighting as well as hunting.

'Digitalis' a preparation made by extraction of dried seeds and leaves of the **purple foxglove** *Digitalis purpurea*, found certain application in the control and management of dropsy. Later on, in 1785, a noted Scottish physician William Withering first introduced the use of '**digitalis**' in heart therapy and this became a spectacular success and tremendous achievement for curing heart patients.

The active components of **digitalis** are glycosides of **digitoxigenin**, **digoxigenin** and **gitoxigenin** and afford these glycones on acid hydrolysis. The free **aglycones** or **genins** are only weekly active.



The **salient features** of the abvoe *three* **genins** are enumerated below :

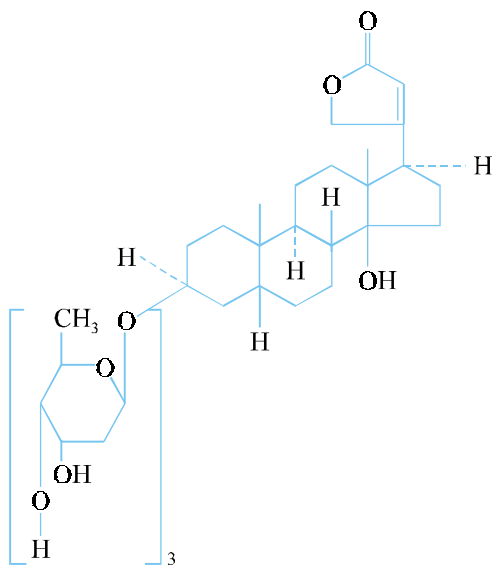
(*i*) All the above three genins have an α, β-unsaturated five-membered lactone ring.

(*ii*) All of them have 3β and 14β hydroxy groups ; **digoxigenin** has an additional 12β-hydroxy group and gitoxigenin a 16β-hydroxy group.

(*iii*) The unsaturated lactone ring and the 14β-hydroxy group are both essential to cardiac activity.

The corresponding glycosides **digitoxin** and **digoxin** are all **triosides** of comparable high cardiotonic activity. They are described briefly here :

A. *Digitoxin* INN, BAN, USAN,



Card-20 (22)-enolide, 3-[(*o*-2, 6-dideoxy-β-D-*ribo*-hexopyranosyl-(1 → 4)-*o*-2, 6-dideoxy-β-D-*ribo*-hexopyranosyl-(1 → 4)-2, 6-dideoxy-β-D-hexopyranosyl) oxy]- 14-hydroxy, (3β, 5β)- ; BP ; USP ; Eur. P ; Ind. P ;

Crystodigin(R) (Lilly).

Digitoxin is the most potent of the **digitalis glycosides** besides being the most cumulative in action.

It enhances the force of myocardial contraction and in the case of heart failure this dominating inotropic effect results in a much modified cardiac output with regard to more complete emptying of the ventricle at systole, an apparent decrease in the elevated end-diastolic ventricular pressure, and above all a positive reduction in the size of the dilated heart. It is used in the treatment of congestive heart failure.

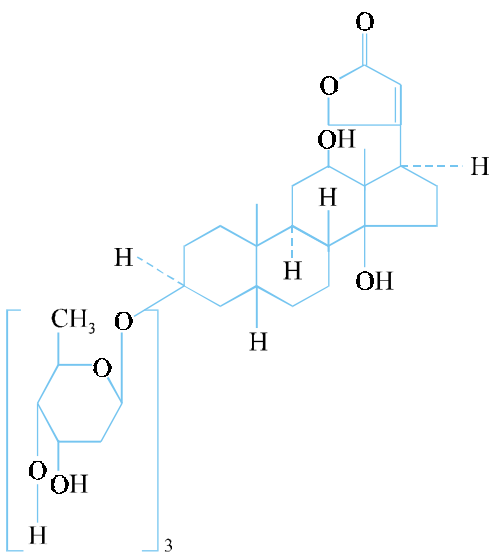
Dose. *Adult, initial, 600 mcg, followed by doses of 200 to 400 mcg every 6 hours as necessary; For slow digitalisation, 300 mcg has been given twice daily for 4 days ; Maintenance dose ranges from 50 to 200 mcg per day.*

B. Digoxin INN, BAN, USAN,

3β-[*o*-2, 6-Dideoxy-β-D-*ribo*-hexopyranosyl-(1 → 4)-*o*, 2, 6-dideoxy-β-D-*ribo*-hexopyranosyl-(1 → 4)-2, 6-dideoxy-β-*ribo* hexopyranosyl) oxy]-12β,-14-dihydroxy-5β-card-20 (22)-enolide ; BP ; USP ; Eur. P. ; Int. P ; Ind. P ;

Lanoxicaps(R) (Burroughs Wellcome) ;

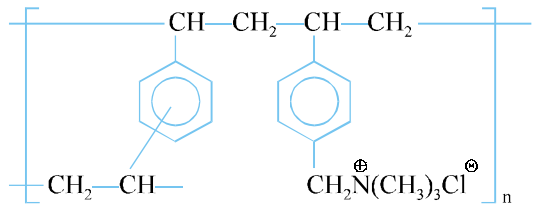
Its uses and actions are very similar to those of **digitoxin**.



Dose. *For rapid digitialization, 0.75 to 1.5 mg orally followed by 250 mcg, every 6 hours until the desired therapeutic effect is achieved.*

3.3.1. Mechansim of Action

The **mechansim of action** of **digitoxin** and **digoxin** are treated in the sections that follows :



(I)

3.3.1.1. Digitoxin

The '**drug**' usually gets absorbed almost completely after oral administration ; of course, with an exception when **cholestyramine(I)** is used concomitantly. It is found to exhibit its optimal activity within a span of 4 to 12 hour. However, after **full digitalization,** the duration of action extends upto 14 days. It gets protein bound in plasma upto almost 97%. Its volume of distribution (v_d^{ss}) is approximately 0.6 mL g^{-1}. It has been duly established that a plasma concentration of 15-25mg mL^{-1} are regarded to be therapeutic range ; whereas, 35-40 ng mL^{-1}, or even more to be toxic. However, significant variation in the plasma concentration may be afforded by plasma K^+ and Ca^{2+} levels along with other such factors. It has been osberved that the ensuing '**hepatic metabolism**' usually accounts for 52-70% of the entire elimination of this '**drug**'. The β-half-life varies between 2.4 to 9.6 (average 7.6) days.

CAUTION. Phenytoin. (anticonvulsant) and phenobarbital (long-acting barbiturate) can induce hepatic microsomal enzymes and thereby retard the half-life significantly ; and, therefore, ultimately interfering with the prevalent efficacy of the 'drug'.

3.2.1.2. Digoxin

The '**drug**' is invariably used IV for accomplishing rapid digitalization because of its high degree of purity ; and its action becomes manifest within a span of 15-30 minutes, eventually attaining its peak in 2-5 hours. However, after full digitalization its duration of action extends upto 6 days (unlike 14 days for digitoxin). The '**drug**' is bound to protein in plasma between 20-30%. Its volume of distribution (v_d^{ss}) stands at 5.1 L. kg^{-1} in normal adults ; whereas, in patients with a history of renal failure v_d^{ss} is nearly 3.3 L. kg^{-1}. It has been observed that an observed **extensive intracellular binding** is usually responsible for the large volume of distribution.

The renal excretion in adults normally accounts for 60-90% of its total elimination ; a small quantum gets converted in the liver to **dihydrodigoxin**. The elimination half-life in adults (normal) ranges between 29 to 135 hours (normally 36-41 hour). It has been observed that an enhanced GI motility lowers and decreased motility augments absorption.

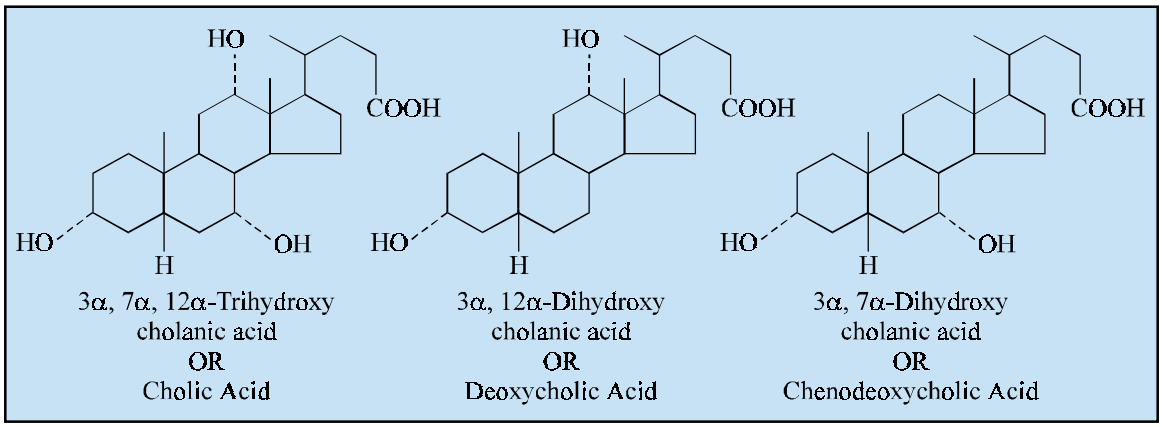
CAUTION. Bioavailability of 'digoxin' gets altered due to the presence of such drugs as : antacids, antineoplastic agents, cholestyramine resins, dietary fibre, erythromycin, neomycin, tetracyclines, metoclopramide, sulphasalazine and propantheline.

3.4. Bile Acids

The liver secretes a clear, golden yellow viscous liquid known as '**bile**'. It is stored in gall bladder and is solely useful for the digestive system. It mainly consists of the inorganic ions like HCO_3^-, Cl^- Na^+, K^+, etc., in addition to organic compounds such as bile acids, bile pigments, liquid fatty acids and cholesterol. **Cholic Acid ; Deoxycholic Acid ; Chenodeoxycholic Acid.**

The bile acids are usually present as the salt of amide with either glycine or taurine, for instance ; **sodium glycocholate** (**glycine + cholic acid**), and **sodium taurocholate** (**taurine + cholic acid**).

In all twelve natural bile acids have been identified and characterised duly. Of these the most abundant bile acids in human bile are : **cholic acid** (26-60% of total bile acids) ; **deoxycholic acid** (5-25%), and **chenodeoxycholic acids** (30-35%), whose structures and chemical names are stated below :



The **bile acids** may be isolated from the bile by cleaving the peptide linkage present in them by hydrolysis with alkali. From the resulting solution the bile acids are conveniently isolated either by crystallization from organic solvent or by treating the ethereal solution of the acids with various concentration of hydrochloric acid, for instance ; the trihydroxy, dihydroxy and the monohydroxy acids may be isolated by treating the ethereal solution with 15%, 25% and concentrated hydrochloric acid respectively.

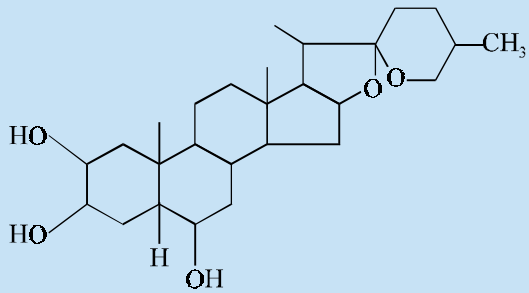
3.5. Sapogenins

Saponins are the plant glycosides that have the characteristic of forming colloidal aqueous solutions which normally foam upon shaking. Like other glycosides, **saponins** usually vary in their chemical structures. **Saponins**, in general possess an unique property to effect hydrolysis of red-blood cells (RBC) even in high dilutions. In this respect, they are very toxic to cold-blooded animals. In general, **saponins** have a bitter taste and are very irritating to the eyes and the nose. The more commonly and abundantly occurring saponins are those found in soap bark, soap root, snake root, similax and cacti.

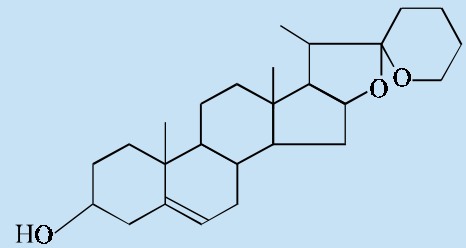
Saponins on hydrolysis yield sugars such as glucose, galactose, rhamnose and xylose together with an aglycone (**sapogenin**) *i.e.*, the non-sugar moiety. They have been used extensively in medicine, as foaming agents in fire extinguishers and as fish poisons.

Following are a few examples of **steroidal saponins** with their respective sources :

Source	Saponin	Sapogenin	Sugars
Digitalis purpurea or ***Digitalis lanata***	Digitonin	Digitogenin ($C_{27}H_{44}O_5$)	Glucose, Galactose
Trillium erectum	Trillin	Diosgenin ($C_{27}H_{42}O_3$)	Glucose



Digitogenin



Diosgenin

Probable Questions for B. Pharm. Examinations

1. Write short notes on the following :

(*a*) Nomenclature of Steroids

(*b*) Diel's hydrocarbon

(*c*) Sterols.

2. Give a brief account of the ANDROGENS. How would you synthesize Testosterone from :

(*a*) Cholesterol

(*b*) Dehydroepiandrosterone.

3. What are Follicular Hormones ? Classify them and describe the synthesis of one potent drug from each class.

4. Name a prominent **Corpus Luteum Hormone** and discuss its synthesis from a glycoside obtained from *Digitalis lanata.*

5. Discuss **'Cardiac Glycosides'** by giving its plant source, **three** important known genins, structure of the corresponding glycosides and their uses.

6. Give a comprehensive account of the **'Bile Acids'**. How are they isolated from the natural bile ? Support your answer with the structure of known bile acids.

7. Naturally occurring plant sources yield **'Sapogenins'.** Discuss their importance and usage in medicine and steroidal chemistry.

8. Hugh's total synthesis of **OESTRONE** from 1-(3-methoxy)-phenyl propyl bromide offers a comparatively simpler method than others. Explain.

9. Give the names and official status of at least **five** derivatives of :

(*a*) Testosterone

(*b*) Estradiol

which are used in medicine.