



# GONADAL HORMONES





# CONTRACEPTIVES

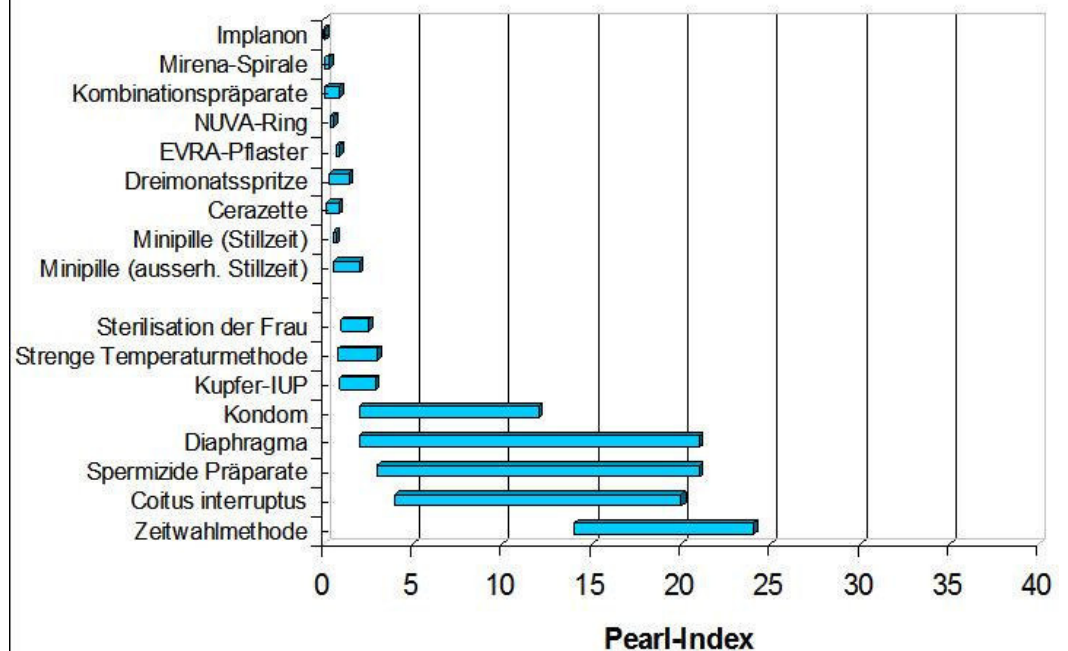


# THERAPEUTIC USE OF PROGESTINS

- Contraception with or without estrogen.
- Hormone replacement therapy.
- Secondary amenorrhoea, bleeding disorders
- Luteal-phase support to treat infertility
- Premature labour
- Progestins have been used as palliative measure for metastatic endometrial carcinoma, and is used as a second line treatment of metastatic carcinoma.
- Diagnostic uses:
  - to test endometrial responsiveness with or without estrogen.

# PERL INDEX

Without protection	80
Vaginal lavage	25-45
Coitus interruptus	12-42
Vaginal tablets	10-42
Ogino-Knaus	12-40
Vaginal, cervical pessarium	6-32
Condom	6-28
Minipill	2-8
IUD	0.8-8
Classic combinational	0.2-1.5



Number of unwanted pregnancies X 1200  
Application time in months

# ORAL CONTRACEPTIVES

## ■ 4 types:

- monophasic: Loestrin, Levlen, Levora, Levlite, Desogen, Lo/Ovral, Ortho-Cept, Nordette, Demulen, Ovcon, Modicon, Zovia, Loestrin, Apri, Microgestin, Yasmin, Ortho-Cept, Levora, Alesse
- biphasic: Ortho-Novum 10/11, Nelova 10/11, Necon 10/11, Jenest-28, Mircette
- triphasic: Ortho-Novum 7/7/7, Tri-Norinyl, Tri-Levlen, Triphasil, Trivora-28, Estrostep
- progestin-only: Micronor, Nor-QD, Ovrette

# ESTRAGEN AND PROGESTAGENE FIX COMBINATIONS

	Ethinylestradiol	levonorgestrel
■ OVIDON	0.05 mg	0.25 mg
■ RIGEVIDON	0.03 mg	0.15 mg
■ LOETTE	0.02 mg	0.10 mg
		desogestrel
■ MARVELON	0.03 mg	0.15 mg
■ MERCILON	0.02 mg	0.15 mg
■ NOVYNETTE	0.02 mg	0.15 mg
■ REGULON	0.03 mg	0.15 mg
		gestodenum
■ FEMODEN	0.03 mg	0.075 mg
■ HARMONET	0.02 mg	0.075 mg
■ MELIANE	0.02 mg	0.075 mg
■ MINULET	0.03 mg	0.075 mg
■ TRI-MINULET	0.03 mg	0.05 mg beige
	0.04 mg	0.07 mg brown
	0.03 mg	0.1 mg white
■ LINDYNETTE	0.02 v. 0.03 mg	0.075 mg
■ MINESSE	0.015 mg	0.06 mg
		norgestimate
■ CILEST	0.035 mg	0.25 mg
		chlormadinon
■ BELARA	0.03 mg	1.71 mg
		drospirenone
■ YADINE	0.03 mg	3.0 mg
■ YASMINELLE	0.02 mg	3.0 mg

# ESTROGEN AND PROGESTAGEN SEQUENTIAL COMBINATIONS

	EOD	levonorgestrel	
■ ANTEOVIN	0.05 mg	0.05 mg	white
	0.05 mg	0.125 mg	pinkish
■ TRINORDIOL	0.03 mg	0.05 mg	purplebrown
	0.04 mg	0.075 mg	white
	0.03 mg	0.125 mg	okkeryellow
■ TRIQUILAR	0.03 mg	0.05 mg	
	0.04 mg	0.075 mg	
	0.03 mg	0.125 mg	
■ TRIREGOL	0.03 mg	0.05 mg	pinkish
	0.04 mg	0.075 mg	white
	0.03 mg	0.125 mg	okkeryellow
		desogestrel	
■ GRACIAL	0.04 mg	0.025 mg	blue
	0.03 mg	0.125 mg	white
		gestodenum	
■ TRIODENA	0.03 mg	0.05 mg	beige
	0.04 mg	0.07 mg	darkbrown
	0.03 mg	0.1 mg	white
■ MILLIGEST	0.03 mg	0.05 mg	
	0.04 mg	0.07 mg	
	0.03 mg	0.01 mg	

# PROGESTAGEN ONLY CONTRACEPTIVES

- CONTINUIN (Etonodiol diacetate 0.5 mg)
- DEPO PROVERA (medroxyprogesteron 150 mg) every 3<sup>rd</sup> month 1 inj.
- MIRENA levonorgestrel (IUD)
- IMPLANON (etonogestrel 68 mg) implant, (3 years!)
- CERASETTE (desogestrel 0.075 mg) 28 tbl. (Minipill!)
  
- morning after pill contraceptives
  - RIGESOFT (0.75 mg levonorgestrel)
  - POSTINOR (0.75 mg levonorgestrel)
  - ESCAPELLE (1.5 mg levonorgestrel)



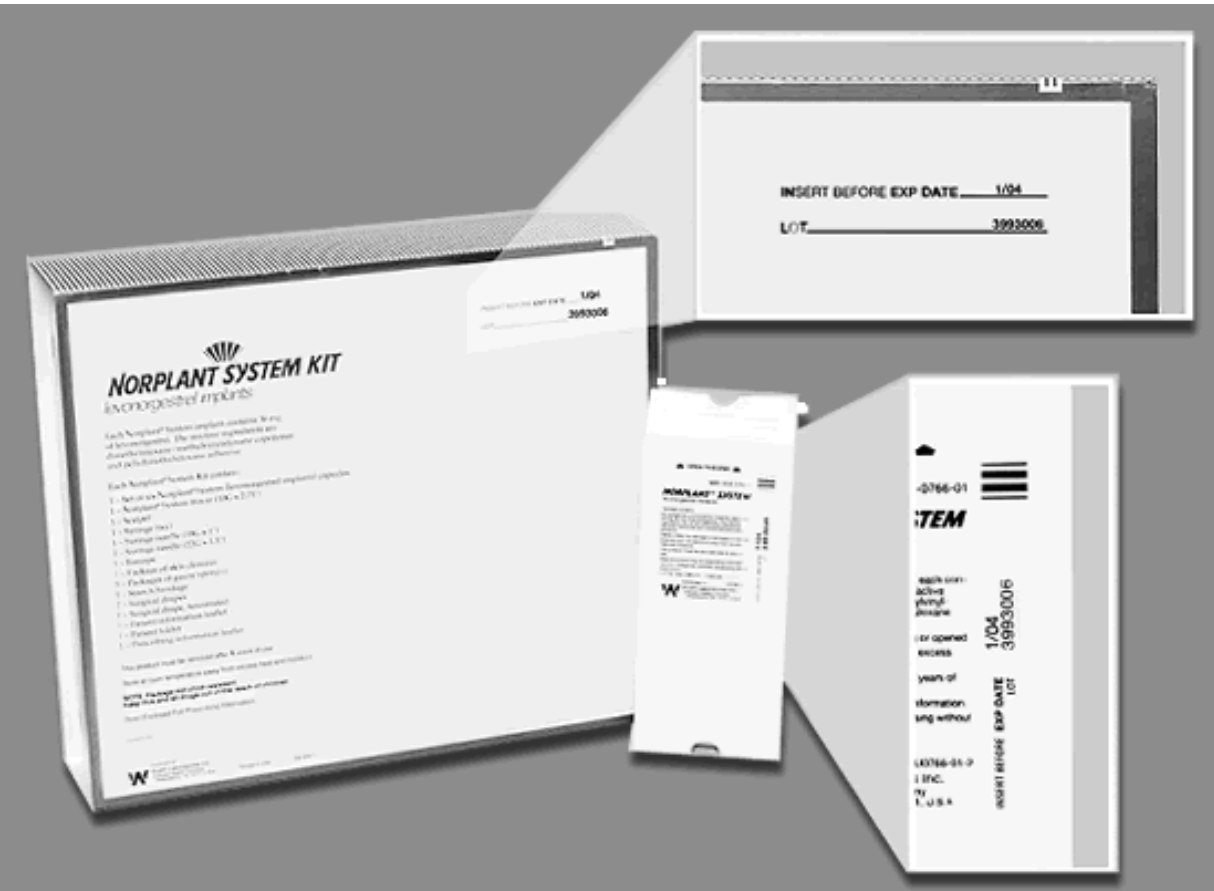
# GENERIC

- Examples of Generic Oral Contraceptives
  - Apri (same as Desogen and Ortho-Cept 28)
  - Aviane (same as Alesse-28)
  - Lessina (same as Levlite 28)
  - Necon (same as Ortho-Novum 1/35)
  - Ogestrel (same as Ovral)
  - Sprintec (same as Ortho-Cyclen-28)
  - Microgestin Fe (same as Loestrin Fe)
  - Kariva (same as Mircette)
  - Enpresse (same as Triphasil-28)

# OTHER CONTRACEPTIVE PRODUCTS

- levonorgestrel implants (Norplant system)
- intrauterine progesterone contraceptive system (Progestasert)
- medroxyprogesterone contraceptive injection (Depo-Provera)
- nonoxynol contraceptive creams and gels

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# EMERGENCY CONTRACEPTIVES

- drugs used for the prevention of pregnancy following unprotected intercourse or a known or suspected contraceptive failure
- to be effective these must be taken within 72 hours of intercourse
- two products are available:
  - Plan B: 0.75 mg levonorgestrel
  - Preven: 0.25 mg levonorgestrel and 0.05 mg ethinyl estradiol (this product includes a pregnancy test kit)



**Table 9** Spectrum of hormonal activities of progestogens. The data are mainly based on animal experiments and are compiled from the literature<sup>202,204,236–244</sup>. The clinical effects of the progestogens are dependent on their tissue concentrations

<i>Progestogen</i>	<i>A-E</i>	<i>EST</i>	<i>AND</i>	<i>A-A</i>	<i>GLU</i>	<i>A-M</i>
Progesterone	+	–	–	(+)	+	+
Chlormadinone acetate	+	–	–	+	+	–
Cyproterone acetate	+	–	–	+	+	–
Medroxyprogesterone acetate	+	–	(+)	–	+	–
Medrogestone	+	–	–	–	?	–
Dydrogesterone	+	–	–	–	?	(+)
Norethisterone	+	+	+	–	–	–
Levonorgestrel	+	–	+	–	–	–
Gestodene	+	–	+	–	(+)	+
Etonogestrel (3-keto-desogestrel)	+	–	+	–	(+)	–
Norgestimate	+	–	+	–	?	?
Dienogest	+	–	–	+	–	–
Tibolone metabolites	+	+	++	–	–	–
Drospirenone	+	–	–	+	–	+
Trimegestone	+	–	–	(+)	–	(+)
Promegestone	+	–	–	–	+	–
Nomegestrol acetate	+	–	–	+	–	–
Nestorone	+	–	–	–	–	–

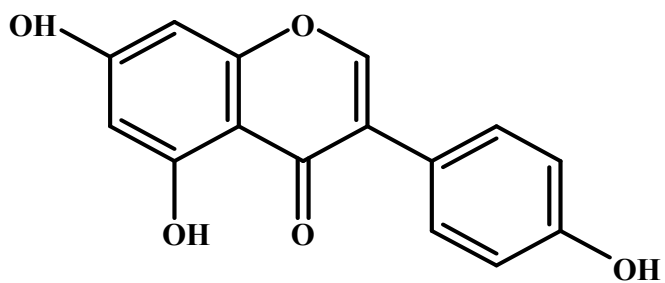
A-E, antiestrogenic; EST, estrogenic; AND, androgenic; A-A, antiandrogenic; GLU, glucocorticoid; A-M, antimineralocorticoid activity

++, strongly effective; +, effective; (+) weakly effective; –, not effective; ?, unknown

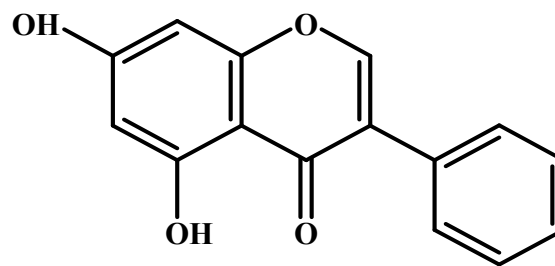
# PLANT ESTROGENS: PHYTOESTROGENS

- A variety of compounds exist in plant which possess estrogenic activity
- Soy products contain flavonoids and lignin derived compounds which have estrogenic activity
- Extractum agni casti fructus (illatos barátcserje termés kivonat)
- Extractum cimicifugae rhizomae (black cohosh, poloskavész, indiánasszonygyökér kivonat)

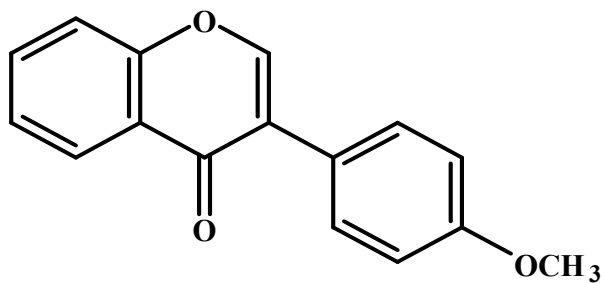




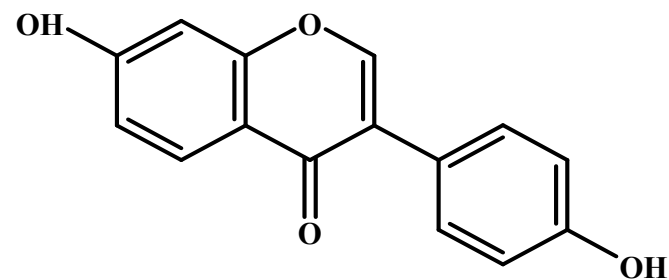
**GENISTEIN**



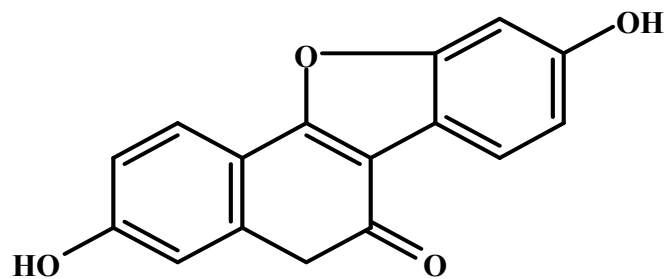
**BIOCHANIN A**



**FORMONONETIN**



**DAIDZIN**



**COUMESTROL**

# BLACK COHOSH (REMIFEMIN)

- *Cimicifuga racemosa*
- medicinally used parts: dried rhizomes and roots
- used for the symptoms of PMS and climacteric complains
- active ingredients:
  - triterpenes: cimifugoside, actein, 27-deoxyactein
  - Quinolizine alkaloids: cytisine, methyl cytisine
  - Other: isoferulic acid
- binding to estrogen receptor causes a suppression of LH release





# SIDE EFFECTS OF ORAL CONTRACEPTIVES

- Estrogen component (EOD)
  - Mastalgia, bloating, headache, nausea, vomitus, gall stone formation
- Progestin component
  - Hirsutism, weight gain, acne, tiredness, depression, ↓HDL, ↑LDL

# ANDROGENS

- prototype is testosterone (produced by interstitial cells of testis)
- main function: development and maintenance of primary and secondary sex characteristics in males (androgenic)
- protein retention (anabolic action)
- other naturally occurring androgens: androsterone, isoandrosterone, dehydroandrosterone, dehydroisoandrosterone

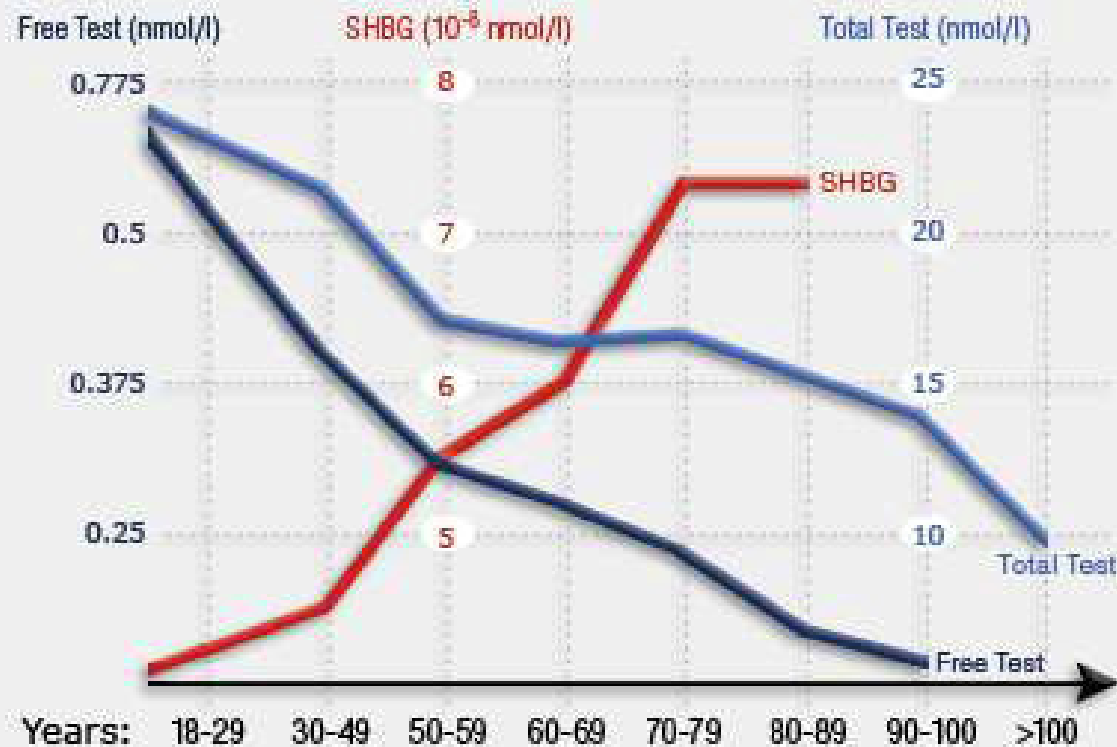
## Uses:

- Male hypogonadism
- Anabolic actions
- Illicit use in athletics

# PHYSIOLOGICAL EFFECTS OF TESTOSTERONE

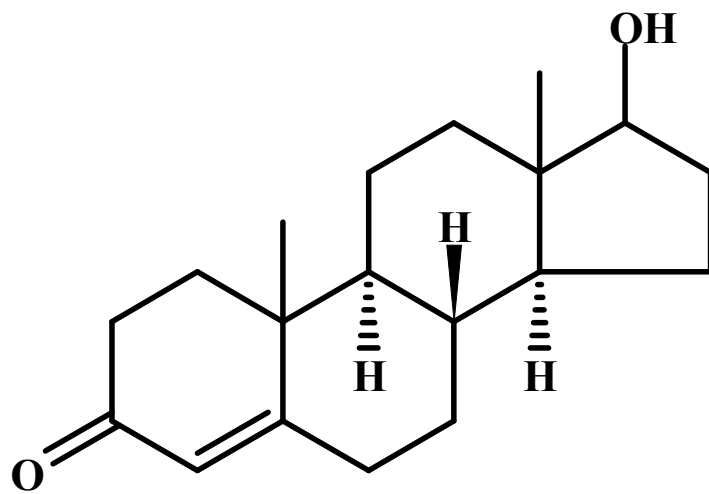
- pubertal transformation:
  - enlargement of testes, penis and scrotum
  - pubic and axillary hair
  - bone growth
  - red cell mass increase
  - skeletal muscle mass increase
  - larynx enlarges - deepening of the voice
  - increase in sebaceous glands - often cause of acne
  - beard development

## Age-related Decline In Testosterone Levels

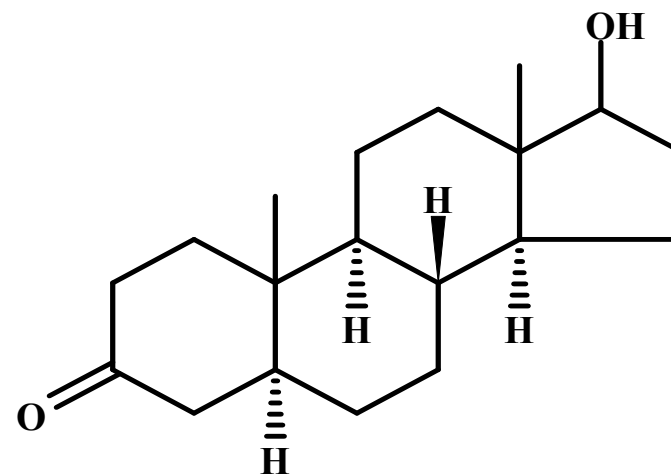


Starting around age 35 to 40, testosterone levels (Total Test) in men will decline by roughly 1% each year. It's not only a decrease in production that causes the testosterone deficiency, but an increase in Sex Hormone-Binding Globulin (SHBG). SHBG is a glycoprotein that binds to testosterone and prevents it from becoming active. Only the so-called "Free" testosterone (Free Test) is biologically active. The drop in Free testosterone is even greater, roughly 1.2% a year.

# NATURAL ANDROGENS

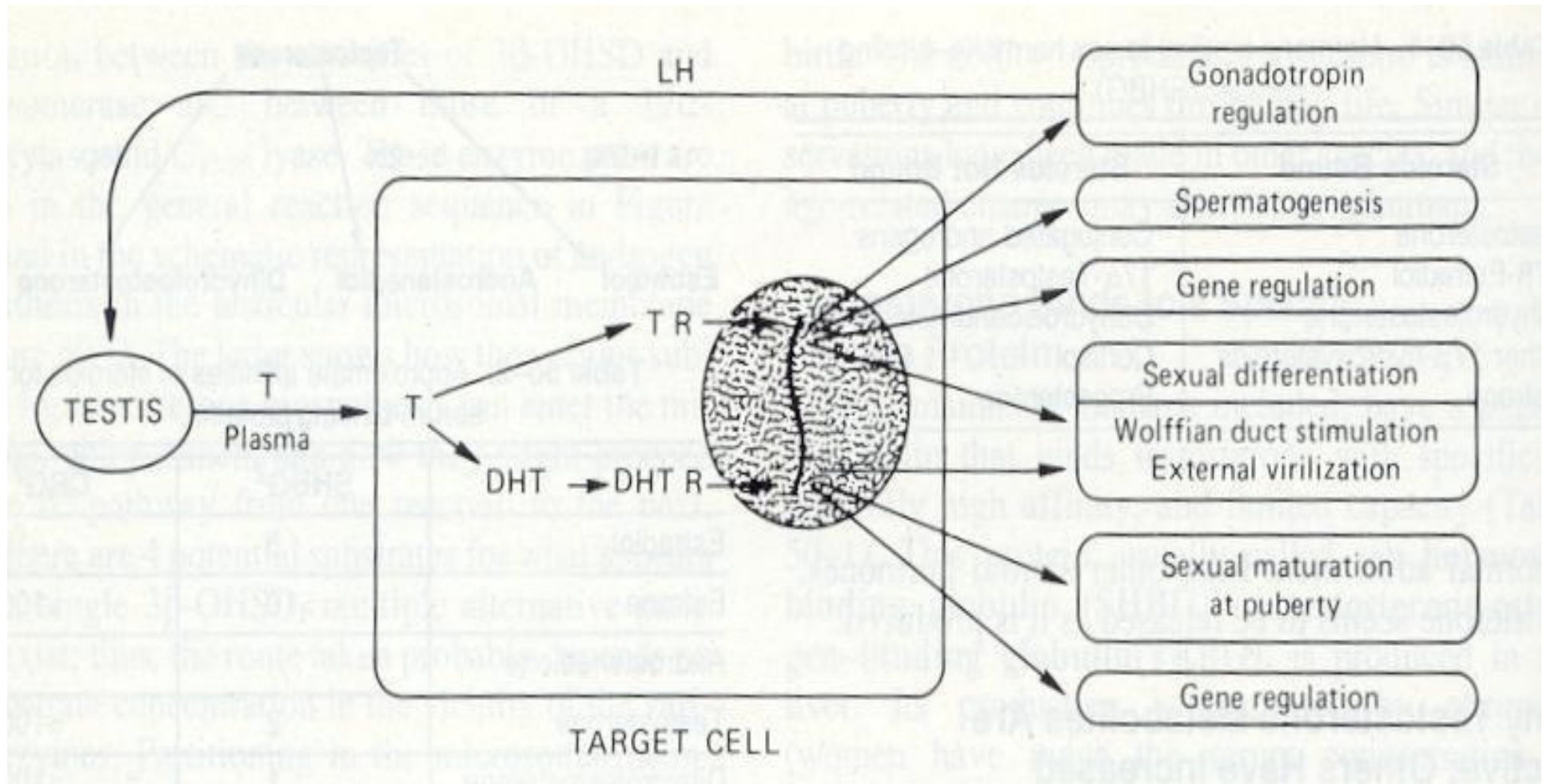


**TESTOSTERONE**



**DIHYDROTESTOSTERONE**





# TESTOSTERONE PRODUCTS

- testosterone in aqueous suspension (short-acting)
- testosterone propionate in oil
- testosterone enanthate in oil (Delatestryl)
- testosterone cypionate in oil (Depotest)
- testosterone pellets (Testopel)
- testosterone transdermal system (Androderm)

# ANDROGEN PRODUCTS IN HUNGARY

- Testosterone

- ANDRIOL

- ANDROGEL

- NEBIDO

- TOSTRAN

- Mesterolone

- PROVIRON



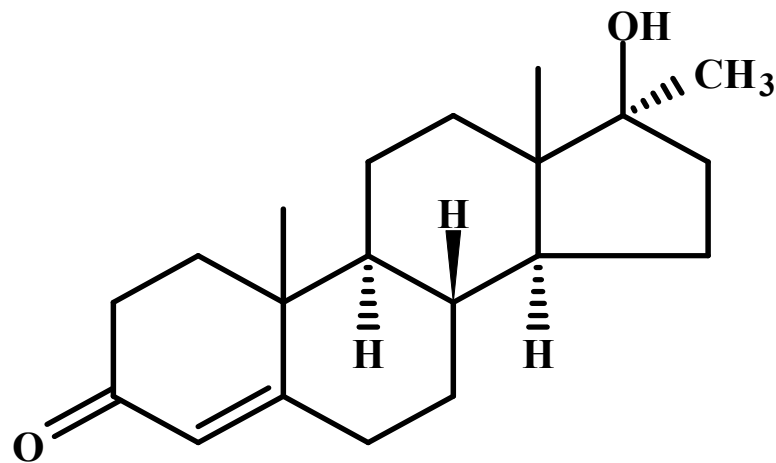
# USES FOR ANDROGENS

- replacement therapy in hypogonadism
- delayed puberty
- cryptorchidism
- metastatic breast cancer in women
- postpartum breast pain/engorgement
- male climacteric

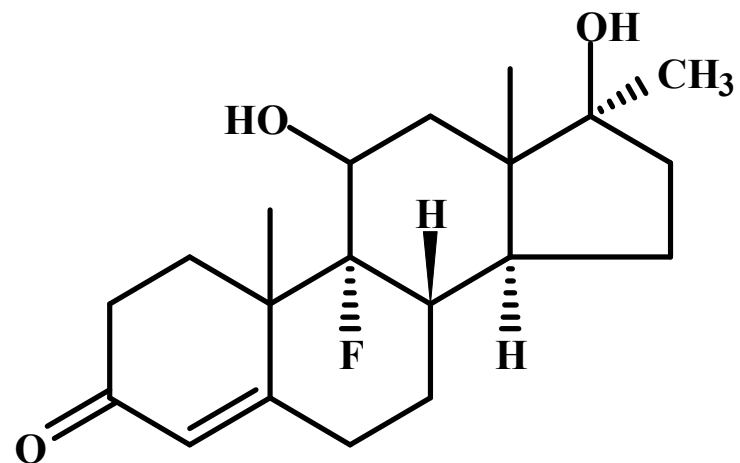
# SIDE EFFECTS OF ANDROGENS

- Excessive masculinization (virilization in the baby as well)
- Cholestatic jaundice
- Premature closure of epiphyses
- Aggression ((Ste)roid rage)
- Dependence

# SEMI-SYNTHETIC ANDROGENS

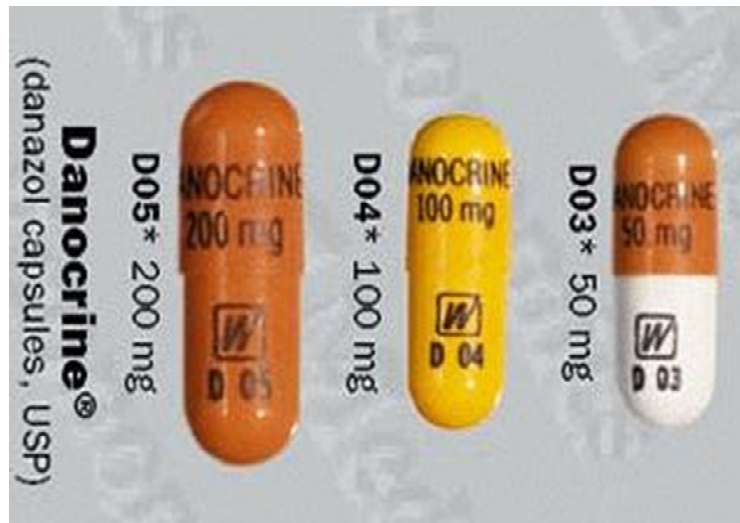


**METHYLTESTOSTERONE**



**FLUOXYMESTERONE (HALOTESTIN)**

- Frequently classified as 17-alpha alkylated androgens;
- alkylation confers more oral effectiveness



*Up to 20 mg/day*

**OXANDRIN®**  
oxandrolone, USP @  
2.5 mg tablets

Co-marketed by Ross Products

Division, Abbott Laboratories

Manufactured for BTG Pharmaceuticals

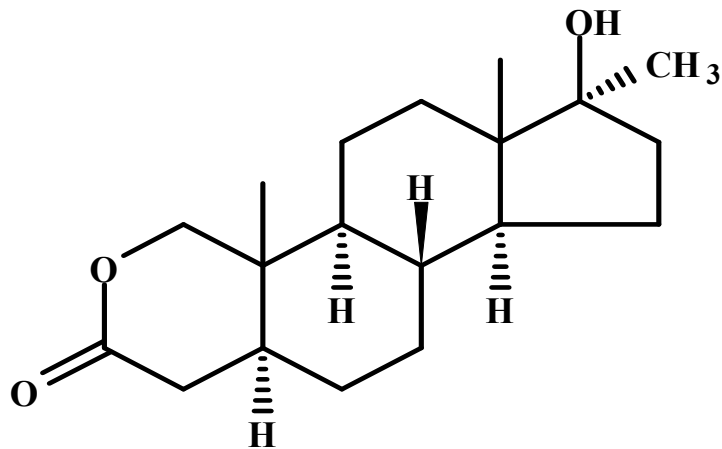
For more information:

[www.oxandrin.com](http://www.oxandrin.com)

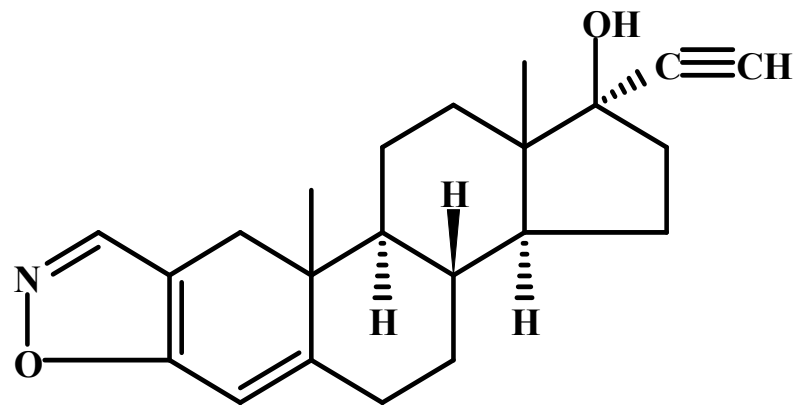




# ANABOLIC STEROIDS



**OXANDROLONE (OXANDRIN)**

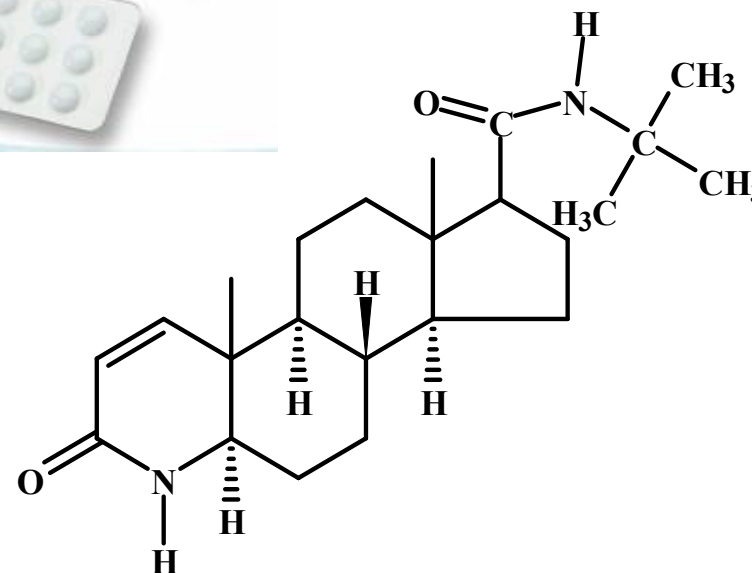


**DANAZOL (DANOCRINE)**

■ Also classified as 17-alpha alkylated androgens

# FINASTERIDE (PROSCAR, PROPECIA)

- An anti-androgen used in the treatment of BPH (benign prostatic hypertrophy)
- also used to manage male pattern baldness (Propecia)
- Can be teratogenic!
- MOA: Inhibits  $5\alpha$ -reductase enzyme  $\rightarrow$  Testosterone-DHT formation is inhibited



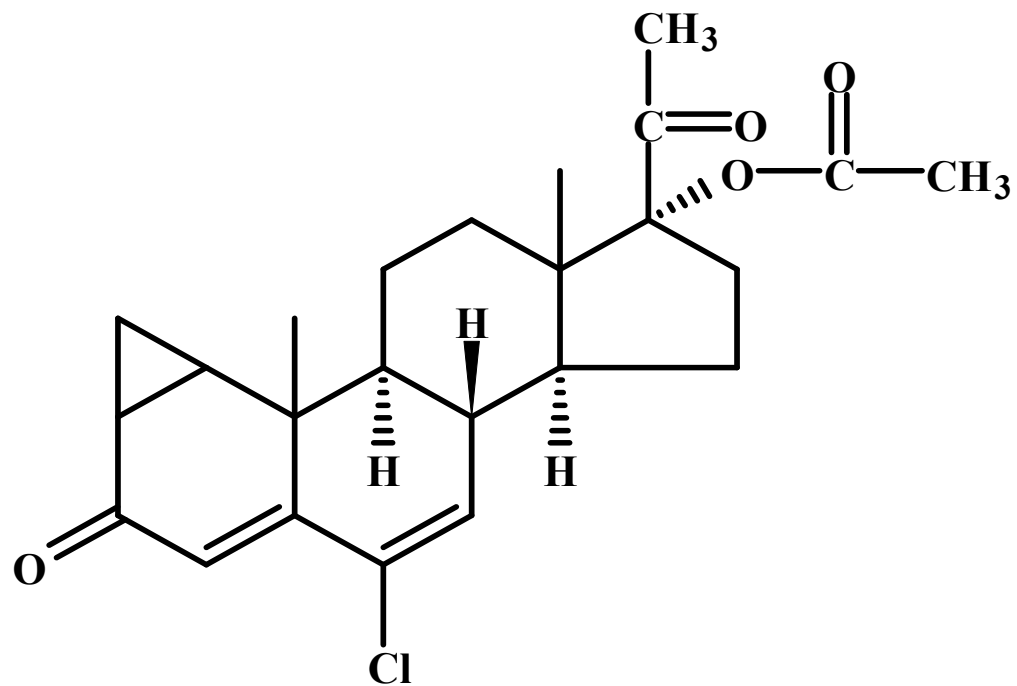
FINASTERIDE (PROSCAR)

# FINASTERIDE : PROSCAR AND PROPECIA



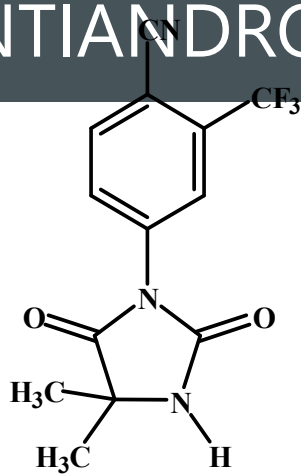
# CYPROTERONE ACETATE

■ Antiandrogenic properties

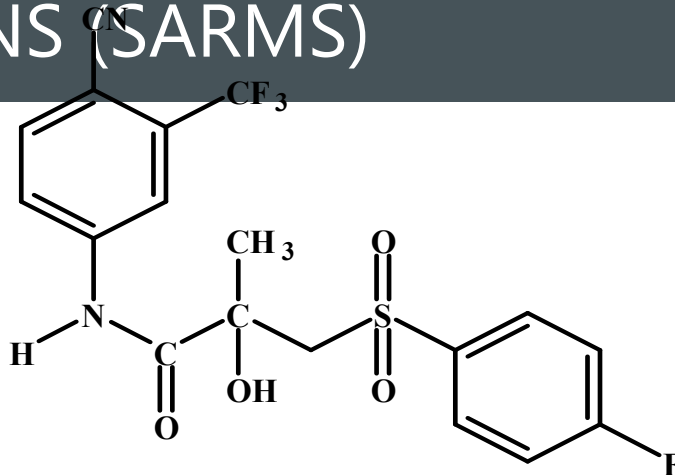


**CYPROTERONE ACETATE (ANDROCUR)**

# ANTIANDROGENS (SARMS)

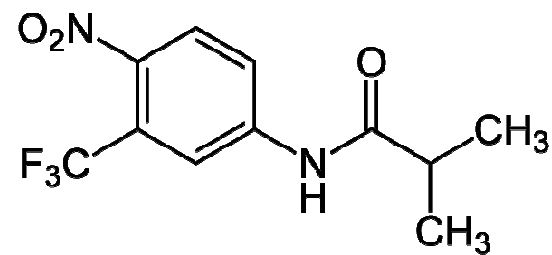


**NILUTAMIDE (NILANDRON)**



**BICALUTAMIDE (CASODEX)**

Use in metastatic prostate carcinoma

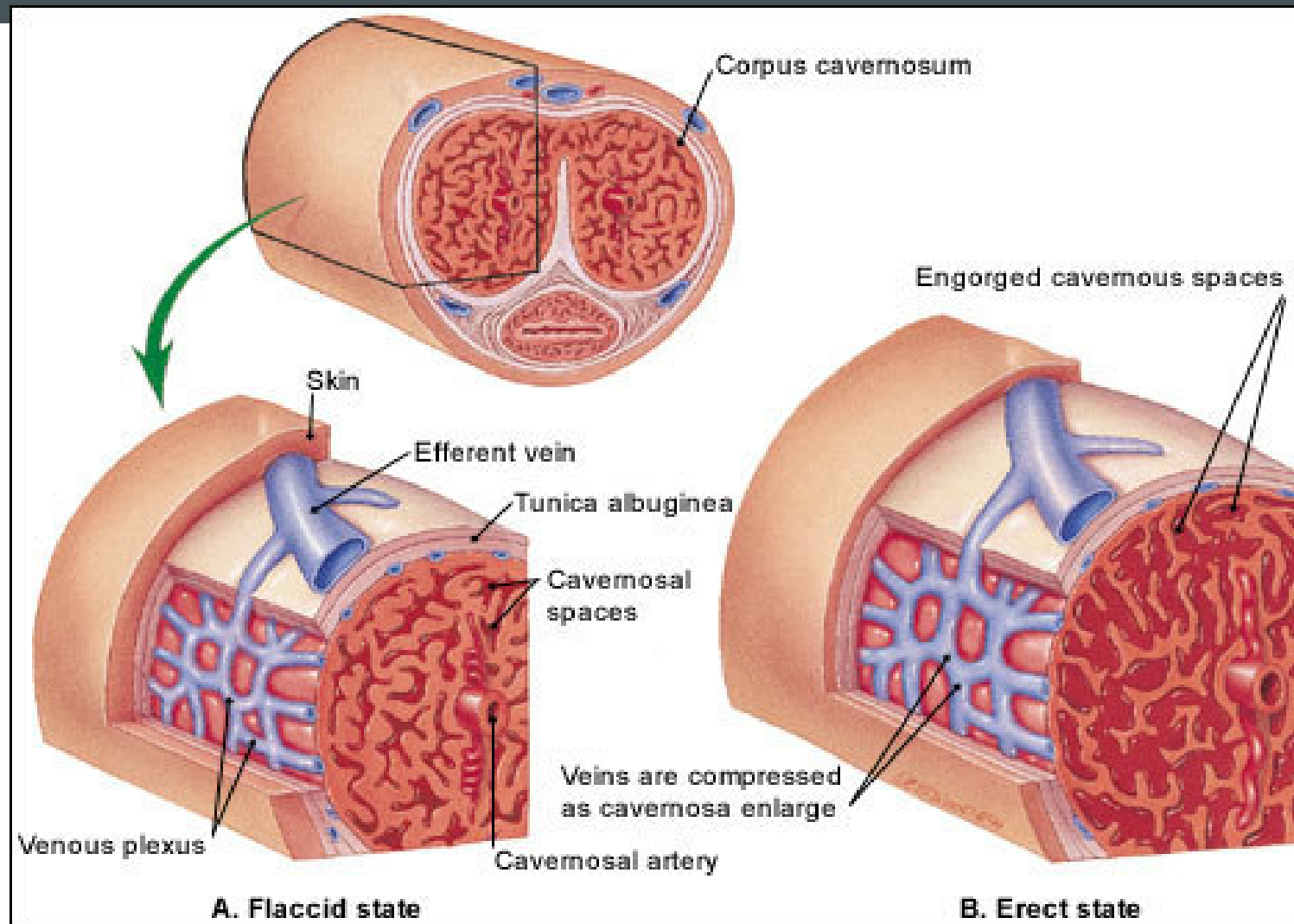


**Flutamide**

# Antiandrogen drugs



# TREATMENT OF ERECTILE DYSFUNCTION



# PDE5 INHIBITORS

- Sildenafil (VIAGRA)
- Tadalafil (CIALIS)
- Vardenafil (LEVITRA)
- Alprostadil (CAVERJECT)
- Phentolamin
- Papaverin
- PDE5 inhibitors are used in the treatment of pulmonary hypertension as well!
- Sildenafil is metabolized mainly by the cytochrome P450 3A4 pathway (79%) and to a lesser extent by 2C9 (20%).
- Vardenafil is metabolized in a similar manner, mainly by 3A4 with a smaller contribution by 2C9. Tadalafil is metabolized almost solely by 3A4.
- Contraindicated to co-administer with nitrates!!!  
(Severe hypotension may occur.)



# PDE5 INHIBITORS



Vardenafil

