

كل شي حكت عنه
الدكتورة مهم
مكتوب عنده
بالاحمر ❤️



تفريغ ميديسينال

محاضرة: *Hormones*

الصيدلانية: *Yara Mani*



لجان الرفعات



Hormones (14)

- Are chemical released by a cell or a gland in one part of the body that send out messages that affect cells in other parts of the organism. Only a small amount of hormones is required to alter cell metabolism.
- In essence, they are chemical messenger that transport a signal from one cell to another.
 - Secreted by endocrine gland
 - Specific to target
 - Activate cellular change

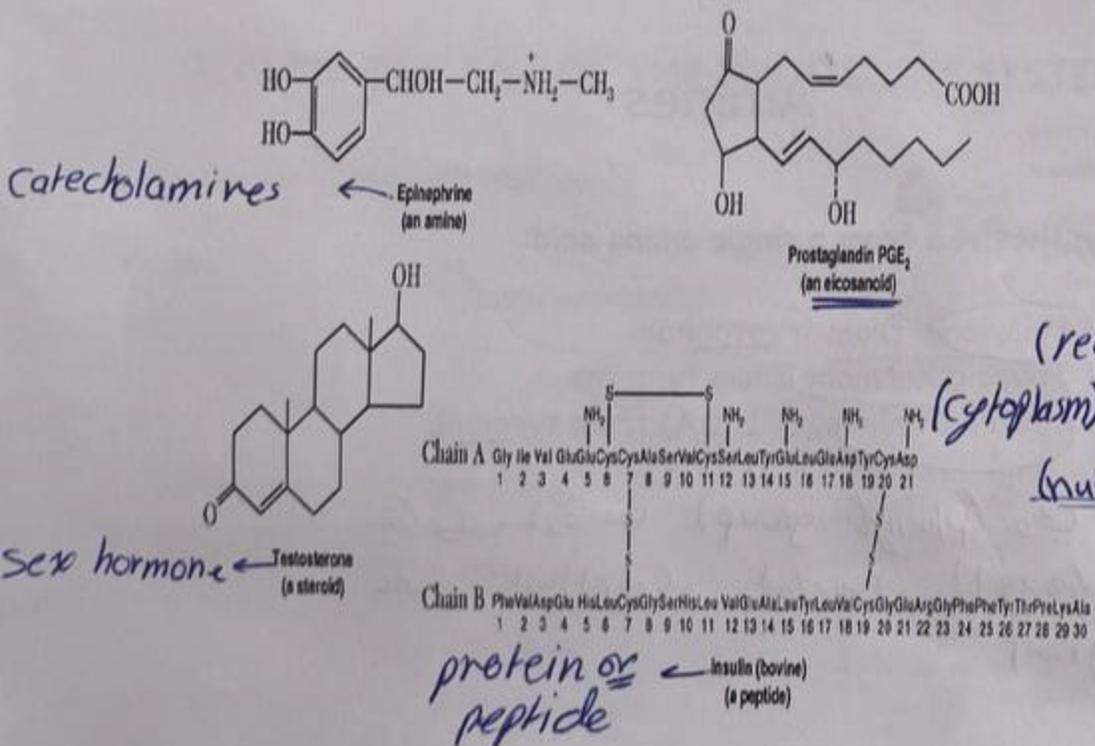
هورمونيات معروفه
الانواع

Chemical characteristics of hormones

- Amines (from tyrosine)
 - hydroxylation - catecholamines
 - iodination - thyroid hormones
- Peptides/proteins → insuline
- Steroids (from cholesterol)
 - adrenocorticoids
 - sex hormones
 - active metabolites of vitamin D_X
- Ecosanoid
 - Prostaglandins

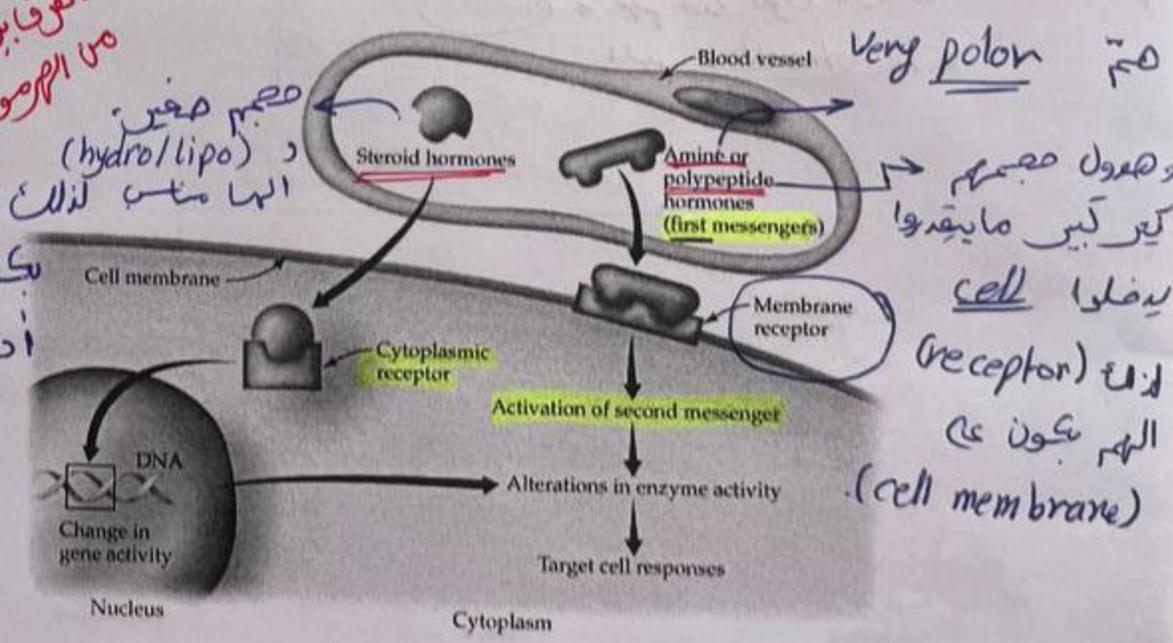
Dopamine.
epinephrine.
Norepinephrine.

هورمون الريح نرسهم
هاد ليد



ليتر مهم معروف
من الهرمون
الفرق بين كل نوع

Hormone + Receptor



Very polar
وهول مصيهم
كيس مايقدوا
يدلوا cell
لذ (receptor)
الهم يكون على
(cell membrane)

Protein/Peptide Hormones

هاد شئ الهم ←

- Hydrophilic
- Large
- Can't pass through membrane
- Second messenger mechanism of action
- Most hormones are polypeptides in nature
- Example: Insulin

Steroid Hormones

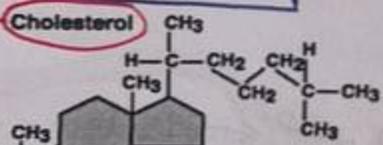
- Small
- Hydrophobic/Lipophilic
- Travel in blood w/carrier
- Have Cytoplasmic or nuclear receptors
- Affect protein synthesis
- Example: estradiol

Steroid Hormones

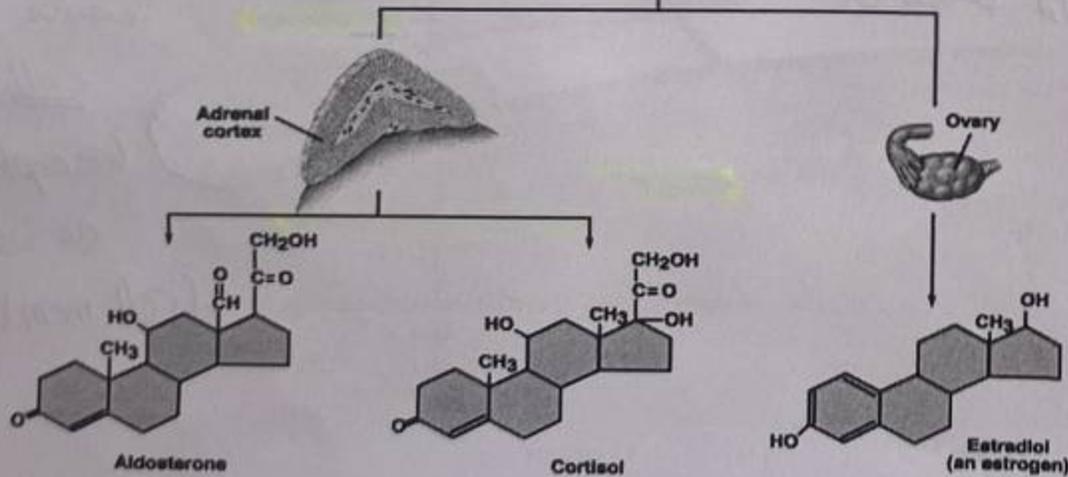
ovary/sex organ

Adrenal cortex ← يصنع هورمون في مكانين

(precursor) ← مهم جدا فرق شوهو (cholesterol) = الهم



is modified by enzymes to make steroid hormones such as



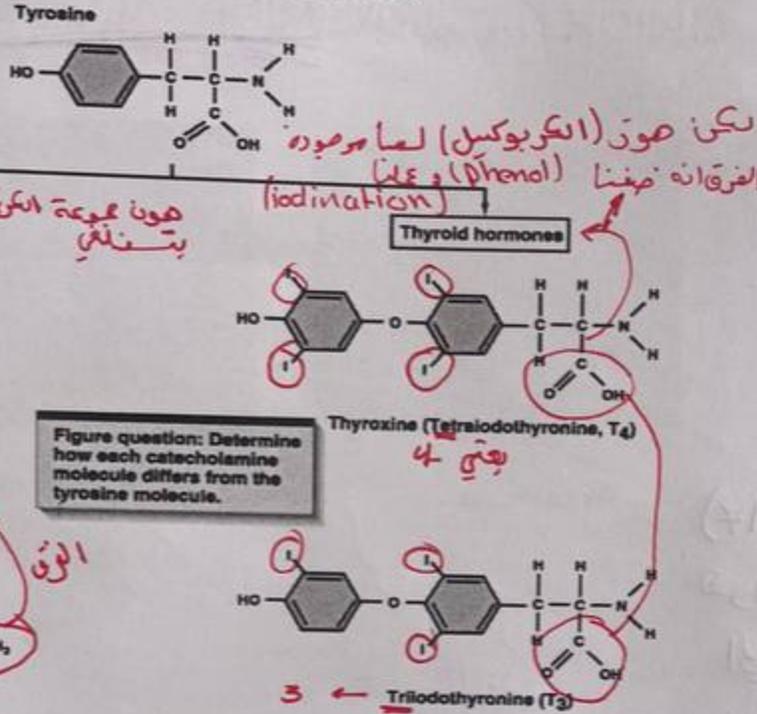
Amines

- Synthesized from a single amino acid:
- Melatonin from tryptophan
- Thyroid hormone from tyrosine
- Catecholamines (EPI, DA) from tyrosine

يتكون عبارة عن (phenyl group) وفي
على (ortho) و (meta) - hydroxy (group)

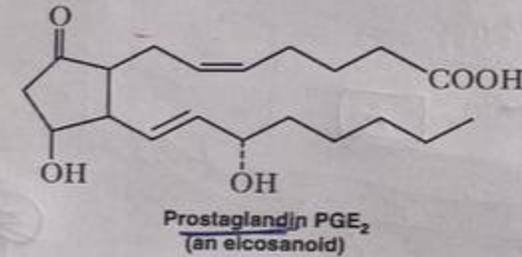
Amine hormones

هذا يتبرصهم تعرفه



Eicosanoid

- Produced from 20-carbon fatty acid, arachidonic acid
- Produced in all cells except RBCs
- Act as 2nd messenger
- Prostaglandins and leukotrienes are among these hormones
- Play a major role in inflammation process

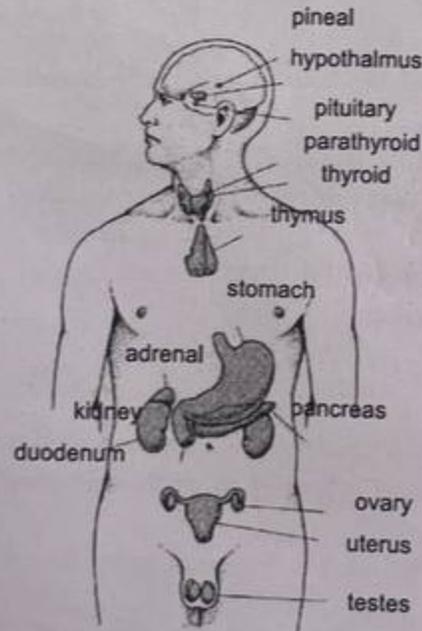


HUMAN ORGANS OF THE ENDOCRINE SYSTEM

Steroid hormones are synthesised primarily in:

- Adrenal Cortex - Adrenocorticoids
- Ovaries, testes - Sex steroids

Steroid secretion is generally controlled by peptides secreted from the Hypothalamus and pituitary



Steroidal hormones

These hormones are classified as:

1. Sex hormones produced by genital glands: estrogens, progestins & androgens.

2. Adrenocortical hormones:

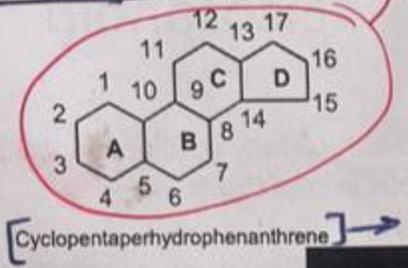
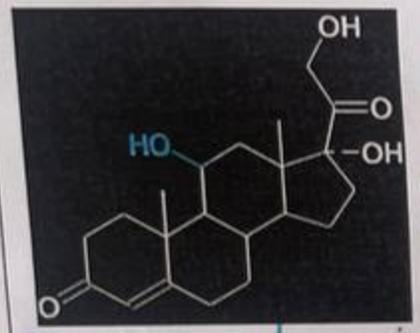
a. Mineralocorticoids: control salts & water

b. Glucocorticoids: indicated in the treatment of collagen diseases (rheumatoid arthritis), asthma, hay fever, serum sickness & various skin & eye disorders.

هو ما هو يعرف الاستظاماتهم المهم يعرف (SAR)

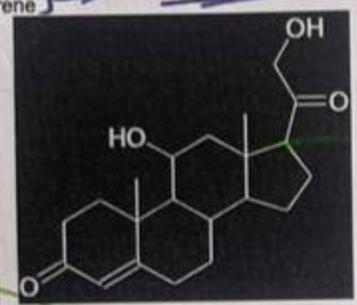
هم جدًا مبدئي في وصول الأرقام (نظفهم) عنان الامتحان يتساءلنا عن
 هذا (position) بنعله هيك أو صيغته.

MAJOR NATURAL GLUCOCORTICOIDS



سؤال في الامتحان
 مهة

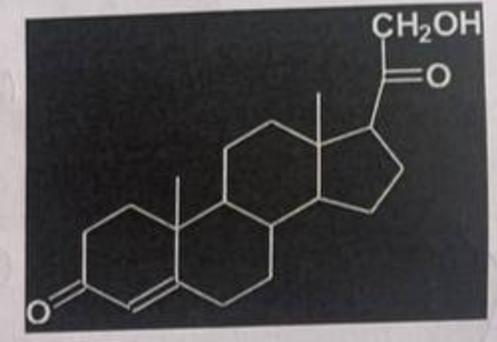
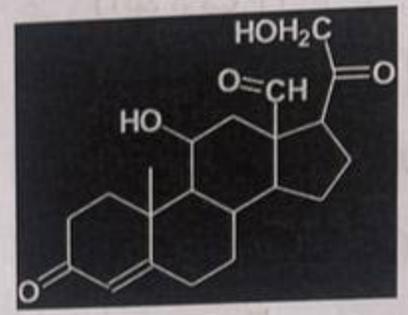
Backbone



1 Cortisol (hydrocortisone)
 الفرق بينهم نفس
 هاد (OH) تحولت إلى
 هاد (OH)
 (hydrocortisone)

3 Corticosterone (OH)
 هون (OH) التي كانت موجودة عليها رامت

MAJOR NATURAL MINERALOCORTICOIDS

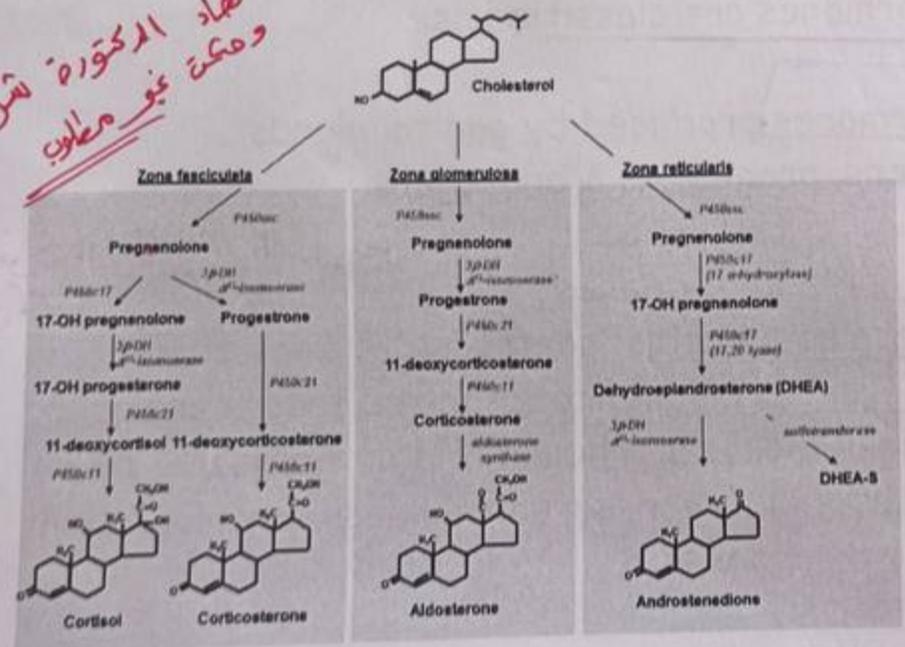


Aldosterone

desoxycorticosterone

Biosynthesis OF Mineralocorticoids and Glucocorticoids

هاد الركيزة شرحتها
 وبعدها غير مطلوب



ANTIINFLAMMATORY EFFECTS OF GLUCOCORTICOIDS

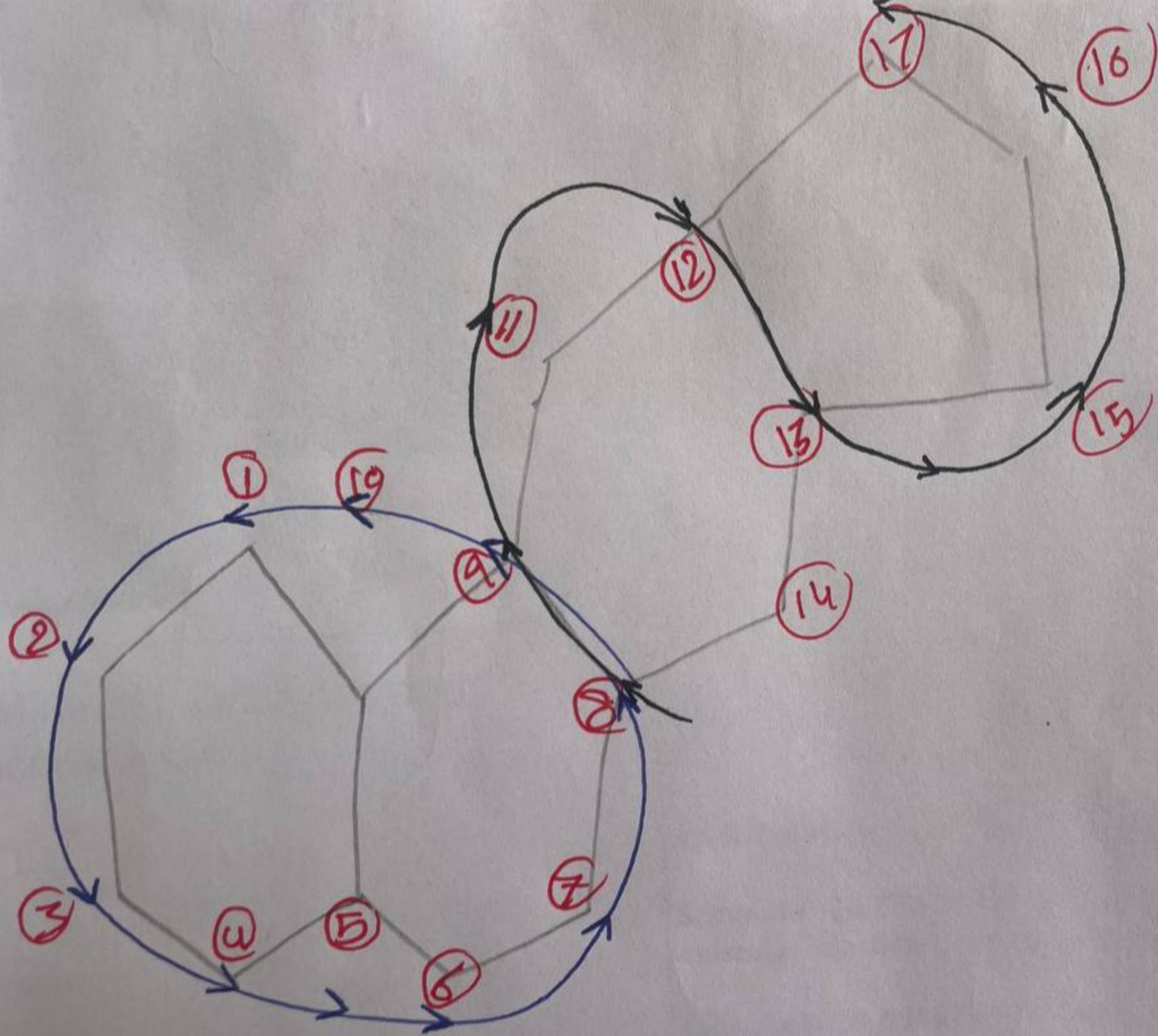
April, 1948 1 Gram cortisone isolated by Kendall

September 21, 1948 Hensch administers 100mg of cortisone by intramuscular injection to patient Mrs. G. suffering chronic Rheumatoid Arthritis

September 28, 1948 Mrs. G. first time in years walks downtown to go shopping.

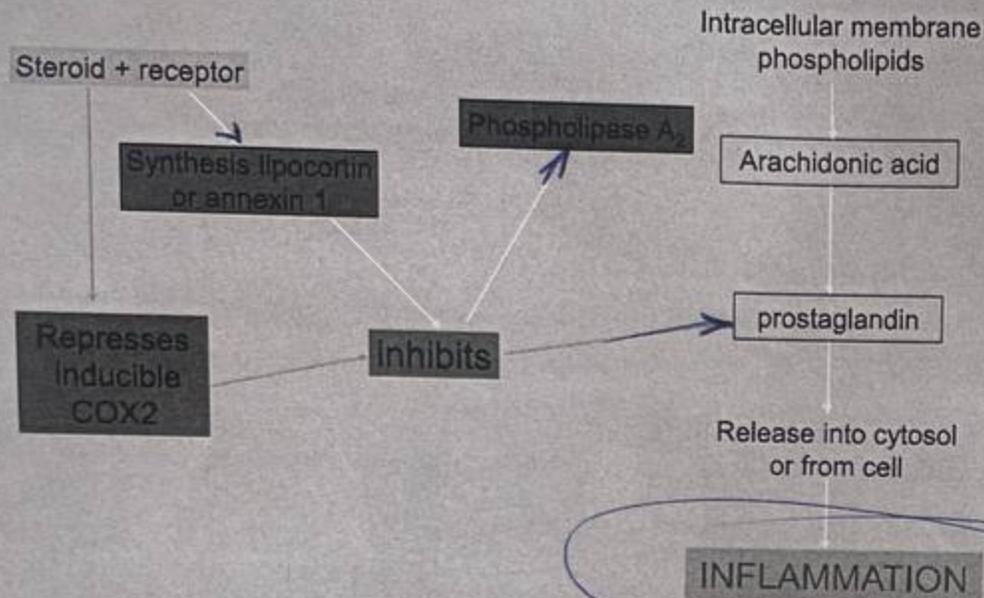
Represented a new approach to therapy with natural hormones by utilizing a dose much higher than that naturally produced by the body

i.e. pharmacological rather than physiological dose.



فكرة الذاكرة
 بكيفية حفظ
 الترتيب، بنفس
 باتجاه اليمين

MODE OF ACTION of GLUCOCORTICOIDS IN PREVENTING INFLAMMATION



THERAPEUTIC APPLICATION ADRENOCORTICOIDS

Glucocorticoids (GR)

Agonists - adrenal insufficiency
- rheumatoid disease and allergic manifestations
(eg. severe asthma, rheumatoid arthritis, rheumatic fever)

Palliative therapy only not curative

Antagonists - Cushing's Syndrome (hyperadrenocorticism or hypercorticism).

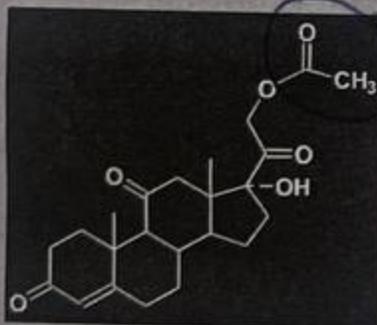
Mineralocorticoids (MR)

Agonists - adrenal insufficiency, generally glucocorticoids used in this application

Antagonists - Cushing's syndrome
- test functioning of hypothalamo-pituitary axis

CORTISONE PREPARATIONS

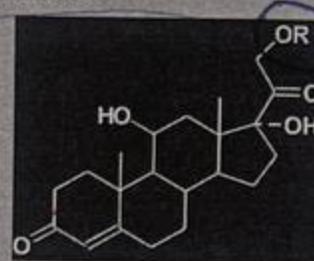
Cortisone is primarily used as its 21-acetate because of increased stability and longer duration of action



Oral or intramuscular dose usually 25 mg 4 times daily

Topically 1 to 2.5% lotion

Other 21-ester derivatives available include:



Hydrocortisone cypionate R =

Hydrocortamate sodium succinate
R = Na⁺-OOCCH₂CH₂CO⁻ (water soluble)
Intravenous, emergency treatment

RELATIVE POTENCIES OF CORTICOSTEROIDS

Compound	Na ⁺ retention	Hepatic glycogen deposition	Antiinflammatory effect
Cortisol	1	1	1
Cortisone	0.8	0.8	0.8
Corticosterone	15	0.35	0.3
11-desoxycortisone	100	0	0
Aldosterone	3000	0.3	0.3

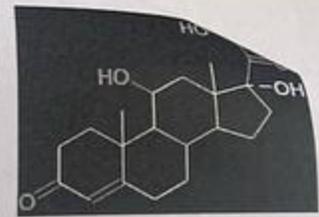
Most natural or synthetic compounds have some activity at both GR and MR receptors

oral (oral) (ionized) (ionized)

STRUCTURE-ACTIVITY OF GLUCOCORTICOIDS

لا ينجح إلا إذا (mineralocorticoid)
 جعل (water retention)
 بتزويد كمية الستيرويد
 وينقل كمية الستيرويد

SAR

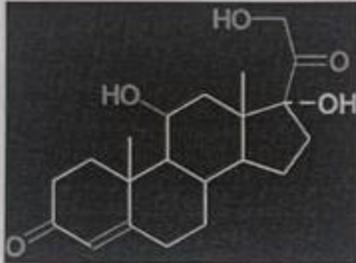


Intensive efforts for compounds with reduced mineralocorticoid activity

Structure-activity for glucocorticoid activity

Required for activity

- 1 3-keto group
- 2 4,5-double bond
- 3 11-oxygen (keto or alcohol)
- 4 17-β keto sidechain



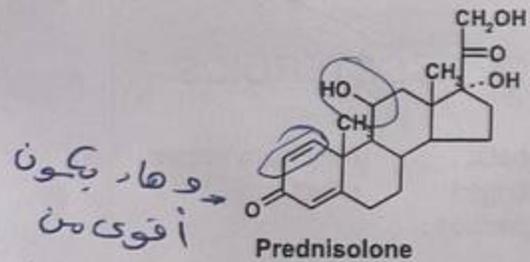
يعني على كورتيزون
 لا زال مهم

اهم شي لا زال يبقى

1. The steroid is a mineralocorticoid if it contains no oxygen-function at C11.
2. Oxygen at C11 is essential for glucocorticoids and alcoholic is superior than ketonic one.
3. Introduction of 17-α-OH increases glucocorticoid activity.
4. Introduction of 6-α-F or 9-α-F increases both glucocorticoid & mineralocorticoid activity.
5. Double bond at C1 increases antiinflammatory activity & decreases mineralocorticoid effects.

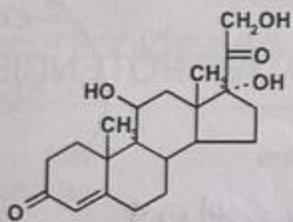
22

Synthetic Corticosteroids



Prednisolone

وهذا يكون أقوى من



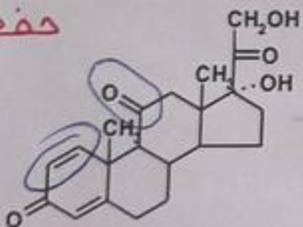
Hydrocortisone

Prednisone Hydrocortisone: 11-β, 17-α, 21-trihydroxy-pregn-4-ene-3,20-dione.

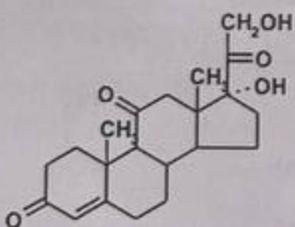
(brand name) مثل حقن

مطلوب منا نعرف من (α) ومن (β).

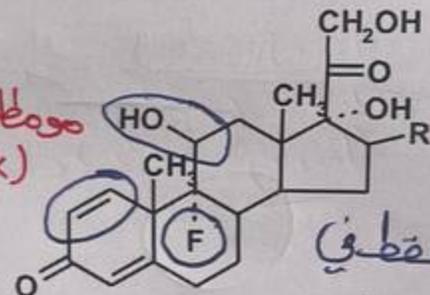
في التسمية مثل حفظ.



Prednisone



cortisone



بمختلفة عن بعض فقط في
 CH₃ (orientation)

- Diproflose: (R = 16-β-CH₃) Betamethasone.
- Decadron: (R = 16-α-CH₃) Dexamethasone.
- Kenacort: (R = 16-α-OH) Triamcinolone.

أما هذا بإضافة (OH) أقل جداً
 (mineralocorticoid activity)

Triamcinolone acetonide is the acetone ketal with Both (OH) at C-16 & C-17.

24

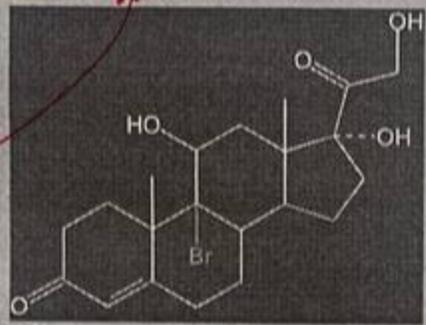
هذه مهم نعرف (substitution) الى صبار؛ لانه ممكن يعرف لسؤال
 عند مقارنة بين مركبات من أقوى (mineralo/glucocorticoids)

Synthetic Corticosteroids

F < Cl < Br < I

9 α -bromo analogue

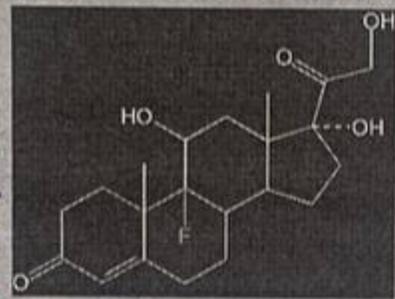
1/3 activity of cortisone acetate



Glucocorticoid activity inversely Proportional to size of 9 α -halogen

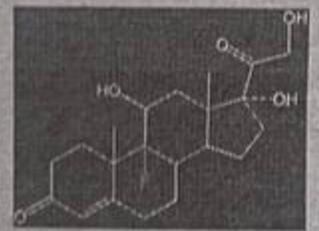
11 times activity of cortisone acetate

Fludrocortisone

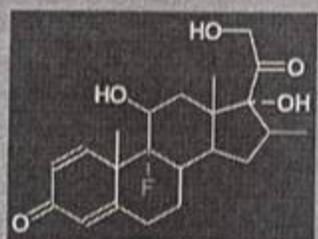


بما انه (F) زاد فعالية الستيرويد مرتين تقريباً (halogen) ثاني. فيما (Br) ؛ لكن بسبب حجمه العكس قلّت الفعالية. بالنسبة لـ (Cl) الفعالية رح تكون متوسطه؛ لكن الافضل (F)

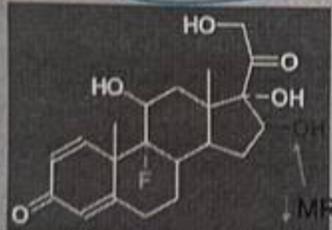
SYNTHETIC GLUCOCORTICOIDS



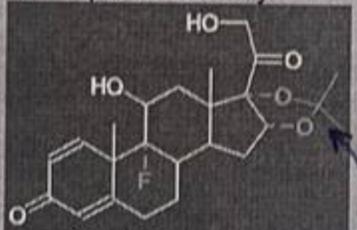
Fludrocortisone (GR activity 11) MR activity 300-800 fold



betamethasone GR 35 fold Rheumatic and dermatologic disorders Short period use only



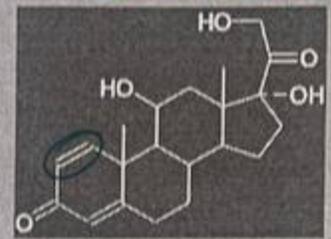
triamcinolone GR 5 fold MR activity 20% more effective than prednisolone Unusual toxic side effects



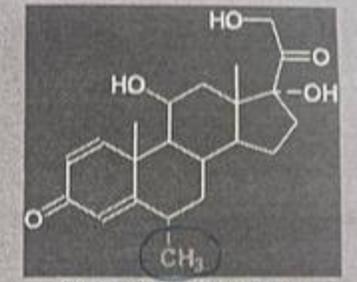
triamcinolone acetonide Used topically for treatment of psoriasis and other skin conditions

SYNTHETIC GLUCOCORTICOIDS

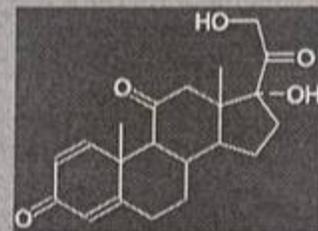
Prednisolone (GR 4 MR unchanged)



Rheumatoid arthritis 2-4 mg /day



Methylprednisolone (GR 5 MR unchanged)



Prednisone (GR 4 MR unchanged)

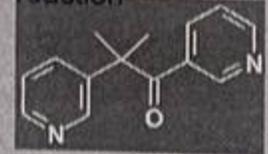
Greater activity allows smaller doses to be used reducing side effects

Prednisone and Prednisolone can be used interchangeably

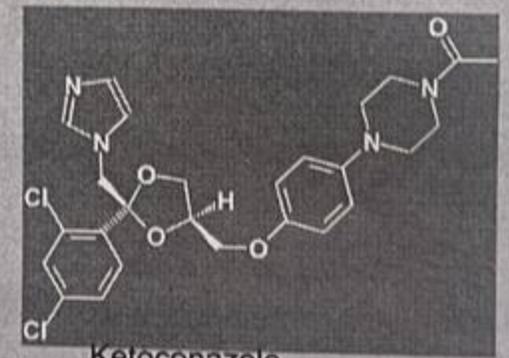
INHIBITORS OF BIOSYNTHESIS OF CORTICOSTEROIDS

Metyrapone

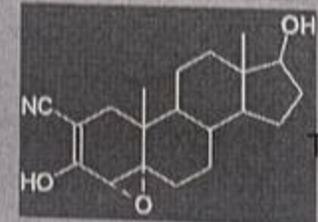
inhibits 11 β -hydroxylation reaction



Used for diagnosis hypothalmo-pituitary malfunction

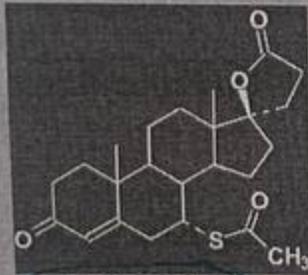


Ketoconazole blocks cholesterol sidechain cleavage in the adrenal (Cushings Syndrome)



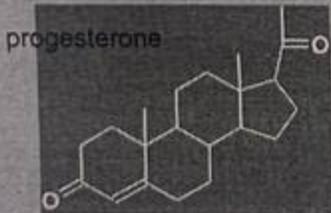
Trilostane inhibits 3 β -hydroxysteroid dehydrogenase (Cushings Syndrome - currently not recommended)

ADRENOCORTICOID ANTAGONISTS

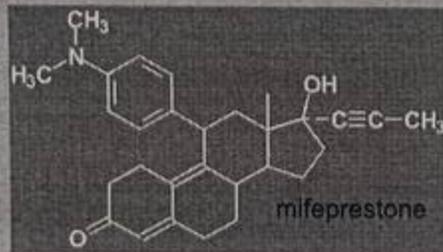


Spironolactone

Diuretic response of increased Na⁺ excretion and K⁺ retention



progesterone
mineralocorticoid antagonist



mifepristone
glucocorticoid antagonist

ممن نفوق عن (antagonists)

هدول (natural)

Summary

1. Glucocorticoids modulate carbohydrate metabolism ie cortisol, cortisone
2. Mineralocorticoids modulate water balance and Na⁺/K⁺ transport ie aldosterone and desoxycorticosterone
3. Biosynthesis of corticosteroids starts with cholesterol the pregnenolone then progesterone and then final hormone
4. Antiinflammatory effects of glucocorticoids mediated by inhibition of phospholipase A₂, inducible COX2 and annexin I → عشان هتأثر بـ (lipocortin) هونفسا
5. 17-esterification facilitates administration
6. All corticosteroids contain both glucocorticoid and mineralocorticoid activity
7. SAR for glucocorticoid activity: 3-keto, 4,5-double bond, 11-oxy, 17-β ketol all essential for activity

مثال

ممن جزاً ندرينه

وهاد يفضل يكون الـ OH

هاد جزاً ممن . عليه الأسترة هادي
خلته (prodrug) و هاد بنفرد نفوقه
(oral)