



تفريغ ميديسينال

Hormon

محاضرة:

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لجان الرفعات



Hormones

شو تعرفهم؟

- Are chemical released ¹ by a cell or a ² 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 الغدد الصماء
 - Specific to target
 - Activate cellular change

Chemical characteristics of hormones

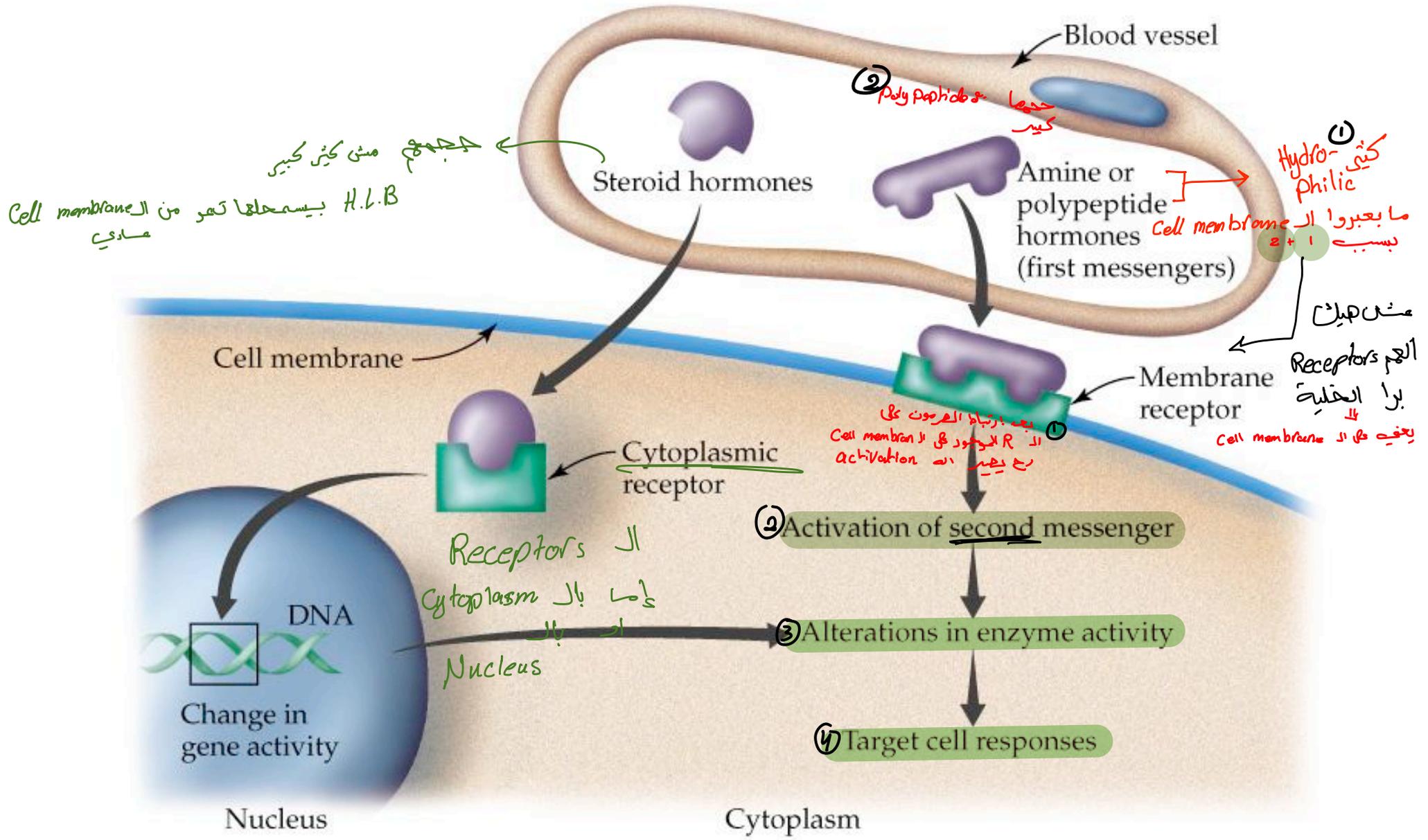
- **Amines (from tyrosine)**
 - hydroxylation - catecholamines
 - iodination - thyroid hormones
- **Peptides/proteins**
- **Steroids (from cholesterol)**
 - adrenocorticoids
 - sex hormones
 - active metabolites of vitamin D
- **Eicosanoid**
 - Prostaglandins

العصبية بزر الحبال
منه ما راجه نخاعي عصبهم

الى تصيب
هم امثلة عليهم

Handwritten flourish

Hormone + Receptor



Protein/Peptide Hormones

نفس الكلام الى على
الرسمة

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

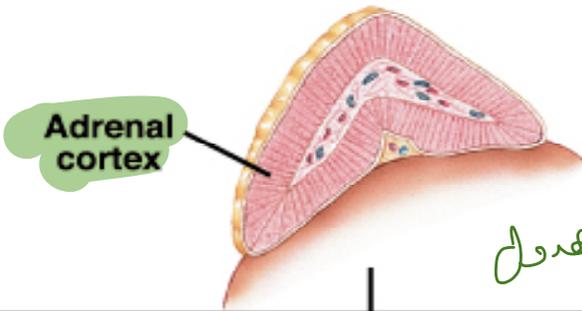
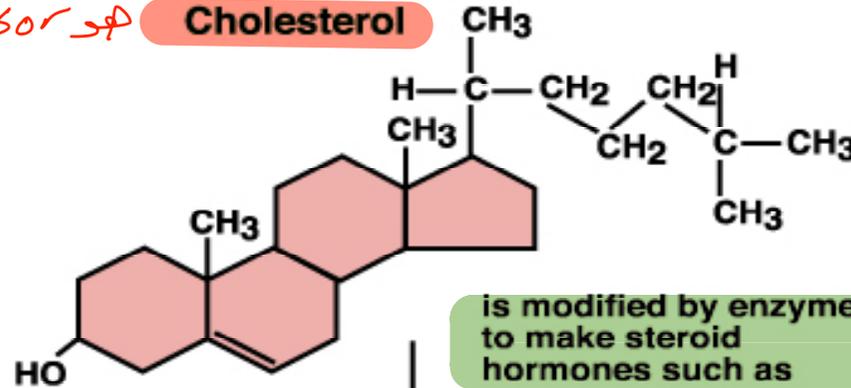
Steroid Hormones

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

Steroid Hormones

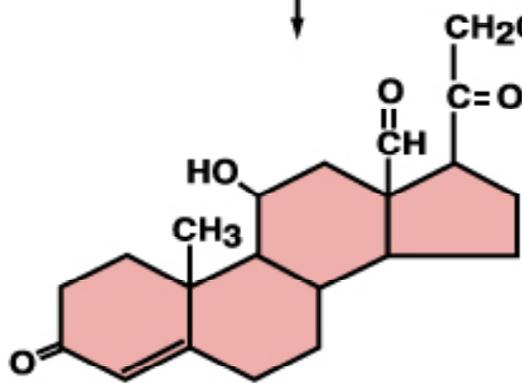
precursor →

Cholesterol

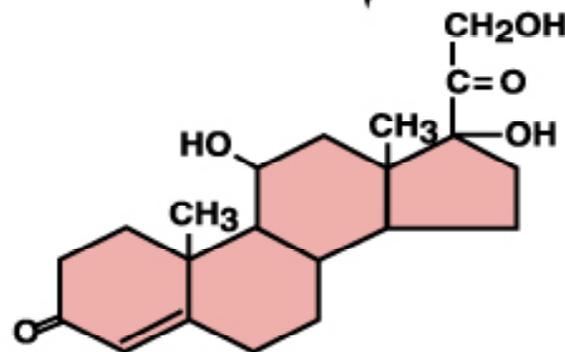


فإنه ← راجع
تركز على الهدول

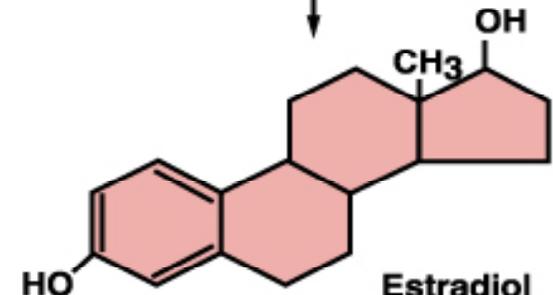
هدول
العم شابتي
لحال



Aldosterone



Cortisol



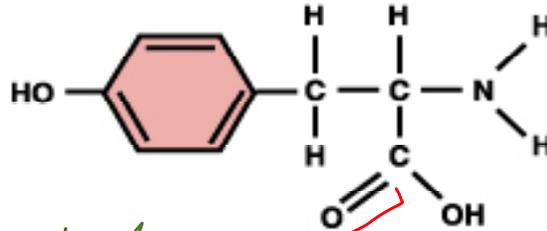
Estradiol
(an estrogen)

Amines

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

Amine hormones

Tyrosine

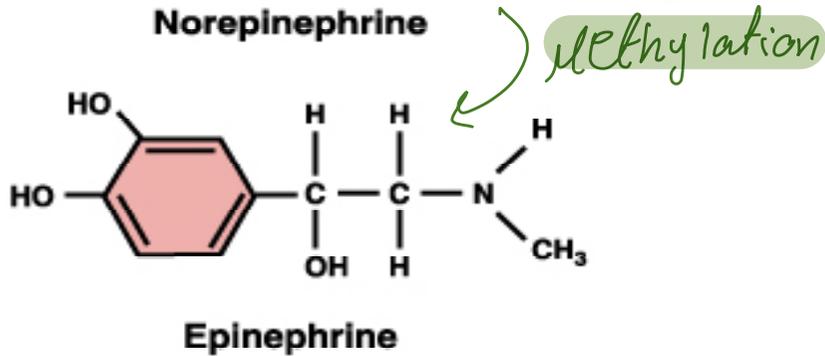
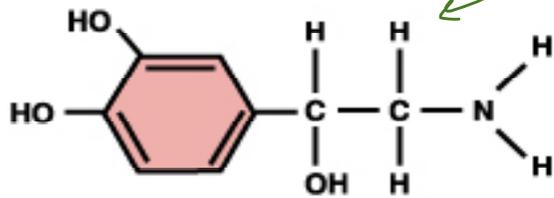
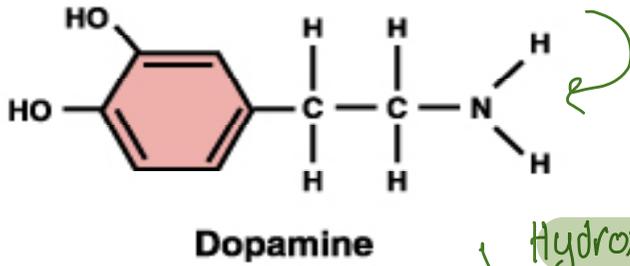


Decarboxylation

دوره از دست دادن
از قاعده آمینو
decarboxylation

addition to phenol Group + Iodin → No decarboxylation

Catecholamines

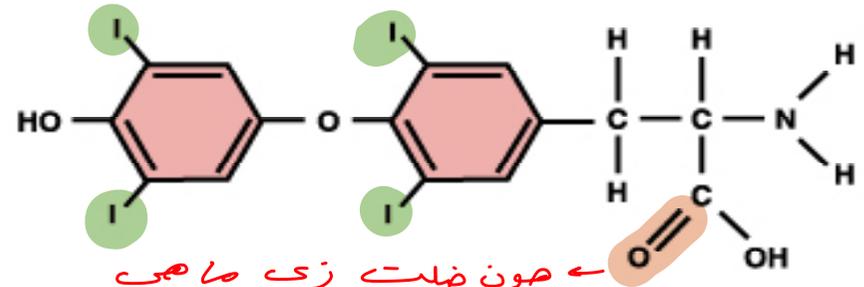


Hydroxylation

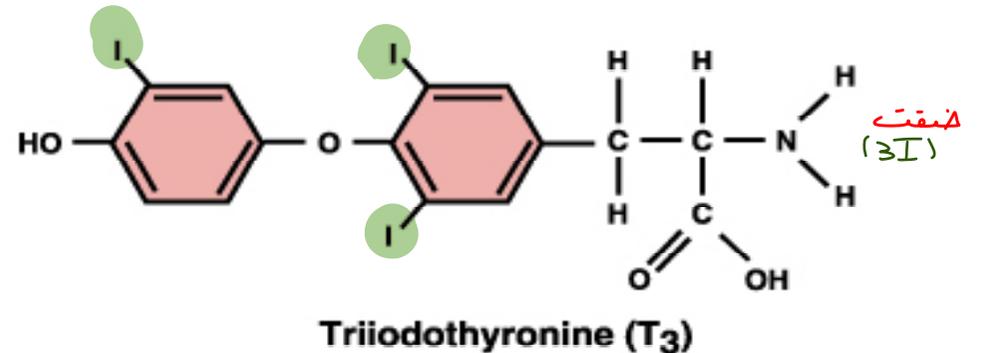
Figure question: Determine how each catecholamine molecule differs from the tyrosine molecule.

Methylation

Thyroid hormones



هفت (4I)



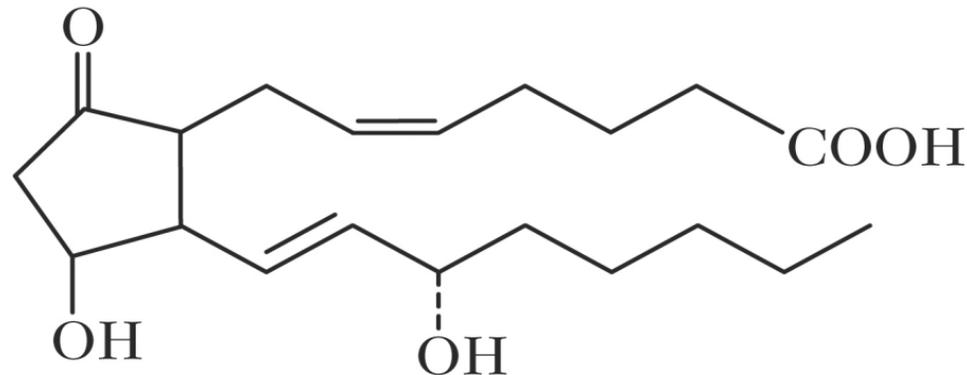
هفت (3I)

Eicosanoid

هذا ال precursor

- 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

حكيئا عنهم بالفارسي



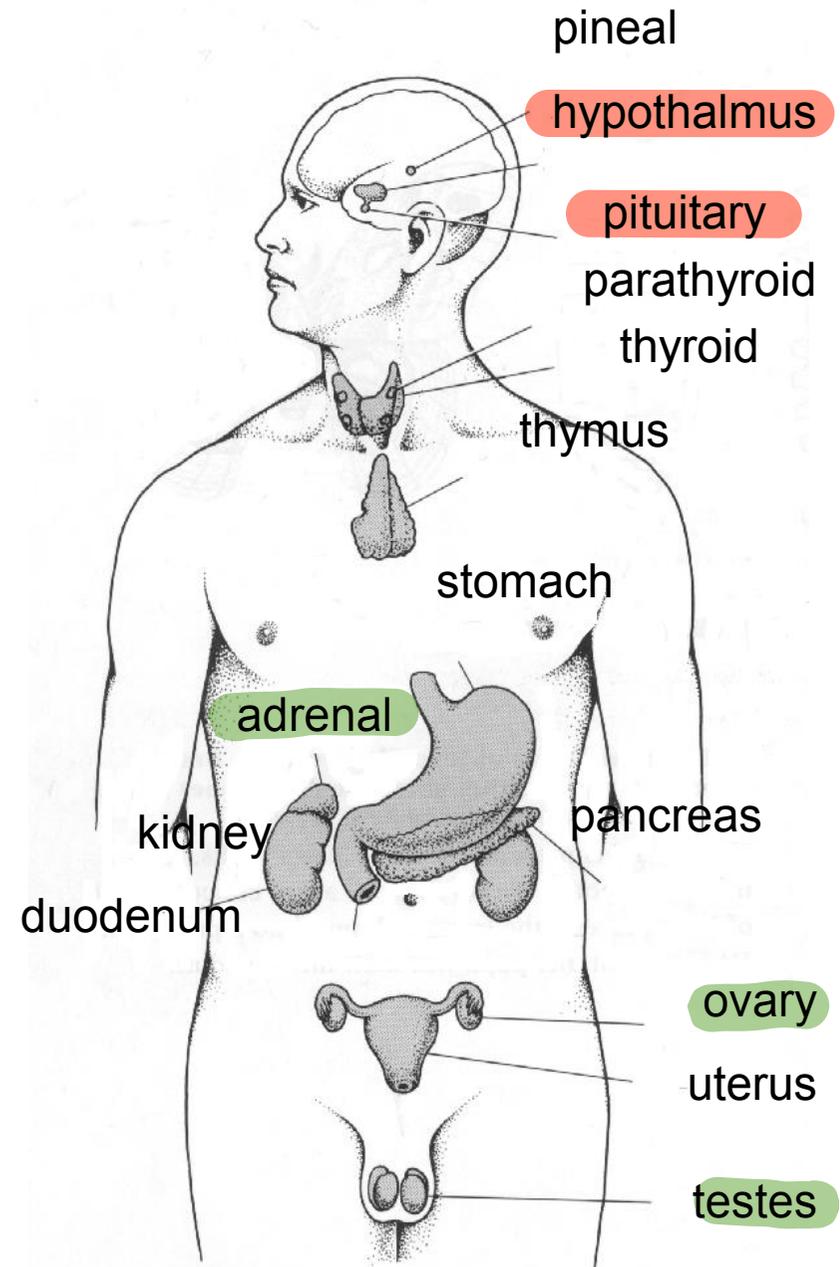
Prostaglandin PGE₂
(an eicosanoid)

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:

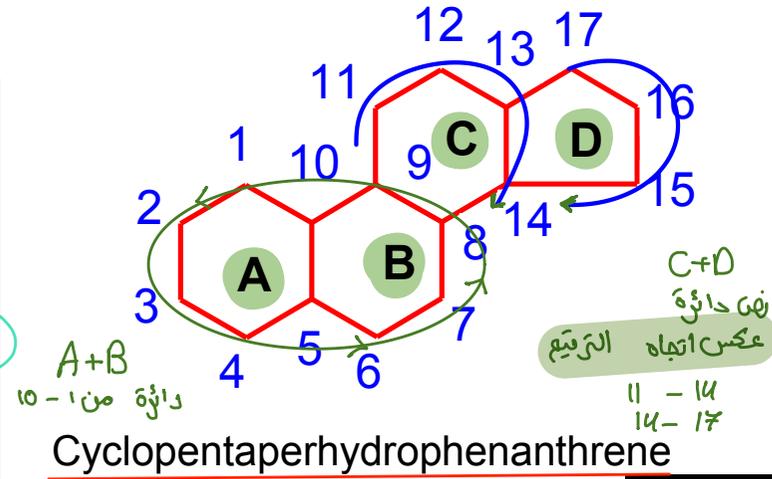
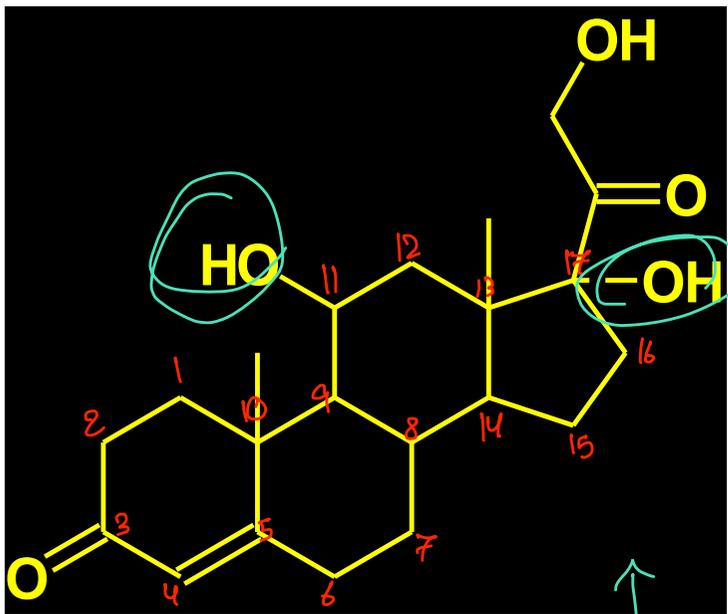
1. Sex hormones produced by genital glands: estrogens, progestins & androgens.

2. Adrenocortical hormones:

- ✓ a. Mineralocorticoids: control salts & water
- ✓ b. Glucocorticoids: indicated in the treatment of collagen diseases (rheumatoid arthritis), asthma, hey fever, serum sickness & various skin & eye disorders.

حطت انه الإستخدامات مش كثير مهمه
بس بما انه آخذناهم بالفارما مش خلا تراجمهم

MAJOR NATURAL GLUCOCORTICOIDS



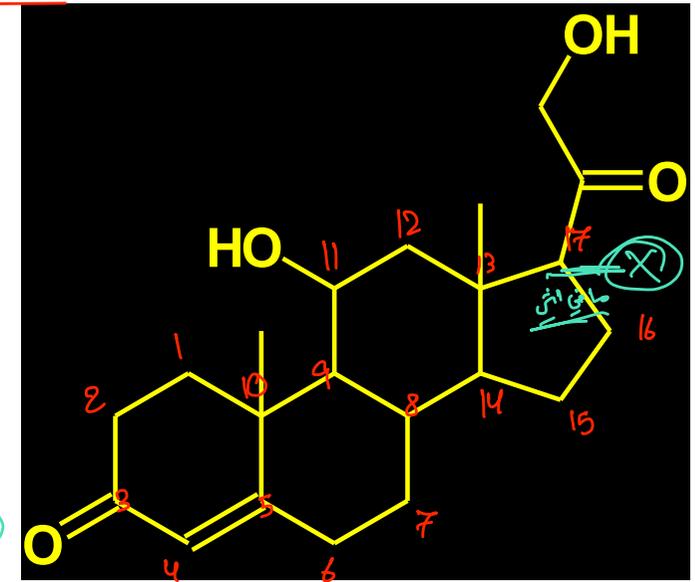
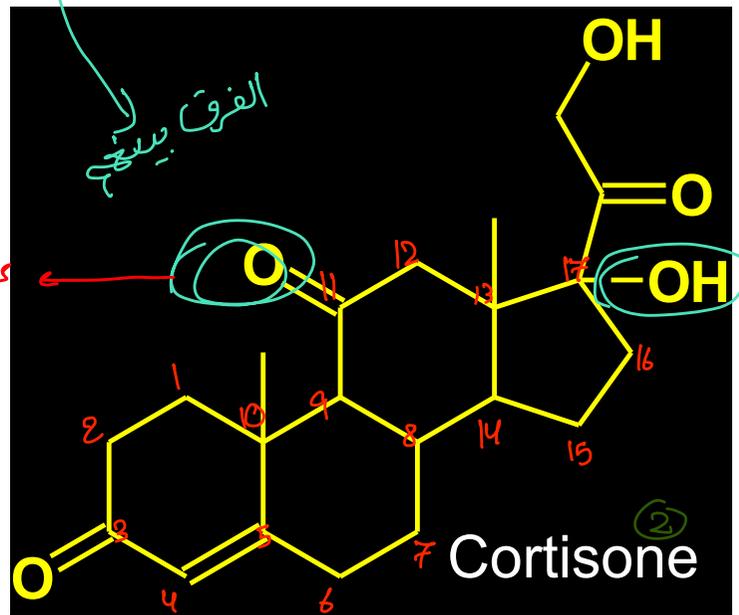
مجموع جده
نعرف المكان
والرقم لكل
كربون

Cyclopentaperhydrophenanthrene

Back Bone
هي موجودة
activity له

1 Cortisol
(hydrocortisone)

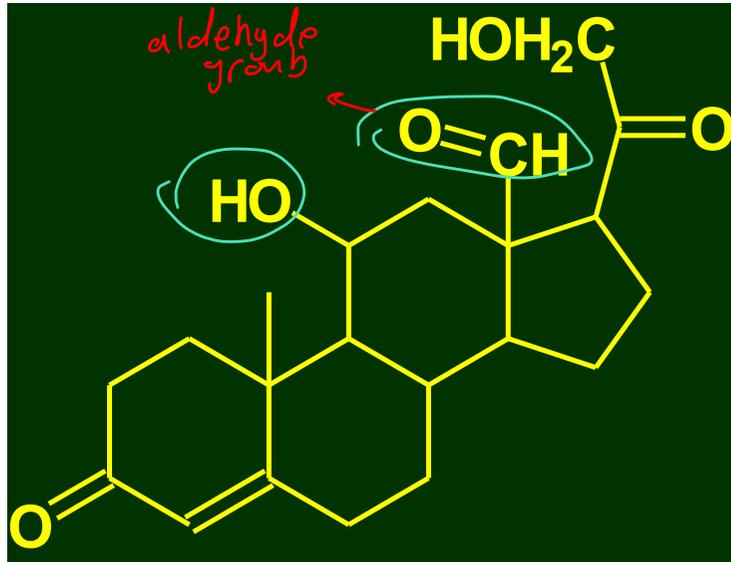
كانت (OH) بال Cortisol
بس مارت Carbonyl بال
Cortisone



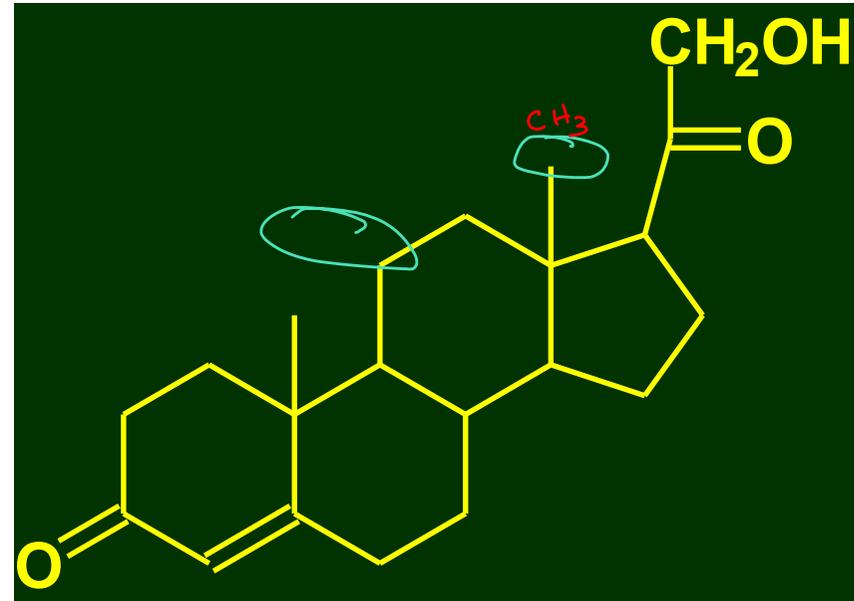
3 Corticosterone

بال Cortisone لا (C17) كان عليها OH بس
انخفضت وصار اسمه Corticosterone

MAJOR NATURAL MINERALOCORTICIDS



Aldosterone

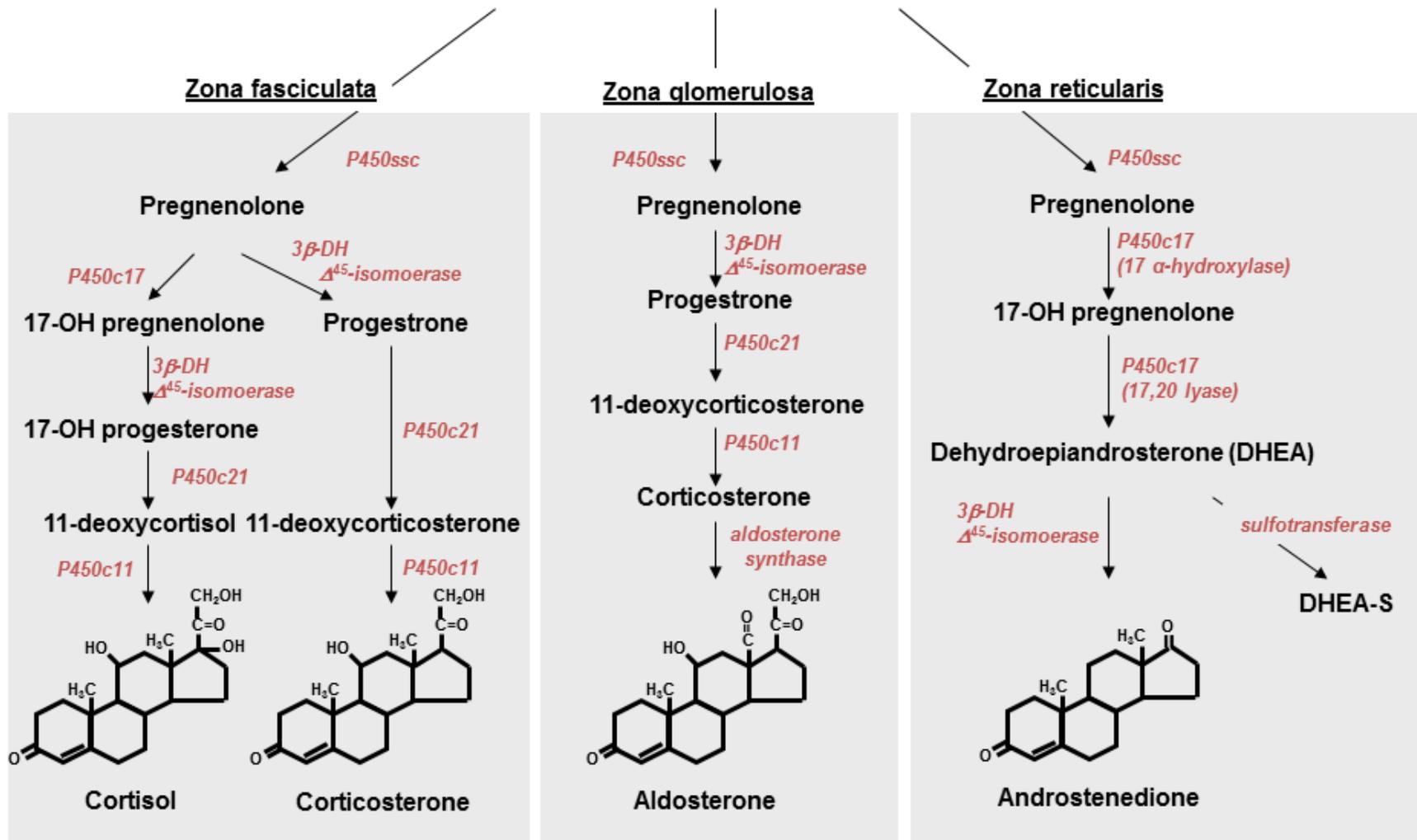
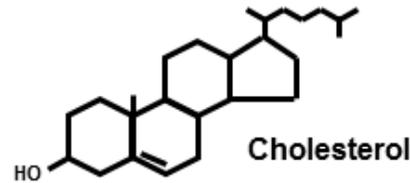


desoxycorticosterone

Biosynthesis OF Mineralocorticoids and Glucocorticoids

صارگت علیہ

Adrenal cortex باج



ANTIINFLAMMATORY EFFECTS OF GLUCOCORTICOIDS

مشويه تاريخ

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.

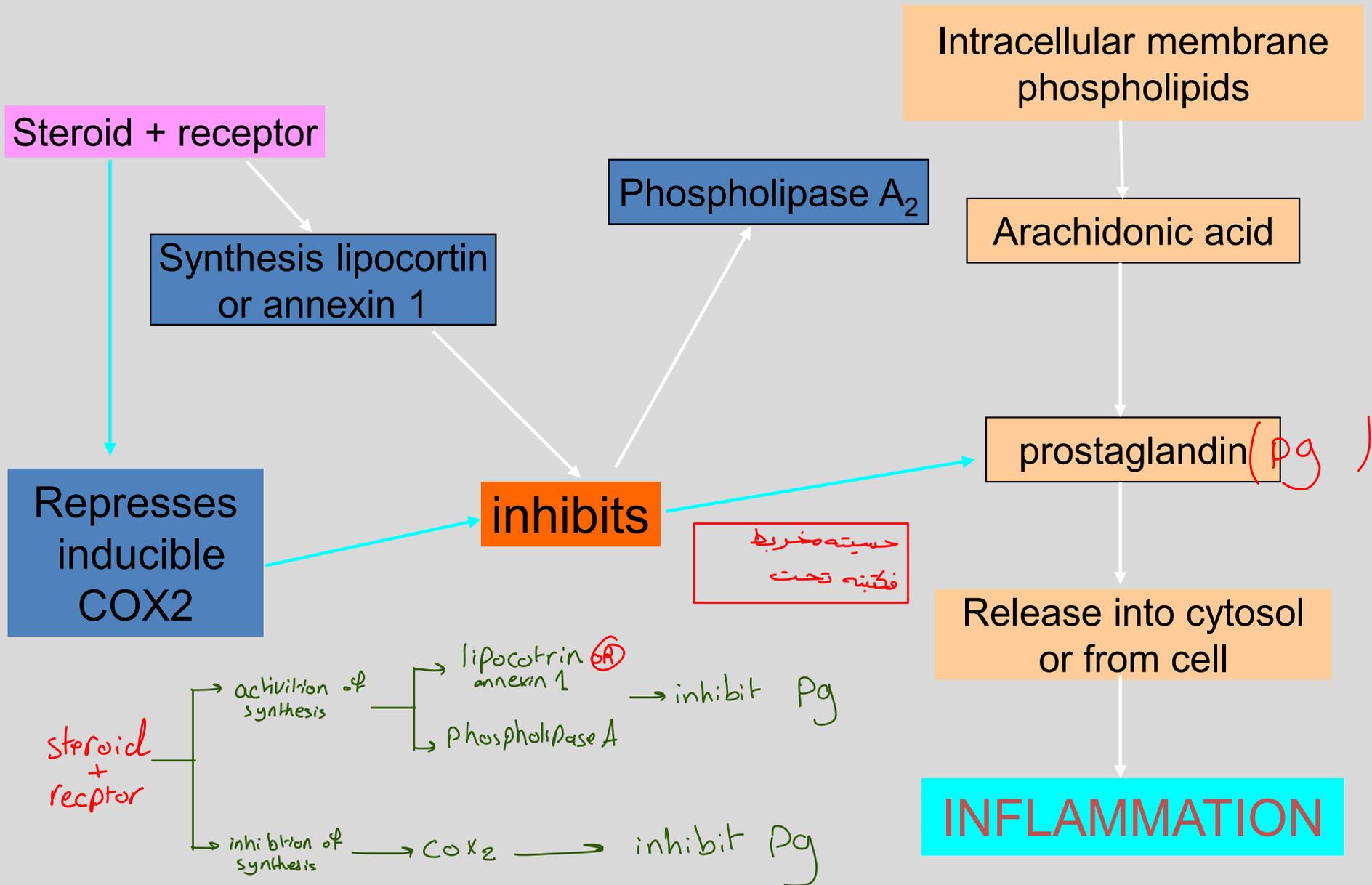
هون بحطيلك انه كانت اول مرة بنعطي ال Pharmacological dose اعلى بطور
Physiological dose لحق يعطي ال effect



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.

MODE OF ACTION of GLUCOCORTICOIDS IN PREVENTING INFLAMMATION



THERAPEUTIC APPLICATION ADRENOCORTICOIDS

منزل حكمة

فاحفظوهم

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).

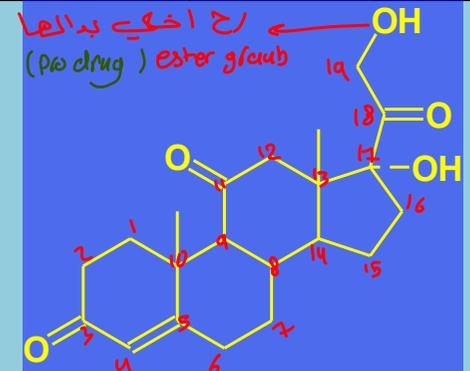
Mineralocorticoids (MR)

Agonists - adrenal insufficiency, generally glucocorticoids used in this application

Antagonists - Cushing's syndrome

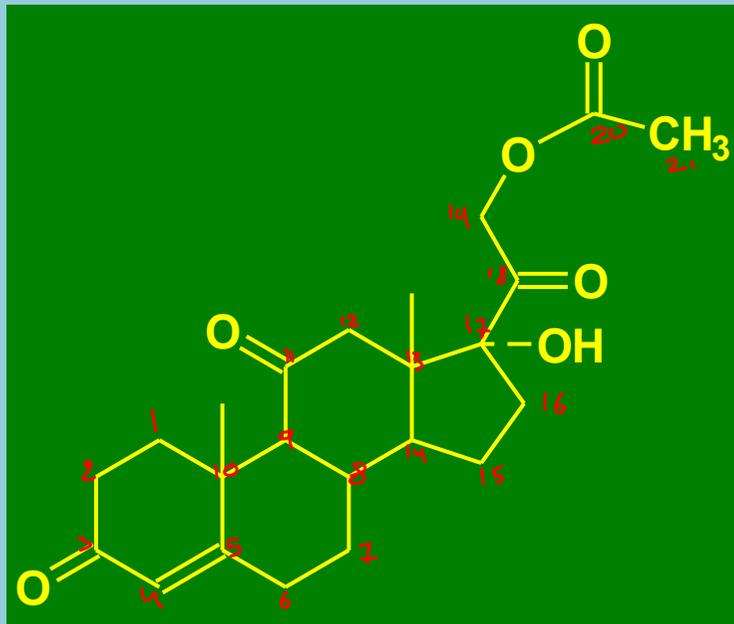
- test functioning of hypothalamo-pituitary axis

CORTISONE PREPARATIONS



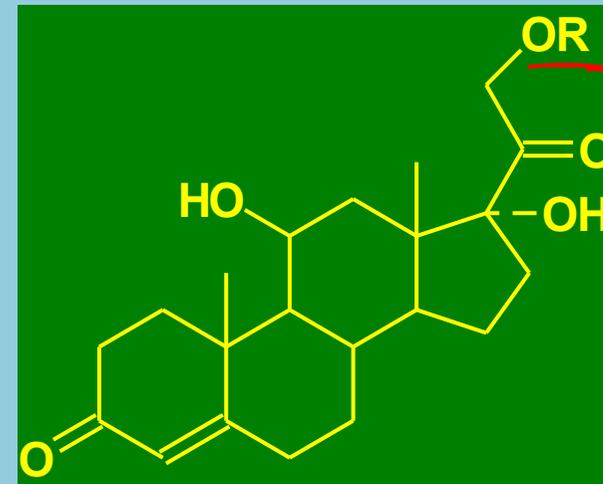
pro drug ح ا خ ي ب د ا ل ل ا

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



acetate group

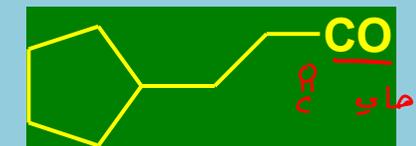
Other 21-ester derivatives available include:



Oral or intramuscular dose usually 25 mg 4 times daily

Topically 1 to 2.5% lotion

Hydrocortisone cypionate R =



Hydrocortamate sodium succinate \rightarrow (-) charge \rightarrow Non oral available
 R = $\text{Na}^+ \text{-OOCCH}_2\text{CH}_2\text{CO-}$ (water soluble)
Intravenous emergency treatment

RELATIVE POTENCIES OF CORTICOSTEROIDS

Compound	Mineralocorticosteroid activity 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-desoxycorticosterone	100	0	0
Aldosterone	3000	0.3	? around 0.6

mineralocorticosteroid activity
+
glucocorticosteroid activity

لا يوجد له نشاط لـ OH على C-17
glucocorticosteroid activity

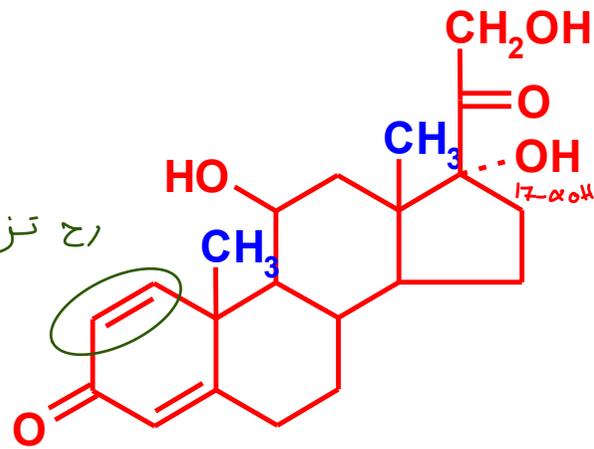
ال OH على C-11
احتياج ادنا في
mineralocorticosteroid activity
و لاني glucocorticosteroid activity

وجود ال aldehyde group
mineralocorticosteroid activity
بس يكون في OH على C-11
glucocorticosteroid activity

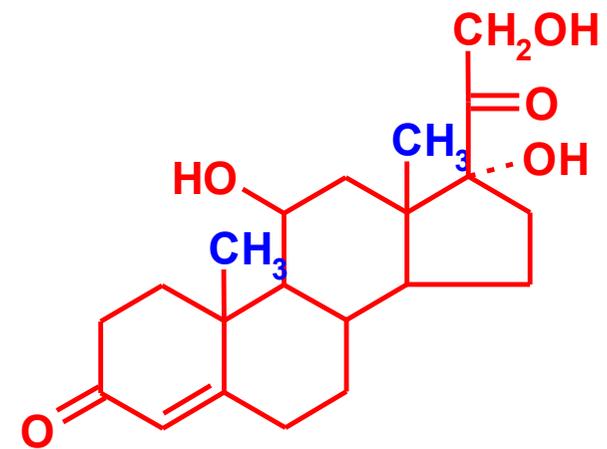
Most natural or synthetic compounds have some activity at both GR and MR receptors

glucocorticosteroid activity

ر ح تزید اد



Prednisolone



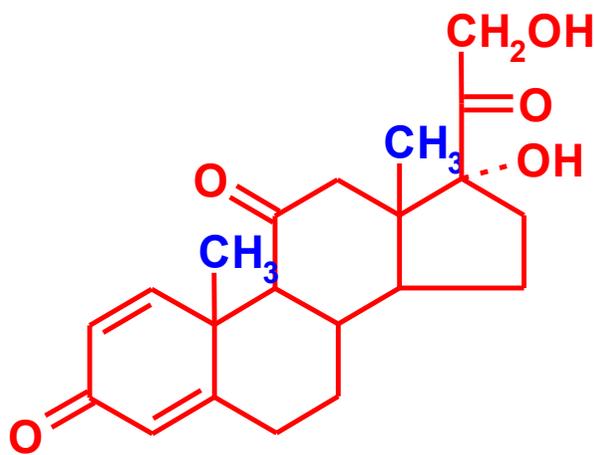
Hydrocortisone

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

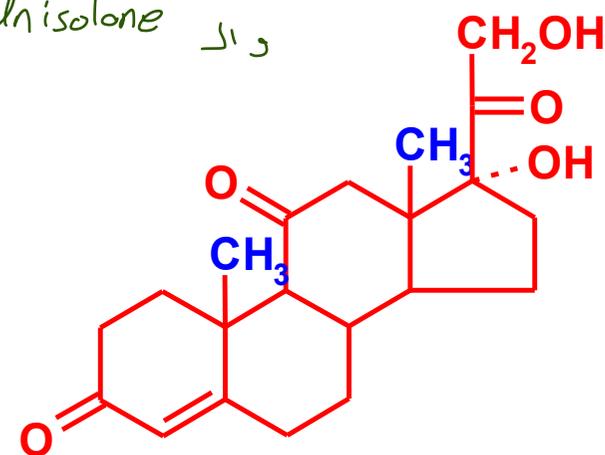
وجود اد OH على 11 (بخلي المركب الـ Potency اكثر
صا لما تـكون ح عـ (عكينا فوق انه بزيـل تكون لـه لو ح)

Cortisone < hydrocortisone الـ Potency

Prednisone < prednisolone واد



Prednisone

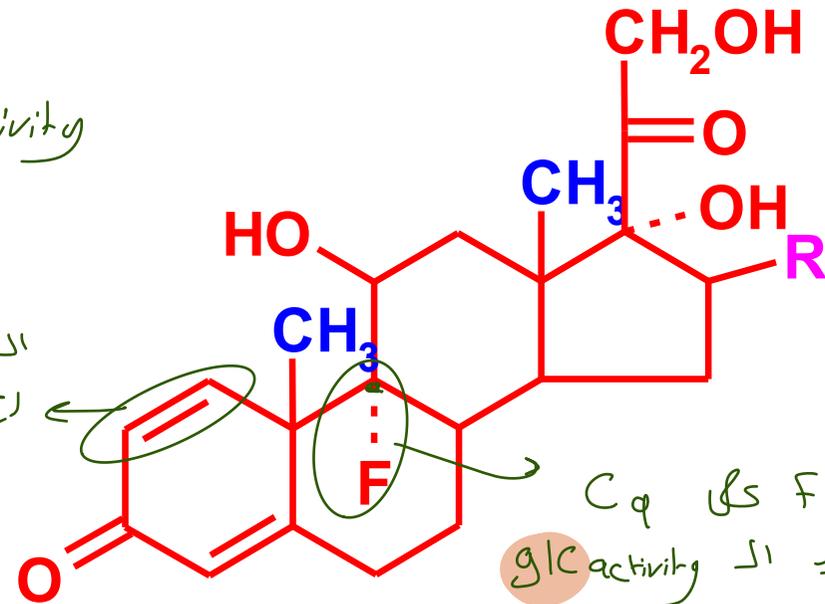


cortisone

Synthetic Corticosteroids

کمزور عشان یزیدوا ال
glucocorticosteroid activity

ال (C) بین ال C₁ وال C₂
g/c activity ←



ال F الی C₉
تیزید ال g/c activity
وال mineralocorticosteroid
activity الی ان موجود

Diprofose: (R = 16-β-CH₃) Betamethasone.

Decadron: (R = 16-α-CH₃) Dexamethasone.

Kenacort: (R = 16-α-OH) Triamcinolone.

وجود ال F مع الأسماء الثانية الی
لمفتها ح یغی المركب الی انوی
glucocorticosteroid activity
Anti-inflammatory effect

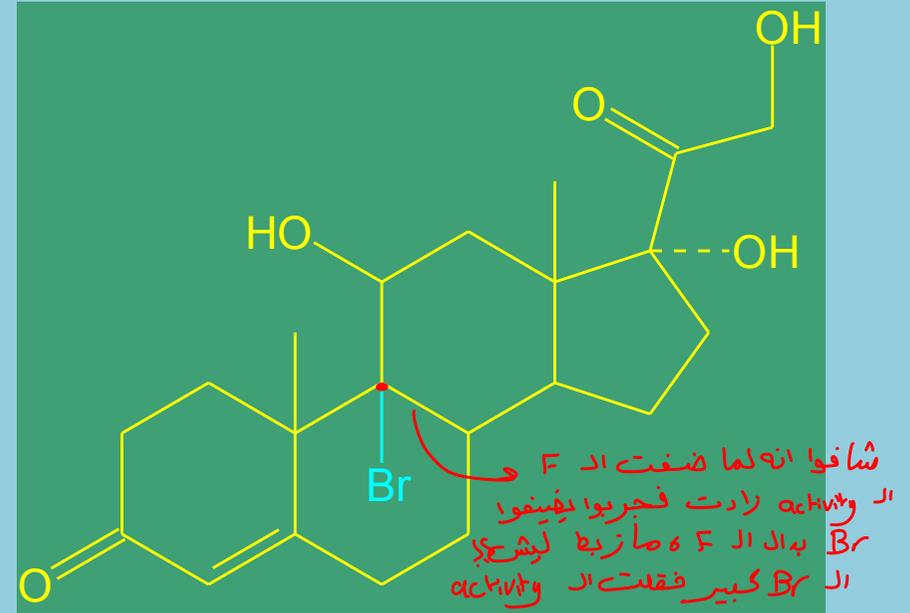
Triamcinolone acetonide is the acetone ketal with Both (OH) at C-16 & C-17.

Synthetic Corticosteroids

9 α -bromo analogue

1/3 activity of cortisone acetate

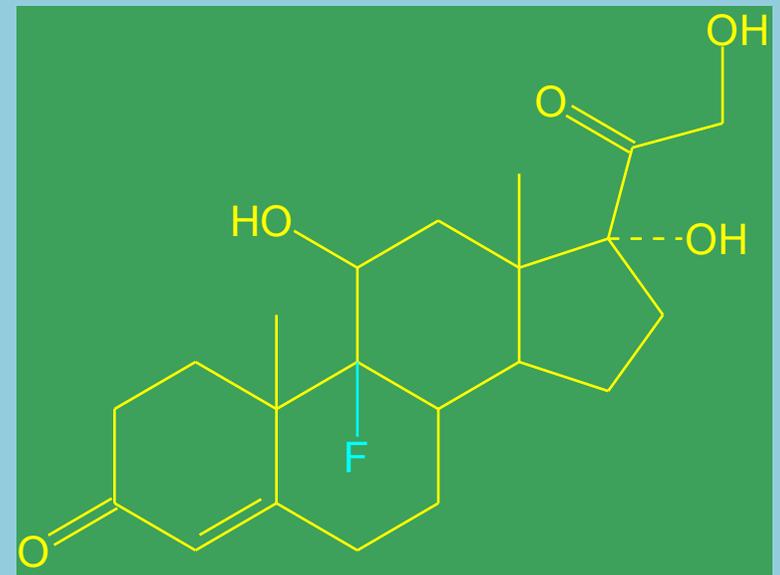
Glucocorticoid activity inversely
Proportional to size of 9 α -halogen



11 times activity of cortisone acetate

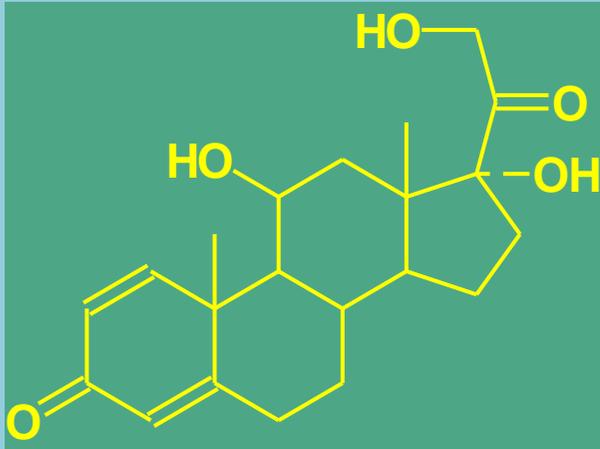
Fludrocortisone

طيب إذا ضافوا الـ F به الـ F رح يكون الـ activity اقل من المركب الي فيه الـ F و اعلى من الـ F فيه (بستنتج انه كلما زاد الحجم زادت الـ activity)

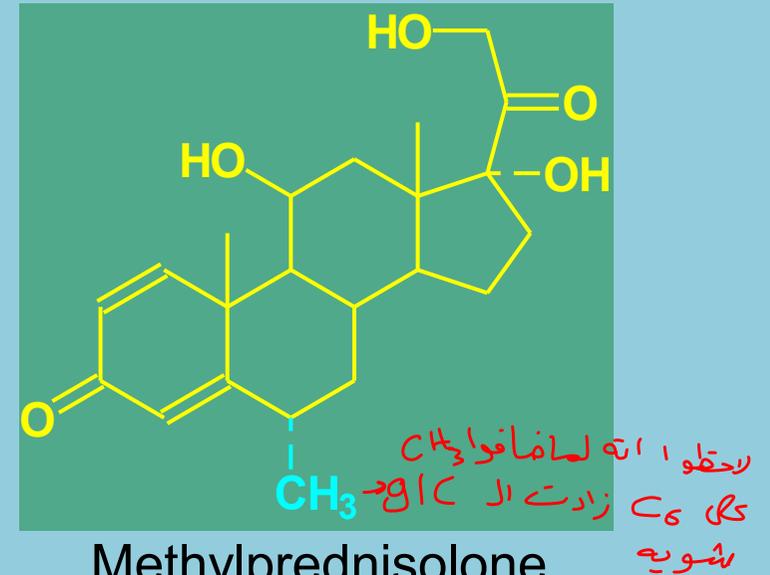


SYNTHETIC GLUCOCORTICOIDS

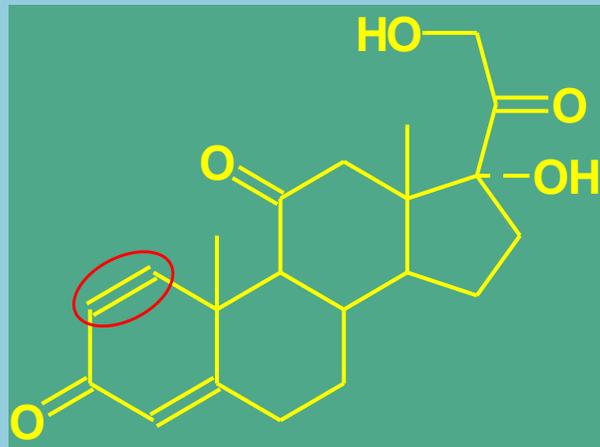
Prednisolone
(GR 4 MR unchanged)



Rheumatoid arthritis 2-4 mg /day



Methylprednisolone
(GR 5 MR unchanged)

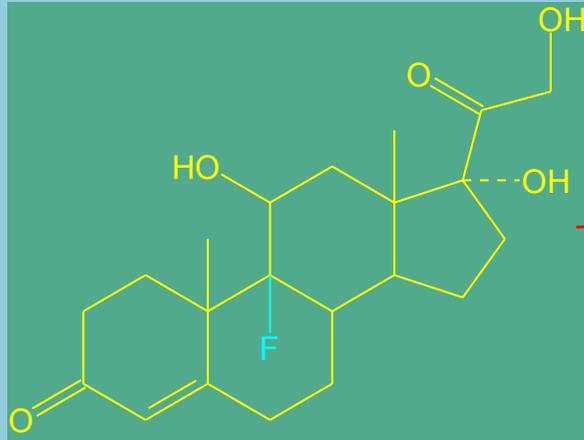


Prednisone
(GR 4 MR unchanged)

Greater activity allows smaller doses to be used reducing side effects

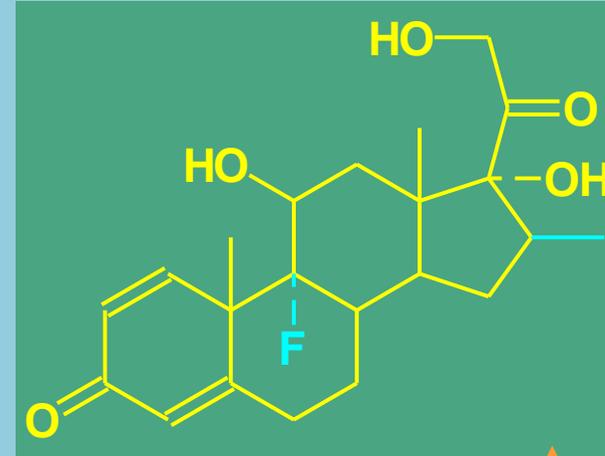
Prednisone and Prednisolone can be used interchangeably

SYNTHETIC GLUCOCORTICOIDS

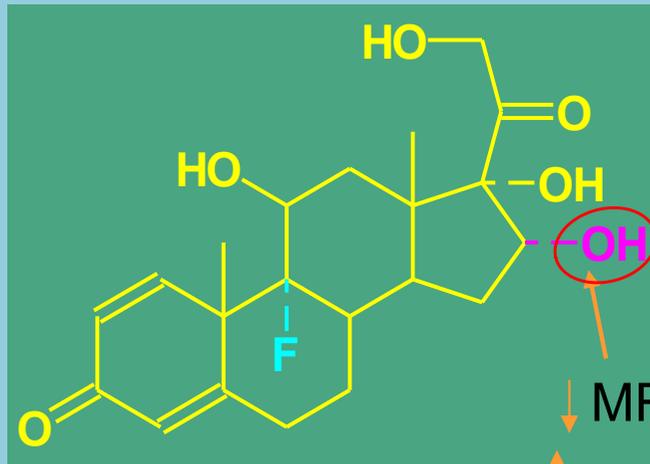


سازم استفاده
بسبب اثر MR
العالیه

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



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

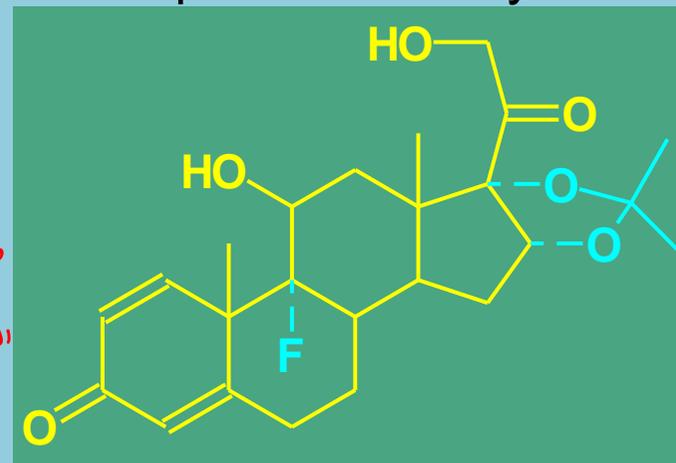


وجود هایدروکسیل
فعلی C₁₆ خلت
در فعالیت منرالو-
یکون کثیر قلیل

MR activity ↓
triamcinolone GR ↑ 5 fold

20% more effective than prednisolone
Unusual toxic side effects

SE ↑
شکایت هیک
ما نهضیه orally
پس topical



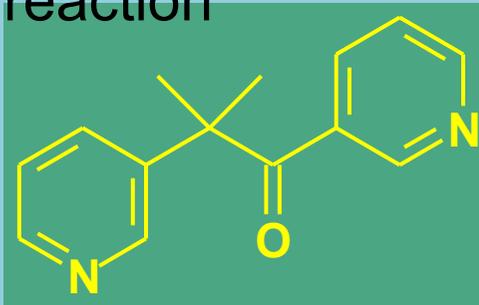
triamcinolone acetonide

Used topically for treatment of
psoriasis and other skin conditions

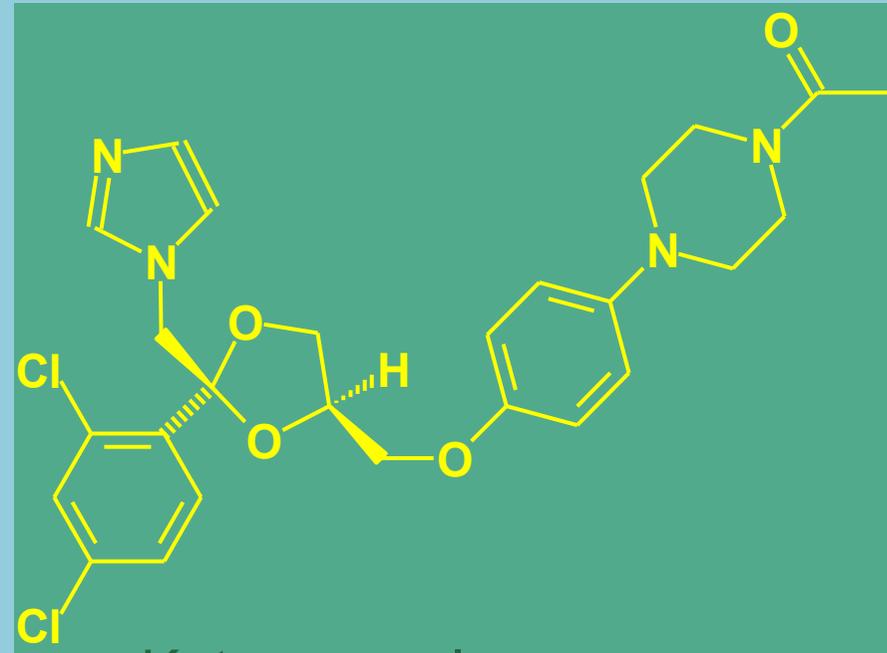
INHIBITORS OF BIOSYNTHESIS OF CORTICOSTEROIDS

Metyrapone

inhibits 11β -hydroxylation reaction

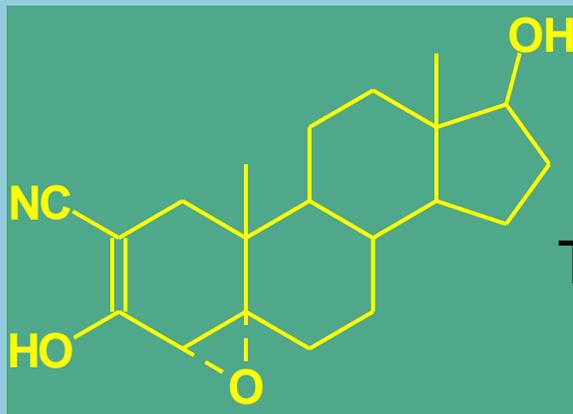


Used for diagnosis hypothalamus-pituitary malfunction



Ketoconazole

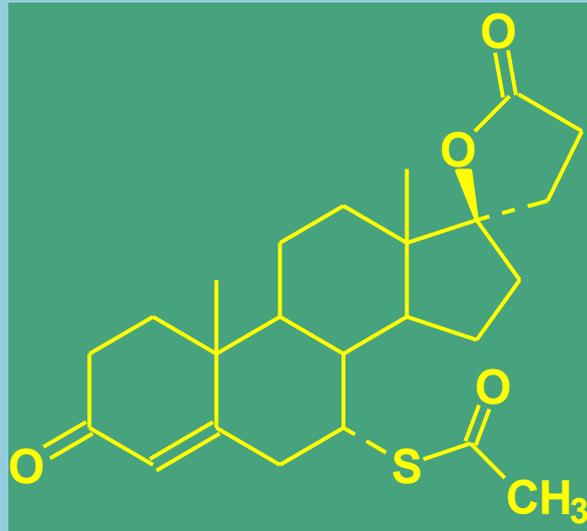
حکمت
میں مطلوب } blocks cholesterol sidechain cleavage in the adrenal (Cushings Syndrome)



Trilostane

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

ADRENOCORTICOID ANTAGONISTS



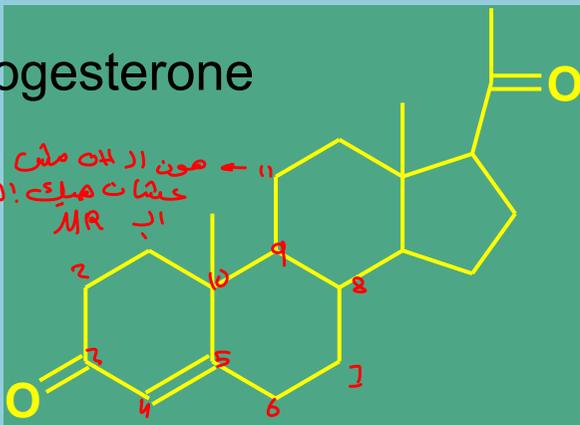
Spironolactone

ال extra binding group على ان هيك ربحي Antagonist

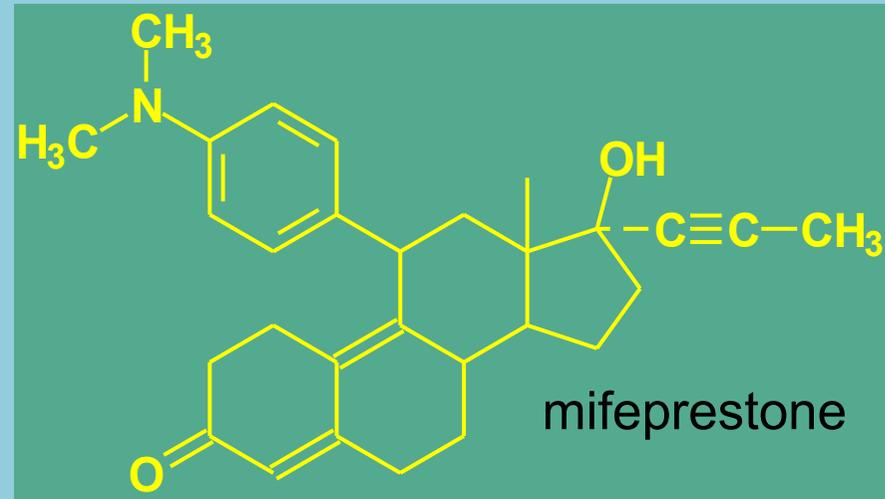
Diuretic response of increased Na⁺ excretion and K⁺ retention

progesterone

صون ال OH مثل موجوده
عشقات هيك! تشغل بلي
MR ال



mineralocorticoid antagonist



glucocorticoid antagonist

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 A_2 , inducible COX2 and annexin I
5. 17-esterification facilitates administration
6. All corticosteroids contain both glucocorticoid and mineralocorticoid activity → هذا باء natural synthesis بهنوب ما يكون في mineraloc activity
7. SAR for glucocorticoid activity: 3-keto, 4,5-double bond, 11-oxy, 17- β ketol all essential for activity *glucocorticoid activity* اذا راحت وحده منهم رح تروح اد

بمادة الفانيل دانا ود اسماء رگزوا كثر على ال SAR فهم تدرسووا

الStructure وتفهمو صنيح صنيح

لا تنسوا زصيلنا ايهم من دعائكم

