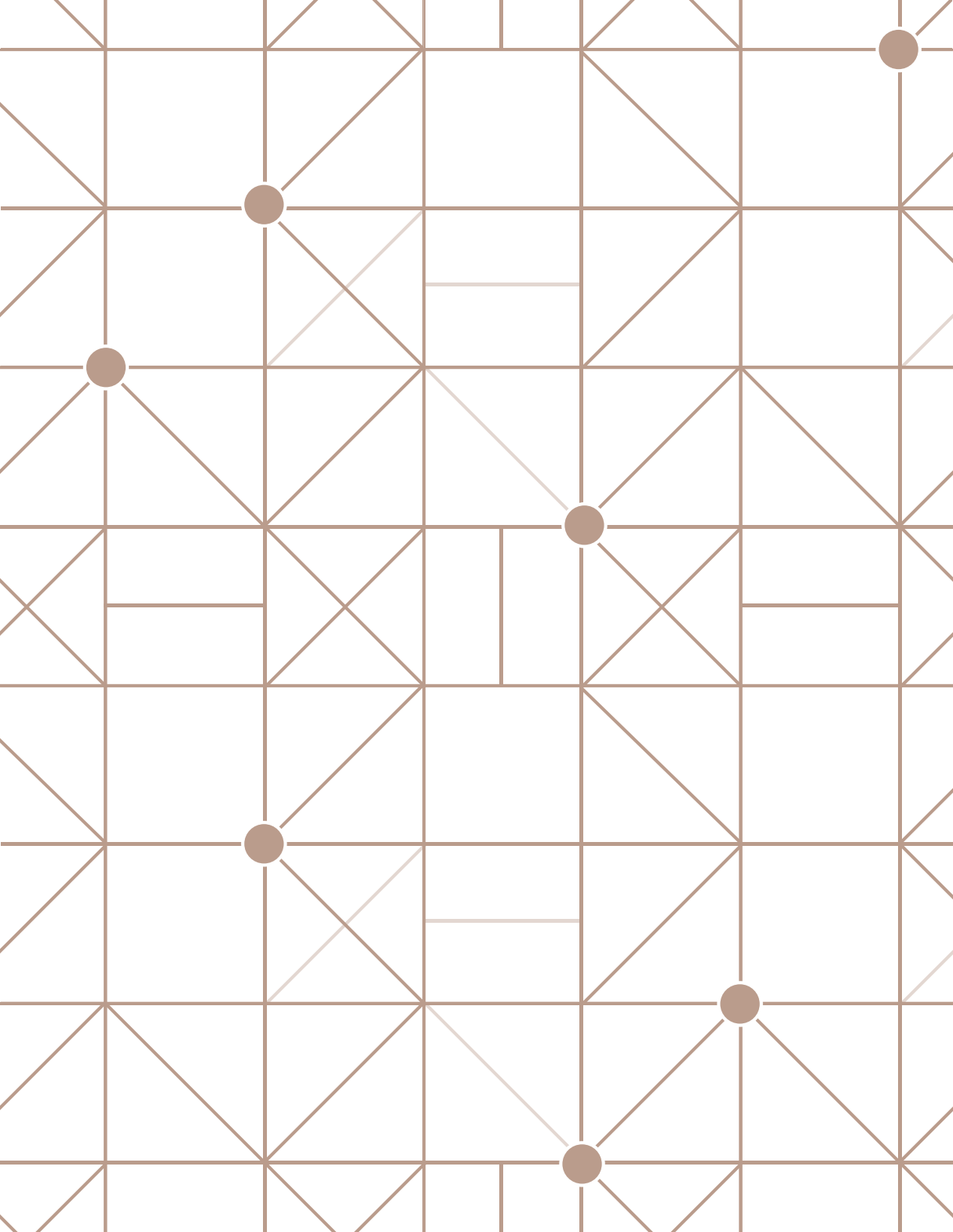

pharma principle of ④ Codynamics

Mechanisms of drug action

	The way	Examples
physical action	produce a therapeutic response ↓ Because it's physical properties	Very Bulky - parenteral (بالحقن) pur esis = little ○ Mannitol → Diuretics way :- Increasing Osmolarity Elimination Conc → Edema - Toxicity - flush ○ Radio-isotopes way :- Emit ionizing radiation use → Treatment Cancer - Thyroid diseases
Simple Chemical reaction	produce a Chemical reaction	○ Gastric Antiacid way :- neutralizing stomach acidity with Alkaline (base) Ex → Magnesium Sulfate ○ Chelating agent way :- bing heavy metals in body (Toxic substances)
Receptors	○ is a - specialized - target - macromolecule ○ present on - cell surface - Intracellular ○ produce pharmacological action	○ Mostly ▭ protein - Enzyme - neuclic acid □ Legand - peptide - Hormones - Drug - neurotransmitter small molecule ←

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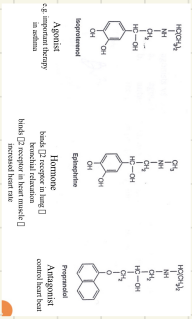
legand - Receptor :-

- endogenous
Hormones - neurotransmitter
- exogenous
Drugs

Interactions 4



- Change Conformation (3D shape) of receptor molecule
- Alter the shape at different part of protein
- Change interaction of receptor - associated biochemicals
- Cellular respond mediated

1 full agonists :- Activate the receptor → Maximal biological response

بيه

Natural endogenous ligand → Greatest efficacy

(full agonist) (100% efficacy)

2 Partial agonists :- Don't activate receptor thoroughly → Partial agonist

معهم الأدوية

(0 - 100% efficacy)

3 Antagonists :- Don't activate receptor (even if it's bind to receptor)

→ Receptor Blockage
→ Inhibiting the binding of agonists
→ Inverse agonists

(The efficacy is Constant)

لا يزيد ولا يقل

4 Inverse antagonists :- Reduce the activity of receptors

↓

Inhebiting their Constitutive activity

(Negative efficacy) ↓

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Drug-receptor Bonds

1 2 3

Chemical forces

	Type	Kinds	Examples
Covalent	irreversible under biologic function	○ very strong ○ not necessarily ○ prolonged & The duration is frequently	□ Don't use in Rational Drug Design □ تستخدم في صناعة الأسلحة الكيماوية (غاز الخردل)
Electrostatic weak bond more selective highly specific very precise fit ↳ example nov > pec > probamol more weak weak strong more use less side effect	reversible	○ much more common ○ Strong linkages → Between permanetly ionic molecules ○ Weaker linkag → Hydrogen bonds ○ Very weaker linkage → Dipole interactions & Van Der Waals forces	
Hydrophobic	reversible	○ quite weak ○ for D_3 vitammis thyriod hormones	○ Inter actions between & – Highly lipid soluble drugs with lipids of cell membrane – Drugs with internal walls of receptor (pockets)

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Duration of drug action

① The effect last only
- During occupies the receptor
- Dissociation of drug
  → Automatically terminates the effect

② The action may persist after dissociated
→ some molecule is still present in activated form (Casecade)

③ Covalently drugs :
→ The affect may persist
→ Until the complex destroyed
New receptor is synthesized

Many receptor-effector system
→ incorporate Desensitization mechanisms
→ preventing excessive activation
(when agonist molecule continue to be present for long period)

Classification of receptors

↓

Based on type of transduction mechanism

4

- Transmembrane ligand-gated ion channel :-

- place → wall of ionchannels in Cell membrane

- way → 1) They activated with their specific ogenist
  2) Open these ion channels
  3) Change in membrane potenial - movement of ions during membrane
  Change in Electric activity - Change in ionic Concentration withen cell

- Mideates diverse functions → 1) Muscle Contraction
  2) Cardiac Conduction
  3) Neurotransmission

	Cholinergic nicotonic (PNS)	Y-aminobutyric acid
Receptor	OPen-OPerated Na^+ channel	Gama receptors
function	Activation of contraction muscle	Hyper-polarization of respective cells
Way	- stimulated the channels - open channels - increase influx of Na^+ cross cell membrane of : 1) neurons 2) NMJ neuromuscular junction in skletal muscle	يعزز تثبيط (ليس تنشيط) - Inhace the stimulation of receptor - Increased influx of Chloried استقطاب Inhibit nervous system

○ Transmembrane G-protein (Coupled-receptors) :-

- Seconed messenger system - segnal transduction
- Way → 1) Receptors stimulated by their ogenist
  2) Activate regularly G-protein in cell membrane
  3) change activity of membrane enzymes

↓

① Adenyl cyclase ② phospholipase C

leading to change in intercellular level of seconed messenger

cAMP — cyclic Adenosin monophosphate

IP_3 - DAG — inosilol triphosphate

↓

Cell response

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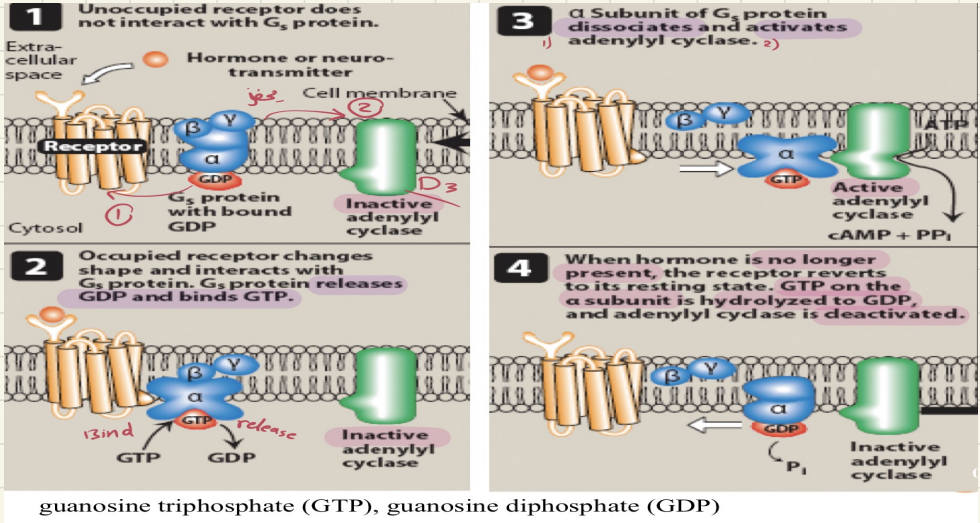

guanosine triphosphate (GTP), guanosine diphosphate (GDP)

- **Ex:** Receptors for transmitters
  - → Stimulation of Muscarinic Receptors (M_1 - M_3) (2 PNS)
  - → for Ach
  - → Activate G-protein
  - → Leads to Increase intracellular level of IP_3 - DAG

- **Enzyme-linked receptors:-** Extracellular → binds to specific agonist

  Intracellular → Contain a.a : Tyrosine (Cytoplasmic domain)

way →
1) Activation receptors → Extra
2) phospholiration → Tyrosine → Intra
3) Acquirs Kynase actively
4) Activation Intracellular Substrats - E
5) Cell response

Ex →
1) Insulin
2) Growth factors → EGF - PDGF
3) Immune Cytokines

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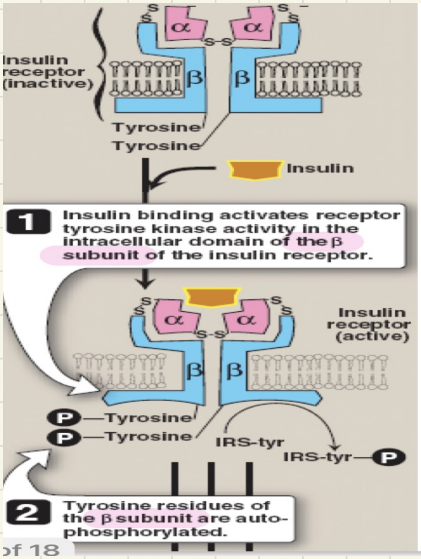

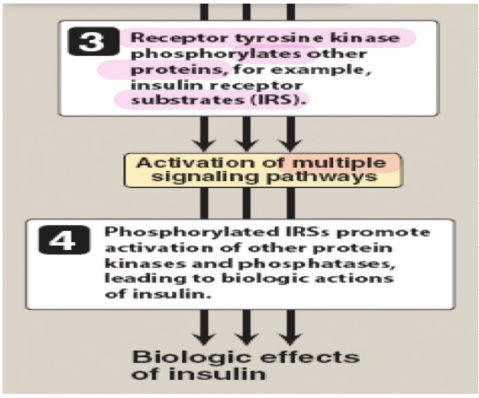

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○ Intracellular receptors :- [lipophelic]

سؤال امتحان

place → 1) Cytoplasm → Steriod receptors

2) Nucleus → Thyroid Hormones - Vitammins D_3

way → 1) Ogenist Cross cell membrane
2) Activation receptors
3) Bind to DNA gene response elements in nucleus
4) Change in gene transcription
5) Synthesis of new protein