University of Mosul
Lecture No.:3
College of Veterinary Medicine
Date:
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Website:

Lecture title: Polypeptides

Lecturer Affiliation: College of Veterinary Medicine

Summary:

POLYPEPTIDES

Vasoactive peptide

1-Angiotensin.

2-Plasmakinin.

3-Vasopressin.

4-Natriuretic peptide.

5-Vasoactive intestinal polypeptide.

6-Substance P.

Renin-angiotensin-aldosterone system

a. Angiotensinogen: Is an α2-globulin synthesized in the liver and is present in the circulation. It is the precursor for all angiotensin.

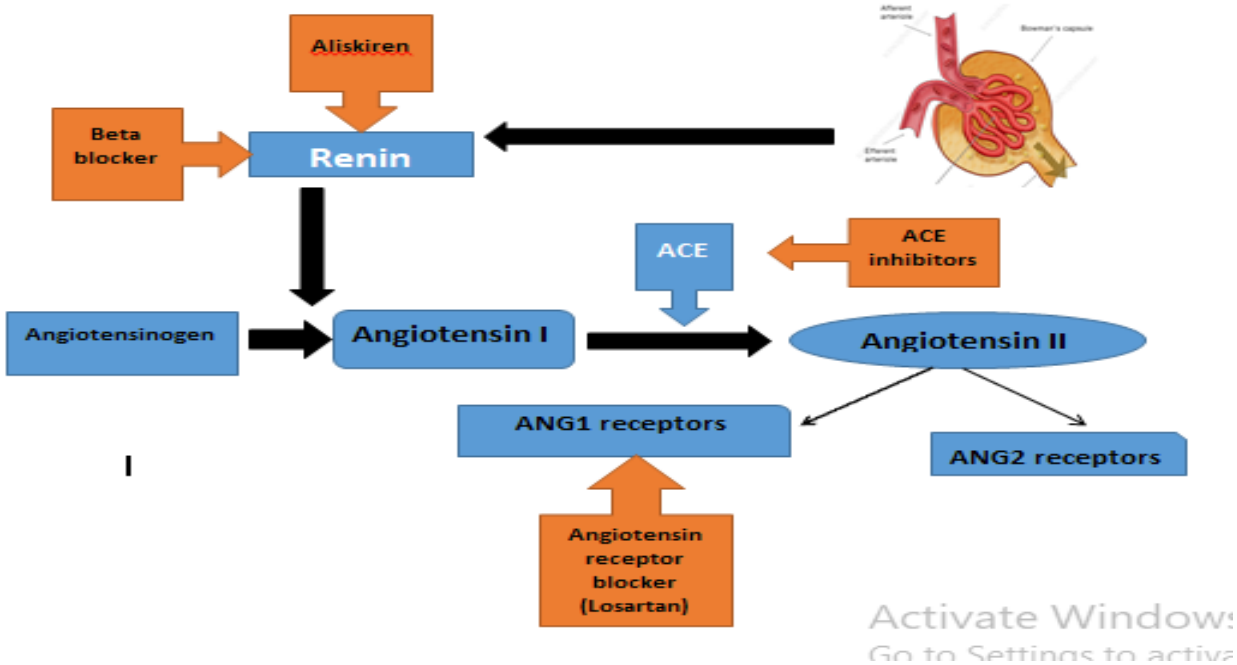
b. Renin: Is an enzyme secreted by juxtaglomerular cells in the renal arterioles, which metabolizes angiotensinogen to form angiotensin I.

c. Angiotensin-converting enzyme (ACE): an enzyme found in large amounts in lung capillary endothelial cells as well as in other vascular beds, metabolizes **angiotensin I** to the **angiotensin II.**

d. Angiotensin II: is metabolized by an aminopeptidase to angiotensin III that has less biologic activity than angiotensin II.

Receptors

AT1(Gq) receptor and **AT2(Gi) receptor**. AT1 receptors are stimulatory, whereas AT2 receptors are inhibitory, which mediate effects usually are opposite to those of AT1.



Pharmacological effects.

CVS	• ANGII very potent vasoconstriction • ANGII 40 time more potent than NE • ANGII rapid onset about 10-15 second
Adrenal medulla	ANGII stimulate autonomic ganglia leading to increase NE and E release
Adrenal cortex	ANGII stimulate aldosterone synthesis and release

Kidney	ANGII cause renal VC, inhibit renin release and increase Na and water reabsorption from proximal tubule.
Brain	• ANGII increase sympathetic outflow • ANGII increase release of ACTH and ADH (vasopressin)
Cell growth	Mitogenic effect hypertrophy and remodeling of heart and BV.

Antagonists of the renin–angiotensin system.

1- ACE Inhibitors: -

Mechanism of action	• ACE inhibitors block the conversion of angiotensin I to angiotensin II • ACE inhibitors inhibit the degradation of bradykinin (vasodilator substance).
Adverse effect	1. Dry persistence cough and angioedema due to increase levels of bradykinin. 2. Hyperkalemia due to decrease aldosterone secretion. 3. Renal impairment 4. Fetopathic potential (teratogenicity) decrease organogenesis of lung and fetal abnormalities and may cause fetal death.
Drug interaction	1. K+ sparing diuretics → hyperkalemia 2. NSAIDs → due to decrease PGs →hyperkalemia and decrease renin secretion

	3. Angiotensin receptor blocker 4. Renin inhibitors e.g. Aliskiren
Contraindication	1. Pregnancy 2. Lactation 3. Chronic obstructive pulmonary disease 4. Impaired renal function
Drugs name	1. Enalapril 2. Enalaprilat (only injection) 3. Captopril 4. Ramipril
Uses	Hypertension

2- β1-Adrenergic antagonists:

Catecholamines promotes the release of renin from juxtaglomerular cells via β1-receptors. **Propranolol** antagonizes β1-receptors in the kidney and thereby reduce **renin** release.

3-Angiotensin II (AT_1) receptor antagonists:

Act as competitive antagonism at AT_1 receptor of the angiotensin II.

Losartan, Candesartan, Valsartan

1. Losartan is an angiotensin II receptor blocker (ARB) used to treat hypertension.
2. Patients with ACE inhibitor-associated coughs are switched to ARBs like losartan.

3. Losartan is available as losartan potassium oral tablets as well as a combination tablet of losartan potassium and hydrochlorothiazide.
4. Losartan has an anticancer activity and neuroprotective effects in experiment model systems.

4- Renin receptor inhibitor

Aliskiren.

Mechanism of action: Inhibits the conversion of angiotensinogen to angiotensin I.

Uses: It is for controlling hypertension in humans and animals

Route of administration: orally.

Metabolism: Aliskiren is metabolized by cytochrome P450.