Angiotensin II Overview

Overview:
Angiotensin II is a potent vasoactive peptide involved in regulating blood pressure, electrolyte balance, and fluid homeostasis. It is the main effector molecule of the renin-angiotensin-aldosterone system (RAAS), playing a central role in cardiovascular physiology.

Mechanism of Action:
Angiotensin II binds to two main receptors:

- AT1 receptor (primary): Causes vasoconstriction, sodium retention, and aldosterone release.
- AT2 receptor (minor role in adults): Involved in vasodilation, anti-proliferative effects, and tissue repair.

When Angiotensin II binds to AT1 receptors (GPCRs) on vascular smooth muscle and renal tubules, it activates:

- Phospholipase C (PLC) → produces IP3 and DAG → calcium release → vasoconstriction.
- Stimulates aldosterone secretion from adrenal cortex → sodium and water retention → increased blood volume.

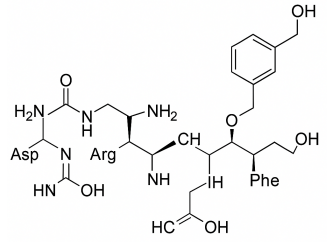
Physiological Functions in the Body:
Vasoconstriction: Increases systemic vascular resistance (SVR), raising blood pressure.
Aldosterone Secretion: Enhances sodium reabsorption in kidneys, promoting fluid retention.
Thirst Stimulation: Increases fluid intake via hypothalamic thirst centers.
Cardiac Remodeling: Promotes hypertrophy in chronic conditions (adaptive, but maladaptive in disease).
Sympathetic Activity: Increases norepinephrine release, boosting blood pressure.

Clinical & Research Use:

- Approved Use: Synthetic Angiotensin II (Giapreza®) is FDA-approved for septic or other distributive shock to raise blood pressure.
- Biomarker Role: Elevated levels seen in hypertension, heart failure, and renal disease.
- Therapeutic Target: Many cardiovascular drugs target the RAAS system, including ACE inhibitors, ARBs (angiotensin receptor blockers).

Dosing (FDA-Approved Context):
Giapreza® IV Dosing: Initial: 20 ng/kg/min, titrated by 15 ng/kg/min every 5 minutes to target MAP ≥ 65 mmHg.
Max dose: 80 ng/kg/min during first 3 hours; maintenance typically 1.25-40 ng/kg/min.

Conclusion:
Angiotensin II is a critical peptide hormone that maintains blood pressure and fluid homeostasis by acting on vascular smooth muscle, adrenal glands, and the CNS. Its central role in the RAAS system makes it a vital target in shock management and cardiovascular disease research.



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