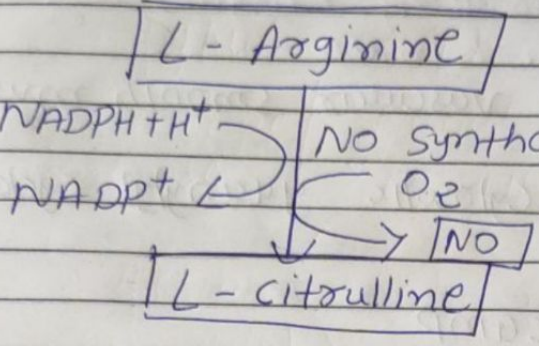
* Nitric oxide / Nitrogen oxide metabolism & function :-

→ Synthesis :-



→ Free radical gas
→ N_2O - Nitrous oxide laughing gas - used anesthetic
→ Endothelium derived relaxing factor
↓
Cause vasodilation by relaxing vascular smooth muscle
→ Act as neurotransmitter in brain
→ prevent platlet aggregation
→ Mediate tumoricidal & bactericidal action of macrophages
→ very short half life in tissue - react with O_2 & O_2^- & converted into nitrates & nitrites including peroxynitrite [$O=NOO^-$]
[Reactive nitrogen species [ROS]]

→ Nitric oxide synthase

3 isoenzyme - 2 are constitutive [cNOS]
↓
Calcium - calmodulin dependent & found in endothelium & neural tissue

constantly produced in very low level for vasodilatation & neurotransmission.

1 is inducible Ca^{+2} independent - [iNOS]
present in many cell - macrophage & neutrophills.

→ Nitric oxide & vascular endothelium

↓

Synthesized by eNOS in endothelial cells

↓

diffuses to vascular smooth muscle

↓

activate cytosolic guanylyl cyclase

↓

Form cGMP

↓

⊕ protein kinase G

↓

phosphorylate Ca^{2+} channel

↓

Decreased entry of Ca^{2+} into smooth muscle cells

↓

↓ Smooth muscle contraction & cause relaxation.

→ Is endogenous vasodilator.

→ Drug - Nitroglycerin - metabolized to NO

↓

Cause relaxation of vascular smooth muscle & lower blood pressure

→ Under hypoxic condition → Nitrite can be reduced to NO

↓

bind to deoxyhemoglobin

Nitric oxide & macrophage bactericidal activity

In macrophage - iNOS activity normally low stimulated significantly by bacterial LPS [lipopolysaccharide] & by release of IFN-γ & TNF-α in response to infection.

- Activated macrophage form O_2^- radical that combine with NO & form intermediates that decompose, producing highly bactericidal OH^- radical.