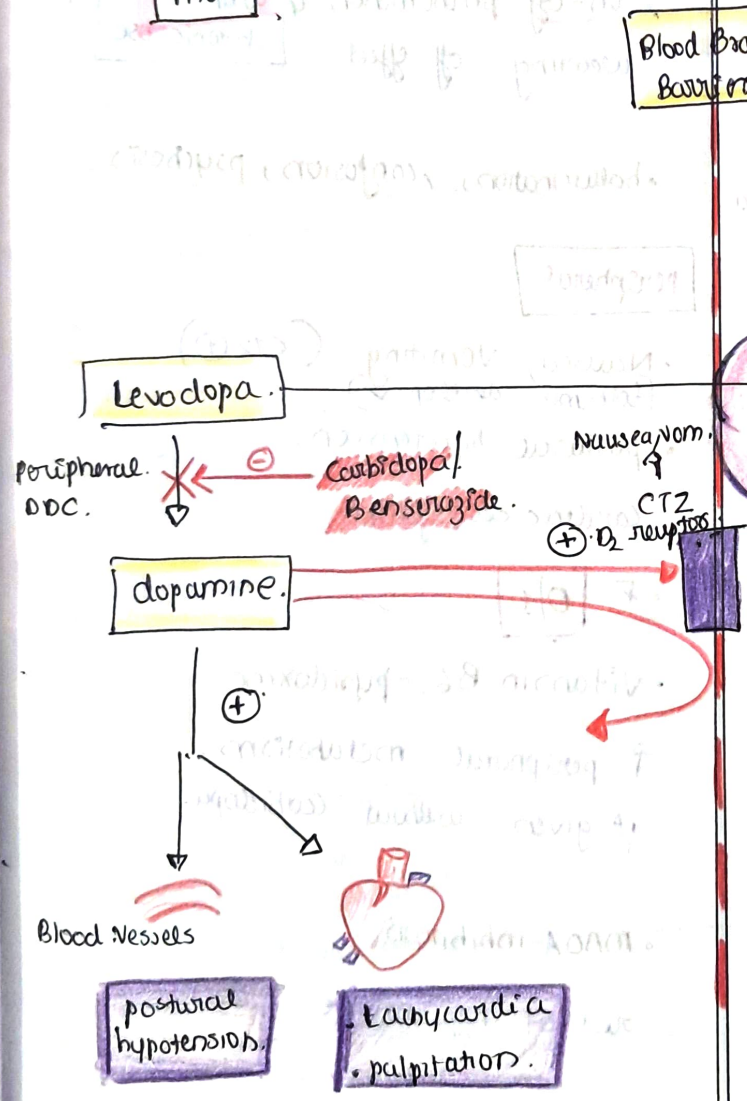


# Levodopa

- dopamine precursor.
- used in idiopathic parkinsonism.
- usually given as (Levodopa + Carbidopa) combination to reduce peripheral metabolism.

# MOA



peripheral

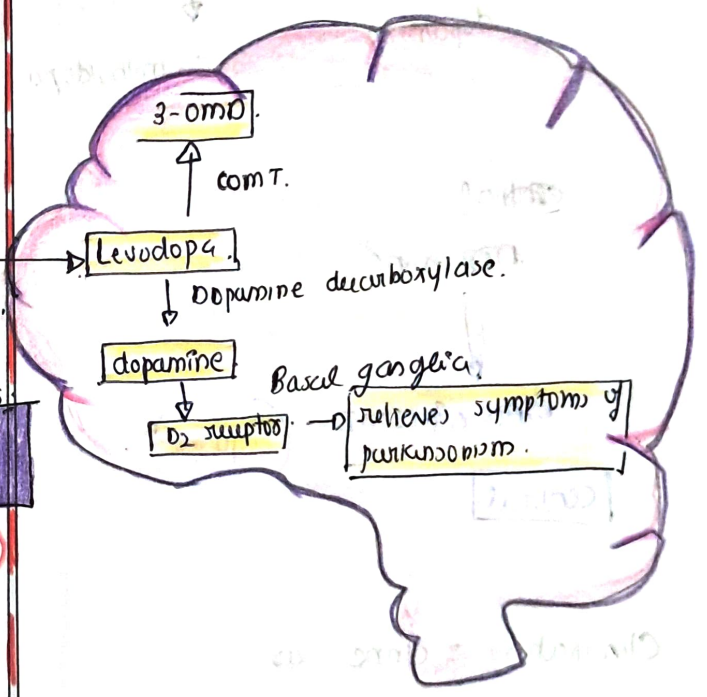
COMT - Catechol-O-methyl transferase.

MAO - Monoamine oxidase.

HVA - homo vanillic acid.

3-OMD - 3-O-methyldopa.

# Blood Brain Barrier



central.

**PK**  $T_{1/2} = 1-2h.$

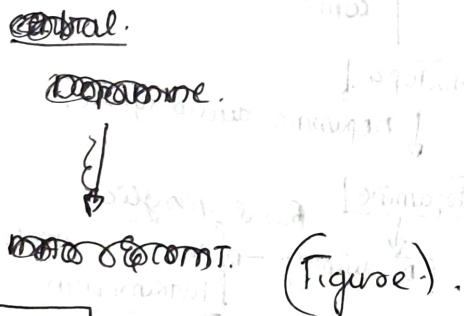
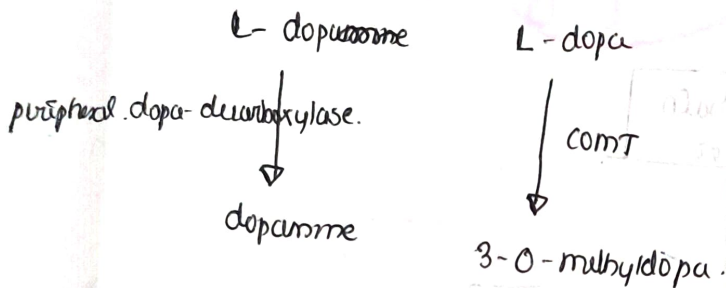
Absorption: oral.

↓ with high protein meal.

distribution: crosses BBB via.

LAT.

Metabolism: **peripheral**; ~~central~~.



**central**

Elimination: same as.

Homovanillic acid.

DOPAC.

## USES

• parkinson's disease

↓

Symptomatic treatment

## ADR

**CNS** { due to ↑ Basal dopamine }

• ~~nausea~~  
• ~~dyskinesia~~ { chorea, dystonia }  
(No tolerance).

• on-off phenomenon & wearing-off effect. **with chronic use**

• hallucinations, confusion, psychosis.

## peripheral

• Nausea, vomiting (CTZ ⊕)  
(tolerance develops)

• postural hypotension.

cardiac arrhythmias.

• **O/I**

• Vitamin B6 - pyridoxine.

↑ peripheral metabolism if given without carbidopa.

• MAOA-inhibitors.

risk of hypertensive crisis.

# Pharmacological actions (UQ)

## CNS

- correct symptoms.
- Hypokinesia, rigidity resolves first, later tremors.
- cannot arrest progression of ds.
- not given in drug induced P.D.

## CVS

- tachycardia
- postural hypotension.

## GI

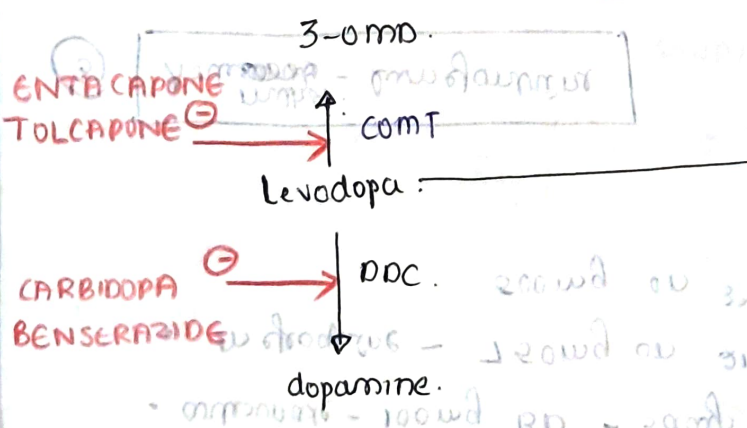
- nausea, vomiting.

## Endocrine

- ↓ prolactin release.
- ↑ GH release

## Metabolism

### periphery



# Advantage of L-dopa + Carbidopa

- 1. Carbidopa ⊖ peripheral conversion into DA. ↓ more L-dopa in brain.
- 2. Systemic concentration of Dopamine is reduced ↓ reduces peripheral side effects of dopamine.
- 3. Enhanced central effect as more L-dopa in CNS.
- 4. L-dopa dose is reduced to ~ 1/4th.
- 5. 'on-off' phenomenon is minimized.
- 6. pyridoxine reversal of Levodopa effect doesn't occur.

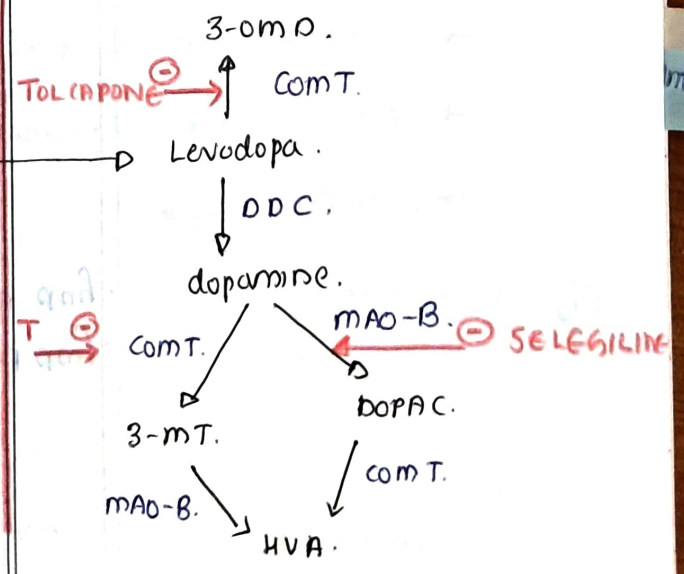
## problems accentuated.

- Involuntary movements, dyskinesia.
- Behavioral abnormalities
- postural hypotension.

## DOOPANE

Next page ★

## BRAIN



## Dosage

• Started with a small dose



Carbidopa + L dopa x 3 times  
25mg 100mg daily.

• most patients ultimately

require



CD  
25mg

+

Ldopa { - 3-4 times }  
250mg day.

COMT Ⓟ

near morphine.

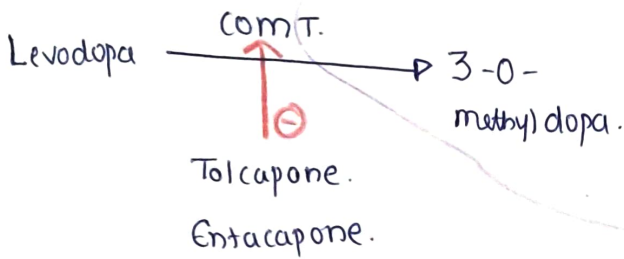
## COMT Inhibitors

Catechol-O-methyltransferase.

Tolcapone.

Entacapone.

## MOA



• ↑ central dopamine levels.

## USES / advantages.

• ↑ T<sub>1/2</sub> of L-dopa & ↑ B.A. in CNS.

• 'on' time is prolonged. - {↓ on-off / wearing off phenomenon}

• Tolcapone → peripheral + central ⊖

• Entacapone → peripheral only.

• used as adjuncts.

L-dop + Carbidopa + Entacapone.

## ADR

- dyskinesia.
- nausea
- diarrhoea.
- hypotension
- confusion.

Tolcapone.  
↓  
hepatotoxic.

Entacapone  
↓  
No hepatotoxicity

## PB

• use of Trihexyphenidyl / Bexthexol in drug induced parkinsonism.

in drug induced P.

→ dopamine receptors are blocked.

→ there is no deficiency of dopamine.

## PB

• drug induced parkinsonism {antipsychotics etc}

↓  
dopamine receptor blockade in nigrostriatal pathway.

↓  
relative ↑ in cholinergic activity in striatum

Bexthexol → centrally acting antimuscarinic.

↓  
blocks muscarinic R in striatum.

↓  
restore DA : Ach balance.

↓  
Improved rigidity & tremor.

