Kerbala University
College of Pharmacy
Dep. of Pharmaceutical Chemistry
Organic Pharmaceutical Chemistry II

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14-Oct-2014

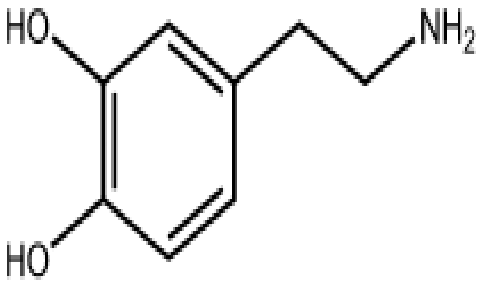
Adrenergic Agents

Adrenergic Agents

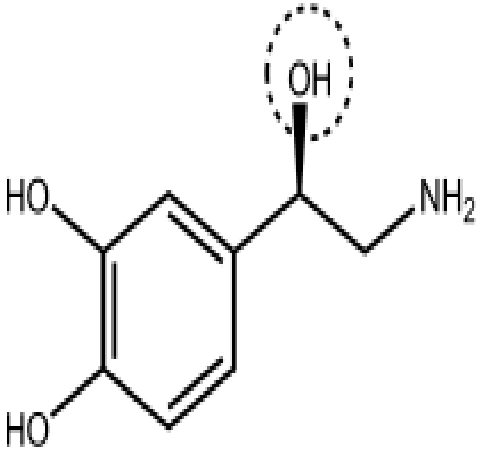
- **Agonists**
- Sympathomimetics
- Adrenergic stimulants
- Adrenergic agonists

- **Antagonists**
- Sympatholytics
- Antiadrenergics, or
- Adrenergic-blocking agents

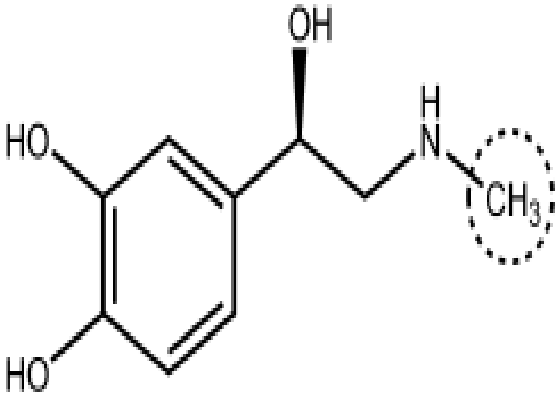
Endogenous Catecholamines (Adrenergic Neurotransmitters)



Dopamine (DA, Log P = 0.12)



NE (Log P = -0.63)



E (Log P = 0.28)

Dopamine

- Differs from NE in lacking of 1-OH group.
- It is the immediate precursor of NE.
- Regarding the structure of dopamine, dopamine has a short DOA with no oral activity. Explain why?

Norepinephrine (NE)

- Differs from DA only by addition of a 1-OH substituent.
- Differs from E only by lacking the N - methyl group.
- Like DA, it is polar and rapidly metabolized by both COMT and MAO, resulting in poor oral bioavailability and short DOA (1 or 2 minutes even when given intravenously).

Epinephrine (E, Adrenalin)

- Differs from NE by the addition of an N - methyl group.
- Like the other CAs, E is light sensitive and easily oxidized on exposure to air because of the catechol ring system.
- The development of a pink-to-brown color indicates oxidative breakdown.
- To minimize oxidation, solutions of the drug are stabilized by the addition of reducing agents such as sodium bisulfite

DRUGS AFFECTING ADRENERGIC NEUROTRANSMISSION:

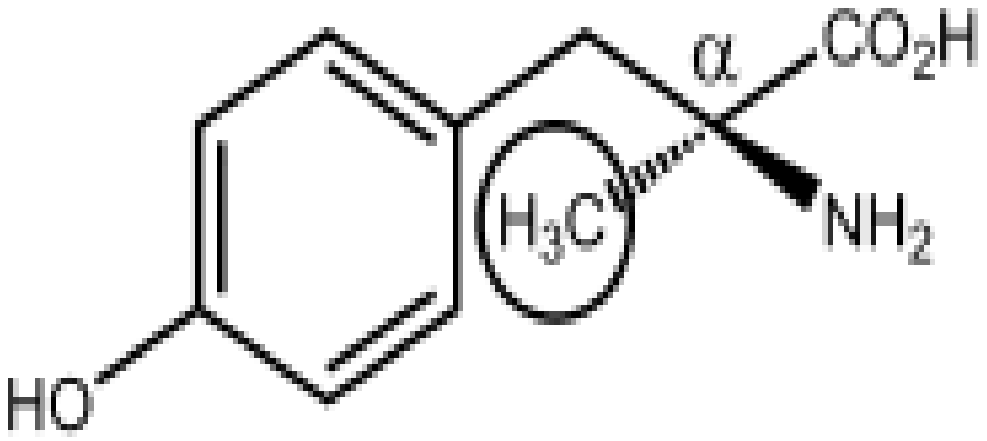
A. *Drugs Affecting Catecholamine Biosynthesis*

B. *Drugs Affecting Catecholamine Storage and Release*

Drugs Affecting Catecholamine Biosynthesis

Metyrosine:

- Metyrosine is a much more effective competitive inhibitor of E and NE production than agents that inhibit any of the other enzymes involved in CA biosynthesis. Why?



Drugs Affecting Catecholamine Storage and Release

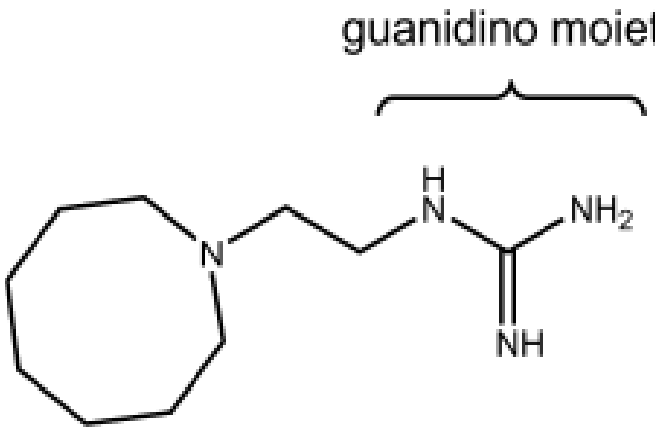
Reserpine

- Reserpine is an indole alkaloid obtained from the root of Rauwolfia serpentina found in India.

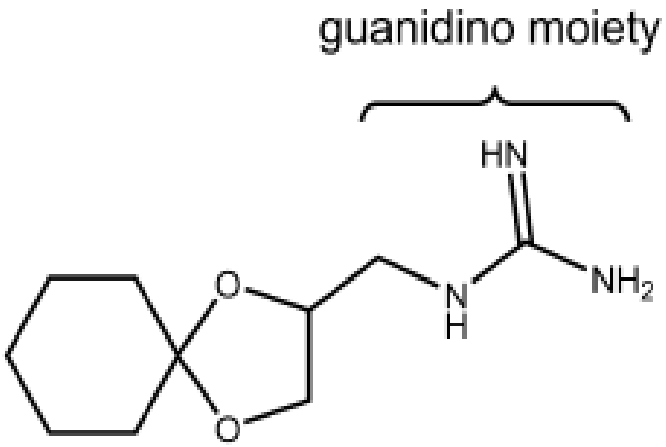
- Reserpine is known as “NT Depleter”. Explain why?

Guanethidine and guanadrel

- These drugs bind to the storage vesicles and stabilize the neuronal storage vesicle membranes, making them less responsive to nerve impulses.



Guanethidine
pKa = 13.43
No CNS activity



Guanadrel
pKa = 12.76
No CNS activity

References:

- Wilson and Gisvold Textbook of Organic Medicinal and Pharmaceutical Chemistry; Delgado JN, Remers WA, (Eds.); 12th ed., 2011.
- https://pubchem.ncbi.nlm.nih.gov/search/search.cgi