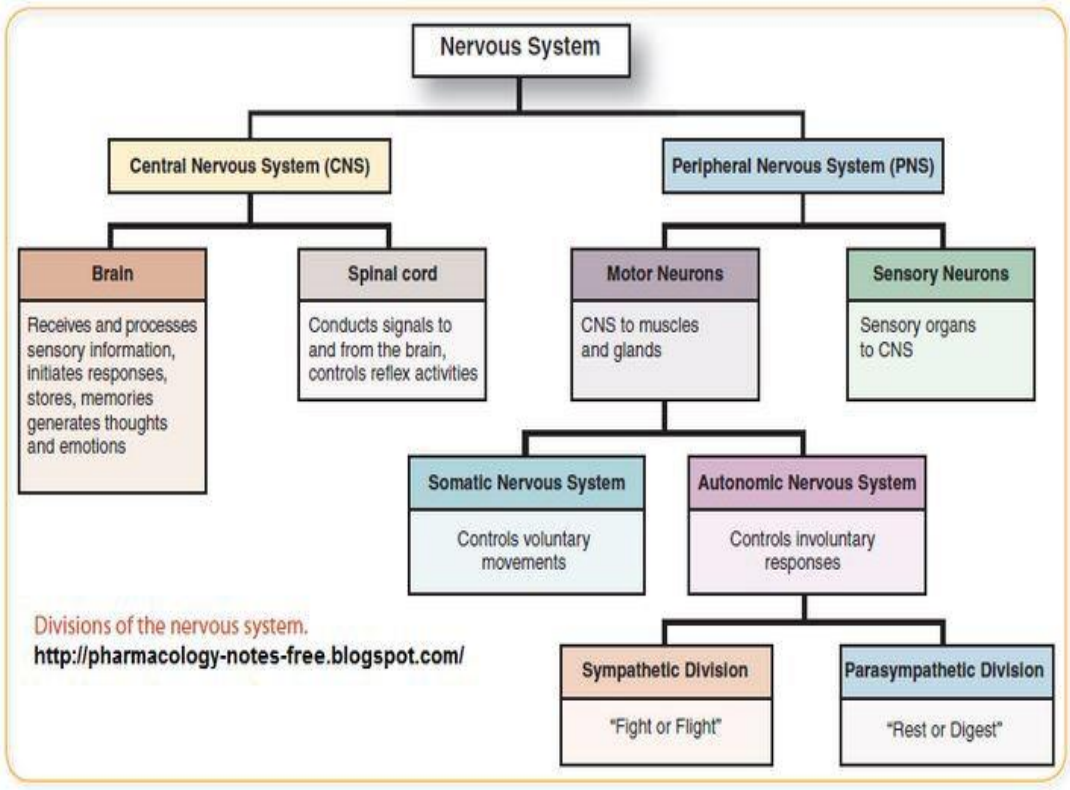
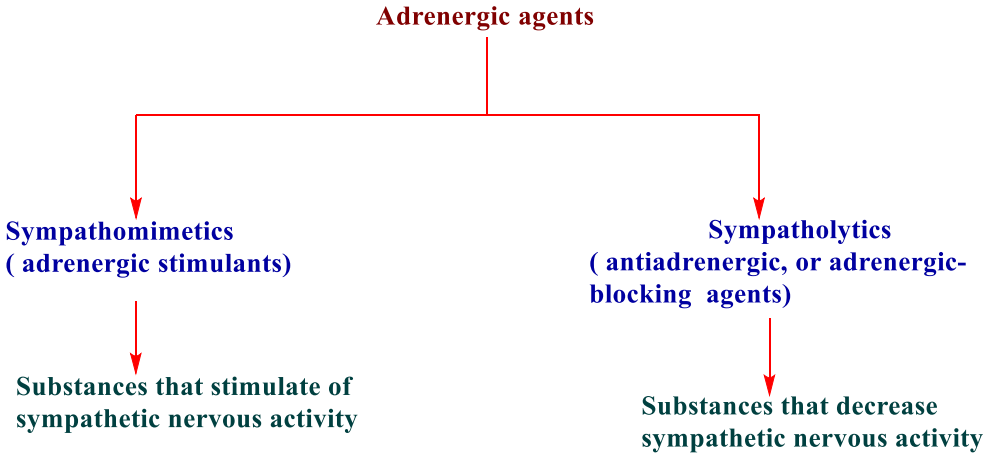


Adrenergic Agents

Adrenergic drugs: - are chemical agents that exert their principal pharmacological and therapeutic effects by either enhancing or reducing the activity of the various components of the sympathetic division of the autonomic nervous system.



Because of the important role that the sympathetic nervous system plays in the normal functioning of the body, adrenergic drugs find wide use in the treatment of a number of diseases.

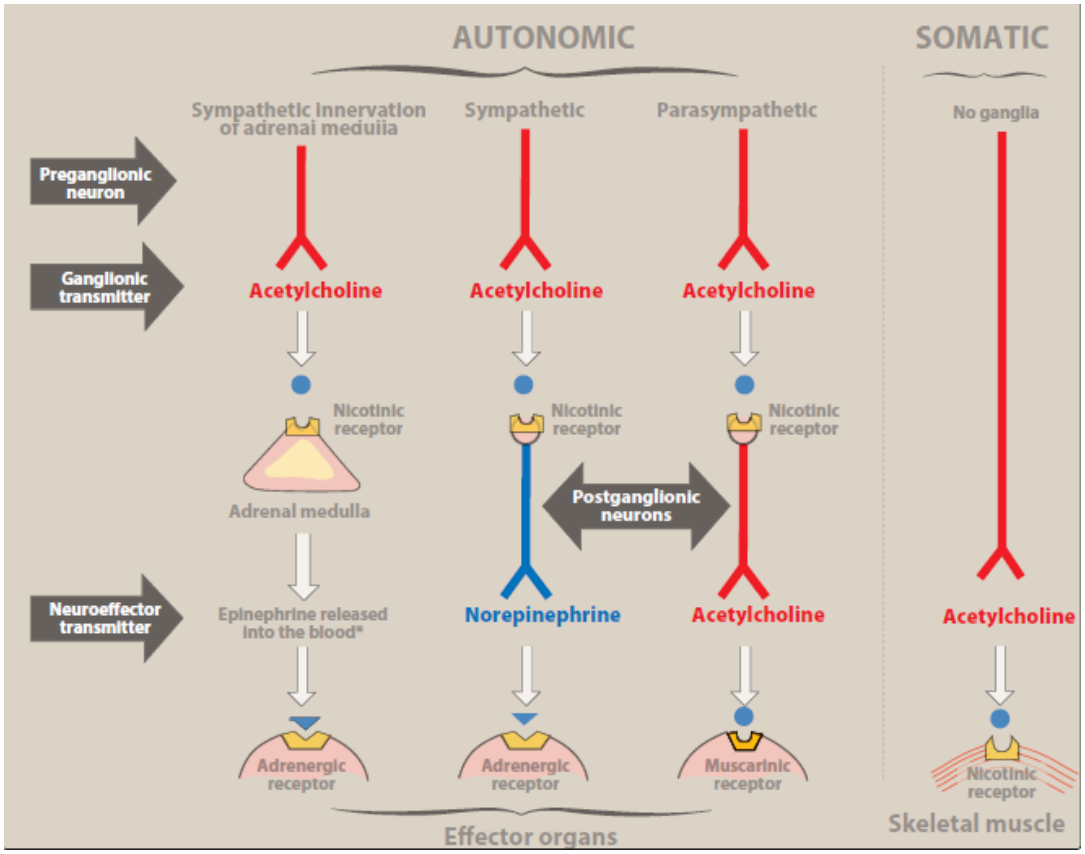
Adrenergic neurotransmitters (NTs):-

1- **Norepinephrine (NE, noradrenaline)** is the neurotransmitter of the postganglionic sympathetic neurons. As a result of sympathetic nerve stimulation, it is released from sympathetic nerve endings into the synaptic cleft, where it interacts with specific presynaptic and postsynaptic adrenergic receptors.

Another endogenous adrenergic receptor agonist is epinephrine.

2- **Epinephrine (E, adrenaline).** it is a neurohormone that synthesized and stored in the adrenal medulla, from which it is released into the blood circulation.

Epinephrine is not released from peripheral sympathetic nerve endings, as is NE.

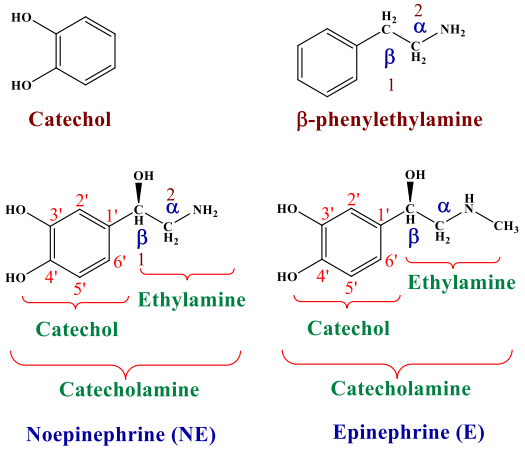


Structure and Physicochemical properties of adrenergic neurotransmitters

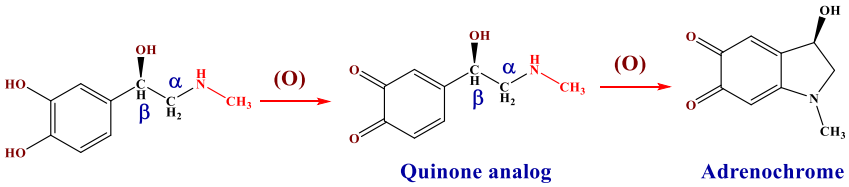
NE, E and DA: - are chemically catecholamines (CAs) which refer to all organic compounds that contain a catechol nucleus (ortho-dihydroxybenzene) and an ethylamine group.

Why this name was given to these compounds?

Because they contain an amino group attached to an aromatic ring that contains two hydroxyl groups situated ortho to each other, the same arrangement of hydroxyl groups as found in catechol.

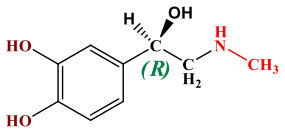


- **The catechol functional groups in CAs are highly susceptible to facile oxidation. E and NE undergo oxidation in the presence of oxygen (air) or other oxidizing agents to produce a quinone analog, which undergoes further reactions to give mixtures of colored products, one of which is adrenochrome. Hence, solutions of these drugs often are stabilized by the addition of an antioxidant (reducing agent) such as ascorbic acid or sodium bisulfate.**

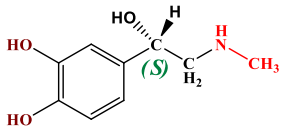


Oxidation of epinephrine

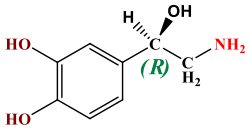
- **Epinephrine and NE each possess a chiral carbon atom; thus, each can exist as an enantiomeric pair of isomers. The enantiomer with the (R) configuration is biosynthesized by the body and possesses the biological activity. This R configuration of many other adrenergic agents also contributes to their high affinity to their corresponding adrenoceptor.**



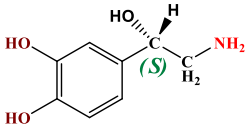
(R) isomer of Epinephrine



(S) isomer of Epinephrine



(R) isomer of Norepinephrine



(S) isomer of Norepinephrine

- **E contains one secondary amino group and three hydroxyl groups, the calculated log P for E is (Clog P= -0.63), which would be expected the molecule is polar and soluble in water.**
- **E is a weak base (pK_a= 9.9) because of its aliphatic amino group.**
- **E is a weak acid (pK_a= 8.7) because of its phenolic hydroxyl group.**
- **It can be predicted that ionized species (the cation form) of E at physiological pH is predominate (log D at pH 7= -2.75).This largely accounts for the high water solubility of this compound as well as other CAs.**
- **Because log P with a value of 0-3 is an optimal window for absorption, we can predict that E has poor absorption and poor central nervous system (CNS) penetration.**