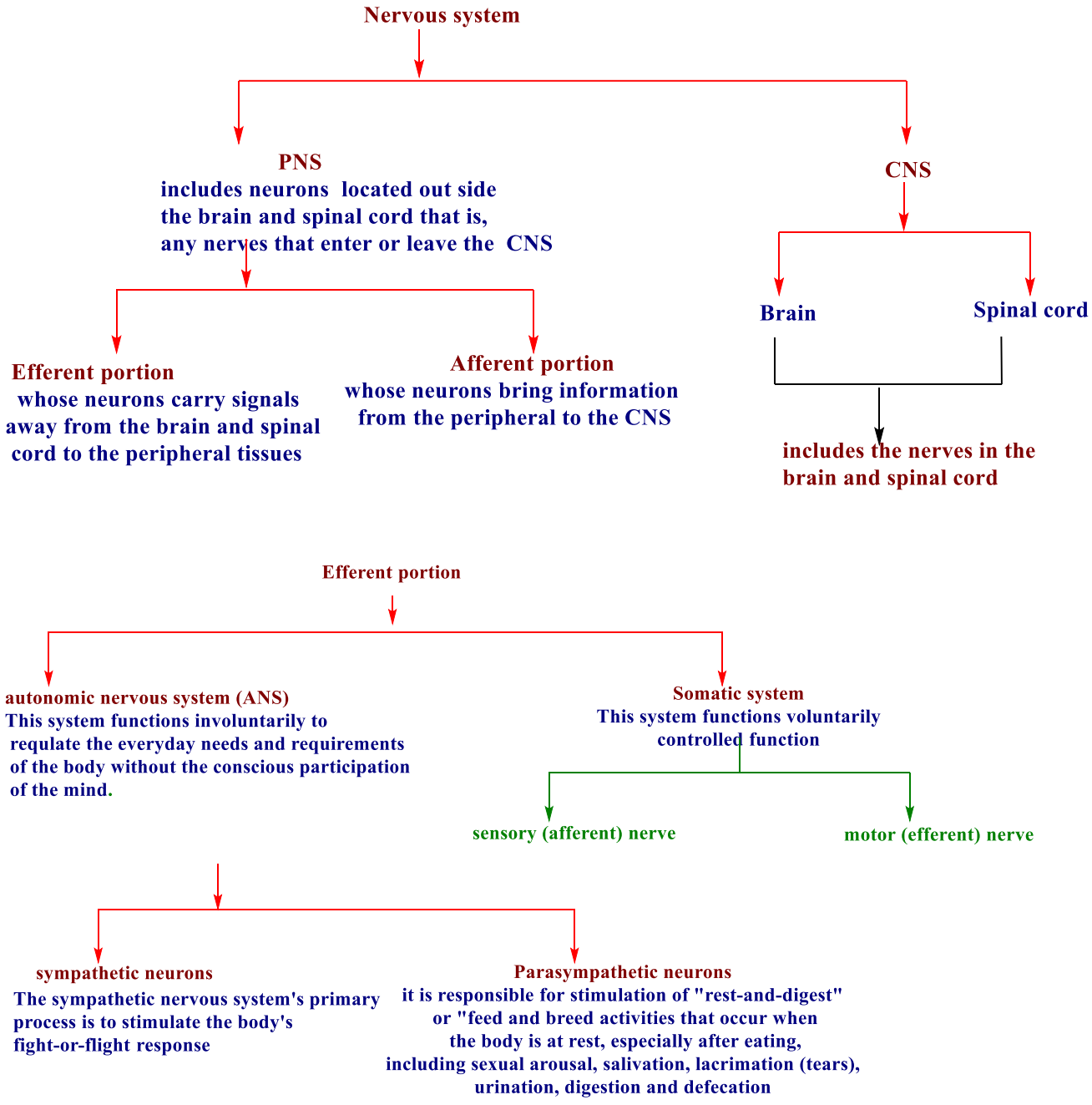
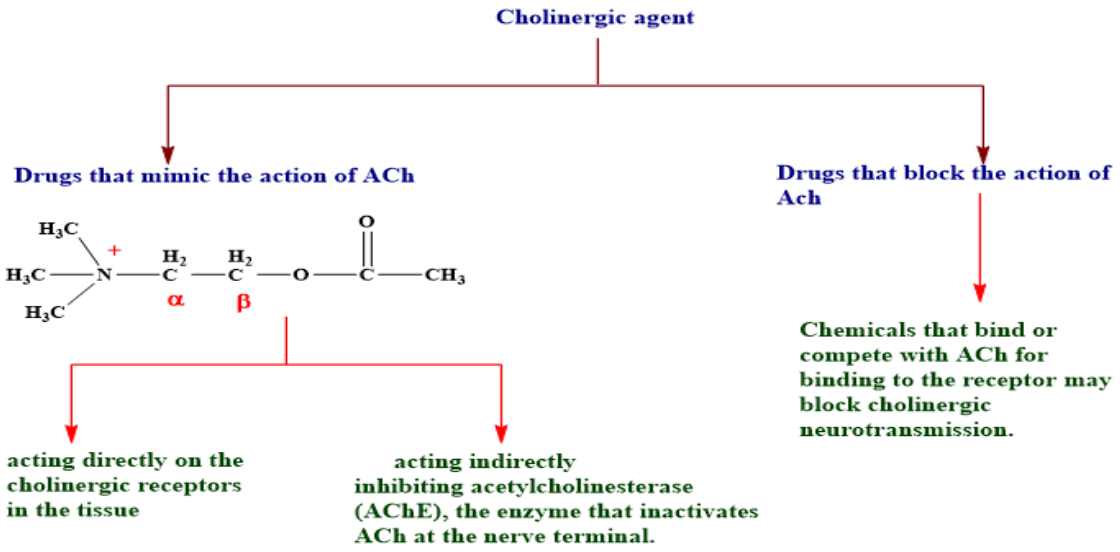
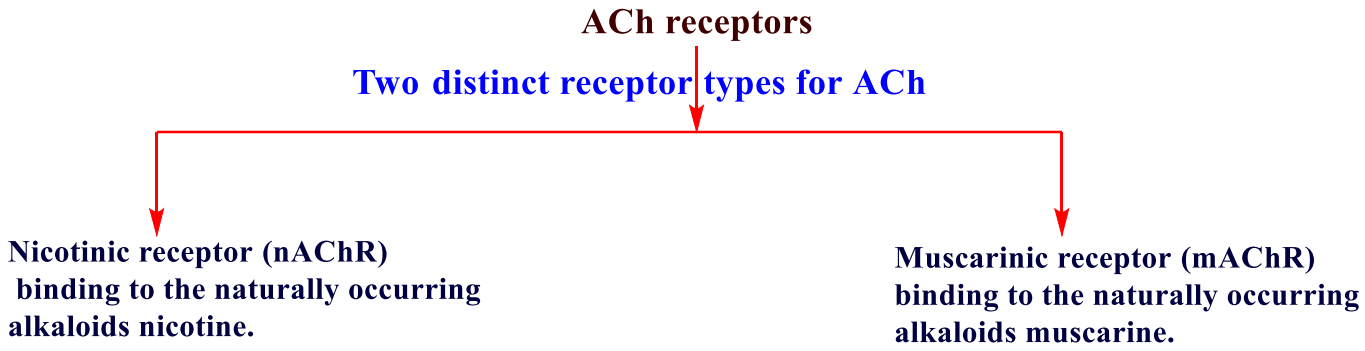
Cholinergic Drugs and Related Agents



Cholinergic agents: - are drugs and chemicals that act on cholinergic nerves or Tissues they innervate to either mimic or block the action of ACh.



CHOLINERGIC RECEPTORS



Nicotinic Receptors:- (ionotropic receptor, ligande gate ion channel)
when stimulated by their neurotransmitter they themselves become an ion channel.

Ion channels are responsible for:-

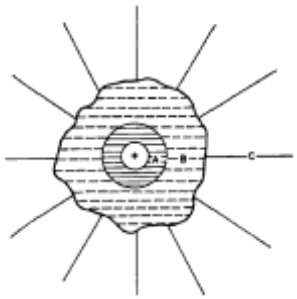
- The electrical excitability of nerve and muscle cells.
- The sensitivity of sensory cells.

The channels are pores that open or close on time scales ranging from 0.1 to 10 milliseconds to provide aqueous pathways through the plasma membrane that ions can transverse.

Factors affecting selectivity of ion pores include both:-

- The charge of ions.
- The size of ions.

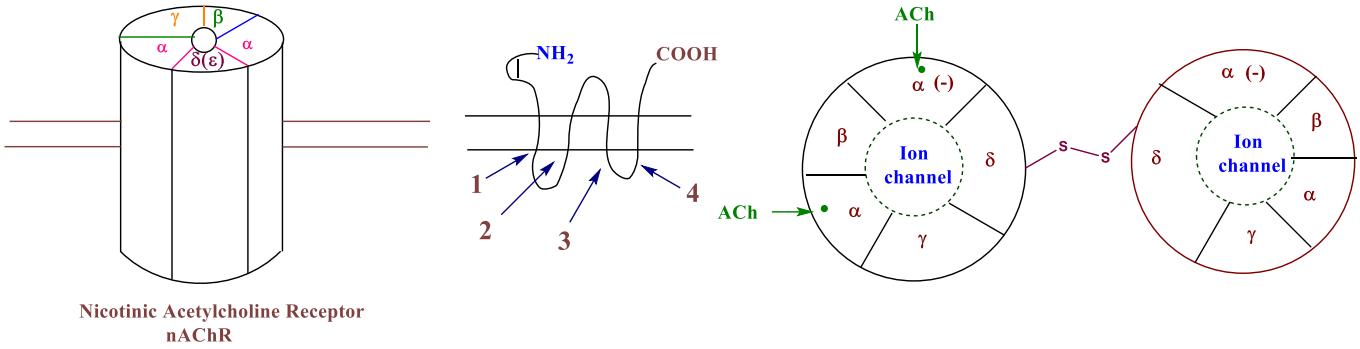
Ions in aqueous solution are hydrated. The water around the ion is characterized by the presence of two distinct water structures: a tightly bound, highly ordered layer immediately surrounding the ion and a second, less structured layer. The degree of organization of the water structure determines the energy required to remove the hydration shell and is a factor in the selectivity of that ion channel.



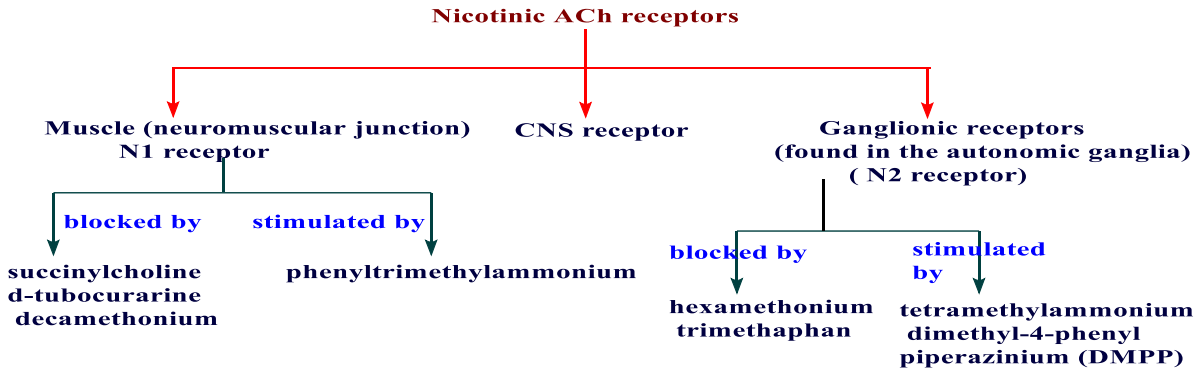
These ion channels are made of five subunits polypeptide chains, of which two appear to be identical, 2α, β, γ, and δ (ε) and they are arranged symmetrically around a central pore through which ions travel when opened. Each α chain contains a negatively charged binding site for the quaternary ammonium group of ACh . The receptor appears to exist as a dimer of the two five-subunit polypeptide chain monomers linked through a disulfide bond between δ chains. When stimulated by either Ach or nicotine. This is going to cause a conformational change in the shape of the ion channel, which is going to open the central pore to allow passage ions (Na^+, K^+, Ca^{+2}) through.

. The physiological effect is to temporarily depolarize the end plate. This depolarization results in muscular contraction at a neuromuscular junction or, as occurs in autonomic ganglia, continuation of the nerve impulse.

Neuromuscular nicotinic ACh receptors are of interest as targets for autoimmune antibodies in myasthenia gravis and for muscle relaxants used during the course of surgical procedures. Nicotinic receptors in autonomic ganglia, when blocked by drugs, can play a role in the control of hypertension.

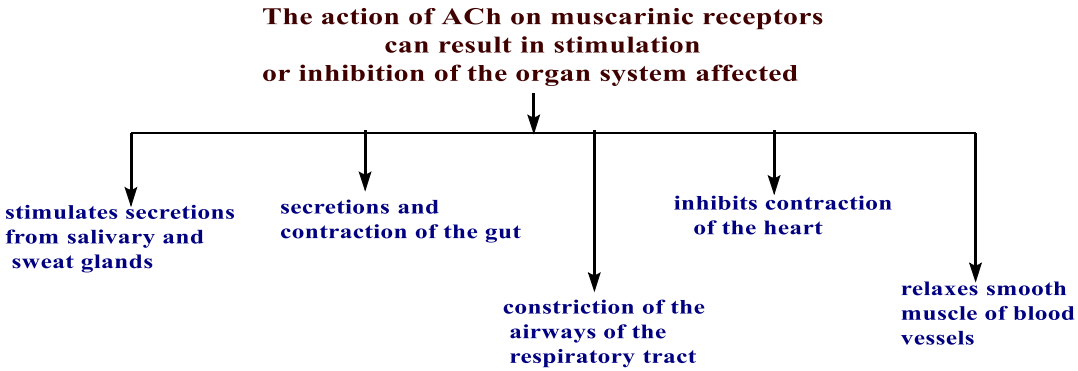


NICOTINIC RECEPTOR SUBTYPES



Muscarinic Receptors:- play an essential role in regulating the functions of organs innervated by the autonomic nervous system to maintain homeostasis of the organism.

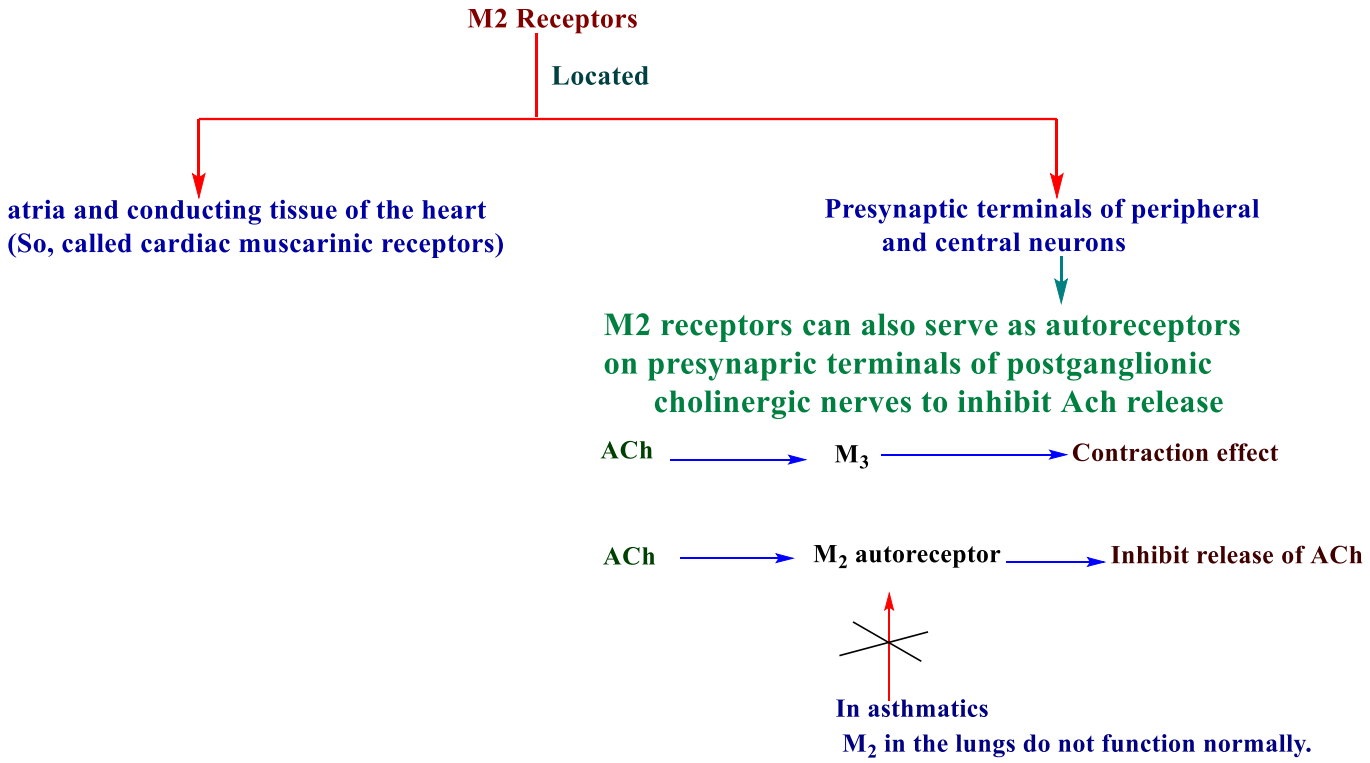
Muscarinic receptors mediate their effects by activating guanosine triphosphate (GTP)-binding proteins (G- protein).



Muscarinic Receptors subtypes

Subtypes of muscarinic receptors are located in the CNS and peripheral nervous system

M2 receptor:- are also called cardiac muscarinic receptors because they are located in the atria and conducting tissue of the heart.



M4 Receptors: - M_4 receptors, like M_2 receptors, act through G_i, protein to inhibit adenylate cyclase. They also function by a direct regulatory action on K^+ and Ca^{+2} ion channels. M_4 receptors in tracheal smooth muscle, when stimulated, inhibit the release of Ach in the same manner that M_2 receptors do.