



Compiled and circulated by Dr. Parimal Dua, Assistant Professor,
Dept. of Physiology, Narajole Raj college

Unit V: Introduction and classification of the drugs

acting on:

a. Autonomic nervous system

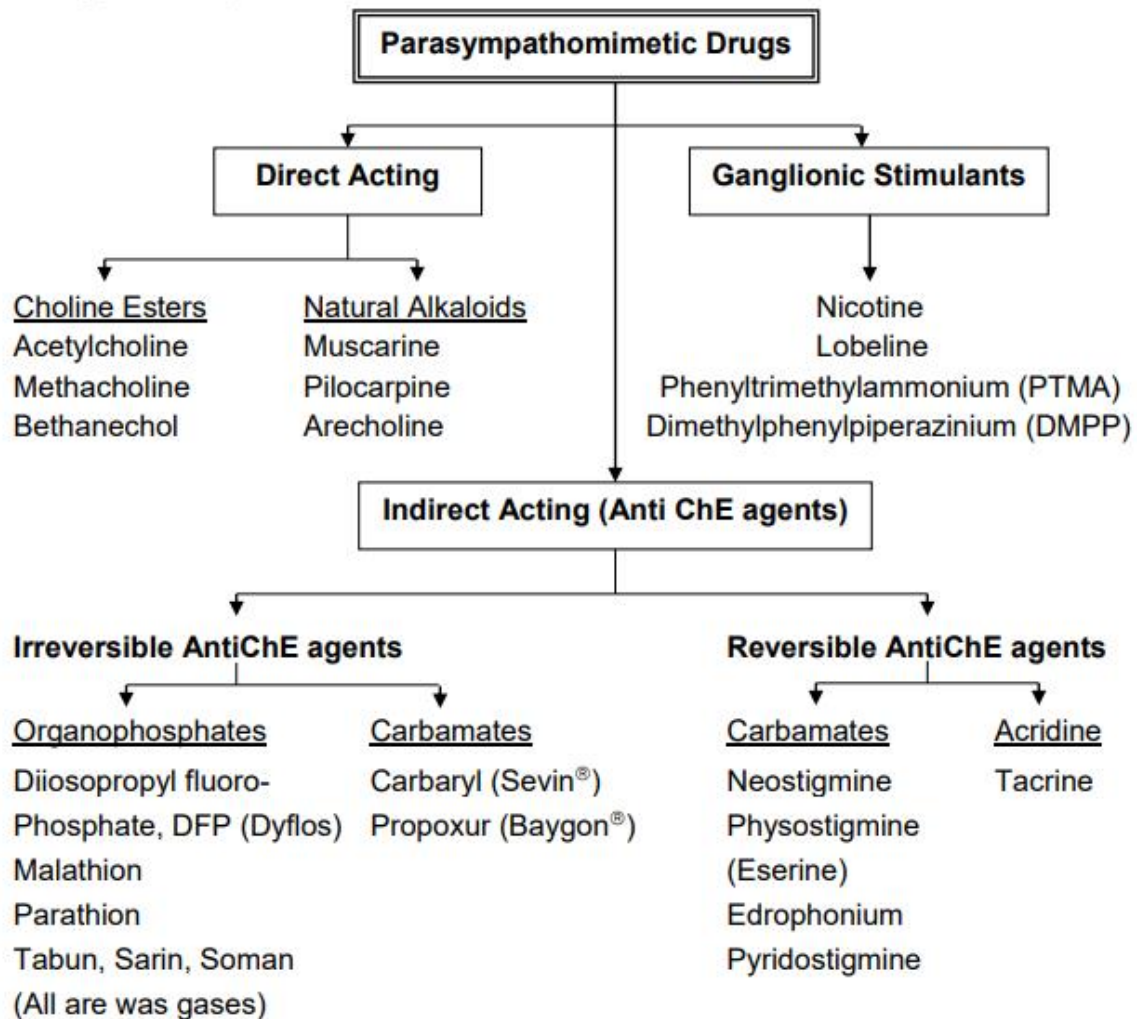
Introduction:

The autonomic nervous system is a coordinated motor system that consists of innervated cardiac muscle, smooth muscle, and glands. The ANS maintains homeostasis and provides a coordinated response to external stimulation. Much of homeostasis occurs involuntarily, but some autonomic processes have a degree of voluntary control (urination, sexual activity). The major components are the sympathetic and parasympathetic nervous systems.

❖ Cholinergic Drugs (Parasympathomimetics):

These are the drugs which mimic the effects of parasympathetic postganglionic nerves or those of acetylcholine. These are also called as cholinergics, cholinergic agonists or cholinomimetics. These drugs also have agonistic action on cholinergic receptors at autonomic ganglia, neuromuscular junction etc.

CLASSIFICATION:



(I) Choline Esters:

1) Acetylcholine (ACh): Although is essential for maintenance of body homeostasis, it is not used therapeutically for two important reasons:

- (i) It acts simultaneously at various tissue sites and no selective therapeutic response can be achieved.
- (ii) Its duration of action is quite brief because it is rapidly inactivated by the cholinesterases. Parasympathomimetic Drugs Direct Acting Ganglionic Stimulants Indirect Acting (Anti ChE agents).



Compiled and circulated by Dr. Parimal Dua, Assistant Professor,
Dept. of Physiology, Narajole Raj college

2) Methacholine (Acetyl- β -methylcholine): It is a synthetic choline ester used occasionally in human therapeutics but infrequently (rarely) employed in veterinary medicine.

Methacholine causes muscarinic effects on cardiovascular function similar to those produced by ACh, but it is considerably less active on GI system. Methacholine lacks nicotinic action.

Methacholine is a cholinomimetic of choice for controlling tachycardias of atrial origin. It will cause slowing of heart, reduction of the force of contraction & generalized vasodilatation. Main site of action of methacholine is the pacemaker.

3) Carbachol (Carbamoylcholine): It is an extremely potent choline ester that is active at both muscarinic and nicotinic receptors and therefore caused pharmacological effects similar to changes evoked by ACh. These are particularly prominent on the nicotinic receptors of autonomic ganglia; however, this drug is also very potent at muscarinic sites. For instance, intravenous injection of doses as small as $2\mu\text{g}/\text{kg}$ causes a transient slowing of heart rate and hypotension owing to muscarinic effects. Carbachol is sometimes used for the emergency treatment of colic in the horse and ruminal stasis in cattle. Administration of carbachol is done with great care and the drug is given in repeated small doses of 1-2 mg subcutaneously.

4) Bethanechol (Carbamoylmethylcholine): It is somewhat similar to methacholine and carbachol, however it is primarily a muscarinic agonist, and has little stimulant effects on nicotinic receptors.



Compiled and circulated by Dr. Parimal Dua, Assistant Professor,
Dept. of Physiology, Narajole Raj college

Table: Showing properties of choline esters

Choline esters	Hydrolyzed by		Actions		Selective actions on
	AChE	BuChE	Muscarinic	Nicotinic	
ACh	++	+	+	+	Non-selective
Methacholine	+	–	+	±	CVS
Carbachol	–	–	+	+	GIT, Bladder
Bethanechol	–	–	+	–	GIT, Bladder

Therapeutic uses of choline esters:

- (i) Methacholine and bethanechol are not used frequently in clinical veterinary medicine. Methacholine has been used in human medicine to control tachycardia of supraventricular origin.
- (ii) Bethanechol, 1 mg administered subcutaneously b.i.d. has been used to treat urinary bladder atony in cats after incidence of urolithiasis.
- (iii) Carbachol has been used in the treatment of colic and impactions of the intestinal tract. It is also used in the treatment of ruminal atony and impaction in cattle. However, none of the above have proved satisfactory results, so, now-a-days, these are not used clinically on routine basis.

(II) Natural Alkaloids:

(1) **Pilocarpine:** It is obtained from the leaves of Brazilian shrubs *Pilocarpus jaborandi* and *P. microphyllus*. It has prominent muscarinic actions and also stimulates ganglia – mainly through ganglionic muscarinic receptors. Pilocarpine is particularly effective in stimulating flow of secretions from exocrine glands, including salivary, mucous, gastric and digestive pancreatic secretions. As with acetylcholine, it causes contraction of GI smooth muscle, thereby increasing smooth muscle tone and peristaltic activity. Of considerable importance, Pilocarpine has a potent constrictor effect on the pupil. Applied to the eye, it penetrates cornea and promptly causes miosis, ciliary muscle contraction and fall in intraocular tension lasting 4-8 hours.



Compiled and circulated by Dr. Parimal Dua, Assistant Professor,
Dept. of Physiology, Narajole Raj college

- (2) **Arecholine:** It is an alkaloid found in the beetle nut, the seed of the beetle palm (*Areca catechu*). It has muscarinic as well as nicotinic actions including those on skeletal muscle end plate. It is similar to Pilocarpine in scope of activity but is considerably more potent. It stimulates secretion of the glands of the digestive tract and increases peristaltic movement of the gut. Increased flow of the saliva occurring within 5 minutes following a subcutaneous injection and lasting for an hour is particularly noticeable. Arecholine contracts the urinary bladder.
- (3) **Muscarine:** It is found in the poisonous mushrooms *Amanita muscaria*, and has only muscarinic actions. It is not used therapeutically, but, is of toxicological importance.

Therapeutic uses of cholinomimetic alkaloids:

- (i) Clinically, solutions of 0.5 to 2% of pilocarpine are used for instillation into the conjunctival sac for treatment of glaucoma.
- (ii) Other uses of pilocarpine as a miotic are – to counteract mydriatics after they have been used for testing refraction and to prevent or break adhesions of iris with lens or cornea by alternating it with mydriatics.