SHAMBHUNATH INSTITUTE OF PHARMACY

3rd Sessional Examination 2019-20

D. Pharm. Final Year

Subject- Pharmacology

Time: - 90 minutes. **Max. Marks: 20**

Roll no. - **Subject code: 214206**

Note: Attempt any **four** questions. **(4x5=20)**

1. Write in detail about cholinergic system with their agonists and antagonists.
2. Give the classification, mechanism of action, therapeutic use and pharmacokinetics of following topics:
   a) Ganglion blockers
   b) Anti parkinsonism agents
3. Write in detail about adrenergic receptor blockers with their examples (classification).
4. Give the classification, mechanism of action, therapeutic use and pharmacokinetics of following topics:
   a) Drugs used in glaucoma
   b) Anti cholinesterase drugs
5. Write in detail about Local anesthetics.

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Solutions:

1. Synthetic insecticides are still widely used in plant protection. The main target for their action is the nervous system, in which the cholinergic system plays a vital role. Currently available insecticides have low selectivity and act on the cholinergic systems of invertebrates and vertebrates. Acetylcholine, a cholinergic system neurotransmitter, acts on cells by two types of receptors: nicotinic and muscarinic. In mammals, the role of muscarinic acetylcholine receptors (mAChRs) is quite well-known but in insects, is still not enough. Based on data indicating that the muscarinic cholinergic system strongly affects mammalian metabolism, we investigated if it similarly occurs in insects. We investigated the influence of agonists (acetylcholine, carbachol, and pilocarpine) and antagonists (tropane alkaloids: atropine and scopolamine) of mAChRs on the level of selected metabolites in *Tenebrio molitor* beetle trophic tissues. We analyzed the glycogen content in the fat body and midgut, the total free sugar concentration in the hemolymph and the lipid amount in the fat body. Moreover, we analyzed the levels of insulin-like peptides in the hemolymph. The tested compounds significantly influenced the mentioned parameters. They increased the glycogen content in the fat body and midgut but decreased the concentration of free sugars in the hemolymph. The observed effects were tissue-specific, and were also time- and dose-dependent. We used nonligated and neck-ligated larvae (to eliminate the influence of head factors on tissue metabolism) to determine whether the observed changes are the result of direct or indirect impacts on tissues. The obtained data suggest that the cholinergic system affects the fat body and midgut indirectly and directly and a pleiotropic role for mAChRs exists in the regulation of energy metabolism in insects. Moreover, tested compounds significantly affected the level of insulin-like peptides in hemolymph. Our studies for the first time showed that mAChRs are involved in regulation of insect metabolism of trophic tissues, and act on them directly and indirectly. Improved knowledge about insect cholinergic system may help in searching more selective and environment-friendly solutions in pest management.
2. **Ganglion blockers-**

   A ganglionic blocker (or ganglioplegic) is a type of medication that inhibits transmission between preganglionic and postganglionic neurons in the Autonomic Nervous System, often by acting as a nicotinic receptor antagonist. Nicotinic acetylcholine receptors are found on skeletal muscle, but also within the route of transmission for the parasympathetic and sympathetic nervous system (which together comprise the autonomic nervous system). More specifically, nicotinic receptors are found within the ganglia of the autonomic nervous system, allowing outgoing signals to be transmitted from the presynaptic to the postsynaptic cells. Thus, for example, blocking nicotinic acetylcholine receptors blocks both sympathetic (excitatory) and parasympathetic (calming) stimulation of the heart. The nicotinic antagonist hexamethonium, for example, does this by blocking the transmission of outgoing signals across the autonomic ganglia at the postsynaptic nicotinic acetylcholine receptor.

Uses-

Ganglionic blockers are used less frequently now than they were in the past, because antihypertensives with fewer side effects are now available. Hexamethonium has been described as the "first effective antihypertensive drug".[4] However, they are still used in some emergency situations, such as aortic dissection or autonomic dysreflexia.

3. Anti parkinsonism agents-

Antiparkinsonian agents are used in the treatment of Parkinson's disease (PD), RLS, and PLM disorder. PD is a neurodegenerative movement disorder that results from a depletion of dopaminergic neurons in the substantia nigra. Approximately 74–98% of patients with PD experience some form of a sleep disorder (Bhatt et al., 2005), including insomnia, OSA, parasomnias, PLM disorder, RLS, REM sleep behavior disorder, EDS, and circadian rhythm disturbances. Difficulty falling asleep may be due to parkinsonian tremors or RLS symptoms. Problems staying asleep may also be due to tremors, which can also occur during light S1 sleep but rarely in S3 or S4 sleep (Hening et al., 1999), nocturnal akinesia, PLMs, OSA, or REM sleep behavior disorder. It is not known if these sleep disorders are a consequence of the disease pathology itself, the medications used to treat PD, or from other psychiatric complications such as depression.

Drug	**Adverse effects**
Dopamine agonists	Compulsive behavior (i.e., pathological gambling) (Dodd et al., 2005)
	Uncontrollable somnolence (Avorn et al., 2005)
	Insomnia (Horn and Stern, 2004)
	Dizziness (Etminan et al., 2003)
	Orthostatic hypotension (Horn and Stern, 2004)
	Levodopa phobia (Kurlan, 2005)
	Serotonin syndrome (Bainbridge et al., 2008)
Levodopa	Headache, dizziness, somnolence (Horn and Stern, 2004)
COMT inhibitors	Somnolence/insomnia (Horn and Stern, 2004)
Anticholinergics	Confusion (Horn and Stern, 2004)
MAO B inhibitors	Insomnia (Thornton et al., 1980)
	Headache (Horn and Stern, 2004)
	Serotonin syndrome (Bainbridge et al., 2008)

4. **Drugs used in glaucoma-**

Drugs to treat glaucoma are classified by their active ingredient. These include: prostaglandin analogs, beta blockers, alpha agonists, carbonic anhydrase inhibitors, and rho kinase inhibitors. In addition, combination drugs are available for patients who require more than one type of medication.

Types of Medications

Alpha Adrenergic Agonists

This medication both reduces aqueous humor production and increases its outflow. Allergic reactions frequently occur with this class of medication.

Examples include:

- Apraclonidine (Iopidine)
- Brimonidine (Alphagan)
- Epinepherine (Gluacon and Epifrin)
- Dipivefrin (Propine)

Beta Blockers

This type of medication works to lower eye (intraocular) pressure by reducing aqueous humor production and decreasing the rate at which the fluid flows into the eye.

Examples include:

- Timolol (Timoptic XE Ocumeter and Timoptic)
- Levobunolol (Betagan)
- Carteolol (Ocupress)
- Metipranolol (OptiPranolol)
- Betatoxol (Betoptic)

Carbonic Anhydrase Inhibitors

These are eye drops or pills that reduce fluid production in the eye. Examples include:

- Dorzolamide (Trusopt)
- Brinzolamide (Azopt)
- Acetazolamide (Diamox): an oral medication
- Methazolamide (Neptazane): an oral medication

b) **Anti cholinesterase drugs- Anticholinesterase**, any of several drugs that prevent destruction of the neurotransmitter acetylcholine by the enzyme acetylcholinesterase within the nervous system. Acetylcholine acts to transmit nerve impulses within the parasympathetic nervous system—i.e., that part of the autonomic nervous system that tends to induce secretion, to contract smooth muscles, and to dilate blood vessels. In preventing the destruction of acetylcholine, anticholinesterase permits high levels of this neurotransmitter to build up at the sites of its action, thus stimulating the parasympathetic nervous system and in turn slowing the heart action, lowering blood pressure, increasing secretion, and inducing contraction of the smooth muscles.

Physostigmine and neostigmine are among the principal anticholinesterases. These drugs have only a few clinical uses, mainly in augmenting gastric and intestinal contractions (in treatment of obstructions of the digestive tract) and in augmenting muscular contractions in general (in the treatment of myasthenia gravis). Anticholinesterase drugs that are used more widely in the clinic are those that inhibit acetylcholinesterase in the brain. The most useful application of such agents is in the treatment of Alzheimer disease, in which reduced transmission of acetylcholine contributes to the neuropathology of the disease. When the breakdown of acetylcholine is inhibited, levels of the neurotransmitter can return to near normal, and the degeneration of neurons—and hence the degeneration of cognitive ability—is slowed. Agents that have been developed for this purpose include donepezil, tacrine, and galantamine. However, the potentially

dangerous side effects of these drugs has limited their use. For example, liver toxicity caused by tacrine has restricted its availability by prescription. In addition, although donepezil, which is marketed as Aricept, was found to marginally benefit some persons with early-onset Alzheimer disease, its use has been primarily limited to individuals with late-stage disease, for whom the benefits outweigh the risks of side effects.

5. **Local anesthetics-**

Local anesthetics are medications used for the purpose of temporary and reversible elimination of painful feelings in specific areas of the body by blocking transmission of nerve fiber impulses. Local anesthesia is any technique to render part of the body insensitive to pain without affecting consciousness. Local anesthetics are a group of structurally related compounds which share as principal mechanism of action the blockade of voltage-gated sodium channels, resulting in reversible interruption of nerve signal transduction. Currently used local anesthetics are divided into amino amides, or amino esters. Each substance has distinct physicochemical properties, and local anesthetics can be administered continuously or together with adjuvants, allowing clinicians to tailor their anesthetic to procedure and patient. Next to sodium channel blockade, local anesthetics interact with other targets, for example calcium and potassium channels, and G-protein coupled receptors. The latter mode of action explains the anti-inflammatory properties of local anesthetics. Clinical application of existing local anesthetics, and development of novel local anesthetics, is hampered by systemic and local toxicity. Among the additives to local anesthetics, epinephrine is helpful in prolonging duration of action of medium-acting local anesthetics, and to reduce systemic absorption of any local anesthetic. Buprenorphine is an effective additive and has local anesthetic properties but causes excessive nausea and vomiting. Dexmedetomidine and clonidine are popular additives as well but can cause dose-dependent systemic side effects such as sedation, bradycardia and hypotension. Dexamethasone has the least systemic side effects, and the longest prolongation of nerve block duration. Emerging developments in the field of local anesthetics include the development of subtype-specific sodium channel blockers, cell type-specific or heat-assisted delivery, and various modes of encapsulation.