Antihistaminics

BP-503T

Antihistaminic agents

- By convention, the generic term ‘antihistamine’ usually refers only to the H1-receptor antagonists that are used for treating various inflammatory and allergic conditions
- These drugs act as competitive antagonists at H1 receptors, and Conventionally, the antihistamines are classified into ‘first generation’, which cross the blood–brain barrier and often have sedating actions, and ‘second generation’ drugs, which broadly speaking, do not; i.e. on the basis of CNS penetration and anticholinergic properties.
- In addition to these, there are several others that are primarily used topically (e.g. in nasal sprays or eye drops) in the treatment of hay fever and other allergic symptoms. These include antazoline, azelastine, epinastine, olapatadine and emedastine. In addition to their H1 antagonist activities, some antihistamines (e.g. ketotifen) may also have ‘mast cell stabilising’ and other anti-inflammatory properties unrelated to histamine antagonism

Comparison of some commonly used systemic antihistamines

Type	Drug	Common anti-allergic use	Comments
'Sedating'	Alimemazine	U	Strong sedative action. Sometimes used for anaesthetic premedication
	Chlorphenamine	AE, H, U	—
	Cinnarizine	—	Also used to treat nausea, vomiting, motion sickness
	Clemastine	H, U	—
	Cyclizine	—	Also used to treat nausea, vomiting, motion sickness
	Cyproheptadine	H, U	Also used for migraine
	Hydroxyzine	U	May cause QT interval prolongation
	Ketotifen	H	Mast cell 'stabilising' properties.
	Promethazine	H, U, AE	Strong sedative action. Also used to control nausea and vomiting
'Non-sedating'	Acrivastine	H, U	—
	Bilastine	H, U	—
	Cetirizine	H, U	—
	Desloratadine	H, U	Metabolite of loratadine. Long-lasting action
	Fexofenadine	H, U	'Cardio-safe' metabolite of terfenadine
	Levocetirizine	H, U	Isomer of cetirizine
	Loratidine	H, U	—
	Mizolastine	H, U	May cause QT interval prolongation
	Rupatadine	H, U	Also antagonises PAF (see Ch. 18)

AE, allergic emergency (e.g. anaphylactic shock); *H,* hay fever; *PAF,* platelet activating factor; *S,* sedation; *U,* urticaria and/or pruritus.
(Data from various sources, including the British National Formulary, 2017.)

Source: Rang and Dale's Pharmacology Ninth Edition

First Generation Anti-histaminics

Highly sedating	Moderately sedating	Mildly sedating
Diphenhydramine	Pheniramine	Chlorpheniramine
Dimenhydrinate	Cyproheptadine	Mepyramine
Promethazine	Meclizine	Cyclizine
Hydroxyzine	Buclizine	Clemastine
Doxepin	Cinnarizine	

USES:

Based on H_1 blocking action	Based on anticholinergic properties	Other uses
1. Allergic conditions like *itching, urticaria, hay fever* etc. 2. *Insect bite, ivy poisoning* and to prevent the adverse effects due to histamine releasers.	1. *Common cold* (to control rhinorrhoea) 2. *Motion sickness* (as prophylactic agents) 3. *Parkinsonism* (promethazine may be used) 4. *Acute muscular dystonia*	1. Antihistaminics are drug of choice for *idiopathic pruritis* 2. Cinnarizine is useful in *vertigo*.

Pharmacokinetic aspects

- Most of orally active H1-receptor antagonists are well absorbed and remain effective for 3–6 h, although there are some prominent exceptions (e.g. loratidine, which is converted to a long-acting metabolite). Most appear to be widely distributed throughout the body, but some do not penetrate the blood–brain barrier, for example the non-sedating drugs mentioned above given Table. They are mainly metabolised in the liver and excreted in the urine. Many antihistamines have peripheral anti-muscarinic **side effects**. The commonest of these is dryness of the mouth, but blurred vision, constipation and retention of urine can also occur. Unwanted effects that are not mechanism-based are also seen; GI disturbances are fairly common, while allergic dermatitis can follow topical application

Second Generation Anti-histaminics

- These drugs have little CNS penetration, thus do not cause sedation, and do not possess anticholinergic activity. Some drugs like **cetirizine** and **azelastine** possess additional **antiallergic** mechanisms.
- Terfenadine is the fastest acting antihistaminic drug. In overdose, it blocks cardiac K+ channels and may result in ventricular tachycardia (torsades de' pointes). Use of this drug with microsomal enzyme inhibitors like ketoconazole, erythromycin, clarithromycin and itraconazole increases the risk of this arrhythmia.

Terfenadine is metabolized to an active metabolite "fexofenadine" (available as a separate drug) that lacks K+ channel blocking property.

- Astemizole is slowest and longest acting agent and possesses arrhythmogenic property similar to terfenadine.
- Loratidine is another long acting second generation antihistaminic and is metabolized to desloratidine (available as a separate drug).
- Cetirizine is an active metabolite of a first generation antihistaminic drug, hydroxyzine.