AJPMHS GLOBAL RESEARCH NETWORK

AMERICAN Journal of Pediatric Medicine and Health Sciences
Volume 3, Issue 5, 2025 ISSN (E): 2993-2149

Analysis of General and Specific Pharmacological Properties of Antiallergic Drugs

Sokhib Rashidov Zamon o‘g‘li, Murodjon Nabiev Mukhammadkarim o‘g‘li, Mo‘tabar Yoqubjonova Khusanboy qizi, Shakhzodakhon Bekmurodova Po‘latjon qizi, Jumanazar To‘ychiev Saidqul o'g'li
Department of pharmacology, Tashkent medical academy
rashidovsohib9295@gmail.com

Abstract: Widespread proinflammatory and inflammatory activation, strong cytokine and chemokine signaling, and diverse immunological and endothelial responses are all features of the allergy cascade that eventually result in allergic reaction symptoms. Released from granules found in mast cells, basophils, lymphocytes, and other reservoirs, histamine is a tiny peptide with intrinsic vasoactive qualities. It interacts with histamine receptors to control a variety of cellular processes related to allergic inflammation and immunological regulation. The primary target of suppressive medication is the H1-receptor, which is most obviously linked to increased effector function and proinflammatory immune cell activity potentiation among the known histamine receptors. As highly selective, long-acting H1-receptor agonists at its specific receptor, second-generation oral H1-antihistamines, including cetirizine, desloratadine, fexofenadine, levocetirizine, and loratadine, are cornerstones of allergy treatment. Further research is required to establish the role of antihistamines like desloratadine in anti-inflammatory therapy, as evidenced by the ongoing identification of immune effector cells and mediators implicated in the allergic cascade. Members of an interprofessional team that oversees the treatment of patients with conditions that respond to histamine receptor blockade need to be aware of the indications, contraindications, activity, adverse events, and other crucial aspects of antihistamine therapy in the clinical setting.

Keywords: Desloratadine, second-generation antihistamines, urticaria, allergic rhinitis, antihistamines, anti-inflammatory drugs.

Introduction. One of the most researched molecules in medicine, histamine plays a crucial role in the development of allergic rhinitis (AR) and urticaria. It interacts with a special set of membrane-bound receptors that are widely distributed across immune cell subtypes and participate in complex bidirectional messaging between cytokines and inflammatory cells or their precursors. It also helps cells migrate to inflammatory sites, stimulates lymphocyte activity, and modifies the behavior of eosinophils, neutrophils, and mast cells.1–4 It is directly responsible for the development of the classic allergic symptoms, including rhinorrhea, sneezing, congestion, nasal, ocular, and dermal pruritus, hives, and flushing [1-4]. The cascade of allergies. Degranulation is brought on by mast cell mediators, such as cytokines, which also support lymphocyte activity, immune cell migration to inflammatory areas, and bidirectional communication with other inflammatory cells or their progenitors. MBP, or mannose-binding protein; MHC II, or major histocompatibility complex; PGs, or prostaglandins; Ig, or immunoglobulin; IL, or interleukin; LT, or leukotriene; ECP, or eosinophil cationic protein;

ICAM, or intracellular adhesion molecule [5,6]. The primary focus of suppressive therapy for AR and urticaria using second-generation H1-antihistamines, such as cetirizine, desloratadine, ebastine, fexofenadine, levocetirizine, loratadine, and rupatadine, is the interaction between the H1-histamine receptor and histamine. The receptor is most obviously linked to the modulation of proinflammatory immune cell activity. These antihistamines work well together as a class to relieve the symptoms of histamine-mediated illnesses. Second-generation antihistamines virtually eliminate unwanted central nervous system (CNS) side effects including somnolence when taken as prescribed. They are also far less likely to produce other undesired anticholinergic side effects that are typical of first-generation antihistamines. According to current management guidelines, first-line treatment for urticaria and AR should use second-generation antihistamines [7-10]. Individual second-generation antihistamines differ in their pharmacology and, potentially, in their capacity to inhibit proinflammatory mediators linked to an allergic reaction. While certain anti-inflammatory actions of antihistamines appear to be receptor-independent, others appear to require early contact with the histamine receptor. To ascertain whether these variations in anti-inflammatory pharmacology result in effects that are clinically significant, more research is required. The second-generation oral antihistamine desloratadine, the active metabolite of loratadine, has demonstrated effectiveness in randomized, controlled clinical trials with a safety and tolerability profile comparable to that of a placebo. Desloratadine is approved by the European Union to treat urticaria and intermittent and persistent AR in adults and children ≥1 year. Perennial AR and chronic idiopathic urticaria (CIU) in adults and children aged ≥6 months, as well as seasonal AR in adults and children aged ≥2 years, can be treated with desloratadine in the US [11-14]. Similar to antihistamines like levocetirizine (the active enantiomer of cetirizine) and others, desloratadine suppresses a variety of inflammatory mediators in addition to displaying strong H1-receptor antagonism, according to in vitro, animal model, and in vivo research. This review will offer new data that broadens desloratadine's antihistaminic, anti-inflammatory, and antiallergic properties [15-18].

The main purpose of the presented analytical manuscript is to provide a brief overview based on many years of scientific research devoted to the analysis of the general and specific pharmacological properties of antiallergic drugs.

Pharmacological Factors Associated with Antihistamine Sedation. A class of pharmacological medications known as antihistamines is used to treat illnesses that are mediated by histamine. Histamine receptors can be divided into two major classes: H-1 and H-2. Allergies and allergic rhinitis are typically treated with antihistamine medications that bind to H-1 receptors. Upper gastrointestinal disorders brought on by too much stomach acid are treated with medications that bind to H-2 receptors. First- and second-generation agents are used to further categorize H-1 antihistamines. In contrast to second-generation H-1 antihistamines, first-generation H-1 antihistamines have an easier time entering the central nervous system (CNS) through the blood-brain barrier. While second-generation medications selectively bind to peripheral histamine-1 receptors, first-generation medications will bind to both central and peripheral histamine-1 receptors; this results in distinct therapeutic and adverse effect profiles [5-13].

The H1-histamine receptor. The effects of histamine are mediated by four specialized, widely distributed receptors (designated H1, H2, H3, and H4). The type of effector response that is elicited depends on the local concentration of histamine and the predominant type of histamine receptor that is undergoing activation. The majority of cells involved in inflammatory reactions express H1, H2, and H4 subtypes, with the H1-receptor playing a major role in potentiation of proinflammatory immune cell activity and effector responses essential to an allergic reaction; the H2-receptor, on the other hand, appears to suppress inflammatory and effector functions, while there is little information about the function of the H4-receptor in immune response [4-11]. The G-protein coupled receptor family includes the transmembrane protein known as the H1-receptor. Following the interaction of a particular ligand or agonist, the GCPR gets activated, resulting in signal transduction from the extracellular to the intracellular environment. A subunit

of the G-protein then separates and influences intracellular communication, including downstream signaling carried out by a number of intermediaries, including calcium, cyclic AMP, cyclic GMP, and nuclear factor kappa B (NF-κB), a ubiquitous transcription factor believed to be crucial for immune-cell chemotaxis, the production of proinflammatory cytokines, the expression of cell adhesion molecules, and other inflammatory and allergic disorders [15-21].

Antihistaminic, anti-inflammatory, and antiallergic effects of desloratadine. The H1-receptor affinity. The assay's effector end point was the measured change in histamine-induced intracellular calcium. Desloratadine binds avidly and noncompetitively to a recombinant human H1-receptor, exhibiting 52, 57, 194, and 153 times more potency for the interaction than cetirizine, ebastine, fexofenadine, and loratadine, respectively. Only 37% of desloratadine is free at 6 hours after binding, indicating pseudo-irreversibility and indicating a prolonged duration of effect. Once bound, desloratadine dissociates from the receptor slowly [3-6]. Inverse agonism was exhibited by desloratadine, a second-generation antihistamine, which decreased downstream messaging by spontaneously activated receptors. In one study, desloratadine significantly decreased baseline NF-κB activity compared to equal amounts of cetirizine, fexofenadine, loratadine, or pyrilamine by efficiently inhibiting downstream signaling of a constitutively active human H1-receptor linked to NF-κB production. Furthermore, desloratadine was more effective than comparators at preventing the increase of NF-κB following histamine exposure-induced receptor activation [9-13].

Impact on Immune Cells: Migration, Survival, and Eosinophil Activation. Recruited from the circulation to areas of inflammatory activity, eosinophils—important effector cells in the allergic response—participate in immune responses and release a variety of preformed cytotoxic cationic proteins, including major basic protein, cationic protein, peroxidase, and neurotoxin protein. Leukotrienes, chemokines, neuromodulators, and cytokines are also produced by eosinophils. Desloratadine may have an impact on the activation, survival, precursors, and chemoattractants of eosinophils [1-5]. The main chemoattractant for eosinophils, monocytes, and t-lymphocytes, desloratadine decreases the production of NF-κB, a known inducer of RANTES (regulated upon activation, normal T-cell produced and released). RANTES stimulates basophil histamine release and eosinophil activation. In response to tumor necrosis factor (TNF), eosinophil cationic protein, and activated mast cells, desloratadine suppressed the release of RANTES by nasal polyp epithelial cell lines; this suppression was also reflected in decreased tryptase and leukotriene C4 synthesis [11-15]. The idea that desloratadine prevents these cells from migrating from circulation to inflammatory sites in nasal tissue may also be supported by the statistically significant drop in nasal lavage eotaxin observed in the desloratadine group when compared to the placebo group. Peripheral blood eosinophils incubated with human epithelial cell conditioned medium from nasal mucosa or nasal polyp tissue showed a dose-dependent decrease in survival following preincubation with desloratadine in a study evaluating eosinophil survival at the site of upper airway inflammation [18-21].

Negative Impacts. Depending on the particular drug class used, antihistamine medications can have a wide range of side effects. The side effects of H-1 receptor antihistamines are typically dose-dependent and clinically significant. First-generation antihistamines are considerably more likely to cause these negative effects. The adverse effect profile of second-generation antihistamines is much more constrained since they have a harder time passing through the blood-brain barrier. With the exception of cimetidine, H-2 receptor antihistamines rarely cause side effects, in contrast to H-1 receptor antihistamines. Only the first generation of antihistamines primarily exhibit the adverse effect-inducing anticholinergic characteristics of H-1 receptor antihistamines. They are generally sedative, but some users may experience sleeplessness as a result [5-11]. Dry mouth is a quite common side effect because of its anticholinergic qualities. Tinnitus and vertigo are experienced by some users. Euphoria and impaired coordination can also happen at greater dosages, and delirium is a possible side effect at even higher dose levels. Due to their impact on QTc prolongation, antihistamines may also be cardiotoxic to certain users. Although most users tolerate H-2 receptor antihistamines well, there

is a chance of rare side effects. Constipation and diarrhea are among the gastrointestinal abnormalities that are visible. There are reports of exhaustion, lightheadedness, and disorientation. Cimetidine is one particular medication in this class that has the potential to have a number of negative side effects. Its antiandrogenic properties are associated with the potential for male gynecomastia. It can result in galactorrhea in women [13-18]. Drug toxicity and combinations with other drugs might result from H-2 receptor antihistamines' suppression of the cytochrome system, particularly cimetidine. Antihistamines should be used cautiously in patients who have hemodynamic changes, elevated intraocular pressure, or increased urine retention because these problems may worsen [19,20,21].

Many possible targets and mechanisms for desloratadine's modulation of histamine-receptor activity, down-regulation of inflammatory cytokines and chemokines, or stimulation of inflammatory cell migration and survival are provided by the biochemical and effector pathways triggered by the allergic reaction. Desloratadine's anti-inflammatory effects on inflammatory cell activity and mediator release are supported by in vitro evidence. Nevertheless, desloratadine concentrations used in these investigations are usually higher than those found in clinical settings at currently advised dosages. Desloratadine dose escalation may provide a stronger anti-inflammatory response, as evidenced by dose-dependent suppression of the inflammatory response observed in vitro. Desloratadine may influence elements of inflammation through mechanisms other than H1-histamine receptor inhibition, according to mounting evidence. More research is needed to determine potential processes [17-21].

Discussion. Antihistamines are a class of pharmaceutical drugs that act to treat histamine-mediated conditions. There are two main classes of histamine receptors: H-1 and H-2. Antihistamines that bind to H-1 receptors are typically used to treat allergies and allergic rhinitis, while those that bind to H-2 receptors can treat upper gastrointestinal conditions caused by excessive stomach acid. This activity reviews the indications, contraindications, activity, adverse events, and other important aspects of antihistamine therapy in the clinical setting as they relate to the critical information required by members of an interprofessional team managing the care of patients with conditions that respond to histamine receptor blockade [1,4,5,7]. Patients with allergic rhinitis benefit greatly from antihistamines that target the histamine H1 receptor in order to preserve and improve their quality of life. A classification based on the specific properties of second-generation medications is required for their safer and more effective usage, as advised by numerous standards. First-line antihistamines shouldn't have sedative or central depressive properties. Central histamine neuron inhibition is linked to sedative effects, such as tiredness and decreased performance. One helpful metric that has been demonstrated to correspond with indices based on clinical findings is brain H1 receptor occupancy (H1RO). Based on H1RO, antihistamines are divided into three groups: non-sedating (<20%), less-sedating (20–50%), and sedating (≥50%). According to the H1RO, fexofenadine and bilastine are categorized as "non-brain-penetrating antihistamines" under the non-sedating group [8-12]. Numerous chemical characteristics of these two medications are similar. Bilastine, on the other hand, binds to the H1 receptor more strongly and has a longer half-life. Even at twice the recommended dosage (20 mg), bilastine has no effect on psychomotor or driving performance in well-controlled studies that use objective markers. A number of circumstances should be taken into account while choosing antihistamines for allergic rhinitis. According to this evaluation, the first-line treatment for mild allergic rhinitis should involve non-brain-penetrating antihistamines [9,14,15,17]. When prescribing antihistamines, healthcare professionals like doctors, nurse practitioners, and physician assistants should exercise caution and ensure that the patient's medication profile is reviewed by the pharmacist to spot any clinically significant drug interactions, particularly in older patients [18,19,20].

Conclusions. The class of drugs known as antihistamines is further classified into H-1 and H-2 groups. The primary purpose of H-1 antihistamines, which are further classified into first and second generations, is to treat allergy symptoms and diseases that are mediated by comparable pathways. Acid reflux, gastritis, and gastrointestinal ulcers can all be treated with H-2

antihistamines by reducing excessive stomach acid. Because antihistamines may be purchased off-the-shelf at pharmacies, pharmacists act as both dispensers and educators of these drugs. They play a vital role in advising the patient to use the appropriate dosage and to be aware of any negative effects and contraindications. In addition to providing advice on side effects and noting the therapeutic efficacy of these drugs, nurses should be ready to respond to inquiries about them and share any results with the clinician. Physicians, nurse practitioners, and physician assistants who prescribe antihistamines should exercise caution and ensure that the patient's medication profile is reviewed by the pharmacist to identify any clinically significant drug interactions, particularly in older patients, and that the healthcare team is informed of the recommendation.

References.

1. Farzam K, Sabir S, O'Rourke MC. Antihistamines. [Updated 2023 Jul 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538188/
2. Canonica GW, Blaiss M. Antihistaminic, anti-inflammatory, and antiallergic properties of the nonsedating second-generation antihistamine desloratadine: a review of the evidence. World Allergy Organ J. 2011 Feb;4(2):47-53. doi: 10.1097/WOX.0b013e3182093e19.
3. Monczor F, Fernandez N. Current Knowledge and Perspectives on Histamine H1 and H2 Receptor Pharmacology: Functional Selectivity, Receptor Crosstalk, and Repositioning of Classic Histaminergic Ligands. Mol Pharmacol. 2016 Nov;90(5):640-648.
4. Schaefer TS, Patel P, Zito PM. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Mar 10, 2024.
5. Antiemetic Histamine H1 Receptor Blockers. Curto-Barredo L, Giménez-Arnau AM. Treatment of chronic spontaneous urticaria with an inadequate response to H1-antihistamine. G Ital Dermatol Venereol. 2019 Aug;154(4):444-456.
6. Kuna L, Jakab J, Smolic R, Raguz-Lucic N, Vcev A, Smolic M. Peptic Ulcer Disease: A Brief Review of Conventional Therapy and Herbal Treatment Options. J Clin Med. 2019 Feb 03;8(2)
7. Pirahanchi Y, Sharma S. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Jul 11, 2023.
8. Physiology, Bradykinin. Heda R, Toro F, Tombazzi CR. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): May 1, 2023.
9. Physiology, Pepsin. Kawauchi H, Yanai K, Wang D-Y, Itahashi K, Okubo K. Antihistamines for Allergic Rhinitis Treatment from the Viewpoint of Nonsedative Properties. International Journal of Molecular Sciences. 2019; 20(1):213. https://doi.org/10.3390/ijms20010213
10. Bowman JD, Kim H, Bustamante JJ. Drug-induced gynecomastia. Pharmacotherapy. 2012 Dec;32(12):1123-40.
11. Farzam K, Tivakaran VS. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Jul 2, 2023.
12. QT Prolonging Drugs. Boley SP, Olives TD, Bangh SA, Fahrner S, Cole JB. Physostigmine is superior to non-antidote therapy in the management of antimuscarinic delirium: a prospective study from a regional poison center. Clin Toxicol (Phila). 2019 Jan;57(1):50-55.
13. Heda R, Toro F, Tombazzi CR. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): May 1, 2023.
14. Physiology, Pepsin. Okubo, K.; Kurono, Y.; Ichimura, K.; Enomoto, T.; Okamoto, Y.; Kawauchi, H.; Suzaki, H.; Fujieda, S.; Masuyama, K. Japanese guidelines for allergic rhinitis 2017. *Allergol. Int.* 2017, *66*, 205–219.

15. Yanai, K.; Yoshikawa, T.; Yanai, A.; Nakamura, T.; Iida, T.; Leurs, R.; Tashiro, M. The clinical pharmacology of non-sedating antihistamines. *Pharmacol. Ther.* 2017, *178*, 148–156.
16. Panula, P.; Chazot, P.L.; Cowart, M.; Gutzmer, R.; Leurs, R.; Liu, W.L.; Stark, H.; Thurmond, R.L.; Haas, H.L. International Union of Basic and Clinical Pharmacology. XCVIII. Histamine receptors. *Pharmacol. Rev.* 2015, *67*, 601–655.
17. Shan, L.; Dauvilliers, Y.; Siegel, J.M. Interactions of the histamine and hypocretin systems in CNS disorders. *Nat. Rev. Neurol.* 2015, *11*, 401–413.
18. Bosma, R.; van den Bor, J.; Vischer, H.F.; Labeaga, L.; Leurs, R. The long duration of action of the second generation antihistamine bilastine coincides with its long residence time at the histamine H1 receptor. *Eur. J. Pharmacol.* 2018, *838*, 107–111.
19. Hashiguchi, K.; Wakabayashi, K.I.; Togawa, M.; Saito, A.; Okubo, K. Therapeutic effect of bilastine in Japanese cedar pollinosis using an artificial exposure chamber (OHIO Chamber). *Allergol. Int.* 2017, *66*, 123–131.
20. Okubo, K.; Gotoh, M.; Asako, M.; Nomura, Y.; Togawa, M.; Saito, A.; Honda, T.; Ohashi, Y. Efficacy and safety of bilastine in Japanese patients with perennial allergic rhinitis: A multicenter, randomized, double-blind, placebo-controlled, parallel-group phase III study. *Allergol. Int.* 2017, *66*, 97–105.
21. Novák, Z.; Yáñez, A.; Kiss, I.; Kuna, P.; Tortajada-Girbés, M.; Valiente, R. Safety and tolerability of bilastine 10 mg administered for 12 weeks in children with allergic diseases. *Pediatr. Allergy Immunol.* 2016, *27*, 493–498.