INTRODUCTION

The H1 antihistamines were discovered by Bovet and Staub in 1937.\(^1\)

Phenbezamine was the first clinically useful antihistamine. Pyrilamine maleate, diphenhydramine, and tripelemnamine were synthesized few years later and are currently used till date.

Today more than 40 H1 antihistamines are available which stays the most widely used for the treatment of urticaria among all the medications.\(^2\)

H1 antihistamines are inverse agonists and not receptor antagonists.

Antihistamines are known to inhibit the effects of histamine at H1 receptors.

First-generation antihistamines are lipophilic, easily crossing the blood-brain barrier leading to central nervous system (CNS) adverse effects such as sedation, decreased perceiving, and drowsiness. They also have short half-lives and require multiple daily doses.

Hence, newer antihistamines were introduced to reduce the adverse effects of 1st generation drugs. A major advancement in antihistamine development took place in the 1980s with the introduction of second-generation H1 - antihistamines.

“Second generation” antihistamines are lipophobic, having low capacity to cross the blood-brain barrier, thus reducing sedation and cognitive impairment. They have a lower affinity for non histamine receptors and higher specificity for binding to H1 receptors. These have longer half-lives, allowing once-or-twice-daily dosing.\(^3\)

The commonly used second-generation H1-receptor antagonists are desloratadine, fexofenadine, levocetirizine, bilastine, ebastine, rupatadine, and olopatadine.

A Google scholar search for second-generation antihistamines was done using the words “second generation H1 antihistamines,” “bilastine,” “ebastine,” “olopatadine,” “rupatadine,” “levocetirizine,” “fexofenadine,” “desloratadine,” “histamine,” “allergy,” and “urticaria.” All the articles were retrieved and classified into review articles, studies, double-blinded trials, and case reports. The final data were then analyzed and presented in a narrative fashion.

HISTAMINE AND ALLERGY

Although histamine plays an important physiologic role in human health via four subtypes of receptors, its activity at...
H1 histamine receptors are involved in allergic reactions.[3] Histamine being one of the several mediators involved in the pathophysiology of allergy has a vital role in allergic immediate reaction.[4] Degranulation following entry of an allergen to immunoglobulin E (IgE)-sensitized mast cells, causes the release of histamine.

Histamine effect in allergic reaction is mediated through H1 receptors both active and inactive forms of g-protein-coupled receptors. Histamine being an agonist leads to effects such as muscular contraction, endothelial permeability upregulation, bronchospasm, and activation of cough receptors and sensory nerves by pushing the balance to the active side.[5]

H1 antihistamines work as inverse agonists and suppress histamine effects by pushing the balance toward the inactive side.

Hence, the effects are not antagonistic, but a balance between active and inactive forms of H1 receptors.[3]

**BILASTINE**

It is a new antihistamine belonging to the piperidine class of antihistamines and structurally is 2-[4-2-(4-(1-(2-ethoxyethyl)-benzimidazole-2-yl)piperidin-1-yl)ethyl]phenyl-2-methylpropane acid, having a molecular weight of 463.6 daltons.[6,7]

Bilastine is a new, well-tolerated, nonsedating H1 receptor inverse agonist having a high specific affinity for H1-receptor. It possesses both antihistaminic and anti-inflammatory properties in vitro and in vivo.[8,9]

*In vivo* studies have shown an inhibition of histamine-induced wheal and flare response activity of skin in the human population with bilastine 20 mg as with cetirizine 10 mg.[10]

**Pharmacokinetics**

Mean oral systemic bioavailability of bilastine of 61% in healthy adults have been reported.[11]

Bilastine should be taken at least 1 h before and not before 2 h after a meal, as absorption is slowed when taken with food. It is best absorbed in the fasting state.[12,13]

It has no impact on CYP450 enzyme of liver. It does not have any drug interactions, except that there is an increased uptake of bilastine if taken simultaneously with diltiazem, erythromycin, or ketoconazole.[7]

The maximum plasma concentration of bilastine 20 mg was 1.3 h post administration, the half-life was 14.5 h, and plasma protein binding was 84–90%.[7]

Bilastine is not metabolized in humans, with almost 95% of the administered dose is excreted intact in feces or urine, as unchanged bilastine.[7]

**Clinical studies**

Bilastine is well tolerated. A double-blinded, crossover study of the safety of bilastine in 30 healthy individuals did not show any cardiac effects of bilastine 20 or 100 mg when taken once daily.[14]

Clinical studies have shown the equal efficacy of bilastine 20 mg and levocetirizine 5 mg in the treatment of chronic idiopathic urticarial (CIU). The study also demonstrated bilastine 20 mg to be more effective than placebo in reducing the discomfort and disruption of sleep and thereby improving the quality of life (QoL) of patients with chronic urticaria.[15]

Research into pharmacokinetics, efficacy, and the adverse effect of bilastine in children under 12 years of age is needed.

**OLOPATABINE**

Olopatadine hydrochloride is newly developed second-generation, selective histamine H1 – receptor antagonist. It inhibits the release of lipid mediators, such as leukotriene and thromboxane from human polymorphonuclear leukocytes and eosinophils.[16]

It is a tricyclic compound having a chemical structure: 11-[(Z)-3-(di-methylamino)propylidene]-6,11–dihydrodibenz[b, e] oxepin-2-acetic acid monohydrochloride.[17]

Olopatadine was shown to be more stable and potent compared to other commonly used second-generation antihistamines in double-blind clinical trials.

Despite being a second-generation antihistamine, CNS side effects have been reported with olopatadine.[18]

**Pharmacological properties**

*Mode of action*

Olopatadine has shown an affinity for the histamine H1 receptor in receptor binding *in vitro* studies.[19]

Studies have shown its selectivity for histamine H1 receptor and a lack of interaction with H2 and H3 – histaminergic, α-β-adrenergic, dopaminergic, muscarinic, and numerous other receptors have also been demonstrated.[20]

Olopatadine inhibits the histamine-enhanced expression of intercellular adhesion molecule 1 and E-selectin.[21]

Yanni *et al.* reported olopatadine to inhibit histamine-induced secretion of interleukin 6 (IL-6) and IL-8 from human conjunctival epithelial cells.[22]
Olopatadine is more potent as an inhibitor of histamine-enhanced tumor necrosis factor-α-stimulated adhesion molecule expression.[19]

Olopatadine also inhibits anti-human IgE-induced histamine release from human conjunctival tryptase/chymase-containing mast cells.[20]

According to these data, it is clear that olopatadine offers additional therapeutic benefits which complement histamine H1-receptor antagonistic activities.

**Tolerability and adverse events**

Olopatadine has shown to have little effect on CNS, peripheral nervous system, autonomic nervous system, cardiovascular system, digestive and urogenital system in rats, dogs, guinea pigs, rabbits, mice, and cats at antiallergic doses.[21]

An extensive systemic and topical ophthalmic toxicology profile, mutagenicity, single and multiple-dose toxicity, the effect on reproduction, fertility, fetal development, and ocular tolerance for olopatadine have been studied in detail, and it has been declared safe for use.[22-25]

Olopatadine has very little possibility to cause ventricular arrhythmia, as it did not show the QT prolongation in hypokalemia-anesthetized dogs with doses 1 and 5 mg/g, intravenous.[26]

**Pharmacokinetics**

Olopatadine was absorbed rapidly, under fasting conditions after a single oral administration to healthy males at doses of 5, 10, 20, 40, and 80 mg.[27] The elimination half-lives were 7.13–9.36 h within this dose range.

The drug-drug interaction is very unlikely to occur, as olopatadine is excreted through renal route without extensive metabolism.

Under both fasting and nonfasting conditions, the renal clearance remains constant.

The effect of food on the absorption of olopatadine is unremarkable.

The plasma concentrations of olopatadine at a dose of 10 mg/body, after single oral administration in elderly subjects were higher than those after administration to healthy subjects. However, the half-live values were almost the same.[28]

**Metabolism**

Olopatadine is a renal clearance drug having poor metabolism.

It has no inhibitory effect on the drug-metabolizing activities that are catalyzed by the isoforms of cytochrome P450.

**Clinical studies**

In one study, 73 patients with chronic urticaria were screened for the safety and efficacy of olopatadine at daily doses of 2, 5, and 10 mg (b.i.d.) for 2 weeks. None of the groups showed serious adverse effects, and thus, olopatadine was considered highly useful in the dose range of 2–10 mg/day.[29]

Another study for investigating the optimal dose of olopatadine for chronic urticaria in a total of 233 patients at three dose levels (0.4, 2 and 10 mg b.i.d) for 2 weeks were compared. 10 mg/day group was found to be superior to the 2 mg/day and 0.4 mg/day groups in the rate of disappearance of itching after 1 week of treatment. Therefore, the optimal dose was estimated to be 10 mg/day.[29]

A study for the purpose of investigating the safety and efficacy of olopatadine on long-term administration using the 10 mg/day dose for 8 weeks in a total of 82 patients was conducted. The only adverse effects observed after 20 days of administration were sleepiness and increase in body weight in one patient each. Hence, it was concluded that olopatadine would also be highly useful on long-term administration with significantly lower incidence of adverse reactions.[30]

Olopatadine was compared with cetirizine for its suppressive effects on histamine-induced wheal and flare reaction in a double-blind, cross-over, placebo-controlled study. Olopatadine was found to have comparable effects to cetirizine.[31]

Makino *et al.* compared the suppressive effects of both the 5 mg/day and 10 mg/day dose of olopatadine with chronic urticarial itch in well-controlled subjects. The result showed that treatment with 5 mg olopatadine was as effective as 10 mg olopatadine for controlling the symptoms of chronic urticaria (CU). No adverse events such as sedation and drowsiness were reported. Thus, it was concluded that treatment with olopatadine at 5 mg once daily can maintain the improvement of urticarial symptoms the same as 10 mg/day with lesser CNS side effects and hence appears safe and effective for the management and prevention of CU.[32]

Hence, olopatadine is an effective treatment option for CU with sedation being a side effect in about 10% of patients.

**EBASTINE**

It is a selective, long-acting, non-sedating, second-generation H1-receptor antagonist. It has an oxypiperidine-based structure: (4-diphenylmethoxy-1-[3-(4-terbutylbenzoyl)-propyl] piperidine).
Ebastine itself is extensively metabolized to carebastine, an active carboxylic acid metabolite. Carebastine is even more potent as an antihistamine and exerts most of the pharmacological actions associated with ebastine administration. It is used in the treatment of symptoms of CIU as once-daily administration.\[37\]

**Pharmacokinetics**

Ebastine is absorbed well and is detected up to 24 h. The peak plasma concentrations are 3.61 ± 1.06 and 3.70 ± 0.76 h for 10 mg and 50 mg of ebastine, respectively. The elimination half-lives are 10.3 ± 2.6 and 12.5 ± 1.9 h with 10 mg and 50 mg, respectively.\[38\]

In one study, ebastine 10 mg inhibited the histamine-induced wheal for up to 24 h with peak reduction in histamine wheal occurring between 2 and 6 h. The mean maximum inhibition of wheal occurred at 4 h after taking the dose.\[38\]

Ebastine is completely metabolized into one or more active metabolites.

**Clinical studies**

Vincent et al. in their study have found significant antihistamine effect of ebastine at a dose of 10 mg. It had no effect on autonomic or cardiovascular effects in humans. This dose did not impair psychomotor performance.\[38\]

In one study, ebastine was used in thirty patients of chronic spontaneous urticaria in higher doses. It was observed that seventeen patients became symptom-free with 10 mg ebastine, eight with 20 mg, and two patients benefited with 40 mg ebastine. Only one patient with 40 mg of ebastine complained of mild sedation. This study clearly proves that ebastine is safe and effective in higher doses in patients with chronic spontaneous urticaria.\[39\]

Frossard et al. observed ebastine 20 mg to be superior in efficacy when compared to 10 mg of ebastine and 10 mg of cetirizine after 24 h of the last dose of a 6-day long treatment on the skin wheal response.\[40\]

In one German study, it was observed that ebastine 20 mg is safe and effective in preventing dermographic urticaria.\[41\]

Thus, once daily ebastine is an effective alternative to other second-generation antihistamines for the first-line treatment of chronic urticaria.

**RUPATADINE**

It is a new novel drug that has been used to manage urticaria. It has potent anti-platelet-activating factor (PAF) activity (~30 × potency of loratadine and ~ 40 × potency of Fexofenadine) and is a potent H1-antihistamine (~8 × potency of loratadine and ~ 10 × potency of Fexofenadine).\[43\]

Its chemical structure is 8-chloro-11-[(5-methyl-3-pyridinyl) methyl] piperidin -4-ylidene]-6,11-dihydro-5H-[1,2-b]pyridine fumarate.

**Pharmacokinetic profile**

Rupatadine is rapidly absorbed in all species, having a \( t_{\text{max}} \) of 0.75–1 h.\[44\]

It has an oral bioavailability of more than 50% with a half-life of ~ 6 h (range 4.3–14.3 h).\[44\]

The highest plasma concentration is observed after 5 h of ingestion of the drug. It has prolonged and sustained inhibition of the flare reaction even after 72 h, indicating that it penetrates and resides inside the tissue. This explains its long duration of action, facilitating once-daily administration.

Rupatadine is 98–99% plasma protein bound. It is well distributed in other tissues facilitating it to reach its target receptor.

It has a mean elimination \( t/2 \) of 5.9 h.

Rupatadine is eliminated through biliary excretion. When given orally rupatadine undergoes pre-systemic metabolism and, therefore, the amount of unaltered active substance found in feces and urine are extremely low.\[43\]

**Drug interactions**

Rupatadine, when given with ketoconazole or erythromycin, does not lead to any electrocardiographic (ECG) changes or changes in any vital signs, but its co-administration with ketoconazole and erythromycin is not advisable as it may lead to marked increase in its concentration.

Rupatadine co-administered with azithromycin or fluoxetine at therapeutic doses is considered safe and is well tolerated.

**Anti-histaminic activity**

Rupatadine has better antihistaminic activity when compared to terfenadine, loratadine, cetirizine, hydroxyzine, and diphenhydramine.\[46\]
The long-lasting effect of rupatadine may be due to some of the metabolites which also show anti-histaminic activity in vitro.

Rupatadine at single doses in a range of 10–80 mg has not shown any anticholinergic effects in humans.\[47\]

**Wide spectrum of action**

Rupatadine is the only antihistamine to exhibit significant PAF antagonist activity.

It has shown to inhibit the inflammatory cytokines production after in vitro activation of human T cells.\[48\]

Rupatadine also inhibits hypersensitivity reactions in vivo, including active and passive anaphylaxis.

**Clinical studies**

In one study to evaluate the long-term safety of rupatadine, the most frequent adverse effects noticed were somnolence (6%), headache, dry mouth, fatigue, and rash (<1%).

There were no ECG or lab abnormalities evidenced throughout the study.\[49\]

Donado et al. demonstrated that rupatadine even at 10 times the therapeutic dose, did not exhibit any pro-arrhythmic side effects.\[50\]

Vuurman et al. evaluated the effects of rupatadine on driving and compared it with hydroxyzine 50 mg or placebo in healthy human volunteers. They concluded that there was no difference between rupatadine and placebo. However, driving performance was impaired by hydroxyzine.\[51\]

Gimenez-Arnau et al. reported improvements in mean number of wheals and mean pruritus severity scores after 4 weeks treatment with rupatadine 10 and 20 mg in patients with chronic spontaneous urticaria.\[52\]

Metz et al. in their study on cold urticaria patients demonstrated that rupatadine 20 mg significantly lowered the threshold temperature along with the symptoms of cold urticaria such as pruritus and burning.\[53\] Hence, it was concluded that rupatadine 20 mg, when given to patients with acquired cold urticaria, has high efficacy and is well tolerated.

Dubertret et al. studied the effect of treatment with rupatadine 5, 10, and 20 mg for 4 weeks in cases of moderate to severe CIU. The 10 and 20 mg doses reduced pruritus severity by 62.05% and 71.87%, respectively. The reductions in total symptom scores were 54.8% for 10 mg and 65.9% for 20 mg.\[54\]

In two randomized, double-blind, placebo-controlled studies of 538 patients with chronic urticaria, treatment with rupatadine 20 mg daily showed a reduction in symptoms up to 75% in a higher percentage of patients as compared with rupatadine 10 mg.\[55\]

Thus, rupatadine is an effective treatment option for chronic spontaneous urticaria.

It has also shown to be effective in other conditions such as cold-induced urticaria.

**LEVOCETIRIZINE**

Levocetirizine is a second generation antihistamine.

It is the R-enantiomer of cetirizine which has favorable pharmacokinetic and pharmacodynamics characteristics.

Levocetirizine or (R)-[2-[4-[(4-chlorophenyl) phenylmethyl]-1-piperazinyl] ethoxy] acetic acid dihydrochloride is a potent histamine H1 receptor antagonist with anti-inflammatory and antiallergic properties.\[56\]

**Pharmacokinetic profile**

Levocetirizine has rapid absorption from the gastrointestinal tract. It has high bioavailability thereby giving a fast onset and long duration of antihistaminic effect. Its mean peak plasma levels are reached 1 h post administration.

Levocetirizine is 95% plasma protein bound, having a low distribution volume, indicating low potential for adverse effects.\[57\]

It has an elimination half-life of about 4 h. Excretion is through urine by glomerular filtration and active tubular secretion. Hence, the time between doses should be prolonged in cases with chronic renal failure.

Levocetirizine does not undergo metabolism in the liver via cytochrome P450 enzyme system. Hence, there are no drug interactions with other drugs which are metabolized through this pathway.\[58\]

**Safety profile**

Levocetirizine shows a low potential for drug interactions. It has no negative effects on alertness or ability to drive vehicles after one or more doses at the recommended dosage of 5 mg/day, as documented from clinical studies.\[59-63\] Apart from drowsiness, no effect on memory and psychomotor functions have been noted.\[61\]

Verster et al. evaluated the effects of treatment with levocetirizine (5 mg) and diphenhydramine (50 mg) administered once daily on four consecutive days on
psychomotor abilities, mood and memory in 48 healthy volunteers. They concluded that single or repeated doses of levocetirizine had no effect on memory, attention, and motor skills as compared to diphenhydramine which showed a significant reduction in attention and motor skills even after the first dose.[59]

Potter during his 6-week study with levocetirizine (5 mg/day) and placebo reported the absence of any significant adverse events. There were no cases reported with increased QT interval on ECG.[63]

A recent study on 52 healthy subjects treated with 5 and 30 mg of levocetirizine confirmed the absence of cardiotoxicity 24 h post administration.[64]

Mild adverse reactions noted with levocetirizine during treatment included fatigue, dizziness, headache, and dry mouth.[63] These do not interfere with the patient’s well-being even in cases of chronic treatment.

Ekiz et al. have reported a case of levocetirizine induced hepatotoxicity in a 64-year-old male patient of chronic urticaria. There was no evidence of other liver disease. It was considered a case of idiosyncratic drug reaction. The liver enzymes normalized after withdrawal of the drug. Hence, physicians should be aware of hepatotoxicity due to levocetirizine.[65]

**Levocetirizine efficacy**

A study on 18 healthy volunteers after a histamine prick test at a concentration of 100 mg/ml demonstrated a higher efficacy and more prolonged action of levocetirizine in inhibiting histamine-induced wheal formation as compared with ebastine (10 mg), fexofenadine (180 mg), mizolastine (10 mg), and loratadine (10 mg).[66]

Purohit et al. concluded in their study that levocetirizine has a greater reduction of histamine wheal for a longer duration of time as compared to desloratadine.[67]

In a double-blind, placebo-controlled study in 258 patients with CIU, levocetirizine at doses 2.5, 5, and 10 mg showed a significant improvement in pruritus intensity, duration, number, and size of wheal. The therapeutic effect of levocetirizine was significant even at a minimum dosage of 2.5 mg throughout the entire study duration (4 weeks).[68]

A comparative study of levocetirizine and cetirizine demonstrated 2.5 mg once daily dose of levocetirizine to inhibit histamine-induced wheal formation entirely in 18 normal subjects. This effect was comparable to 5 mg of cetirizine.[69]

Anuradha et al. in their study to compare the therapeutic efficacy and tolerability of levocetirizine and loratadine in patients suffering from CIU concluded levocetirizine to be superior to loratadine for CIU.[70]

In a randomized, double-blind, active-controlled, parallel group pilot study of 64 patients with CIU who received once-daily desloratadine 5 mg and levocetirizine 5 mg for 6 weeks concluded levocetirizine to be independently associated with a better therapeutic response than desloratadine. The findings suggested levocetirizine had better control than desloratadine for severe CIU.[71]

Hence, based on examined studies, levocetirizine is a potent, consistent, and long-lasting medication for the treatment of CIU.

**FEXOFENADINE**

Fexofenadine, the active metabolite of terfenadine, is a non-sedating, selective histamine H1 receptor antagonist with rapid and long-acting activity. Fexofenadine or (+)-4-[1 hydroxy-4-[(4-hydroxydiphenylmethyl)-1-piperidinyl]-butyl]-α, α-dimethyl benzeneacetic acid also appears to exhibit some anti-inflammatory activity.

**PHARMACODYNAMICS**

Fexofenadine does not cross the blood-brain barrier. It has no anticholinergic or alpha1-adrenergic receptor-blocking effects. Unlike terfenadine, it does not block potassium channels in cardiocytes. It does not affect the QTc interval.[72-73]

Fexofenadine modulates the release of pro-inflammatory mediators and adhesion molecules from human nasal epithelial cells.[74,75]

Human histamine skin wheal and flare studies have shown that the antihistaminic effect of fexofenadine can be detected 1 h post ingestion. Maximum effect is seen 2–3 h later. There is no evidence of intolerance and can be used for long periods. Its effect is seen even 12 h after administration.[72-73,76]

**Pharmacokinetics**

Fexofenadine is absorbed rapidly after oral administration. It is not affected by food.[77]

Peak plasma concentrations are achieved in about 2.6 h. It is 60–70% plasma protein bound mainly albumin and alpha 1-acid glycoprotein. Fexofenadine metabolism is independent of cytochrome P450 activity.[78]
It has an elimination half-life of 14.4 h. Approximately, 5% of the total dose is metabolized in the liver. Only 0.5–1.5% is converted by cytochrome P450, remaining (80%) is excreted in feces, and (12%) in urine.\[72-73\]

Hepatic diseases do not interfere with pharmacokinetics of fexofenadine. However, reduced renal function slows the drug elimination.\[72-73]\n
**Safety and side effects**

Fexofenadine is free of CNS adverse effects. Being a nonsedating drug, it has no effect on the driving performance after being taken in the recommended dosage.\[79]\n
Fexofenadine is potentially useful and safe for aircrews.\[80]\n
The most common side effects noted are a headache, throat irritation, dyspepsia, dysmenorrhea, nausea, fatigue, and drowsiness.\[72-73]\n
Clinical studies have shown that fexofenadine does not have major cardiovascular side effects. However, rarely palpitations, chest pain, chest tightness, and arrhythmia are found during treatment, which resolves on stopping fexofenadine. Fexofenadine even at doses up to tenfold higher than daily recommended dose have no effect on QTc. There was no significant increase in QTc when fexofenadine was co-administered with ketoconazole and erythromycin. In controlled trials, no case of fexofenadine-associated torsades de pointes was observed.\[81-83]\n
Fexofenadine is classified as pregnancy category C. There is insufficient data regarding excretion of fexofenadine in breast milk.\[72]\n
**Drug interactions**

Fexofenadine does not undergo extensive hepatic metabolism, hence, can be safely given with drugs that are metabolized by cytochrome P450. Inhibitors of P-glycoprotein (such as ketoconazole, itraconazole, erythromycin, verapamil, and ritonavir) decrease the intestinal absorption and increase the peak concentration of fexofenadine. However, dose adjustment is not necessary when fexofenadine is co-administered with these drugs, as there is no increased incidence of side effects or QTc abnormalities.\[84]\n
Rifampin increases the fexofenadine clearance.

**Clinical studies**

In double-blind controlled studies, it was found that fexofenadine 60 mg BD or 120 mg OD was more effective and significantly better than daily 10 mg of loratadine in wheal inhibition\[85\] and also in improving the QoL.\[86\]

Finn et al. concluded that fexofenadine 180 mg or 240 mg/day reduced pruritus and the total symptom score in patients of chronic urticaria when compared with placebo.\[87]\n
In a study in 14 children, fexofenadine 30 or 60 mg/day was effective and safe in suppressing wheals and flares.\[88]\n
Recommended dose range of fexofenadine is 120–180 mg daily.\[82]\n
One study has reported fexofenadine to be effective in higher doses in chronic spontaneous urticaria. The only side effects noted during the study were a headache and sedation.\[89]\n
In a study on 512 patients of CIU, fexofenadine 180 mg at a single daily dose was found to be well tolerated and was considered an effective nonsedating antihistamine, devoid of any significant side effects.\[90]\n
Thus, fexofenadine appears quite promising among newer antihistamines in the treatment of chronic urticaria.

**DESLORATADINE**

Desloratadine is a new, nonsedating, second generation H1 receptor antagonist. It is the primary active metabolite of loratadine.\[91]\n
Desloratadine also inhibits important cytokine and cellular activity, suggesting anti-inflammatory and an antiallergic profile. It improves the QoL, by providing long duration of symptom relief.

**Pharmacokinetics**

It is metabolized primarily to a 3-OH form by glucuronidation. The \( t_{1/2} \) of desloratadine is 21–24 h, allowing once-daily dosing. A 5 mg once daily dose is effective for treatment of CIU. Dose adjustments are not required for patients 12 years of age or older as its pharmacokinetic parameters are not altered by sex, age, or race. The bioavailability and absorption of desloratadine are not affected significantly by food, hence, can be administered with or without meals.\[92]\n
**Drug interactions**

ECG studies have revealed no clinically significant interactions between desloratadine and erythromycin or ketoconazole.\[93,94]\n
**Adverse effects**

Till date, no clinically significant effects on vital signs or laboratory tests have been reported in any studies. The most frequently observed side effect is a headache.

Desloratadine has had no relevant effects on ECG parameters in any clinical studies to date.
It does not impair wakefulness or psychomotor performance and has no psychomotor impairment when taken with alcohol.

Vuurman et al. demonstrated that desloratadine does not impair driving performance during an over-the-road driving test.[95]

Clinical studies
In an open-label, observational study, 5 mg desloratadine once daily significantly decreased symptoms of patients with CIU and improved the QoL.[98]

Monroe et al. in their study concluded treatment with desloratadine 5 mg once daily in patients with CIU to be effective and well tolerated. Adverse effects including somnolence was similar in desloratadine and placebo groups in their study.[97]

In a double-blind study, 190 patients with at least 6-week history of CIU were treated with 5 mg of desloratadine once daily or placebo for 6 weeks. The investigators rated the overall condition of CIU and response to treatment as being better in desloratadine group.[98]

In summary, desloratadine has a potent antiallergic activity. It provides excellent clinical efficacy and safety in the treatment of patients with CIU.

CONCLUSION
Urticaria treatment begins with elimination of any known causative factors. However, as the causes of nonphysical or autoimmune-based chronic urticaria are by definition unknown, treatment focuses on symptom relief. H1 antihistamines are the cornerstone of urticaria treatment. Newer, second-generation agents, are preferred over sedating first-generation antihistamines due to their proven efficacy and favorable safety profiles.

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