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THE CLINICAL EFFICACY OF DESLORATADINE, A NON-SEDATING ANTIHISTAMINE, IN THE MANAGEMENT OF ALLERGIC CONDITIONS: A REVIEW OF THE EVIDENCE

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Desloratadine is a relatively new, second-generation, tricyclic antihistamine which came into medical use in 2001. This study aimed to review the available evidence in the literature around the clinical efficacy of desloratadine on a range of allergic conditions. A database search in Medline, PubMed, Embase, and Google Scholar was conducted for the research articles published until July 2020, using the keyword desloratadine. An additional reference lists search and citation tracking were also performed. Research articles in English pertaining to desloratadine and its efficacy were considered for inclusion. Study designs, including randomized controlled trials (RCT), observational/case-control studies, and case series were considered. The collective evidence from the current literature shows superior efficacy of desloratadine compared to placebo and some of the other treatment options in the management of seasonal allergic rhinitis (SAR), perennial allergic rhinitis (PAR), chronic idiopathic urticaria (CIU), and asthmatic symptoms. There is also evidence for potential new roles introduced for desloratadine such as acne treatment, chronic otitis media, and chronic rhinosinusitis, which warrants further investigation. In most studies, desloratadine's safety and tolerability were comparable with placebo. Current evidence suggest that desloratadine is an ideal option for most of the allergic conditions due to its efficacy as well as favourable safety and tolerability profile. Further large-scale studies are needed to establish the efficacy and safety profile of desloratadine and to compare its effectiveness against other treatments in the management of allergic conditions.

INTRODUCTION

Upon the introduction of second-generation H1-antihistamines, the use of first-generation antihistamines became limited due to their high penetration across the blood–brain barrier resulting in sedation, impaired cognitive function, and reduced quality of life (QoL). Currently, second generation non-sedating antihistamines are recommended as a first-line therapy by many international therapeutic guidelines for the management of allergic disorders such as allergic rhinitis and chronic idiopathic urticaria.

Among the second generation H1-antihistamines, desloratadine is a relatively

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new agent which was first approved in 2001 by the US Food and Drug Administration with an indication for allergic rhinitis (AR). Currently, it is indicated for all types of AR irrespective of conventional classification (i.e. seasonal/perennial) or the more recent Allergic Rhinitis and its Impact on Asthma (ARIA) classification (i.e. intermittent or persistent) in both adult and paediatric populations. Its indication has also been approved for the treatment of chronic idiopathic urticaria although other indications have also been introduced for this medication. This study aimed to review the current evidence around the clinical efficacy of desloratadine, in the management of a variety of allergic conditions.

Methods and Search Strategy

An initial scoping search was conducted in Google Scholar to determine the potential keywords. A database search was then conducted in Embase, Medline, PubMed, and Google Scholar for the published literature. Research articles in English published between 2001 and July 2020 were considered for this review. The review included the original research with a variety of methodologies, including randomized controlled trials (RCTs), observational/case-control studies, retrospective evaluations, case series, and short communication reports. Case reports, abstracts, letters to the editor, reviews, meta-analyses, and expert opinions were excluded. Moreover, *in-vitro* pharmacological studies as well as *in-vivo* clinical studies on healthy volunteers without an allergic pathology were also not considered. Wherever possible, a complementary reference list search and citation tracking were also performed to include any articles that might have been missed in the initial database search.

Seasonal or Intermittent Allergic Rhinitis
Desloratadine vs. Placebo

Studies have documented efficacy of desloratadine in improving all parameters related to seasonal allergic rhinitis (SAR) symptom scores, including total symptom scores (TSS), total nasal symptom scores (TNSS), and total non-nasal symptom scores (TNNSS) compared to placebo (Table 1)[2-9].

Looking at individual symptoms, desloratadine was found to attain superior efficacy in decreasing the nasal symptom scores resulting in marked improvement in the severity of nasal congestion, rhinorrhoea, and sneezing[7&10&11]. Similarly, the overall and individual ocular symptoms, including eye tearing, burning/itching, and eye redness have reportedly experienced significant reduction with desloratadine[7&10]. Dermal symptoms, as well as total symptom scores also decreased significantly with desloratadine treatment[10]. Another study indicated that symptoms including nasal discharge, nasal itching, and sneezing as well as eye redness, itchy ears, throat, and palate in the morning and evening showed significantly greater decline[5]. According to the findings of a post-marketing surveillance, desloratadine treatment resulted in significant reduction in all TSS and individual symptom scores (including nasal, ocular, dermal, and asthma symptom scores) compared to baseline[12].

Looking at the evidence around nasal congestion and patency measures, the efficacy of daily desloratadine 5 mg on improving the nasal airflow in patients with grass pollen SAR was studied[2]. Patients treated with desloratadine had a significantly less drop in their nasal airflow after exposure to grass pollen allergen than the placebo and over the entire exposure time. The combined findings of three separate RCTs enrolling 948 patients with SAR indicated a significant reduction in the average reflective morning and afternoon nasal congestion severity scores with desloratadine daily treatment over a 2-week treatment that sustained for four weeks[13]. Other RCTs confirm these findings where administration of desloratadine to patients with SAR/IAR significantly improved nasal congestion/stuffiness, reduced nasal congestion scores, and improved nasal airflow compared to placebo[11&14]. The decongestant effects of desloratadine were observed from day 2 of the trial and sustained over the 2-weeks of the study period[14]. The superior efficacy of desloratadine in comparison with placebo was demonstrated in another RCT in which the efficacy of desloratadine on improving nasal patency measures among 218 patients with SAR was studied[5]. The assessment of nasal patency parameters indicated a significantly greater descending expiratory nasal airflow in the desloratadine group, but non-significant increase in the nasal airflow at the ascending inspiratory phase. Further, the placebo group

experienced a significantly larger increase in the total inspiratory nasal airway resistance compared with desloratadine treatment[5]. In a prospective study of 602 patients, nasal congestion measures indicated by peak nasal inspiratory flow (PNIF) also improved with desloratadine compared to the baseline measures[7]. In one study, however, although numerically improved, the mean nasal inspiratory flow scores did not show a significant improvement with desloratadine[9].

Subjective patient and physician reports have also provided insights into the effectiveness of desloratadine therapy in SAR. Through the subjective assessment of efficacy nearly 65% of both physician and patient respondents stated that the onset of action of desloratadine was faster than their previous treatment with other antihistamines[10]. When assessed for the interference of their allergic disorder with sleep patterns and activities of daily life, taking desloratadine resulted in significant improvement in sleep and daily activities of SAR patients[10&12]. One study employed a patient subjective assessment of the allergic symptoms using a visual analogue scale (VAS). The VAS rating of symptoms also indicated a significant reduction in desloratadine group[8]. More than 85% of the subjects in one study reported complete or marked relief of their allergic symptoms with the use of desloratadine compared to baseline[7].

The impact of desloratadine therapy on SAR patients' QoL has been the focus of some studies. The outcomes of these studies are generally in agreement that patients treated with desloratadine demonstrated significantly greater improvements in QoL scores compared to placebo as measured by common tools like Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ)[4-5&8-9].

Desloratadine vs. other treatment agents

The superior efficacy of both desloratadine and diphenhydramine in improving the TSS as well as TNSS of AR was reported when compared to placebo[15]. Diphenhydramine also showed superior efficacy than placebo in improving the TNNSS, the TSS, TNSS, and individual symptom scores, including nasal congestion in comparison with desloratadine[15&16]. However, diphenhydramine, had the highest percentage of adverse effects (AEs) reported, compared to desloratadine and placebo (35%, 16%, and 8%, respectively) with somnolence being the most common AE[16]. Also, diphenhydramine treatment was associated with significantly meaningful impairment in all the studied cognitive parameters including vigilance, psychomotor speed, working memory, reasoning/computation, and divided attention compared to desloratadine[15].

Another RCT evaluated the efficacy of once daily desloratadine 5 mg and rupatadine 10 mg in patients diagnosed with SAR[17]. Overall, both drugs showed superior efficacy compared to placebo in reducing the total symptoms score of SAR as well as significantly improving both nasal and non-nasal symptoms[17]. There was no clinically significant superiority between the two active agents, although the symptom reduction was slightly better with desloratadine than rupatadine (49% vs. 46%).

In another RCT, azelastine was shown to have superior efficacy compared to desloratadine and placebo after 4-6 hours of administration although desloratadine, was also significantly more effective than placebo[18]. Moreover, azelastine showed a faster decrease in both TNSS and major nasal symptoms score with an onset of action of 15 min. versus 150 min. for desloratadine. Azelastine also showed significantly better results compared to desloratadine in investigator-scored outcomes with 74% satisfactory outcomes compared to 56% for desloratadine[18].

A comparative RCT examined the clinical efficacy as well as the onset and duration of action of once daily desloratadine 5mg against levocetirizine 5mg in patients with ragweed-induced AR[19]. The findings of this trial showed both medications acted significantly better than placebo. However, greater improvement was produced by levocetirizine in a 24-hrs. period, compared to desloratadine in alleviating major symptoms such as nose blows, sneezes, runny nose, itchy nose, watery eye and TSS[19]. Moreover, nasal congestion was found to resolve to a greater extent with levocetirizine than desloratadine while desloratadine did not show a significant alleviation of nasal congestion in comparison to placebo. Levocetirizine also showed advantages in terms of faster onset of action compared to desloratadine (1hr vs. 3hrs) [19]. Another RCT compared the efficacy of a single dose of

levocetirizine 5 mg and desloratadine 5 mg in 24 patients with grass-pollen allergy and rhinitis[50]. Levocetirizine was more successful than desloratadine in inhibiting the sneezing and rhinorrhoea while none of the substances were able to inhibit nasal congestion significantly[20]. Albumin extravasation, as an early allergic marker in the nasal lavage, was significantly inhibited by levocetirizine, but not desloratadine[20].

Using a similar methodology, Bhatia *et al.*[21] compared the effects of daily oral desloratadine and nasal budesonide for two weeks on improving nasal peak inspiratory flow (NPIF) in subjects with a history of seasonal allergy to tree or grass pollens. During the two-week study period, nasal budesonide worked better than desloratadine in terms of the number of days with an improved morning, evening, and overall NPIF values from baseline[21]. While both medications appeared to significantly alleviate the symptom scores compared to their baseline, no significant differences between two medications were detected in this regard[21].

Desloratadine efficacy was further investigated in a comparative study comparing it against ketotifen fumarate ophthalmic solution or their combination in resolving seasonal allergic rhino-conjunctivitis[22]. When evaluated for the ocular symptoms after four weeks, the subjects in the ketotifen or ketotifen/desloratadine combination group attained significantly lower mean ocular itching scores compared to the desloratadine group alone. Comparatively, the ketotifen therapy alone resulted in significantly less ocular redness compared with desloratadine and ketotifen/desloratadine combination at 15 and 20-min time points after allergen induction[22]. When assessed for the amount of tear production, desloratadine treatment resulted in less tearing compared with other groups, though such difference did not achieve statistical significance. The study suggested that using ophthalmic ketotifen in combination with oral desloratadine shows higher efficacy in rhino-conjunctivitis than using desloratadine alone[22].

Bachert *et al.*[23] compared the efficacy and safety of desloratadine and bilastine in relieving SAR. Through a randomized double-blind, placebo-controlled, parallel-group trial, the study subjects received once daily doses of desloratadine 5 mg, bilastine 20 mg, or placebo over a 2-week period. According to the findings, both desloratadine and bilastine significantly, but comparably improved TSS, NSS, and NNSS compared to placebo. Similarly, both treatments were equally effective in increasing the RQLQ measures[23]. Looking at the individual domains of QoL, bilastine demonstrated effectiveness except for nasal symptoms, emotional, and sleep components, while desloratadine did not have significant efficacy on nasal symptoms and emotional components[23].

Through an ad hoc analysis, Bachert & Maurer[12], also made a comparison of desloratadine treatment with any previous monotherapy with another second-generation antihistamine. In this subjective assessment, most of the participants (ranging between 60%-88%) reported the efficacy of desloratadine to be higher than cetirizine, loratadine, fexofenadine, and mizolastine[12].

Berger *et al.*[24] compared the efficacy of desloratadine 5 mg/day, fexofenadine 180 mg/d, and placebo among 722 patients presenting with symptomatic SAR. The analyses of morning instantaneous TSS and morning/evening reflective TSS indicated superior efficacy of both desloratadine and fexofenadine treatments to placebo, while demonstrating the comparative efficacy between the two active treatments. Moreover, both fexofenadine and desloratadine were associated with significant improvements in morning instantaneous individual symptoms, including sneezing and itchy nose, throat, and palate[24]. Desloratadine demonstrated a further advantage in this regard than fexofenadine by significantly alleviating the ocular symptoms such as itchy, watery, and red eyes while fexofenadine failed to achieve a significant improvement in these symptoms. Desloratadine provided further advantage in morning/evening symptoms by statistically reducing the severity score of rhinorrhoea compared to fexofenadine[24]. The numerical assessment of the patient and investigator assessed the subjective efficacy also showed an improving trend throughout the 15 days of study.

Table 1: An overview of research studies on clinical efficacy of desloratadine either compared to placebo , baseline measures, or other treatment agents in treatment of seasonal or intermittent allergic rhinitis

Authors/ year	Methodology	Inclusion criteria	No. of patients	Comparator regimen(s)	Outcomes and results
Salmun & Lorber/ 2002	Randomized, multic enter, parallel-group, placebo-controlled, double-blind trial	≥ 12 years old; 2-year history of SAR	1,036	Desloratadine 2.5, 5, 7.5, 10, 20 mg Placebo	Significantly superior to placebo in morning instantaneous TSS score for all doses. Significantly effective than placebo in improving morning/evening TNSS and TNNSS. Significant 24-hour relief of SAR symptoms compared to placebo. Significant improvement in all individual symptoms including the nasal and non-nasal symptoms.
Horak et al./ 2002	Randomized, double-blind, placebo controlled, crossover trial	19 to 45 years old; SAR ≥ 2 years; positive skin prick test response to grass pollen; radioallergosorbent test of class 2 or greater at screening or during the previous 12 months	47	Desloratadine 5 mg/day Placebo (For 7 days)	Significant efficacy in relieving nasal obstruction and increasing the nasal airflow. Significantly lower individual and overall SAR symptom severity scores including sneezing and nasal congestion. Relatively better nasal airflow, less nasal secretions, and less nasal congestion after allergen exposure.
Horak et al./ 2003	Randomized double-blind placebo-controlled crossed over study	SAR for ≥ 2 years; responder to antihistamine treatment; positive skin prick test to grass pollen; a positive radioallergosorbent test (class ≥ 2)	47	Desloratadine 5mg/day Placebo	Superior efficacy in maintaining nasal airflow. Significantly less increase in nasal secretions. Significantly lower SAR symptom scores and nasal congestion.
Pradalier et al./ 2007	Multicenter, double-blind, randomized, parallel-group study	≥ 18 years old; SAR ≥ 2 years confirmed by a positive skin prick test to grass pollen ≤ 24 months before or at screening; having at least moderate seasonal AR (TSS ≥ 8, nasal congestion score ≥ 2, and a TNNSS ≥ 2)	483	Desloratadine 5 mg once daily Placebo	Significantly greater improvements in RQLQ scores compared to placebo. Significant improvement in all individual domains of the QoL assessment including nose symptoms, eye symptoms, sleep problems, practical problems, activity limitation, general problems, and emotional function. Significant decrease in all TSS, TNSS, and TNNSS of AR compared with placebo. AEs comparable with placebo.

Authors/ year	Methodology	Inclusion criteria	No. of patients	Comparator regimen(s)	Outcomes and results
Bachert et al./ 2002	Observational, post-marketing surveillance study	Patients with symptoms of SAR; expected to remain in the study for the treatment period	47,000	Desloratadine (dose not specified) Baseline Any other previous treatment (e.g. loratadine, cetirizine, fexofenadine, unspecified drugs, or multiple treatments)	Superior efficacy compared with the baseline measures in decreasing the total and individual nasal symptom scores. Significant improvement with desloratadine in overall and individual ocular symptoms. Significant efficacy in alleviating dermal and TSS. Significant reduction in asthma symptom scores in patients with SAR and asthma and reduced asthma medication use during the desloratadine treatment period. Reduction in moderate/severe asthma symptoms including wheezing, breathlessness, chest tightness, and cough.
Lorber et al./ 2002	Combination of three separate, randomized, double-blind, placebo-controlled, parallel-group, multicenter studies	≥ 2-year history of SAR; exacerbated asthma symptoms during allergy season; positive skin test response to appropriate seasonal allergens ≤ 24 months; at least moderate rhinorrhea; TNSS ≥ 6, and TNNSS of 5; FEV1 ≥ 70%; total frequency of asthma score and/or bronchodilator use score =2; total reflective scores for 3 days prior to baseline = 42 for TNSS and = 35 for TNNSS; demonstrated reversibility in patients with SAR and asthma; clinically significant disease-free; negative serum pregnancy test and medically accepted method of birth control	948	Desloratadine 5 mg once daily Placebo	Significant reduction in the average reflective morning/evening nasal congestion severity scores compared to placebo. Significantly greater reduction in the mean reflective nasal congestion scores in a subgroup analysis of patients with concomitant SAR and asthma. Similar safety profile to placebo.
Nayak and Schenkel/ 2001	Randomized, placebo-controlled, double-blind study	At least moderate IAR symptomatic at screening and baseline; both nasal and nonnasal symptoms present; ≥ 2-year history of IAR; positive skin prick test ≤ 1 year; clinically significant disease-free	346	Desloratadine 5 mg/daily Placebo (For two weeks)	Significant improvement of nasal congestion/stuffiness and reduction in the nasal congestion scores compared to placebo. Early onset of action and sustainable efficacy over the study period. Placebo-like AE profile with no severe AEs.

Authors/ year	Methodology	Inclusion criteria	No. of patients	Comparator regimen(s)	Outcomes and results
Meltzer et al./ 2005	Randomized, double-blind, placebo controlled, single-center, parallel-group study	18-60 years old, ≥ 2 years history of mild/moderate SAR, positive skin test reaction to a seasonal allergen within 12 months, combined NSS ≥ 6, nasal congestion score of ≥ 2, and TSS ≥ 11 for at least 3/5 of the preceding morning scores, not having significant disease	218	Desloratadine 5 mg daily Placebo (For two weeks)	Significantly greater decrease than placebo in joint patient and investigator-rated symptom scores. Significant decrease in the sneezing scores according to the joint evaluation of individual symptom scores. Significantly superior efficacy than placebo in improving the morning and evening TNSS. Significantly greater decrease in morning individual symptoms for nasal discharge, nasal itching, and sneezing and itching of ears, throat, and palate. Significant improvement in the evening individual symptoms for nasal discharge, sneezing, eye redness, and itching in ears, throat, and palate. Significant improvement in the nasal symptom domain of the QoL assessment. Significantly greater expiratory airflow, but non-significant increase in the nasal airflow at the ascending inspiratory phase. Significantly larger increase in the total inspiratory nasal airway resistance in the placebo group compared with desloratadine treatment. Similar AE profile to placebo.
Meltzer et al/ 2001	Two multicentre, randomised, double-blind, placebo-controlled, parallel-group investigations	≥12 years old, ≥ 2-year history of SAR, positive (prick or intradermal) skin test to seasonal allergens within the past 12 months, clinically symptomatic (score ≥ 2), TNSS ≥ 6, TNNSS≥ 5, general good health and being free of significant disease	346 in spring 328 in autumn	Desloratadine 5 mg once daily Placebo (For two weeks)	Significant improvement with desloratadine treatment in TSS in both seasons. Significant reduction in both nasal and non-nasal symptoms from the baseline in both seasons with desloratadine. No clinically significant differences compared with placebo in sedation AE or ECG data.

Authors/ year	Methodology	Inclusion criteria	No. of patients	Comparator regimen(s)	Outcomes and results
Bousquet et al./2009	Multi-center, multinational, randomized, double-blind, placebo-controlled, parallel-group Phase IV study	≥ 12 years old; ≥ 2-year history of IAR; moderate/severe symptoms; the reflective total 5 symptom score (T5SS) ≥ 6; the sum of the daily averages of the morning plus evening T5SS for 4 days and the morning reflective T5SS on the morning of the randomization ≥ 30; positive skin prick tests to common specified aeroallergens, no medications for AR treatment in the past 14 days	547	Desloratadine 5mg once daily Placebo (For up to 14 days)	Significant improvement in all nasal individual symptoms. Significant reduction in the morning/evening reflective TSS and instantaneous symptom scores than placebo. Greater improvement in QoL scores with desloratadine therapy. Significant reduction in patient-rated subjective symptom severity using a visual analogue scale.
Demoly et al./ 2009	Double-blind, placebo-controlled, randomized, parallel-group study	≥ 18 years old, ≥ 2-year history of AR during the cypress pollen season; clinically symptomatic with cypress pollen AR at baseline; TNSS plus TNNSS 8, nasal congestion score 2; positive skin prick test within 24 months of the screening visit; using a medically acceptable birth control method; a negative urine pregnancy test result at baseline	233	Desloratadine 5 mg daily Placebo (For 15 days)	Desloratadine more effective than placebo in improving the TSS and TNSS. Significant improvement with desloratadine treatment in QoL scores and the global response to therapy. Numerical but non-significant improvement in the mean nasal inspiratory flow scores with desloratadine treatment
Adham/ 2011	Open-label, noninterventional, practice-based study	≥12 years old; 2-year history of SAR or PAR confirmed with skin prick test; TSS 8; nasal congestion score 2; ocular symptom score 2	602	Desloratadine 5 mg once daily Baseline (For 2 weeks)	Significant reduction in the individual nasal and total ocular symptoms. Significant improvement of TSS. Complete or marked relief with of symptoms in 85% of subjects. Improvement in nasal congestion and PNIF.

Authors/ year	Methodology	Inclusion criteria	No. of patients	Comparator regimen(s)	Outcomes and results
Lukat et al./ 2013	Randomized, double-blind, placebo-controlled study	≥ 12 years old; history of SAR ≥ 2 years; positive prick test on the day or within a year of screening visit; clinically symptomatic at screening (NSS ≥ 6, NNSS ≥ 3, and rhinorrhea score ≥ 2); normal electrocardiography and QTc interval values	356	Desloratadine 5 mg/daily Rupatadine 10 mg/daily Placebo	Significant reduction in TSS by desloratadine and rupatadine compared to placebo. Superior efficacy of both desloratadine and rupatadine in improving nasal and non-nasal symptoms than placebo. No statistically significant differences between rupatadine and desloratadine in reducing the baseline symptoms.
Berger et al./ 2006	Randomized, multi-center, double-blind, double-dummy, active- and placebo-controlled	≥ 12 years old; ≥ 2-year history of SAR during study season; positive skin test to prevalent pollen aeroallergen; morning instantaneous TSS ≥ 6; free of clinically significant medical condition	722	Desloratadine 5 mg/day Fexofenadine 180 mg/day Placebo	Superior efficacy of both desloratadine and fexofenadine in morning instantaneous TSS and morning/evening reflective TSS than placebo but comparative efficacy between two active treatments. Both active treatments associated with significant improvements in morning instantaneous individual symptoms (sneezing and itchy nose, throat, and palate). Desloratadine more advantageous than fexofenadine in alleviating ocular symptoms (itchy, watery, and red eyes). Superior efficacy of both active treatments in morning/evening reflective scores by reducing the symptoms of sneezing, itchy nose, throat, palate, ocular symptoms, and nasal congestion. Significant reduction of the severity score of rhinorrhoea with desloratadine compared to fexofenadine. A positive trend in improvement of symptom severity through the subjective assessment by investigators and subjects during the entire study. Relatively more incidence of AEs with fexofenadine followed by placebo and desloratadine.

Authors/ year	Methodology	Inclusion criteria	No. of patients	Comparator regimen(s)	Outcomes and results
Raphael et al./ 2005	Multi-center, parallel-group, randomized, double-blind, double-dummy, placebo-controlled study	12 to 65 years old; at least moderate SAR due to autumn weed pollen; positive skin prick or intradermal test reaction in the past year; a minimum moderate/moderately severe baseline symptoms of SAR	610	Desloratadine 5 mg daily Diphenhydramine 50 mg three time daily Placebo	Statistically and clinically significant improvements in TSS and TNSS with diphenhydramine compared with either placebo or desloratadine. Significant superiority of diphenhydramine in improving all individual SAR symptom scores, while desloratadine only significantly effective on sneezing scores. Diphenhydramine more effective than desloratadine in treating nasal congestion. Higher incidence of AEs and somnolence with diphenhydramine.
Bachert and Maurer/ 2010	Four prospective post-marketing surveillance studies	≥ 12 years old; SAR or chronic idiopathic urticaria	Overall, 77,880 subjects with 47,953 + 5,399 having SAR	Desloratadine 5 mg once daily (mean duration of 40 days) compared to baseline A post hoc analysis in the subgroup of people previously treated with another second-generation antihistamine	Significant reduction in TSS and individual symptom scores (including nasal, ocular, dermal, and asthma symptom scores) from the baseline after desloratadine therapy. Significant reduction in the mean nasal sum scores compared to baseline. Significant reduction in the percentage of subjects reporting moderate and severe symptoms and nasal congestion after desloratadine treatment. Significant reduction in severity of sleep impairment and daily activity impairment associated with SAR. Higher subjective efficacy of desloratadine than cetirizine, loratadine, fexofenadine, and mizolastine in comparative assessment of desloratadine compared with previous antihistamine monotherapy. Fatigue, headache, and dry mouth the most commonly reported desloratadine-related AEs.

Authors/ year	Methodology	Inclusion criteria	No. of patients	Comparator regimen(s)	Outcomes and results
Deruaz et al/ 2003	Double-blind, placebo-controlled, crossover study	18 - 60 years old; positive history of AR during the latest pollen season; nasal reaction threshold ≤ 10,000 standardized quality units/mL grass pollen at screening	24	Single dose desloratadine 5 mg Single dose levocetirizine 5 mg Single dose placebo	Levocetirizine more successful than desloratadine in inhibiting the sneezing and rhinorrhoea. No significant inhibition of nasal congestion by any of the study substances. Significant inhibition of albumin extravasation, as an early allergic marker in the nasal lavage by levocetirizine but not desloratadine. No significant effect by any of the components on late allergic phase mediators such as IL-5, IL-8, and eotaxin.
Day et al./ 2004	Randomised, double-blind, placebo-controlled, parallel-group study	≥ 16 years old, a documented history of ragweed-induced allergic rhinitis for the past two consecutive seasons, a positive skin prick test to ragweed the year prior to study	373 patients with ragweed induced RA	Desloratadine 5 mg/day Levocetirizine 5mg/day Placebo	Both active treatments superior to placebo in improving major symptom complex score. Significantly greater symptom improvement with levocetirizine compared to desloratadine. Faster action with levocetirizine compared to desloratadine. Resolution of nasal congestion to a greater extent with levocetirizine than desloratadine. Patient satisfaction with symptom improvement significantly higher with both active medications compared to placebo.
Bhatia et al/ 2005	Randomized, double-blind, double-dummy, parallel study	Age 18 to 45 years old, a history of allergy to tree or grass pollens, positive skin test to tree or grass allergens, symptomatic during the spring season for the past 2 years	61	Oral desloratadine, 5 mg/day Nasal budesonide, 32 µg/d per nostril Placebo (All for two weeks)	Superior efficacy of nasal budesonide compared to desloratadine in improving the overall NPIF* values and increasing nasal flow. Significant improvement in the RQLQ with both treatments with no differences between treatments. Significant decrease in the symptom scores with both medications, no significant differences between treatments.

Authors/ year	Methodology	Inclusion criteria	No. of patients	Comparator regimen(s)	Outcomes and results
Crampton/ 2003	Randomized, double-masked, placebo- and active controlled, single-centre clinical trial	Age ≥ 18 years old; history of rhino-conjunctivitis; able to follow study instructions; willing to avoid disallowed medications	80	Ketotifen ophthalmic solution 0.025% + placebo tablet Desloratadine 5 mg tablet + placebo eyedrop Ketotifen 0.025% ophthalmic solution + desloratadine 5 mg tablet	Significantly lower ocular itching scores in ketotifen or ketotifen/desloratadine combination group compared to the desloratadine group alone. Significantly less ocular redness with ketotifen therapy alone compared with desloratadine and ketotifen/desloratadine combination at 15 and 20 minutes after allergen induction. No statistically significant efficacy on nasal symptoms between treatments except ketotifen/loratadine combination at 50 minutes timepoint after the conjunctival allergen challenge. Less tearing with desloratadine treatment compared with other groups (non-significant).
Bachert et al./ 2009	Randomized, double-blind, placebo-controlled, parallel-group multicentre study	Age 12–70 years old; history of SAR ≥ 2 years; positive skin prick test to at least one seasonal allergen, positive prick test to perennial allergens but no symptoms of PAR; minimum reflective nasal symptom score of ≥ 36	720	Bilastine 10 mg once daily Desloratadine 5 mg once daily Placebo	Significant improvement in TSS, NSS, and NNSS with both treatments compared to placebo. Both treatments comparable in efficacy. Both treatments equally effective in increasing the RQLQ QoL measures than placebo. Significant efficacy on individual QoL domains except for nasal symptoms, emotional, and sleep components by bilastine, and nasal symptoms and emotional components by desloratadine.

Asthma

Desloratadine vs. Placebo

The anti-inflammatory action of desloratadine was put in test on reducing the systemic inflammation as well as nasal and bronchial inflammation in patients with asthma accompanied with grass pollen-induced AR[25]. Twenty-six patients received either desloratadine or placebo for seven days and then underwent a nasal provocation test by exposing them to grass pollen allergens. Compared to the placebo, desloratadine therapy resulted in a substantial increase in the PNIF before the nasal provocation test. Also, desloratadine significantly reduced the number of circulating eosinophils in allergic inflammation[25]. However, such reduction was not reflected in the eosinophils in nasal mucosa. Bronchial parameters, as demonstrated by the reactions to the methacholine provocation test, did not significantly change with desloratadine treatment. In this study, desloratadine did not show an improvement in the forced expiratory volume (FEV1) values and had limited efficacy in improving the nasal symptoms and PNIF after the nasal provocation[25].

Another RCT evaluated the effect of 5 mg desloratadine on a group of 20 patients with AR and exercise-induced bronchoconstriction where patients underwent an exercise challenge test before and seven days after receiving desloratadine or placebo[26]. Although desloratadine treatment resulted in a significantly less drop in the FEV1 compared to the baseline visits, no statistical difference was observed in this regard between

desloratadine and placebo[26]. Moreover, the area under the curve for percentage fall in FEV1 did not change significantly between the treatment and placebo group[26].

Among patients with seasonal allergic asthma and SAR desloratadine 5 mg led to a significant reduction in the morning/evening TSS[27]. Regarding the asthma-specific outcomes, desloratadine demonstrated superior effectiveness in reducing asthma symptom scores in patients with simultaneous SAR and asthma, individual asthma symptoms such as wheezing, cough, breathlessness, and chest tightness as well as controlling the lower airway symptoms/inflammation and bronchial hyper-responsiveness parameters, and the frequency of beta-agonist inhaler use[10&27]. In a subgroup analysis, among patients with concomitant SAR and asthma, the reduction in the mean reflective nasal congestion scores was significantly greater than placebo[13].

Another evaluation of 69 patients with SAR and concomitant seasonal asthma assessed the effect of treatment with desloratadine 5 mg on inflammatory mediators[28]. Improvements in rhinitis and nasal congestion was in favor of desloratadine treatment in this evaluation. However, desloratadine did not significantly affect the levels of cytokines, including IL-4, IL-10, IL-18, and TGF-beta failing to support the evidence around anti-inflammatory properties of this medication[28].

In another study, children with AR using either regular or on-demand desloratadine used an equal number of decongestant tablets or anti-allergic eye drops. Interestingly, after a 4-week treatment, patients using desloratadine on a regular basis had a significantly lower average salbutamol puffer use than those taking it on-demand. This was in line with the findings of Bachert *et al.*[10] in which more than half of the cases reduced asthma medication use during the desloratadine treatment period.

Desloratadine vs. Other Treatment Agents

In one study, the patients were randomly treated either with oral desloratadine 5mg, montelukast 10 mg, or placebo over a 4-week period. Both treatments achieved significant reductions in instantaneous total asthma symptom scores (TASS) the morning after the first dose as well as significant reductions in morning/evening reflective TASS scores. In terms of the individual asthma symptoms, including coughing, wheezing, and difficulty breathing, both medications were significantly superior to placebo from day 2 of the treatment and throughout the 4-week period[29]. Through an exploratory analysis, this study found that desloratadine achieved a greater 1 to 2-week impact in reducing the TASS in patients with severe asthma symptoms when compared with those with milder asthma. Looking at the pulmonary function test evaluations, both medications resulted in significant but comparable improvements in FEV1. Both desloratadine and montelukast were able to significantly decrease the frequency of beta2 agonist use in patients without a superiority of one to another.

Perennial or Persistent Allergic Rhinitis

Perennial or persistent allergic rhinitis refers to the allergic conditions where symptoms do not subside throughout the year. The ARIA guidelines describe persistent allergic rhinitis (PAR) when the symptoms persist more than 4 days/week and for more than 4 consecutive weeks[30]. The following section summarizes the current evidence around the efficacy of desloratadine on this class of allergic conditions.

Desloratadine vs. Placebo

Desloratadine has been significantly more effective than placebo in reducing the morning and evening nasal congestion scores and the RQLQ measures among patients with PAR as shown in a four-week trial[31]. Such significant improvements commenced as early as day 3 and the efficacy was sustained consistently from day 8 to the end of the study.

In another four-week trial among 1,179 patients with PAR, desloratadine demonstrated superior efficacy to placebo in reducing the morning/evening reflective TSS at all times[32]. Similar efficacy was demonstrated in another RCT between 676 and 716 patients with PAR. Desloratadine treatment was successful in significantly diminishing the morning and evening instantaneous and reflective TSS as demonstrated by a number of studies[32-34]. Regarding the individual symptoms, desloratadine has shown significant reduction in the TNSS and TNNSS in patients with

PAR[32-34]. Improvements in the PNIF from the baseline have also been significant in favour of the desloratadine treatment group. A prospective, open-label non-random study of 47 patients with PAR treated with desloratadine 5 mg daily showed a significant reduction in the median rhinitis symptoms relative to the baseline measurements[35]. Sneezing, rhinorrhoea, and palatal itchiness were the symptoms which were resolved significantly while the changes in nasal obstruction or ocular and nasal itching were not considered statistically significant. The median endoscopic appearance score, which assessed the nasal cavity from the aspects of nasal polyps, nasal discharge, nasal oedema, and septal deviation, also significantly dropped after desloratadine treatment[35].

In concordance with previous reports, desloratadine also demonstrated superior efficacy to placebo in improving the individual domains of the QoL measures[31&33&35]. Individual components of RQLQ QoL, including nasal symptoms, specific activities, general problems, practical problems, sleep problems, and emotional functioning except ocular symptoms have also shown to improve with desloratadine[31]. Another study used the Medical Outcomes Study 36-item short form health survey to assess the health-related QoL – a tool different from the commonly mused RQLQ tool used by previous studies[35]. Of the eight different scales, only the general health perception was found to be statistically improved after treatment, while improvement in social functions was marginal[35].

Paediatric populations with PAR have also been studied for the effectiveness of desloratadine. An open-label observational multi-centre study conducted in a paediatric population from five Latin American countries reported the efficacy of desloratadine in a mixed diagnosis of SAR and PAR, though PAR patients were in the majority (61% vs 39%)[36]. Desloratadine 2.5 mg/day for 6 weeks was associated with a significant reduction in the mean TSS as well as all individual symptom scores including nasal congestion. The efficacy of desloratadine monotherapy was found to be comparable with desloratadine plus corticosteroid treatment in this study [36]. There are other studies in the literature which have studied the efficacy of desloratadine as fixed-dose combination products with secondary agents (Table 2)[37].

Table 2: An overview of the research studies on clinical efficacy of desloratadine either compared to placebo, baseline measures, or other treatment agents in treatment of perennial or persistent allergic rhinitis

Authors	methodology	Inclusion criteria	No. of patients	Comparator regimens	Outcomes and results
Holmberg et al./ 2009	Randomized, double-blind, placebo-controlled trial	18–65 years old, positive skin prick test or radio-allergosorbent test class ≥ 2 to house dust mite or cat dander within 24 months prior to screening, ≥ 2-year history of moderate/severe nasal symptoms, moderate/severe nasal congestion score ≥ 4 of 6 rated on a 7-point scale for ≥ 4/7 days during the screening	584	Desloratadine 5 mg/daily Placebo	Significant efficacy of desloratadine than placebo in reducing the morning and evening nasal congestion scores. Significant improvement in QoL measures. Superior efficacy of desloratadine in improving the individual domains of QoL measures except ocular symptoms. Significant relief in rhinorrhoea and nasal congestion with desloratadine but no significant effect on minor nasal symptoms such as sneezing and itching.

Authors	methodology	Inclusion criteria	No. of patients	Comparator regimens	Outcomes and results
Kim et al./2006	Randomized, double-blind, placebo-controlled, multicenter study	≥ 12 years old; history of PAR ≥ 2 years; baseline TSS ≥ 9, TNSS ≥5, TNNSS ≥ 4; positive skin prick response to an appropriate perennial allergen within 12 months; significant disease-free; negative serum pregnancy test; using an appropriate birth-control method	1,179	Desloratadine 5 mg/daily Placebo (For 4 weeks)	Superior efficacy of desloratadine to placebo in reducing the morning/evening reflective TSS, TNSS, and TNNSS. Significant improvements in the PNIF from the baseline in favour of the desloratadine treatment group (better improvement in morning PNIF). Similar AEs profile between desloratadine and placebo.
Cingi et al./ 2013	Prospective and multi-centric, placebo-controlled clinical trial	20-51 years old; diagnosis of PAR as per ARIA criteria for ≥ 2 years; general good health; non-smoker	40	Desloratadine/montelukast 5/10 mg fixed dose combination Placebo (For three months)	Decreased nasal allergy symptoms including itching, sneezing, discharge, and congestion. Increased minimum-cross sectional area and volume indicating a beneficial effect of treatment on nasal obstruction. Significant improvement than placebo on the RQLQ QoL scores and all domains of the QoL.
Simons et al./ 2003	Randomized, placebo-controlled, double-blind, parallel-group study	≥ 12 years old; history of moderate PAR ≥ 2 years; positive skin test response to ≥ 1 specified allergens within the previous year, having PAR symptoms with a reflective TSS ≥ 10 and no greater than moderate nasal stuffiness/congestion, the summed reflective congestion score ≤ 12 in the 3 days before baseline, the summed TSS ≥ 60, overall rhinitis score ≥ 2 at baseline, good general health; negative serum pregnancy test and use of an accepted method of contraception	676	Desloratadine 5 mg/once daily Placebo (For 4 weeks)	Superiority of desloratadine to placebo in significantly decreasing the PAR symptoms. Significant reduction in the morning/evening instantaneous and reflective TSS. Significant alleviation of individual symptoms scores with desloratadine (significant reduction of the total non-nasal scores as well as nasal symptoms including rhinorrhoea, nasal itching, sneezing, and postnasal drip). Similar occurrence of AEs between desloratadine and placebo.

Authors	methodology	Inclusion criteria	No. of patients	Comparator regimens	Outcomes and results
Bousquet et al./ 2010	Randomized placebo-controlled trial	≥ 12 years old, ≥ 2-year history of ARIA-defined PAR, moderate/severe symptoms, reflective T5SS ≥ 8 at screening, the sum of the daily averages of morning and evening reflective T5SS in 4 days and the morning reflective T5SS on the morning of randomization= 640, positive skin prick test to common aeroallergens, no medication for allergic rhinitis for specified periods (washout) prior to study	716	Desloratadine 5 mg once daily Placebo (For 12 weeks)	Significantly greater reduction with desloratadine in the morning/evening reflective TSS relative to the placebo during the first month and on each individual day. Significant reduction in the individual nasal symptom scores with desloratadine therapy than placebo. Rapid onset of effect from the second day and significant reduction in the morning instantaneous TSS. Significant improvement of QoL measures than placebo. AEs associated with desloratadine comparable with placebo.
Lam et al./ 2007	Prospective, open-label, non-blinded, non-randomised study	> 12 years old, diagnosed with chronic perennial rhinitis (symptoms ≥ 12 weeks), colleagues' rhinitis symptoms score ≥ 2, appropriate washout period with recent medications such as antihistamines and corticosteroids	47	Desloratadine 5 mg once daily for 12 weeks Baseline	Significant reduction in the median rhinitis symptoms after treatment with desloratadine. Significant drop in the median endoscopic appearance score after desloratadine treatment. Significant relief in sneezing, rhinorrhoea, and palatal itchiness but no significant changes in nasal obstruction or ocular and nasal itching. Significant improvement in the general health perception domain of QoL but non-significant changes in other domains.
Tassinari et al./ 2009	Open-label, observational, multicenter study	6 to 12 years old; physician-confirmed diagnosis of either SAR or PAR	455	Desloratadine syrup 2.5 mg/day (5 mL) (For 6 weeks)	Significant reduction in the mean TSS and all individual symptom scores including nasal congestion. Comparable efficacy of desloratadine monotherapy with desloratadine plus corticosteroid treatment.

Authors	methodology	Inclusion criteria	No. of patients	Comparator regimens	Outcomes and results
Wandalsen et al./ 2016	Prospective, multi-center, double-blind, randomized, controlled study of parallel group	2-12 years old, moderate/severe PAR, clinical features consistent with the PAR (recurrent nasal symptoms, and sensitization to airborne allergens by the presence of specific IgE), nasal symptoms scores ≥6 in the past week	195	Desloratadine (0.5 mg/mL) and prednisolone (4 mg/mL) combined in oral solution Dexchlorpheniramine maleate (0.4 mg/mL) and betamethasone (0.05 mg/mL) syrup	Significant but comparable reduction in the nasal and extra-nasal symptom scores by each compound. More than 90% of subjects in both groups reporting to be better/much better after treatment. Somnolence, headache, and fever significantly higher in the dexchlorpheniramine/betamethasone group, while epistaxis significantly higher with desloratadine/prednisolone.
Lee et al./ 2004	Randomized, double-blind, placebo-controlled, cross-over	History of PAR without concomitant asthma, no oral corticosteroids or antibiotics over the past 3 months, a positive skin prick test response to house dust mite, a positive response to nasal AMP challenge at screening	16	Single dose desloratadine 5 mg Single dose fexofenadine 180 mg Single dose levocetirizine 5 mg Placebo	Significant attenuation of the maximum fall in the baseline PNIF with all three active treatments compared to placebo. Significant attenuation of the area under the curve for 60 minutes time-response measures with all active treatments compared to placebo. Equal efficiency of all three treatments in attenuating the allergic reaction to nasal AMP.
Ciprandi et al./ 2004	Randomized double-blind, parallel-group, placebo-controlled	> 18 years old, history of PAR for the last 2 years, rhinitis symptoms in the last 2 weeks, baseline TSS ≥6, moderate/severe nasal obstruction	30	Desloratadine 5 mg/daily Levocetirizine 5 mg/daily Placebo	Superior efficacy of both desloratadine and levocetirizine to placebo in decreasing TSS and individual symptoms. Significant increase in the nasal airflow and significantly lower reversibility of nasal airflow, with levocetirizine compared to baseline but not with desloratadine. Both treatments superior to placebo in increasing the nasal airflow and lowering the reversibility of nasal airflow. Significant reduction in the number of eosinophils compared to pre-treatment baseline with levocetirizine. Both medications superior to placebo in reducing eosinophils.

Authors	methodology	Inclusion criteria	No. of patients	Comparator regimens	Outcomes and results
Bocşan et al./ 2015	Randomized clinical trial	Inclusion: Patients with ARIA-defined PAR, no history of atopy	85	Desloratadine 5 mg/daily Levocetirizine 5 mg/daily (For four weeks)	Significant but comparable reduction in the TSS by both medications. Significant alleviation of the individual symptoms but levocetirizine superior to desloratadine in alleviating nasal congestion. Significant reduction in inflammatory cytokines including IL-1β, IL-6, IL-8, and TNF-α with both active treatments but more pronounced effect with levocetirizine than desloratadine.
Ciebiada et al./ 2006	Randomized, double-blind, placebo-controlled crossover trial using 2 arms	18 to 65 years old; ARIA-defined PAR for ≥ 2 years, nasal congestion score ≥ 2, sensitization to perennial allergens relevant to Central Europe, positive skin prick test	40	First arm: Desloratadine 5 mg/day Montelukast 10 mg/day Combination of both Placebo Second arm: Levocetirizine 5 mg/day Montelukast 10 mg/day Combination of both Placebo	Significant attenuation of the TSS, daytime nasal scores, and daytime ocular scores with the combination therapy. Significant improvement in the individual nasal symptoms such as congestion and ocular symptoms with desloratadine + montelukast combination than desloratadine or montelukast alone. Significantly better outcome in reduction of eosinophil cationic protein with montelukast + desloratadine combination but not with levocetirizine combination Significant increase in the minimal cross-sectional area of the nasal cavity than the baseline and the placebo, but not compared with monotherapy.

Desloratadine vs. Other Treatment Agents

The efficacy of desloratadine 5 mg, fexofenadine 180 mg, and levocetirizine 5 mg, three of the recent second-generation antihistamines was comparatively assessed in a randomized double-blind cross-over trial in patients with PAR[38]. Overall, the three agents demonstrated equal efficiency in attenuating the allergic reaction to nasal adenosine 5-monophosphate (AMP). Administering all three treatments resulted in significant attenuation of the maximum drop in the baseline PNIF and the area under the curve for 60 minutes time-response measures compared to placebo[38].

Both desloratadine and levocetirizine 5 mg/daily demonstrated superior effectiveness than the placebo in decreasing TSS, individual symptoms, and levels of inflammatory cytokines such as IL-1β, IL-4, IL-6, IL-8, and

TNF-α[39&40]. This effect was more pronounced with levocetirizine than desloratadine[39]. Also, levocetirizine had significant superiority to desloratadine in improving nasal airflow, achieving lower reversibility in nasal airflow after induced vasoconstriction, caused a significant increase in total nasal airflow, and reduction in the number of eosinophils[39&40].

The combination therapy of montelukast with desloratadine or levocetirizine offered a number of advantages over monotherapy such as significant attenuation of the TSS, daytime nasal scores, and daytime ocular scores. Specifically, in the montelukast-desloratadine combination, there was a significant improvement in the individual nasal and ocular symptoms compared to desloratadine or montelukast alone. Moreover, montelukast-desloratadine combination resulted in a significantly better outcome than montelukast-levocetirizine in reduction of eosinophil cationic protein as an inflammatory mediator[41].

The efficacy of desloratadine in combination with prednisolone was compared with dexchlorpheniramine/betamethasone combination among children 2-12 years old presenting with moderate to severe PAR[42]. Significant reduction in nasal and extra-nasal symptoms was achieved by both compounds separately and this reduction was comparable between treatments. In the subjective evaluation more than 90% of the subjects in both treatment groups indicated feeling better/much better after the treatment.

Chronic Idiopathic Urticaria

Desloratadine vs. Placebo

Desloratadine has a potential role of oxidative stress in the pathogenesis of chronic idiopathic urticaria (CIU). Desloratadine treatment was also associated with a significant decrease in the levels of alph-1, alpha-2, beta-1 globulins, c-reactive protein, and albumin as inflammation indicators. In patients with chronic spontaneous urticaria (CSU), desloratadine resulted in a significant decrease in leucocytes and basophils compared to before treatment with no significant effect on other hematologic parameters such as neutrophils, lymphocytes, and monocytes[43]. The positive impact of desloratadine on QoL was demonstrated by some studies[44-46].

Response to desloratadine treatment in one study was rated as either a complete relief or a marked relief equally by one-thirds of the patients[46]. Desloratadine group also achieved a significantly better CIU improvement with nearly 70% of the subjects reporting complete relief[47]. Moreover, desloratadine has resulted in significant improvement in interference with sleep and improved sleep as well as interference/disruption in daily activities scores[12&44&45&48-50]. Physician-rated evaluations also show that general state of urticaria also experienced a significant improvement with desloratadine therapy where, according to physician reports more than 88% of the patients achieved wither complete or significant symptom relief[48].

In a number of studies of varying methodologies such as RCT and post-marketing surveillances involving patients with CIU, desloratadine has been shown to be significantly effective in improving the total CIU symptom scores, attenuating the CIU related pruritus and itching severity, and improving mean morning/evening reflective pruritus scores[12&43&45&47-50]. Similarly, desloratadine treatment has shown to significantly reduce the number and size of the wheals, and the size of the largest whealscores[12&43&45&47-50].

Desloratadine vs. Other Treatment Agents

A comparative study of efficacy and safety of rupatadine versus desloratadine therapy in patients with CIU showed the superior safety and efficacy of rupatadine in reducing the eosinophil count, serum IgE levels, and the number of wheals, as well as significantly greater improvement in the AEQLQ[51&52]. In another RCT, the efficacy of rupatadine was compared to desloratadine in pediatric patients aged between 2 to 11 years old with CSU[52]. All active agents showed significant efficacy in improving the urticaria activity scores, but no differences were present between treatments. Both agents were significantly more effective

than placebo in improving mean pruritus scores but superiority of rupatadine to desloratadine was observed. In this study, both treatments resulted in a significant improvement in children's QoL[52].

Desloratadine did not show superiority to levocetirizine in managing CIU[53]. A significantly greater decrease was achieved with levocetirizine in pruritus symptom severity scores as well as the sum of the pruritus severity score and the score for the numbers of wheals throughout the 4-week treatment period[53]. Moreover, relative to desloratadine, levocetirizine was significantly more effective in reducing the duration of pruritus symptoms[53]. Levocetirizine showed superiority to desloratadine in the overall success rate. In non-responders to the maximum dose of one medication, switching desloratadine to levocetirizine resulted in 30% improvement, while no benefit was obtained with switching to desloratadine[54]. Moreover, the results of the improvement level of urticaria-associated discomfort significantly favored levocetirizine over desloratadine. Assessment of the QoL components showed an increasing trend of QoL with increasing the dose of both medications with levocetirizine demonstrating superiority to desloratadine[54].

Another study took a different approach by seeking to understand the effect of adding dipyridamole to desloratadine therapy in managing the patients with chronic urticaria[55]. This study was based on the notion that platelets are involved in the inflammatory reactions through their proinflammatory properties leading to the release of inflammatory mediators when activated. Desloratadine and dipyridamole combination had a significantly greater clinical effectiveness compared to desloratadine alone as 85% percent versus 70% attained complete cure or obvious improvement of their CIU based on Symptom Score Reduce Index, respectively[55]. Both treatments significantly reduced the wheals and pruritus scores, though such decrease in symptoms was greater with the combination therapy. Moreover, the recurrence rate of symptoms after the treatment withdrawal was considerably lower in the combination therapy group compared to desloratadine monotherapy (24% vs. 53%)[55].

Desloratadine and montelukast combination did not provide a marked advantage in reliving CIU symptoms as the effectiveness of desloratadine alone versus desloratadine and montelukast combination were similar in all these efficacy parameters[56]. Superior efficacy of desloratadine and desloratadine/montelukast was observed compared to montelukast alone in alleviating pruritus. Desloratadine monotherapy and desloratadine/montelukast combination were also significantly more effective than montelukast monotherapy in reducing the TSS, pruritus, number, and size of hives, although all treatments improved these measures. In terms of the improving the CIU interference with sleep, both desloratadine mono- and combination therapy showed significant efficacy than placebo and montelukast monotherapy[56].

Higher efficacy of desloratadine was observed compared with previous antihistamine monotherapy including cetirizine, loratadine, and fexofenadine, desloratadine in a post-marketing surveillance study[48]. Also, more than half of the previous antihistamine users reported receiving a faster alleviation with desloratadine than the previous medication[48].

Table 3: An overview of the research studies on clinical efficacy of desloratadine compared to placebo, baseline measures, or other treatment agents in treatment of chronic idiopathic urticaria

Authors	Methodology	Inclusion criteria	No. of patients	Comparator regimens	Outcomes and results
Maaouia et al./ 2016	Prospective case-control design	CSU confirmed by urticarial skin lesions, intermittent or continuous for > 6 weeks	30 CSU patients and 30 controls	Desloratadine 5 mg/day (For 30 days)	Marked reduction in the wheal size and itching severity with desloratadine Significant decrease in the levels of alpha-1, alpha-2, beta-1 globulins, CRP and albumin as inflammation indicators Significant decrease in leucocytes and basophils compared to before treatment but no significant effect on other hematologic parameters.
Lachapelle et al./ 2005	Prospective before and after study	CIU ≥ 6 weeks, current flare of ≥ 3 weeks, ≥ 18 years old, no child-bearing potential, using an acceptable method of birth control, free of any diseases or medication that may interfere with the study	121 consecutive patients	Desloratadine 5 mg daily (For 42 days)	Significant improvement in the total and sub-total QoL scores (except work and school component) evident at day 7 and day 42. Complete relief of the symptoms or marked relief equally by one-third of the patients.
Monroe et al./ 2003	Double-blind, randomized, placebo-controlled trial	≥ 12 years old; documented CIU ≥ 6 weeks; CIU flare ≥ 3 weeks; urticarial lesions ≥ 3 days/week; at least moderate severity CIU at screening and baseline; at least moderate pruritus, and visible hives, total reflective pruritus score ≥ 14 in last 3 days of screening, normal lab/ECG values, negative serum pregnancy test and acceptable contraception method	226	Desloratadine 5 mg/daily Placebo (For 6 weeks)	Significantly superior efficacy of desloratadine in improving the total CIU symptom scores. Significant attenuation of symptoms including pruritus, the number of hives, and the size of the largest hive. Significant reduction in sleep disturbance and improvement of the performance of daily activities. Sustained efficacy from the first 24 hours throughout the entire duration of the study. Similar incidence of AEs between desloratadine and placebo.

Authors	Methodology	Inclusion criteria	No. of patients	Comparator regimens	Outcomes and results
Ortonne et al./ 2007	Randomized double-blind placebo-controlled trial	≥ 18 years old, previous diagnosis of CIU, having active moderate-to-severe CIU, an active CIU flare of ≥ 3 weeks, wheals present ≥ 3 days/week, global CIU severity score ≥ 2, required washout period for a specified list of medications such as corticosteroids, antihistamines, NSAIDs, etc.	137	Desloratadine 5 mg once daily Placebo (For 6 weeks)	Significantly superior efficacy of desloratadine than placebo in improving the pruritus scores. Significant reduction in the sizes of the largest wheals. Significant reduction in the number of wheals from the week 2 of the study onwards. Significantly better CIU improvement with nearly 70% of the subjects reporting complete relief with desloratadine therapy. Sustained efficacy throughout the study period.
Kim and Lynde/ 2008	Open-label, observational, multicenter study	≥ 18 years old; CIU diagnosis; a hive score ≥ 1, pruritus score ≥ 2, overall condition score ≥ 2, 6-week history of CIU, a current flare of ≥ 3-weeks	348	Desloratadine 5 mg daily compared to the baseline (For 14 days)	Significant reduction in the overall condition score. Significant reduction in itching scores. Significant reduction in hive scores and the size of the hives. Significant improvement in interference with sleep and interference with daily outdoor activities. Significant improvement in all ten domains of the AEQLQ QoL tool.
Ring et al./ 2001	Multicentre, randomized, double-blind, placebo-controlled study	≥ 12 years old, ≥ 6-week CIU history, active flare ≥ 3 weeks, wheals visible for ≥ 3 days/week, at least moderate disease severity at screening and baseline, at least moderate pruritus and wheals at screening, total reflective pruritus score ≥ 14 over previous 3 days and the morning of the baseline visit, clinical/laboratory tests within acceptable range	190	Desloratadine 5 mg once daily Placebo (For 6 weeks)	Superior efficacy to placebo in reducing the average mean morning/evening reflective pruritus score. Significant improvement in the morning/evening reflective TSS compared to placebo. Significant reduction in the morning instantaneous pruritus scores. Significant improvement in sleep and daily activity scores. Highly significant reduction in the number of hives and the size of the largest hives.

Authors	Methodology	Inclusion criteria	No. of patients	Comparator regimens	Outcomes and results
Grob et al./ 2007	Multicentre, randomized, double-blind placebo-controlled study	≥ 18 years old, history of CIU with symptoms present for 3 weeks, wheals present for 3 days/ week, flare-up before first visit, good general health, using an effective method of contraception, pruritus score of 2, wheal score of 1, global CIU severity score of 2 at screening and baseline, morning/evening reflective pruritus score of 14 for three consecutive days prior to study	137	Desloratadine 5 mg once daily Placebo (For 42 days)	Significantly greater overall improvement in QoL than the baseline scores compared to the placebo with both DLQI and VQ Dermato QoL assessment tools. Significant improvement in sleep disruption components and reduction in the disruption of daily activities score from the beginning to the end of the study period.
Augusting and Ehrle/ 2009	Observational post-marketing surveillance study	Patients with CIU aged ≥ 12 years old, meeting the desloratadine treatment criteria as outlined in the package insert	9,246	Desloratadine Baseline Any previous antihistamine therapy	Significant decrease in the symptoms of itching/pruritus, number of wheals, and the size of the largest wheal. Significant patient-reported improvement in CIU-impaired sleep and daily activities. More than 88% complete or significant symptom relief with desloratadine treatment. Superior efficacy and earlier onset of action compared with previous antihistamine treatments with cetirizine, loratadine, and fexofenadine.
Bachert and Maurer/ 2010	Four prospective post-marketing surveillance studies	≥ 12 years old with SAR or CIU treated with desloratadine	Overall, 77,880 subjects with 9,246 + 13,183 having CIU	Desloratadine 5 mg once daily compared to baseline (Mean duration of 40.4 days)	Significant improvement in total urticaria symptoms. Significant reduction in the severity of itching, number of wheals and diameter of the largest wheal. Significant effect on sleep and daily activity improvement with desloratadine.

Authors	Methodology	Inclusion criteria	No. of patients	Comparator regimens	Outcomes and results
Kolasani et al./ 2013	Prospective, randomized, open, outdoor-based clinical study	12 - 60 years old; CIU diagnosis	56	Desloratadine 5 mg daily Rupatadine 10 mg daily Placebo (For 4 weeks)	Superior efficacy of rupatadine over desloratadine in improving the TSS and the AEQLQ, though both medications significantly superior to placebo. Rupatadine superior over desloratadine in reducing the eosinophil count and serum IgE levels. Lower (but non-significant) incidence of AEs with rupatadine.
Potter et al./ 2009	Multi-center, randomized, double-blind study	≥ 18 years old; history of CIU ≥ 6 weeks in the last 3 months; pruritus severity score ≥ 2; wheal score ≥ 1 for ≥ 3 days/week prior to study	886	Desloratadine 5 mg once daily Levocetirizine 5 mg once daily (For 4 weeks)	Significantly greater decrease with levocetirizine in pruritus severity scores and the sum of the pruritus severity score + the numbers of wheals compared to desloratadine. Significantly more efficacy with levocetirizine than desloratadine in reducing the duration of pruritus symptoms. Improved DLQI QoL measures with both treatments. Reduced CIU impact on sleep with both treatments.

Authors	Methodology	Inclusion criteria	No. of patients	Comparator regimens	Outcomes and results
Khalaf et al./ 2007	Randomized, double-blind; parallel group study	≥ 16 years old, documented history of CU ≥ 6 weeks with a frequency of ≥ 3 episodes/week, stopping corticosteroids 1 month before the study and other preventive or treatment agents one week prior	64	Desloratadine 5 mg/day + dipyridamole 25 mg TDS Desloratadine 5 mg/day + placebo	Significantly greater clinical effectiveness with desloratadine and dipyridamole combination compared to desloratadine alone (85% percent versus 70% complete cure or obvious improvement of CIU, respectively). Significant reduction in the wheals and pruritus scores with both treatments, but a greater decrease in symptoms with the combination therapy. Lower recurrence rate of symptoms after the treatment withdrawal in the combination therapy group compared to desloratadine monotherapy (24% vs. 53%).
Lorenzo et al./ 2004	Randomized, double-blind, double-dummy, placebo-controlled, parallel-group study	18-69 years old, CIU diagnosis (presence of urticarial lesions for > 6 weeks with > 3 episodes per week), no secondary known causes	160	Desloratadine 5 mg daily + Placebo Montelukast 10 mg + Placebo Desloratadine 5 mg + Montelukast 10 mg	Significant improvement in the TSS, number of hives, and the size of the largest hive with all treatments. No marked advantage with desloratadine and montelukast combination than desloratadine alone. Similar efficacy of desloratadine alone versus desloratadine/montelukast combination in all the efficacy parameters. Superior efficacy of desloratadine and desloratadine/montelukast compared to montelukast alone in alleviating pruritus. Significant efficacy of desloratadine mono- and combination therapy than montelukast monotherapy in improving sleep interference.

Authors	Methodology	Inclusion criteria	No. of patients	Comparator regimens	Outcomes and results
Potter et al./ 2015	Randomized, double blind, placebo- and desloratadine-controlled study	Children aged 2-11 years old with CSU, weighing ≥ 10 kg, documented history of CSU with or without angioedema ≥ 6, Urticaria Activity Score 7 days cumulative score ≥ 12 points; normal ECG values	206	Rupatadine oral solution 1 mg/ml once daily Desloratadine 0.5 mg/ml once daily Placebo (For 6 weeks)	Significant improvement by all active agents in improving the Urticaria Activity Scores but no between-treatment differences. Rupatadine more effective than desloratadine in reducing the mean number of wheals. Both agents significantly effective than placebo in improving absolute change mean pruritus scores but superiority of rupatadine in improving mean pruritus score to desloratadine. Significant improvement in children's QoL with both treatments.
Staevska ey al./ 2010	Double-blind, randomized, 2 parallel-armed trial	19-67 years old; difficult-to-treat chronic urticaria with failure to previous treatment, receiving intermittent systemic corticosteroids up to 3 weeks before inclusion in the study; ≥ 6-week history of moderate/ severe urticaria	80	Desloratadine 5, 10, 20 mg once daily Levocetirizine 5, 10, 20 mg once daily	Significantly more success rate in achieving symptom-free state with increasing the dose of both medications to more than 5mg conventional dose. Superiority of levocetirizine to desloratadine in the overall success rate. 30% improvement after switching maximum dose desloratadine to levocetirizine (bot no effect with switching levocetirizine to desloratadine). Significant improvement in urticaria-associated discomfort in favor of levocetirizine than desloratadine. Increasing trend of QoL with increasing the dose of both medications but superior efficacy with levocetirizine.

Other potential indications

Uremic Pruritus

Uremic pruritus is a common complication in dialysis patients. Only one study was found evaluating the efficacy of desloratadine compared with gabapentin in alleviating chronic haemodialysis with sustained pruritus for more than 2 months[57]. Both treatments resulted in an improvement in the severity of pruritus using a visual analogue scale for pruritus scores, of which only desloratadine's effect was statistically significant compared to the baseline. However, none of the agents were superior to the other. The percentage of patients experiencing at least 50% improvement in their symptoms was significantly higher with desloratadine than gabapentin (58% vs 16%).

Cold Urticaria

Desloratadine has also been proposed to be effective in the treatment of acquired cold urticaria, a condition in which a cold stimulus

provokes the formation of wheals and itching on the skin. Two studies were found investigating the efficacy of desloratadine on treating cold urticaria[58&59]. Desloratadine demonstrated efficacy in reducing the volume of wheals provoked by cold where higher doses of desloratadine was more effective. Thermographic analysis also showed significantly smaller areas of hyperthermic skin lesions with no statistical differences between the doses. Furthermore, the critical temperature threshold (i.e. the maximum temperature causing wheal induction) and the critical stimulation time threshold (i.e. the shortest time required to induce a wheal) were significantly improved with desloratadine administration in both conventional and high dose[59].

The second study evaluated the effect of desloratadine 5 mg daily for 4 days in inhibition of cold urticaria among 12 patients by provoking cold with an ice-cube being in contact with the forearm skin[58]. Desloratadine treatment caused a considerable improvement in the symptoms of cold urticaria, reflected as no confluent wheals or itching after the treatment period. Moreover, desloratadine treatment was associated with significantly lower likelihood of producing ≥ 4 wheals after the cold contact than before treatment[58]. Moreover, it took longer time after desloratadine treatment to generate a weak response (7.0 vs 1.2 min). Analysis of patient opinions indicated a general satisfaction with desloratadine over previous antihistamine treatments such as cetirizine, loratadine, and cyproheptadine for a number of reasons including less itching, less side effects, and better effectiveness[58].

Chronic Rhinosinusitis

One study was found investigating the potential clinical application and efficacy of desloratadine therapy in chronic rhinosinusitis[60]. This study involved 90 patients with chronic sinusitis who had underwent endoscopic sinus surgery and compared the clinical efficacy of the combination of desloratadine citrate disodium with budesonide suspension against budesonide nebulizing suspension[60]. While both treatments resulted in a significant decrease in serum IgE, eosinophils and inflammatory cytokines including IL-6, IL-8, TNF-α, and hs-CRP. Desloratadine and budesonide combination had a significantly higher efficacy for chronic sinusitis and decreasing inflammatory cytokines[60].

Chronic Otitis Media

A retrospective review of case series related to 138 children with chronic otitis media with effusion studied the potential role of desloratadine based on the assumption of the involvement of histamine in the middle ear effusion[61]. Desloratadine was found to be effective in accelerating the alleviation of effusion in the middle ear as demonstrated

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الفعالية السريرية لمضادات الهيستامين غير المهدئة ديسلوراتادين في تدبير حالات الحساسية: مراجعة للأدلة

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[٥] كلية التوظيف الأمريكية ، كاليفورنيا ، الولايات المتحدة الأمريكية

[٦] قسم الصيدلة الاكلينيكية ، كلية الصيدلة ، جامعة شهيد بهشتي للعلوم الطبية ، طهران ، إيران

ديسلوراتادين هو مضاد للهستامين ثلاثي الحلقات جديد نسبيًا من الجيل الثاني دخل حيز الاستخدام الطبي في عام ٢٠٠١. هدفت هذه الدراسة إلى مراجعة الأدلة المتوفرة في المراجع حول الفعالية السريرية لديسلوراتادين في مجموعة من حالات الحساسية. تم إجراء بحث في قاعدة البيانات في Medline و PubMed و Embase و Google Scholar للمقالات البحثية المنشورة حتى يوليو ٢٠٢٠ ، باستخدام الكلمة المفتاحية desloratadine. كما تم إجراء بحث إضافي عن قوائم المراجع وتتبع الاقتباس. تم النظر في المقالات البحثية باللغة الإنجليزية المتعلقة بديسلوراتادين وفعاليته. تم النظر في تصميمات الدراسات ، بما في ذلك التجارب المعشاة ذات الشواهد (RCT) ، ودراسات المراقبة / الحالات والشواهد ، وسلسلة الحالات. يُظهر الدليل الجمعي من المراجع الحالية فعالية فائقة لعقار ديسلوراتادين مقارنة بالعقار الوهمي وبعض خيارات العلاج الأخرى في إدارة التهاب الأنف التحسسي الموسمي (SAR) والتهاب الأنف التحسسي الدائم (PAR) والأرتكاريا المزمنة مجهول السبب (CIU) وأعراض الربو. هناك أيضًا دليل على الأدوار الجديدة المحتملة التي تم نسبتها للديسلوراتادين مثل علاج حب الشباب والتهاب الأذن الوسطى المزمن والتهاب الأنف والجيوب المزمن ، الأمر الذي يتطلب المزيد من التحقيق. في معظم الدراسات ، كانت سلامةاستخدام ديسلوراتادين وتحمله مماثلة للعقار الوهمي. تشير الدلائل الحالية إلى أن ديسلوراتادين هو خيار مثالي لمعظم حالات الحساسية نظرًا

لفعاليته بالإضافة إلى خصائص السلامة والتحمل الملائمة. هناك حاجة إلى مزيد من الدراسات واسعة النطاق لإثبات فعالية وسلامة ديسلوراتادين ومقارنة فعاليته مع العلاجات الأخرى في إدارة حالات الحساسية.