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Review Article

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A REVIEW ON ANTIALLERGIC ACTION OF RUPATADINE

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ABSTRACT

Rupatadine helps alleviate various symptoms of an allergic reaction. It acts as an anti-histamine, which treats urticaria and allergic rhinitis. Certain precautions are necessary when taking Rupatadine, such as liquor consumption should be avoided. Patients who suffer from kidney and liver problems, as well as old aged persons and children below the age of 12, should take the drug only after their doctor approves. Expecting mothers, those trying to conceive and breastfeeding women should also inform their doctor before they start the drug. Over dosage of Rupatadine can lead to severe complications and should be avoided. The drug is meant to be stored at room temperature, preferably in a container that is clean and airtight. The dosage of the drug generally depends on the severity of the allergic reaction. In most cases, doctors prescribe about 10 mg which needs to be taken one time daily. It is an oral drug that should be consumed exactly as prescribed by your health care provider. Information given here is based on the salt content of the medicine. Uses and effects of the medicine may vary from person to person. It is advisable to consult an internal medicine specializer before using this medicine.Rupatadine is a second generation antihistamine and PAF antagonist used to treat allergies. It is available as round, light salmon coloured tablets containing 10 mg of rupatadine as fumarate.

KEYWORDS: Antihistamines, Rupatadine, allergic rhinitis, chronic urticaria

INTRODUCTION

Rupatadine is an effective anti-allergic medicine used to temporarily relieve the symptoms of seasonal allergies. These symptoms may include sneezing, runny nose, itchy eyes, sore throat, etc. This medicine is not recommended for use in children below 12 years of age.Rupatadine is a novel substance which, in addition to being an H1 antagonist, is also a potent platelet-activating factor (PAF) inhibitor. Animal and human models have shown rupatadine to have dual antihistamine and PAF-antagonist properties. It is commercially available in Spain as 10-mg tablets and has already been approved in several other European countries. Rupatadine has been available in Germany for the treatment of allergic rhinitis and chronic urticaria in adults and children aged over 12 years under the tradename Rupafin10 mg since August 1, 2008, and under the tradename Urtimed since 2010. The present article discusses the pharmacology, kinetics, as well as the side effects and interaction profile of this antihistamine.

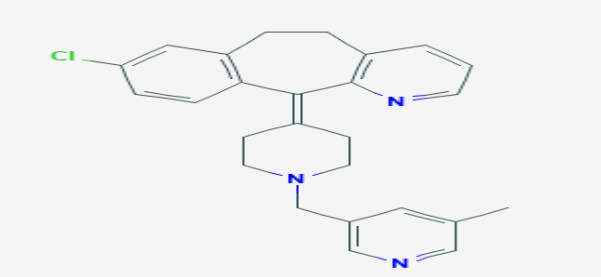
Chemistry of rupatadine

NAME: rupatadine

CHEMICAL NAME: 8-Chloro-11-(1-((5-methylpyridin-3-yl)methyl)piperidin-4-ylidene)-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridine

MOLECULAR FORMULA: C26H26ClN3

MOLECULAR WEIGHT: 416g/mol



PAF antagonist activity

Rupatadine is a benzocycloheptapyridine. Rupatadine is a second-generation tricyclic H1-antihistamine. Rupatadine is a dual histamine H1 receptor and platelet activating factor receptor antagonist that is used for symptomatic relief in seasonal and perennial rhinitis as well as chronic spontaneous urticaria.PAF is an endogenous phospholipid mediator of inflammation made up of inflammatory cells such as alveolar macrophages, eosinophils, mast cells, basophils, platelets and neutrophils, which are released in response to allergic/inflammatory reactions. These reactions are associated with increased vascular permeability, eosinophil chemo attraction, bronchoconstriction and

airway hyperresponsiveness, all of which are involved in the pathophysiology of rhinitis, asthma and anaphylaxis. Moreover, increased plasma levels of PAF have been reported in patients with urticaria and psoriasis compared with healthy controls.

Anticholinergic effects
In contrast to many other first-generation antihistamines, no anticholinergic effects were observed for single doses of rupatadine in the 10- to 80-mg dose range.

Antiinflammatory/ antiallergic effects
Several studies have confirmed that rupatadine exhibits inhibitory effects, e. g. on mast cell degranulation and eosinophil chemotaxis, in various type-1 hypersensitivity models.Rupatadine blocks isolated mast cell degranulation in sensitized dogs. In this particular model, the effects of rupatadine were comparable to those of loratadine, although rupatadine tends to achieve a greater overall effect.In addition to histamine, it was also possible to inhibit the release of LTC4 from peritoneal rat mast cells, as well as the release of tumor necrosis factor (TNF)-α from human mast cell lines. It has been suggested that this property may play a beneficial role in the late phase of allergic reactions. Concentrations of between 10 and 100 nM, rupatadine inhibits human eotaxininduced eosinophil chemotaxis. Rupatadine also inhibits PAF- and LTB4-induced human neutrophil chemotaxis. The inhibitory effects of a number of antihistamines (rupatadine, desloratadine, levocetirizine and fexofenadine) on proinflammatory cytokine (interleukin [IL-6] and IL-8) secretion were investigated in human umbilical venous endothelial cells (HUVEC) activated by histamine. Rupatadine showed the lowest IC50 value, followed by desloratadine, levocetirizine and fexofenadine.

Perennial allergic rhinitis
Rupatadine at doses of 10 or 20 mg once daily was significantly superior to placebo in the treatment of PAR. Compared with other antihistamines, rupatadine proved to be at least as effective as cetirizine, ebastine and loratadine for the relief of nasal and ocular symptoms in patients with PAR.

Persistent allergic rhinitis
A small number of studies and analyses investigated the clinical efficacy and tolerability of rupatadine in PER according to the new ARIA classification .There was a marked improvement in quality of life under rupatadine therapy, 10 mg once daily, compared to placebo. The same beneficial effect was also observed for 10-mg cetirizine.

Chronic urticaria
Several studies have evaluated the efficacy of rupatadine in chronic urticaria patients. The two most relevant scores in the evaluation of chronic urticaria, the mean pruritus severity scores (MPS) and the mean number of wheals scores (MNW), could be significantly reduced. There was a clear difference in favour of rupatadine 10 and 20 mg compared to placebo. Of particular note is rupatadine's fast onset of action. When evaluated in terms of the dermatology life quality index (DLQI), rupatadine again proved to be significantly superior compared with placebo. The efficacy of rupatadine and levocetirizine in chronic urticaria was compared over a 4-week period. By day 28, rupatadine had produced a marked improvement in clinical status and symptom score compared with initial values. Rupatadine also proved to be effective in the treatment of cold urticaria.

Drug interactions
Simultaneous administration of 20 mg rupatadine and ketoconazole or erythromycin (or any other potential CYP3A4 inhibitor) increases systemic rupatadine exposure as measured by the area under the concentration time curve, AUC by 10- and two- to three-fold, respectively. These changes were not associated with any effect on the QT interval or an increase in side effects. Rupatadine is well tolerated in combination with azithromycin or fluoxetine and can be administered in therapeutic doses without risk. Simultaneous intake of grapefruit juice increased rupatadine exposure 3.5-fold. When administering a four times higher dose of rupatadine, as recommended for the treatment of urticaria, together with grapefruit juice, rupatadine exposure may increase more than 10-fold, thereby exceeding the QT/QTc study conditions which, even at a dose of 100 mg, produced no changes in QTc interval. It was possibly potential summation effects of this kind that prompted the manufacturers to contraindicate co-administration of rupatadine 10-mg tablets and grapefruit juice. Food intake increased systemic rupatadine exposure by 23 %; however, exposure to its metabolites remained unaffected. The time to rupatadine's peak plasma concentration (Tmax) was delayed by 1 h, whilst the Cmax was unaffected. These differences were of no clinical significance.

Side effects
- Headache
- Dizziness
- Dry mouth
- Fatigue
- Tiredness and weakness
- Nausea
- Abdominal pain
- Diarrhea
- Vomiting
- Constipation
- Rash

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CONCLUSION

Rupatadine is an effective anti-allergic medicine used to temporarily relieve the symptoms of seasonal allergies. These symptoms may include sneezing, runny nose, itchy eyes, sore throat, etc. This medicine is not recommended for use in children below 12 years of age. This medicine is not recommended for use in breastfeeding women unless absolutely necessary. All the risks and benefits should be discussed with the doctor before taking this medicine. Your doctor may advise you to discontinue the drug or to discontinue breastfeeding based on your clinical condition. Rupatadine is a modern non-sedating H1-antihistamine that also has with additional antagonist effects on platelet-activating factor (PAF). Under the tradenames Rupafin and Urtimed, Rrupatadine is approved registered in Germany for the treatment of allergic rhinitis and urticaria. In this review, the available literature available to date on regarding the pharmacological profile and clinical application of Rrupatadine is reviewed and compared to other conventional histamines. In conclusion finally, the side effects, safety and interaction profile incompatibility of Rrupatadine are discussed. Due to CYP p450 metabolism, Rrupatadine should not be given together with Eerythromycin, Kketoconazole or grapefruit juice. Rupatadine has been found to be effective and safe in a variety of randomized clinical trials both in both seasonal and perennial allergic rhinitis, as well as in but also chronic urticaria Rupatadine has been found as effective and safe.

REFERENCES

1. Simons FE, Simons KJ. Histamine and H1-antihistamines: celebrating a century of progress. J Allergy Clin Immunol, 2011.
2. Merlos M, Giral M, Balsa D, Ferrando R, Queralt M, Puigdemont A, et al. Rupatadine, a new potent, orally active dual antagonist of histamine and platelet-activating factor (PAF) J Pharmacol Exp Ther, 1997.
3. Vuurman E, Theunissen E, van Oers A, van Leeuwen C, Jolles J. Lack of effects between rupatadine 10 mg and placebo on actual driving performance of healthy volunteers. Hum Psychopharmacol, 2007.
4. Izquierdo I, Merlos M, García-Rafanell J. Rupatadine: a new selective histamine H1 receptor and platelet-activating factor (PAF) antagonist.
5. A review of pharmacological profile and clinical management of allergic rhinitis. Drugs Today (Barc), 2003.
6. Merckle Recordati GmbH Hrsg. Rupafin® Fachinformation, 2009.
7. del Cuvillo A, Mullol J, Bartra J, Dávila I, Jáuregui I, Montoro J, et al. Comparative pharmacology of the H1 antihistamines. J Investig Allergol Clin Immunol, 2006.
8. Katiyar S, Prakash S. Pharmacological profile, efficacy and safety of rupatadine in allergic rhinitis. Prim Care Respir J, 2009.
9. Mullol J, Bousquet J, Bachert C, Canonica WG, Gimenez-Arnau A, Kowalski ML, et al. Rupatadine in allergic rhinitis and chronic urticaria. Allergy, 2008.
10. Izquierdo I, Nieto C, Ramis J, Cooper M, Dewland P, Forn J. Pharmacokinetics and dose linearity of rupatadine fumarate in healthy volunteers. Methods Find Exp Clin Pharmacol, 1997.
11. Ring J. Angewandte Allergologie. 3. München: Urban & Vogel, 2004.
12. Ring J, Brockow K, Ollert M, Engst R. Antihistamines in urticaria. Clin Exp Allergy, 1999.
13. Brockow K, Kiehn M, Riethmüller C, Vieluf D, Berger J, Ring J. Efficacy of antihistamine treatment in the prevention of adverse reactions to Hymenoptera immunotherapy: a prospective, randomized, placebo-controlled trial. J Allergy Clin Immunol, 1997.
14. Church MK. Efficacy and tolerability of rupatadine at four times the recommended dose against histamine- and platelet-activating factor-induced flare responses and ex vivo platelet aggregation in healthy males. Br J Dermatol, 2010.
15. Queralt M, Brazís P, Merlos M, Puigdemont A. Inhibitory effects of rupatadine on mast cell histamine release and skin wheal development induced by Ascaris suum in hypersensitive dogs. Drug Development Research, 1998.
16. Barrón S, Ramis I, Merlos M. Rupatadine inhibits the inflammatory component of allergic response: cytokine release, adhesion molecule expression and inflammatory cell recruitment. In: Proceedings of the 23rd EAACI Congress, 2004; 12–16.
17. Ramis I, Giral M, Ferrando R, Merlos M. Inhibition of PAF- and LTB4-induced human neutrophil chemotaxis by rupatadine using a new fluorescent chemotaxis assay. Allergy, 2000.
18. Barrón S, Roman J, Michelena P, Ramis I, Merlos M. Rupatadine inhibits cytokine production and NF-κB activity by histamine H1 receptor-dependent mechanism. Rev Rinol, 2006.
19. Bousquet J, Van Cauwenberge P, Bachert C, Canonica GW, Demoly P, Durham R, et al. Requirements for medications commonly used in the treatment of allergic rhinitis. Allergy, 2003.
20. Bousquet J, Van Cauwenberge P, Khaled NA, Bachert C, Baena-Cagnani CE, Bouchard J, et al. Pharmacologic and anti-IgE treatment of allergic rhinitis (ARIA) update (in collaboration with GA2LEN) Allergy, 2006.
21. Izquierdo I, Valero A, García O, Pérez I, Mullol J, Van Cauwenberge P. Clinical efficacy of rupatadine in allergic rhinitis under ARIA criteria: pooled analysis. Allergy Clin Immunol Int, 2005.

22. Review Pharmacological profile, efficacy and safety of rupatadine in allergic rhinitis. Prim Care Respir J, 2009.
23. Izquierdo I, Nieto C, Ramis J, Cooper M, Dewland P, Forn J. Pharmacokinetics and dose linearity of rupatadine fumarate in healthy volunteers. Methods Find Exp Clin Pharmacol, 1997.
24. Ring J. Angewandte Allergologie. 3. München: Urban & Vogel, 2004.
25. Merlos M, Ramis I, Balsa D, Queralt M, Brazis P, Puigdemont A. Inhibitory effect of rupatadine on TNF alpha release from human monocytes and mast cell line MHC-1. Allergy Clin Immunol, 2000.
26. Queralt M, Merlos M, Giral M, Puigdemont A. Dual effect of a new compound, rupatadine, on edema induced by platelet-activating factor and histamine in dogs: comparison with antihistamines and PAF antagonists. Drug Dev Res, 1996.
27. Merlos M, Balsa D, Giral M, Ferrando R, Garcia-Rafanell J, Forn J. Inhibition of rat peritoneal mast cell exocytosis by rupatadine fumarate: a study with different secretagogues. Methods Find Exp Clín Pharmacol, 1997.
28. In vitro inhibitory effect of rupatadine on histamine and TNF-alpha release from dispersed canine skin mast cells and the human mast cell line HMC-1.
29. Merlos M, Ramis I, Balsa D, Queralt M, Brazis P, Pugidemont A. Inhibitory effect of rupatadine on TNF-α release from human monocytes and mast cell line HMC-1. J Allergy Clin lmmunol, 2000.
30. Barrón S, Ramis I, Merlos M. Rupatadine inhibits the inflammatory component of allergic response: cytokine release, adhesion molecule expression and inflammatory cell recruitment. In: Proceedings of the 23rd EAACI Congress, 2004; 12–16.
31. Ramis I, Giral M, Ferrando R, Merlos M. Inhibition of PAF- and LTB4-induced human neutrophil chemotaxis by rupatadine using a new fluorescent chemotaxis assay. Allergy, 2000.
32. Barrón S, Roman J, Michelena P, Ramis I, Merlos M. Rupatadine inhibits cytokine production and NF-κB activity by histamine H1 receptor-dependent mechanism. Rev Rinol, 2006.
33.