Rupatadine: efficacy and safety of a non-sedating antihistamine with PAF-antagonist effects

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Summary

Rupatadine is a modern non-sedating H1-antihistamine that also haswith additional antagonist effects on platelet-activating factor (PAF). Under the tradenames Rupafin® and Urtimed®, Rrupatadine is approvedregistered in Germany for the treatment of allergic rhinitis and urticaria infor adults and children aged over 12 years. In this review, the available literature available to date onregarding the pharmacological profile and clinical application of Rrupatadine is reviewed and compared to other conventional histamines. In conclusionFinally, the side effects, safety and interaction profileincompatibility 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 Iin a variety of randomized clinical trials both in both seasonal and perennial allergic rhinitis, as well as inbut also chronic urticaria Rupatadine has been found as effective and safe.

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Key words

Antihistamines – platelet-activating factor – Rupatadine – allergic rhinitis – chronic urticaria

Introduction

More than 45 H1 antihistamines (H1 histamine receptor antagonists), forming the largest class of drugs for the treatment of allergic diseases, are available worldwide [1]. Despite comparable efficacy in the treatment of allergic rhinoconjunctivitis, urticaria and other allergic diseases, approved preparations differ in terms of their chemical structure, clinical pharmacology and potential toxicity.

Rupatadine is a novel substance which, in addition to being an H1 antagonist, is also a potent platelet-activating factor (PAF) inhibitor. It belongs to the N-alkyl pyridine derivates. Animal and human models [2] 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 [3, 4]. 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 Rupafin® 10 mg since August 1, 2008, and under the tradename Urtimed® since 2010 [5]. The present article discusses the pharmacology, kinetics, anti-inflammatory effects, clinical efficacy as well as the side effects and interaction profile of this antihistamine.

Pharmacology and kinetics

Rupatadine (8-chloro-11-[1-[(5-methyl-3-pyridinyl) methyl]piperidin-4-ylidene]-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b] pyridine fumarate), a second-generation antihistamine, is a selective, long-acting histamine antagonist with peripheral H1 receptor activity (**Fig. 1**) [2]. Desloratadine and its hydroxylated metabolites are some of the rupatadine metabolites that may contribute to the drug's overall efficacy [5].

In vitro metabolism studies using human liver microsomes show that the cytochrome P450 CYP3A4 is the isoenzyme primarily responsible for the biotransformation of rupatadine [5, 6].

The time to maximum plasma concentration (T_{max}) in adults is between 45 min and 1 h following oral intake (**Tab. 1**). The drug's half-life is 5.9 h. Rupatadine undergoes significant presystemic metabolism when administered orally. The most important biotransformation pathways of rupatadine include oxidative processes, oxidation of the pyr-

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Abbreviations used

ARIA	Allergic rhinitis and its impact on asthma
AUC	Area under the curve
C_{max}	Maximum plasma concentration
CTZ	Cetirizine
CYP	Cytochrome P450
DLQI	Dermatology life quality index
EEG	Electroencephalogram
EKG	Electrocardiogram
EMEA	European Medicines Agency
GM-CSF	Granulocyte macrophage colony-stimulating factor
HERG	Human ether-a-go-go related gene
HUVEC	Humane umbilical venous endothelial cells
IC50	Mean inhibitory concentration
ICH	International Conference on Harmonisation
IL	Interleukin
Ki	Dissociation constant
LCT	Levocetirizine
LOR	Loratadine
mDTSS	Mean daily total symptom score
MNW	Mean number of wheals score
MPS	Mean pruritus severity score
NF-κB	Nuclear factor κ-light-chain-enhancer of activated B cells
nM	Nanomolar
OLP	Olopatadine
PAF	Platelet activating factor
PAR	Perennial allergic rhinitis
PL	Placebo
RQLQ	Rhinoconjunctivitis quality of life questionnaire
RU	Rupatadine
SAR	Seasonal allergic rhinitis
t1/2	Plasma half-life
t_{max}	Time to maximum effect
T_{max}	Time of maximum plasma concentration
TNF-α	Tumor necrosis factor-α

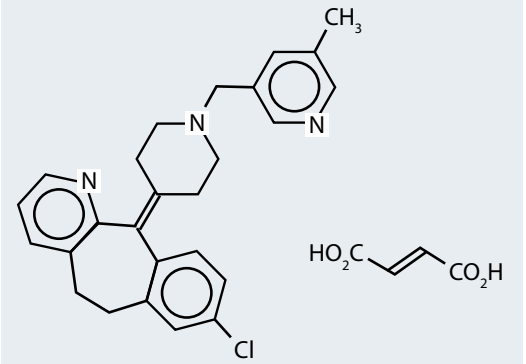

Fig 1. Structural formula of rupatadine (from [4])

idine-methyl group to carboxylic acid, N-dealkylation of piperidine nitrogen and hydroxylation of the 3-, 5- and 6-positions in the tricyclic ring system [7]. Only insignificant amounts of unaltered active substance were found in urine and feces [4, 5, 8, 9].

The pharmacokinetics of rupatadine are linear for doses between 10 mg and 40 mg [5, 8].

The binding rate of rupatadine to plasma protein is 98 %–99 %. Despite this high binding rate, it is well distributed and is able to reach target receptors [6].

Studies have shown that the active substance's maximum plasma concentration is delayed by approximately 1 h when taken with food; despite this delay, the maximum concentration in blood remained unaltered by food intake [5, 8].

Anti-inflammatory and antihistaminergic effects of rupatadine

Rupatadine has a high affinity for the H1 receptor. This activity has been demonstrated in vitro and in a broad spectrum of pharmacological in vivo models in mice, rats, guinea pigs, rabbits, dogs and humans.

Rupatadine inhibits histamine-induced guinea pig ileum contraction at concentrations in the nanomolar range [2]. This ability has been compared in several studies with data on already established antihistamines such as loratadine or terfenadine [8]. The dissociation constant Ki for the three antihistamines was 102, 127 and 144 nM. The same model showed that rupatadine is better than loratadine and fexofenadine at suppressing 3H-mepyramin—a radioligand for the histochemical investigation of histamine receptors – from its H1 binding site (shown in **Tab. 2** as the mean inhibitory concentration IC50) [2].

Rupatadine shows strong selectivity for binding to lung-tissue H1 receptors compared to brain (cerebellum) H1 receptors following oral administration of 0.16 mg/kg in guinea pigs. Similar findings have been reported for loratadine, whilst hydroxyzine showed no differentiation between lung and brain and diphenhydramine blocked lung receptors only weakly (< 10 %) [8].

Merlos and co-workers [2] were also able to show that rupatadine has a selective effect on histamine H1 receptors; however, no effects on acetylcholine, serotonin or leukotriene receptors were observed.

The intensity and duration of inhibition of wheal and erythema formation in the histamine skin prick model increases with dose escalation, reaching peak values of 69 %, 82 % and 93 % following doses of 10, 20 and 40 mg, respectively [9].

Rupatadine's antihistamine activity has been investigated in a number of in vitro models (**Tab. 2**) [2].

PAF antagonist activity

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 chemoattraction, 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 [10, 11, 12].

Rupatadine demonstrates competitive PAF antagonistic activity in the submicromolar range in vitro, with IC50 values of 0.2 and 0.68 μM in models to evaluate thrombocyte aggregation in washed thrombocytes from rabbit or human platelet-rich plasma, respectively. In these models, rupatadine's anti-PAF activity was lower than the specific PAF antagonists WEB-2086 and Ginkgolid B, but significantly higher than that of the antihistamines loratadine, ketotifen, mepyramine, cetirizine or terfenadine [8].

The dose-response relationship of rupatadine in the inhibition of PAF-induced wheals and erythema is shown in **Tab. 3** [9]. The efficacy of rupatadine increases in a linear fashion at increasing doses up to 40 mg; beyond this dose, dose escalation is associated with a slower increase in efficacy [7].

Church [13] showed rupatadine to have long-lasting efficacy at four times the recommended dose over up to 72 h against PAF-induced dermal flares following skin prick testing.

Table 1

Pharmacological data on rupatadine

Parameter	Pharmacological profile	
Mechanism of action	Histamine H1 receptor antagonism PAF receptor antagonism Other anti-inflammatory effects	
Pharmacokinetics	**Single dose**	**Multiple dose**
C_{max} (ng/ml)	2.3	1.9
t_{max} (h)	0.8	0.75–1.0
AUC 0–24 (ng/ml/h)	7.6	8.4
C_{max}/AUC	C_{max} and AUC increase linearly with dosage (10–40 mg)	
Effects when taken with food	Scant, slight increase in tmax	
Protein binding	98%–99%	
Metabolism	Extensive presystemic hepatic metabolism via oxidative glucuronidation Primarily CYP3A4 metabolism, whereby a number of active metabolites are produced	
Elimination T1/2 (h)	4.6	5.8
Elimination	60.9% In feces 34.6% In urine	
Age-specific effects	Slightly increased C_{max} and AUC and reduced clearance, both of little clinical relevance	

AUC, area under the curve; C_{max}, maximum concentration; h, hours; t_{max}, time to maximum effect; PAF, platelet activating factor

Table 2

Antihistamine concentrations required to inhibit histamine-induced guinea pig ileum contraction by 50 % [2]

Antihistamine	Mean IC50 nM (95 % CI)	Relative potency[a]
Rupatadine	3.8 (3.1–4.6)	1
Chlorpheniramine	6.1 (4.6–8.0)	1.6
Ketotifen	21 (12–38)	5.5
Cetirizine	90 (58–140)	23.7
Clemastine	231 (136–391)	60.8
Hydroxyzine	276 (199–382)	72.6
Loratadine	286 (170–480)	75.3
Diphenhydramine	321 (212–485)	84.5
Terfenadine	362 (258–508)	95.3

IC50, mean inhibitory concentration; nM, nanmolar; CI, confidence interval
[a]Concentration required to achieve the same effect as rupatadine

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 [7].

Other 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 [4, 8, 14, 15, 16].

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 [7, 17, 18, 19].

Barrón et al. [20] demonstrated that, at concentrations of between 10 and 100 nM, rupatadine inhibits human eotaxininduced eosinophil chemotaxis.

Rupatadine also inhibits PAF- and LTB4-induced human neutrophil chemotaxis. In Ramis et al.'s model, rupatadine was shown to be more effective than other antihistamines, such as cetirizine, fexofenadine, loratadine and mizolastine [21].

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 [22].

Furthermore, several studies observed inhibition of: secretion of other lymphocyte cytokines (IL-5, IL-6, IL-8, granulocyte macrophage colony-stimulating factor [GM-CSF] and TNF-α), as well as expression of allergy-associated adhesion molecules (CD18 and CD11b) and various transcription factors (nuclear factor κ-light-chain-enhancer of activated B-cells, NF-κB) [8].

Clinical studies

Numerous randomized placebo-controlled double-blind studies on the efficacy of rupatadine in allergic rhinitis and chronic urticaria have been conducted. Comparative studies with various nonsedating H1 receptor antagonists have also been carried out.

The majority of available studies still subdivide allergic rhinitis according to the older system into seasonal (SAR) and perennial allergic rhinitis (PAR), whilst only a small number refer to the new ARIA (allergic rhinitis and its impact on asthma) criteria, which classify allergic rhinitis into intermittent or persistent allergic rhinitis [23, 24, 25].

Interestingly, many authors observed a fast onset of action in patients with SAR, PAR, persistent allergic rhinitis (PER) and chronic idiopathic urticaria in clinical studies on rupatadine. These observations are consistent with the drug's pharmacokinetic profile [7, 8, 13].

Seasonal allergic rhinitis

Clinical studies on rupatadine in patients with moderate to severe SAR are summarized in **Tab. 4**. The

Table 3

Dose–response relationship of rupatadine in the inhibition of PAF-induced wheals and eczema

Rupatadine dose	Early inhibition	Maximum inhibition			Comment
	Extent (%)	Time interval to effect (h)	Extent (%)	Time to maximum effect (h)	
10 mg	n. d.	n. d.	41	24	
20 mg	42	6	56	24	Maintained for up to 48 h
40 mg	68	4	87	6	Remains over 60% for 72 h
80 mg	91	4	93	48	Still effective 96 h following administration

n. d., No data; h, hours; PAF, platelet activating factor

results of these studies confirm the efficacy of rupatadine to reduce mean daily total symptom scores (mDTSS). Covariate analysis found no age- or sex-specific differences.

All rupatadine doses investigated were more effective at reducing SAR symptoms in a dose-dependent manner than placebo. Two studies measured the objective efficacy of rupatadine 10 mg in the reduction of nasal obstruction following allergen provocation; here again, rupatadine was significantly superior to placebo [26, 27].

Overall, doses of 10 mg and 20 mg were the most effective compared to lower doses and, apart from a general trend towards faster symptom relief at 20 mg, significant differences following 1-week treatment were observed [7, 28].

Rupatadine 10 mg once daily was compared with ebastine 10 mg once daily and placebo [29]. After 2 weeks, mDTSS values in the rupatadine group were 33 % lower than placebo ($p = 0.005$). The total symptom score for rupatadine was 22 % lower compared with ebastine; however, this result did not reach statistical significance. Compared with placebo, rupatadine reduced all symptoms with a statistically significant reduction of sneezing, rhinorrhea, lacrimation and nasal itch. The greatest difference between active treatment and placebo was observed for rhinorrhea (rupatadine vs. placebo, $p < 0.001$; ebastine vs. placebo, $p < 0.005$).

The efficacy of rupatadine and levocetirizine was compared for 2 weeks in SAR patients [30]. A significantly greater reduction ($p = 0.004$) in immunoglobulin-E (IgE) levels and overall nasal symptom scores ($p < 0.001$) was observed in the rupatadine group compared with the levocetirizine group. There was an 18.08 % ($p = 0.02$) reduction in the score for the rhinoconjunctivitis quality of life questionnaire (RQLQ) in the rupatadine group, a significantly greater reduction than that seen in the levocetirizine group.

Several studies comparing the 10- and 20-mg doses of rupatadine with the approved daily doses of cetirizine and loratadine showed rupatadine to be beneficial [31, 32, 33].

In a newly published study, the efficacy of rupatadine and olopatadine was compared in SAR patients [34]. The olopatadine group showed a significantly greater reduction in serum IgE values ($p = 0.01$), total nasal symptoms scores ($p < 0.001$) and RQLQ scores ($p = 0.015$) compared to rupatadine.

Perennial allergic rhinitis

Rupatadine at doses of 10 or 20 mg once daily was significantly superior to placebo in the treatment of PAR [35].

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 [35, 36].

Table 4

Summary of efficacy of rupatadine in adults and adolescents (> 12 years) with seasonal allergic rhinitis (SAR)

Study design	RU dose and comparative treatment	Treatment duration (weeks)	No. of patients	Efficacy (mDTSS)	Reference Author (year)
R, DB, PC	PL vs. RU 10 mg/20 mg	2	50/54/45	RU 10 vs. PL* RU 20 vs. PL*	[28] Izquierdo et al. (2000)
R, DB, PC	PL vs. RU 2.5 mg/5 mg/10 mg/20 mg	2	392	RU 2.5 vs. PL* RU 5 vs. PL* RU 10 vs. PL* RU 20 vs. PL*	[4] Izquierdo et al. (2003)
R, DB, PC	PL vs. RU 10 mg vs. EBA 10 mg	2	81/79/83	RU 10 vs. PL* EBA vs. PL ns	[29] Guadaño et al. (2004)
R, DB	RU 10 mg vs. LCT 10 mg	2	60	RU vs. LCT*	[30] Maiti et al. (2010)
R, DB	RU 10 mg vs. CTZ 10 mg	2	124/117	RU vs. CTZ ns	[31] Martínez-Cócera et al. (2005)
R, DB	RU 10 mg/20 mg vs. LOR 10 mg	2	339	RU 10 vs. LOR ns RU 20 vs. LOR ns	[33] Saint-Martin et al. (2004)
R, DB	RU 10 mg vs. OLP 10 mg	2	70	OLP 10 vs. RU 10 ns	[34] Maiti et al. (2011)

R, randomized; DB, double-blind; PC, placebo-controlled; RU, rupatadine; PL, placebo; CTZ, cetirizine; LOR, loratadine; OLP, olopatadine; LCT, levocetirizine; mDTSS, mean daily total symptom score
*$p < 0.05$.

Table 5

Side effects reported during treatment with rupatadine 10 mg vs placebo

Side effect	Patients under rupatadine therapy (%) n = 2025	Patients under placebo therapy (%) n = 1315
Drowsiness	9.5	3.4
Headache	6.8	5.6
Fatigue	3.2	2.0
Weakness/exhaustion	1.5	0
Dry mouth	1.2	0
Dizziness	1.0	0

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 [23, 24, 25, 37, 38]. 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.

Results from the Futura study [38] showed that, with the exception of nasal congestion and secretion, which improved only after the second day of treatment ($p < 0.001$), all symptoms improved markedly in the first days of treatment ($p < 0.001$).

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 score (MPS) and the mean number of wheals score (MNW), could be significantly reduced. There was a clear difference in favour of rupatadine 10 and 20 mg compared to placebo ($p = 0.013$ and $p < 0.0001$) following the first dose. Of particular note is rupatadine's fast onset of action [39, 40, 41].

When evaluated in terms of the dermatology life quality index (DLQI), rupatadine again proved to be significantly superior compared with placebo [40].

The efficacy of rupatadine and levocetirizine in chronic urticaria was compared over a 4-week period [42]. By day 28, rupatadine had produced a marked improvement in clinical status and symptom score compared with initial values. The rupatadine group showed a reduction in serum IgE of 15.3% ($p = 0.024$), a drop in total symptom score of 28.2% ($p = 0.02$) and a reduction in the specific quality of life questionnaire score of 27.3 % [43]. The overall efficacy score for rupatadine was significantly higher ($p = 0.009$) compared to levocetirizine.

Rupatadine also proved to be effective in the treatment of cold urticaria [44].

Tolerability and safety

Results from the clinical phase-III study carried out by Picado et al. [45] in a total of 3490 patients or healthy volunteers are summarized in **Tab. 5**.

In a multicenter phase-IV study, 120 PER patients were treated with rupatadine for 12 months to evaluate the substance's long-term safety in accordance with guidelines of the European Medicines Agency (EMEA) [46, 47]. In par-ticular, headache, drowsiness and dry mouth were the most commonly observed side effects. No clinically relevant changes in electrocardiogram (ECG) were observed. This study confirms rupatadine's good long-term safety profile.

One case of fixed drug eruption was attributed to rupatadine and confirmed by oral provocation testing [48].

Cardiac toxicity

A number of older antihistamines, such as astemizole and later terfenadine, are known to cause prolongation of the QT interval by direct blockade of repolarizing potassium channels, thereby increasing the risk of torsades de pointes arrhythmias [49] [50]. However, these effects are not related to interaction with specific H1 receptors and, as such, are not histamine-specific [8, 51].

The cardiac safety of rupatadine has been extensively and repeatedly investigated in clinical studies [4, 45, 52].

Preclinical studies yielded the following results:

- Rupatadine doses 100 times that of the clinically recommended dose of 10 mg had no effect whatsoever on ECG parameters, blood pressure or pulse rate in rats, guinea pigs and dogs. No arrhythmias or other cardiovascular complications were observed [53].
- Concentrations of rupatadine and one of its most important metabolites in humans (3-hydroxydesloratadine) exceeding at least 2000-fold the C_{max} value (C_{max}: maximum plasma concentration) reached after the administration of a 10-mg dose in humans had no effect on the cardiac action potential in in vitro isolated canine Purkinje fibers [5, 7, 8].
- In a study designed to investigate the effect on a cloned human ether-a-go-go related gene (HERG) potassium channel, the channel was blocked by rupatadine at a concentration 1685 times greater than the C_{max} value reached following administration of 10 mg rupatadine. Tissue distribution studies using radiolabeled rupatadine in rat tissue showed no accumulation of rupatadine in heart tissue [5, 7, 8].
- A QT/QTc study was carried out In line with the guideline recommendations of the EMEA and the

International Conference on Harmonisation (ICH) E14. In the positive control group, moxifloxacin demonstrated the expected changes in QTc interval. ECG data for rupatadine at 10 and 100 mg showed no effects. There were no sex-specific effects and no pharmacodynamic link between rupatadine and its main metabolites, thereby confirming that rupatadine has no particular effect whatsoever on QTc interval. This study demonstrated that rupatadine has no proarrhythmic side effects even at 10 times the therapeutic dose [5, 7, 8].

Central nervous system toxicity

Rupatidine behaves like other second-generation antihistamines and is non-sedating. Even doses as high as 100 mg/kg in a series of tests in rats and mice failed to produce changes in ECG or motor activity [2, 54].

No psychomotor impairment could be detected in humans at doses of up 20 mg. However, dose-dependent impairments were seen at higher doses. Hydroxyzine 25 mg ($p = 0.01$) and rupatadine 80 mg ($p = 0.02$) produced significant impairment of similar degree. The cognitive and psychomotor impairment produced by a single 10-mg oral dose of rupatadine in combination with ethanol was no greater than the impairment produced by ethanol alone, whilst a higher dose (20 mg) in combination with ethanol caused cognitive and psychomotor impairment comparable to that seen with hydroxyzine 25 mg and cetirizine even at therapeutic doses [55, 56].

The effects of rupatadine on fitness to drive were investigated in a study on healthy subjects: at the recommended dose of 10 mg rupatadine, no differences could be seen compared to placebo [3, 57].

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 [5, 7, 8].

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 [13], 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 (T_{max}) was delayed by 1 h, whilst the C_{max} was unaffected. These differences were of no clinical significance [5, 7, 8].

Elderly patients: peak concentration and AUC values for rupatadine are higher in elderly patients than in young adults. Similarly, the mean plasma half-life (t1/2) is 8.7 h compared to 5.9

Conclusion

Rupatadine is a relatively new substance with potent histamine H1 and PAF antagonist activity. It is approved in Germany under the tradenames Rupafin® and Urtimed® 10 mg for the treatment of allergic rhinitis and chronic urticaria in adults and children aged over 12 years.

In addition to its powerful and selective H1 antihistamine activity, rupatadine acts primarily as a PAF antagonist. The drug also has other antiinflammatory effects, such as inhibition of mast cell granulation and eosinophil chemotaxis.

Studies have confirmed the clinical efficacy of rupatadine. At the same time, numerous clinical trials of the drug demonstrated its fast onset of action in patients with SAR, PAR, PER and chronic idiopathic urticaria.

Several studies were able to show that 10- and 20-mg doses of rupatadine were equal or superior to the approved daily doses of cetirizine and loratadine in terms of reducing mean daily total symptom scores.

At doses of 10–20 mg once daily, rupatadine proved to be highly effective in the treatment of chronic urticaria.

Rupatadine has a good safety profile. Isolated reports of side effects include headache or fatigue. No clinically relevant changes were seen on ECG. No psychomotor effects could be seen in humans at doses of up to 20 mg. Rupatadine does not impair driving performance.

Co-administration of rupatadine with erythromycin, ketoconazole and grapefruit should be avoided.

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Conflict of interest

The corresponding author states that there are no conflicts of interest.

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