

Cetirizine inhibits the in vitro and ex vivo chemotactic response of T lymphocytes and monocytes

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We have studied the effect of a nonsedating antihistamine, cetirizine dihydrochloride, on the in vitro chemotaxis of leukocytes from human peripheral blood. We observed that 0.25 µg/ml of cetirizine dihydrochloride in vitro significantly inhibited the chemotaxis of monocytes toward N-formyl-methionyl-leucyl-phenylalanine and leukotriene B₄. Higher concentrations of cetirizine, 1.0 and 2.5 µg/ml, completely inhibited monocyte chemotaxis without affecting cell viability. T-lymphocyte migration was also significantly depressed but not abolished. Pyrilamine (mepyramine) was not inhibitory in equimolar concentrations. According to these in vitro observations, we extended our studies to measure monocyte and T-lymphocyte chemotaxis in an open study, where four healthy volunteers and six patients with atopic dermatitis took 10 and 20 mg/day cetirizine 3 days. We observed a reduction in ex vivo monocyte and T-lymphocyte chemotaxis toward N-formyl-methionyl-leucyl-phenylalanine and leukotriene B₄ without a reduction of the blood cell count. The results were confirmed in an ensuing double-blind, placebo-controlled study of 16 healthy subjects and 14 adult patients with atopic dermatitis, where ex vivo monocyte chemotaxis was reduced or abolished during cetirizine therapy. Serum levels of the two eosinophil-derived granule proteins, eosinophilic protein P and eosinophil protein X, were not changed during the treatment period of 7 days. The results show that cetirizine dihydrochloride has an inhibitory effect on monocytes and T lymphocytes in vitro and ex vivo. Our findings support the clinical observations that cetirizine dihydrochloride has an antiinflammatory effect besides its H₁-blocking activity. (J ALLERGY CLIN IMMUNOL 1995;95:979-86.)

Key words: Cetirizine dihydrochloride, chemotaxis, eosinophil cationic protein, monocytes, T lymphocytes

Cetirizine is a nonsedating, selective H₁-receptor antagonist.¹ A single dose of 10 mg inhibits the wheal-and-flare reaction produced by intracutaneous injections of histamine, compound 48/80, and grass pollen extracts.^{2,3} It also inhibits eosinophils in allergen-induced type I skin reactions⁴ and eosinophil chemotaxis in vitro.⁵ It was demon-

Abbreviations used

BSA:	Bovine serum albumin
CI:	Chemotactic index
ECP:	Eosinophil cationic protein
EPX/EDN:	Eosinophil protein X/eosinophil-derived neurotoxin
fMLP:	N-formyl-methionyl-leucyl-phenylalanine
LTB ₄ :	Leukotriene B ₄

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strated that cetirizine significantly decreased late leukocyte migration into antigen-challenged chambers without any significant alteration in histamine or prostaglandin D₂ levels.⁶ The inhibition of migration of leukocytes is not due to a reduced mediator release but seems to be a direct effect on cells. A number of previous studies indicate that cetirizine may be an antihistamine with a unique

capability of down-regulating the late-phase reaction of inflammatory cells but without altering either early or late mediator production of inflammatory cells.

Previous studies suggested that the dominant phenotypes of cells infiltrating the skin after a type I allergy reaction are CD4⁺ T lymphocytes and activated eosinophils.⁷ On the basis of the evidence that cetirizine can inhibit the cellular late-phase response to allergen-induced skin reactions, we became interested in studying the effect of cetirizine on in vitro and ex vivo chemotaxis of leukocyte subpopulations. We observed that cetirizine can significantly reduce the migration of monocytes and T lymphocytes in their response to *N*-formyl-methionyl-leucyl-phenylalanine (fMLP) and leukotriene B₄ (LTB₄) in vitro, and we further demonstrated how cetirizine inhibits ex vivo chemotaxis of monocytes and T lymphocytes. These results were confirmed in a double-blind, placebo-controlled study, where inhibition of monocyte chemotaxis was confirmed. Serum eosinophil cationic protein (ECP) levels in atopic dermatitis, however, were not reduced during a 7-day treatment period.

METHODS

The study consisted of three successive parts: The first part included 10 healthy volunteers without allergic disease who donated blood for in vitro studies. The second part was an open ex vivo study including four healthy volunteers and six patients with severe atopic dermatitis, who took 10 and 20 mg/day cetirizine for 3 days, after which we measured monocyte and T-lymphocyte chemotaxis against fMLP and LTB₄. The third part included 30 adults, 16 healthy subjects without atopic disease and 14 with atopic dermatitis, who participated in a double-blind, placebo-controlled study of the effect of 10 and 20 mg/day cetirizine for 3 days on ex vivo monocyte chemotaxis toward fMLP and LTB₄.

The donors of blood for the in vitro study were eight men and two women without atopic disease (age range, 22 to 53 years; median age, 35 years). The open ex vivo study participants consisted of seven men and three women (age range, 18 to 48 years; median age, of 24 years). Four had no atopic disease, and six were admitted because of atopic dermatitis. The double-blind, placebo-controlled study participants comprised 30 persons, 16 healthy persons and 14 with active atopic dermatitis. There were 10 men and 20 women (age range, 19 to 61 years; median age, 34 years).

In vitro studies

Mononuclear cells were isolated from 100 ml of heparinized venous blood by Ficoll-Isopaque (Pharmacia, Uppsala, Sweden) gradient centrifugation for 20

minutes (800 g, 4° C). The cells were resuspended in RPMI 1640 with 10% human serum type A and incubated in plastic tissue culture flasks (Nunc, Roskilde, Denmark) for 1 hour at 37° C in 5% CO₂ and atmospheric air. This enables plastic adherence of monocytes.⁸

The nonadherent cell population was washed once in Hanks' balanced salt solution with 1% human serum. T lymphocytes were isolated by incubating nonadherent cells with 2-aminoethylisothiuronium bromide hydrobromide-treated sheep erythrocytes at 37° C for 30 minutes and then performing a second cell separation on Ficoll-Isopaque gradient.⁹ The cells forming rosettes (T lymphocytes) were sedimented on Ficoll-Isopaque gradient, and the erythrocytes were removed by lysis with addition of autologous serum for 5 minutes followed by washing and resuspension in 0.5% bovine serum albumin (BSA) and RPMI 1640 to a concentration of 5×10^6 cells/ml. This cell population was formed of 95% to 98% T lymphocytes.

The adherent cells were detached from the plastic by lowering the temperature to 4° C for 15 minutes. They were washed twice in Hanks' balanced salt solution with 1% fetal calf serum and suspended in RPMI 1640 with 0.5% BSA in a concentration of 1×10^6 cells/ml. More than 90% were monocytes as judged by morphologic criteria and esterase staining.

Neutrophil granulocytes were isolated by mixing 25 ml of heparinized blood with 6 ml of 5% dextran for 45 minutes at 37° C followed by density gradient centrifugation on Ficoll-Isopaque gradient of the supernatant containing leukocytes. Neutrophil granulocytes were pelleted and the contaminating erythrocytes were removed by hypotonic lysis. The cells were suspended in RPMI 1640 with 0.5% BSA at a concentration of 1×10^6 cells/ml before use. The suspension contained more than 97% neutrophilic granulocytes as judged by morphologic criteria.

Pretreatment of cells with antihistamines

Cell suspensions were preincubated with 0, 0.25, 1.0, and 2.5 µg/ml of cetirizine (molecular weight, 461.8 d) at 37° C for 1 hour. These concentrations were chosen because they equal the plasma levels of cetirizine after oral administration of 10 mg, which range from 0.025 µg/ml to peak values of 0.4 µg/ml.¹⁰ We also used pyrilamine (mepyramine) in equimolar concentrations for comparison. The viability of the cells was not affected by the drug (trypan blue exclusion test). The cells were washed in RPMI 1640 with 0.5% BSA just before use in the chemotaxis assay.

Chemotaxis assay

We assessed in vitro chemotaxis by using a 48-well microchemotaxis chamber (Neuroprobe Inc., Cabin John, Md.), which has been described in detail elsewhere.¹¹ Briefly, the chemoattractant was placed in the lower chamber in 26 µl of RPMI 1640 with 0.5% BSA. A polycarbonate polyvinylpyrrolidone-free filter (Nucleo-

pore Corp., Pleasanton, Calif.) was then placed over the lower chambers. The upper chambers were filled with 40 μ l of the various cell suspensions, 1×10^6 /ml for granulocytes and monocytes, and 5×10^6 /ml for T lymphocytes. The pore size of the filters is 8 μ m for monocytes, 5 μ m for T lymphocytes, and 3 μ m for neutrophil granulocytes. Before T-lymphocyte chemotaxis, filters were incubated in sterile water with 3 μ g/ml of collagen (Gibco-BRL, Gaithersburg, Md.) to increase the T-cell adhesion to the filters.

We used fMLP (Sigma Chemical Co., St. Louis, Mo.) in a concentration range from 10^{-10} to 10^{-7} mol/L and LTB₄ in a similar concentration range. These concentrations were known to induce a dose response including maximal chemotaxis in our assay.

The chambers were incubated for 45 minutes (granulocytes), 90 minutes (monocytes), or 120 minutes (T lymphocytes) at 37° C in 5% CO₂ and atmospheric air. Filters were then carefully removed, fixed in 70% methanol, and stained for 5 minutes with Coomassie brilliant blue.

Cells that attached to the lower surface of the filter were counted by measuring their area during microscopy with a video camera connected to a computer system for digital analysis and supported by software for objective determination of chemotactic migration.¹¹ The area covered by stained cells was measured, and a histogram was created where the number of "particles" is arranged according to particle size. The smallest particles are disregarded as "debris," whereas the mean value gives the area of individual cells. This value is then used for calculations of the number of cells in the field.

We measured five fields in each well with a predetermined order of selecting the areas and used triplicate wells for each concentration of chemotaxin. A chemotactic index (CI) was calculated as the number of cells on the lower side of the filter in wells with a chemotaxin versus the number of cells in wells with medium only.

Ex vivo effect of cetirizine

Four healthy persons and six patients with severe atopic dermatitis took cetirizine 10 mg in the morning and 20 mg at night, for 3 days. This dosage was chosen because it would bring serum concentrations of cetirizine within the concentration range, where an effect was observed in vitro. Heparinized blood was drawn at exactly the same time in the morning on days 1 and 3. After the first drawing of blood cetirizine therapy was started. On day 3 blood was drawn 1½ hours after the morning intake of 10 mg cetirizine. Serum was secured for measurements of cetirizine in the four healthy adults together with a skin prick test of 10 U of histamine.

A similar schedule was followed in the double-blind, placebo-controlled study, where blood was drawn at days 1, 3, and 7 during 1 week of therapy with 10 and 20 mg/day cetirizine, or placebo. Mononuclear cells were isolated from heparinized blood and used directly for chemotaxis with the use of 8 μ m filter. This demon-

strates monocyte chemotaxis only as evaluated morphologically by hematoxylin-eosin staining of the membranes.

Eosinophil proteins

We measured ECP and eosinophil protein X and eosinophil-derived neurotoxin (EPX/EDN) in the group of patients with atopic dermatitis during the placebo-controlled, double-blind study. Blood was taken at days 1, 3, and 7 without any anticoagulation and allowed to clot for 1 hour at room temperature. It was then centrifuged for collection of serum, which was kept at -20° C until analysis with ELISA methods as described elsewhere.^{12, 13} The normal range and mean values are ECP, 2.3 to 15.0 ng/ml, mean 6.0 ng/ml; EPX/EDN, 7.8 to 40.0 ng/ml, mean, 17.8 ng/ml.

Statistical methods

We used nonparametric tests for statistical analysis, either the Wilcoxon signed-rank test or the Mann-Whitney two-sample test. A *p* value less than 0.05 was considered significant.

RESULTS

Cetirizine dihydrochloride was found to induce a significant reduction of in vitro chemotaxis of monocytes and T lymphocytes (*p* < 0.0001; Wilcoxon signed-rank test) but not of neutrophil granulocytes (Fig. 1, A). This inhibition occurred for both fMLP and LTB₄. Pyrillamine in equimolar concentrations did not inhibit chemotaxis of any cell type (Fig. 1, B). The viability of the cells was not affected, as judged by trypan blue exclusion tests. Several time-course experiments of the effect of cetirizine on chemotaxis of leukocytes were performed (data not shown). We found that the chemotactic abilities of monocytes and T lymphocytes toward fMLP and LTB₄ began to decrease within 30 minutes of incubation with an optimal concentration (1 μ g/ml) of cetirizine and sharply decreased at 60 minutes without an effect on the viability of cells.

We then continued to study the ex vivo effect on monocytes and T-lymphocyte chemotaxis in an open study. The intake of cetirizine did not lead to a reduction in the percentage of monocytes in peripheral blood in differential counts (results not shown). All persons had a reduction in their monocyte and T-cell chemotactic responses to fMLP and LTB₄ after taking 10 and 20 mg/day cetirizine (Fig. 2). There was no change if only 10 mg cetirizine was given (results not shown, *n* = 4). The chemotactic response of monocytes from patients with atopic dermatitis was lower than that of monocytes from healthy persons, but it did not reach a statistical significant difference (mean CI = 1.97,

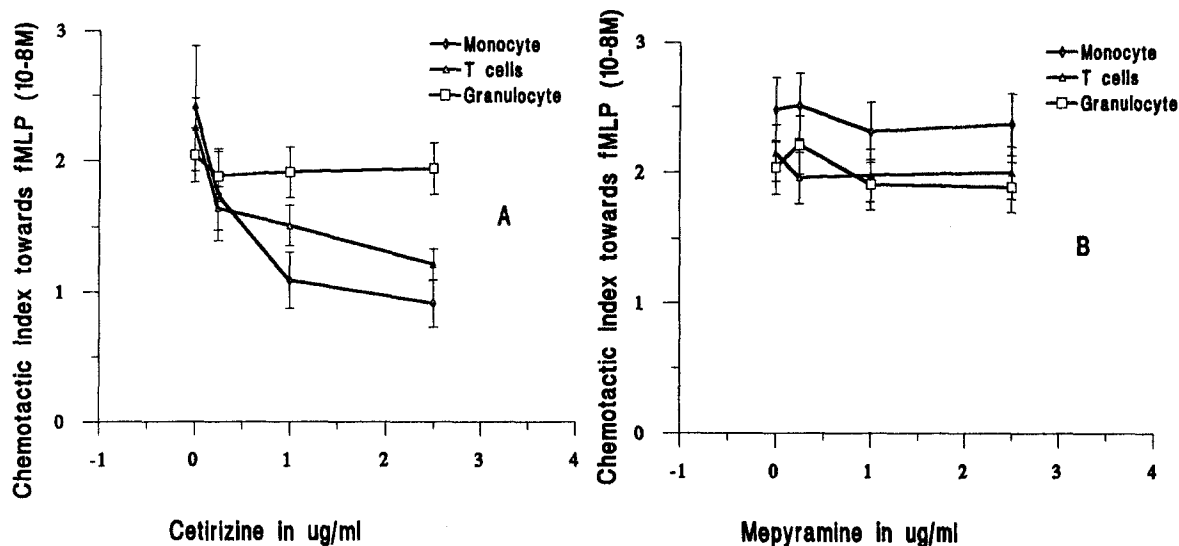


FIG. 1. A, Human peripheral blood leukocyte migration in response to stimulation of fMLP after preincubation with cetirizine. Leukocytes were isolated from peripheral blood of healthy persons and incubated with or without cetirizine before in vitro chemotaxis was measured toward fMLP (10^{-8} mol/L), which induces optimal migration. Concentrations of preincubation with cetirizine were 0, 0.25, 1.0, and 2.5 μ g/ml at 37° C and 5% CO₂ for 60 minutes. Data shown represent triplicate experiments and are from one representative experiment of 10 or eight performed. Results were determined as described in Methods and are expressed as CI and SD. Monocytes, $n = 10$; T lymphocytes, $n = 8$; granulocytes, $n = 8$. Similar result occurred after LTB₄ incubation (results not shown). **B,** Human peripheral blood leukocytes migration in response to stimulation of fMLP after preincubation with pyrilamine (mepyramine). Leukocytes were isolated from peripheral blood of healthy persons and preincubated with pyrilamine at concentrations of 0, 0.25, 1.0, and 2.5 μ g/ml at 37° C and 5% CO₂ for 60 minutes before in vitro chemotaxis was measured toward fMLP in optimal concentration (10^{-8} mol/L). Data shown represent triplicate experiments and are from one representative experiment of four or six performed. Results were determined as described in Methods and are expressed as CI $\pm$ SD. Monocytes, $n = 6$; T lymphocytes, $n = 4$; granulocytes, $n = 4$. Similar result occurred after LTB₄ incubation (results not shown).

$n = 6$; mean CI = 2.67, $n = 4$; respectively; $p > 0.05$). When taking 10 and 20 mg/day cetirizine (day 3), the healthy volunteers had negative histamine skin test reactions. Serum concentrations of cetirizine ranged from 638 to 842 ng/ml, ex vivo monocyte chemotaxis toward fMLP and LTB₄ exhibited an obvious decrease compared with that observed when serum concentrations of cetirizine ranged from 247 to 288 ng/ml (day 1 after the intake of 10 mg/ml cetirizine; data not shown).

The double-blind, placebo-controlled study confirmed that monocytes ex vivo after 10 and 20 mg cetirizine were significantly reduced in their response toward fMLP and LTB₄ in both healthy controls ($p < 0.001$ for both fMLP and LTB₄) (Table I) and in patients with atopic dermatitis ($p < 0.001$ for both fMLP and LTB₄) (Table II). Monocytes from patients with atopic dermatitis were found to have a lower chemotactic response than those from healthy control subjects (Table I

vs Table II; $p > 0.05$). Actually, cetirizine therapy in patients with atopic dermatitis almost abolished chemotaxis (Table II; $p < 0.001$).

The ECP level or EPX/EDN in serum were increased in patients with atopic dermatitis, but no significant change was observed during therapy (Table III). Six of eight subjects in the nonatopic group, receiving 10 and 20 mg/day cetirizine, reported sedation compared with two of eight in the placebo group.

DISCUSSION

Cetirizine dihydrochloride is one of the non-sedating antihistamines and has proven efficacy in treatment of hay fever, urticaria, mosquito bites, and pollen-induced asthma.¹⁴⁻¹⁹ Recently cetirizine was found to induce a significant inhibition of eosinophil migration into skin windows after antigen stimulation,²⁰ and it was found to inhibit in vitro eosinophil chemotaxis after fMLP and plate-

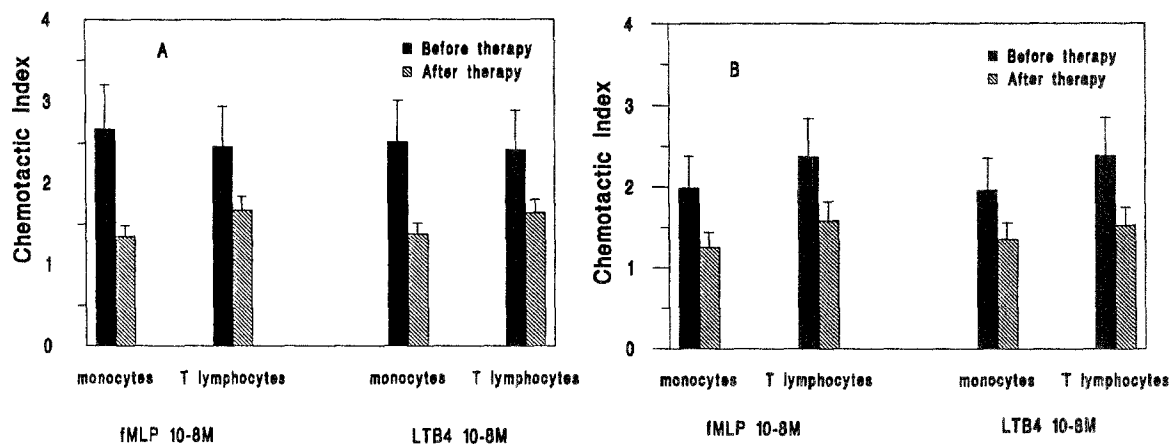


FIG. 2. A and B. Human peripheral blood leukocyte migration in response to stimulation of fMLP or LTB₄ before and after administration. Monocytes and T lymphocytes were isolated from peripheral blood of four healthy subjects and six patients with atopic dermatitis before and 2 days after taking orally 10 and 20 mg/day cetirizine. Cells were exposed in vitro to fMLP and LTB₄ in optimal concentration of 10⁻⁸ mol/L. Data represent triplicate experiments from one representative experiments of each tested group. Results are determined as described in Methods as CI ± SD.

TABLE I. Effect of cetirizine on chemotaxis of monocytes from healthy subjects in double-blind placebo-controlled study

	CI			
	Cetirizine group		Placebo group	
	Before therapy	After therapy	Before therapy	After therapy
fMLP (mol/L)				
10 ⁻⁷	1.70 ± 0.35	1.17 ± 0.27	1.70 ± 0.36	1.79 ± 0.81
10 ⁻⁸	2.62 ± 0.79	1.80 ± 0.67	2.37 ± 0.38	2.23 ± 1.32
10 ⁻⁹	2.40 ± 0.82	1.71 ± 0.52	2.27 ± 0.36	2.21 ± 1.03
10 ⁻¹⁰	1.68 ± 0.52	1.19 ± 0.32	1.21 ± 0.22	1.21 ± 0.36
LTB ₄ (mol/L)				
10 ⁻⁷	1.97 ± 0.37	1.27 ± 0.39	1.69 ± 0.48	1.66 ± 0.63
10 ⁻⁸	2.65 ± 0.62	1.46 ± 0.58	2.06 ± 0.40	2.22 ± 0.96
10 ⁻⁹	2.75 ± 1.41	1.58 ± 0.74	2.32 ± 0.32	2.10 ± 0.96
10 ⁻¹⁰	1.59 ± 0.22	1.22 ± 0.33	1.33 ± 0.23	1.71 ± 0.72

Results of chemotaxis study before and 2 days after 10 and 20 mg/day cetirizine or placebo. Data represent triplicate experiments and are mean values of experiments in each group. Data expressed as mean ± SD.

let-activating factor stimulation.^{4,21} It also inhibited the late-phase response in vivo of type I allergic reactions.⁸

It has been previously shown that cetirizine exerts an inhibitory effect on migration of eosinophils in allergic subjects both in vitro and in vivo. Our results demonstrate a dose-dependent in vitro and ex vivo inhibitory effect of cetirizine on monocyte and to a lesser degree on T-lymphocyte chemotaxis in their response toward fMLP and LTB₄. These findings that cetirizine affects migration of monocytes and T lymphocytes in vitro and ex vivo

are novel. Our results also show that pyrilamine lacks a similar effect in vitro in equimolar concentrations of cetirizine. Additionally, all three types of cells studied (monocytes, neutrophils, and T lymphocytes) exhibit H₁-receptors,²² but cetirizine selectively inhibits the migrations of monocytes and T lymphocytes. These facts strongly indicate that the inhibitory effect on chemotaxis of monocytes and T lymphocytes from cetirizine is not via H₁-receptors on the cells. The production of inflammatory mediators after antigen challenge correlates well with allergy detected by history and

TABLE II. Effect of cetirizine on chemotaxis of monocytes from subjects with atopic disease in double-blind placebo-controlled study

	CI			
	Cetirizine group		Placebo group	
	Before therapy	After therapy	Before therapy	After therapy
fMLP (mol/L)				
10 ⁻⁷	1.14 ± 0.15	1.14 ± 0.15	1.07 ± 0.32	1.02 ± 0.22
10 ⁻⁸	2.48 ± 0.97	1.44 ± 0.87	2.35 ± 0.31	2.12 ± 1.23
10 ⁻⁹	2.00 ± 0.83	1.14 ± 0.26	2.18 ± 0.91	2.83 ± 1.13
10 ⁻¹⁰	1.46 ± 0.50	1.02 ± 0.25	1.22 ± 0.67	1.26 ± 0.40
LTB ₄ (mol/L)				
10 ⁻⁷	1.68 ± 0.54	0.97 ± 0.16	1.11 ± 0.56	1.37 ± 0.71
10 ⁻⁸	2.72 ± 0.80	1.19 ± 0.64	1.40 ± 0.55	2.29 ± 1.18
10 ⁻⁹	2.81 ± 1.45	1.04 ± 0.33	1.57 ± 0.36	1.39 ± 0.50
10 ⁻¹⁰	1.12 ± 0.19	1.11 ± 0.52	1.06 ± 0.37	1.11 ± 0.51

Results of chemotaxis study before and 2 days after 10 and 20 mg/day cetirizine or placebo show dose response toward fMLP and LTB₄. Data represent triplicate experiments and are mean values of experiments in each group. Data expressed as means ± SD.

TABLE III. Levels of ECP and EPX in 14 patients with atopic dermatitis

Day	Cetirizine group (n = 8)		Placebo group (n = 6)	
	ECP (ng/ml)	EPX (ng/ml)	ECP (ng/ml)	EPX/EDN (ng/ml)
1	20.2 ± 9.1	48.8 ± 22.6	12.0 ± 9.1	43.5 ± 12.8
3	14.3 ± 5.9	39.6 ± 16.7	20.9 ± 7.5	41.2 ± 11.8
7	28.4 ± 21.8	60.6 ± 28.4	20.9 ± 14.3	55.9 ± 20.6

Serum levels of ECP and EPX were measured before, during, and 7 days after administration of either 10 and 20 mg/day cetirizine or placebo. Normal ranges: ECP, 2.3 to 15 ng/ml (mean, 6.0 ng/ml); EPX/EDN, 7.8 to 40.0 ng/ml (mean, 17.8 ng/ml).

skin test, but neither the amount of mediators generated during late-phase reaction nor the symptomatic response was predicated by skin sensitivity, specific serum IgE levels, or basophil histamine release.²³ This fact suggests that the generation of late-phase reaction is not a simple result of high sensitivity to antigen. There was, however, a significant correlation between the amount of mediators and symptoms of allergy generated during the early reaction and the corresponding amount during the late-phase reaction.

A number of studies show that eosinophils, T lymphocytes, and monocytes may play an important role in the initiation, the development, and the control of a variety of allergic disorders including atopic dermatitis. The recent observation that cetirizine significantly inhibits the late skin reaction induced by platelet-activating factor and kallikrein in patients with chronic urticaria indicates that cetirizine, besides having antihistamine activity, also has an antiinflammatory effect. Such late cutaneous reactions in these patients are not blocked by previous administration of loratadine

and dexchlorpheniramine.²¹ We now report that, in addition to inhibiting significantly the migration of eosinophils in vivo, cetirizine inhibits the chemotactic migrations of monocytes and T lymphocytes in vitro and ex vivo. This is to our knowledge the first description of a specific nonsedating H₁-receptor antagonist having inhibitory effect on migration of several inflammatory cells including monocytes and T lymphocytes. It supports the clinical observations that cetirizine has an antiinflammatory effect by reducing the migration of inflammatory cells. The mechanism of inhibitory effect of cetirizine on migration of monocytes and T lymphocytes needs to be investigated further.

The serum levels of ECP and EPX/EDN were not influenced by cetirizine. Measurements of ECP and EPX/EDN are strongly influenced by sample processing, which were therefore standardized in our study.¹² A recent study showed that serum levels of ECP in particular, but also serum levels of EPX reflects eosinophil degranulation in vitro. The lack of an effect on ECP and EPX/EDN values from cetirizine may be because the treatment

period was short. It has been shown that 20 mg/day cetirizine given to patients with atopic dermatitis for 4 weeks leads to a significant drop in the number of circulating eosinophils.²⁴ ECP values in serum from patients with atopic dermatitis is known to be increased,²⁵ and this was also found in our patients.

The reduced chemotactic capacity of monocytes from patients with atopic dermatitis reflects disease activity and has been reported before.²⁶

Our data support the view that a potent antihistamine, cetirizine, also has antiinflammatory effects by inhibiting the chemotactic response of cells that are important participants in any allergic reaction, an effect that seems not to be mediated via H₁-receptor blocking. One explanation for our observation may be that cetirizine inhibits the expression of adhesion molecules on cells of the macrophage lineage.^{27, 28} It has recently been demonstrated that cetirizine (100 µg/ml) significantly inhibited the adhesion of eosinophils to endothelial cells when adherence is enhanced by either fMLP or interleukin-1 stimulation.^{29, 30} This raises the possibility that drugs such as cetirizine might affect the function or expression of several adhesion molecules. Our data on the capacity of cetirizine to inhibit migration of monocyte and T lymphocytes in vitro might indicate an important property in the efficacy of this drug in allergic disease. It remains to be seen whether cetirizine has an additional antiinflammatory effect in diseases where monocytes and T lymphocytes form a major part of the disease process, such as psoriasis, rheumatoid arthritis, and ulcerative colitis.

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