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Cinnamaldehyde is an effective anti-inflammatory agent for treatment of allergic rhinitis in a rat model

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ABSTRACT

Objectives: The effect of cinnamaldehyde on the treatment of allergic rhinitis (AR) was investigated in rat model.
Methods: Twenty-eight female Wistar albino rats were randomly divided into four groups: Group 1 (control) (C), Group 2 (AR with no treatment) (AR + NoTr), Group 3 (AR + Azelastine HCl) (AR + Aze), and Group 4 (AR + cinnamaldehyde) (AR + Cin). At day 21, AR + Aze rats were given an Azelastine HCl drop, and AR + Cin rats were given cinnamaldehyde intranasally. In all groups, allergic symptoms histopathological results were evaluated.
Results: The AR + NoTr group showed the worst allergic symptoms, cilia loss and greater inflammation. In the AR + Aze and AR + Cin groups, allergic symptom scores were higher than those in the control group. However, between AR + Aze and AR + Cin groups, there were no significant differences in the allergic symptom scores Histopathological analysis revealed vascular congestion and an increase in goblet cell numbers in the AR + Cin group. However, AR + Cin rat nasal mucosa had less plasma cell infiltration compared with the AR + NoTr group. In rats from the AR + Aze group, analysis of the nasal mucosa revealed less eosinophil infiltration than that seen in the AR + NoTr group. A lower score for mast cell (MC) infiltration was observed in the nasal mucosa of rats treated with Azelastine HCl compared with cinnamaldehyde.
Conclusions: In this study we observed that both Azelastine HCl and cinnamaldehyde reduced allergic symptoms in an AR rat model. Cinnamaldehyde decreased vascular congestion as well as plasma cell, eosinophil, and inflammatory cell infiltration into the lamina propria.

1. Introduction

Allergic rhinitis (AR) is a major condition that occurs in individuals with asthma and is related to inflammation of the upper respiratory tract. AR is a risk factor for the development of asthma, and thus children and adults with AR, especially persistent AR, should be examined for asthma [1].

When considering the role of allergies in sinus diseases, one may speculate that nasal inflammation induced by IgE-mediated mechanisms results in the development of acute and/or chronic sinus infections [2,3]. The mechanisms of allergic inflammation in the nose that predisposes an individual to the development of sinus disease are partially known [4]. Inhaled allergens may reach the sinus mucosa and initiate an allergic reaction, leading to congestion of the sinus mucosa with impaired removal of mucus. However, studies conducted in chronic sinus infection patients failed to demonstrate more severe congestion present in AR patients than in individuals without AR [4]. Allergens are not

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always responsible for severe forms of sinus infections, indicating that other factors besides allergens play a role in the etiopathogenesis of severe sinus infections [5].

AR can depreciate the quality of life by causing fatigue, headaches, cognitive impairment, and other symptoms. To maintain basal levels of inflammation in the body, the regulation of Th1 and Th2 cells is important. Dysregulation of Th responses results in the activation and accumulation of Th cells, which are causes of AR [6].

Cinnamon is a well-known spice distributed mainly in Asia, South America, and the Caribbean [7]. Cinnamon oil (usually diluted 0.5–2.5%) is more often derived from the bark than from the leaves of the tree. Its main components are cinnamaldehyde (65–80%), trans-cinnamic acid (5–10%), and eugenol (4–10%); other constituents include cinnamic alcohol, terpenes (i.e., limonene, tannins, mucilage, and the oligomer procyanidin), and traces of coumarin [8,9].

The pungent taste and smell comes from cinnamaldehyde, an antimicrobial agent [10]. Cinnamaldehyde can also be found naturally in blueberries and cranberries [11]. Other components of cinnamon and cassia include phenolic acids, proanthocyanidins [12,13], cinnamyl alcohol, terpenes, carbohydrates, coumarin, and tannins [11]. Although cassia contains much less cinnamaldehyde than cinnamon, it is much richer in coumarin [14,15].

Cinnamomum cassia is the most popular type of cinnamon. For thousands of years, cinnamomum cassia has been utilized in traditional Chinese medicine for treating various disorders including chronic gastric symptoms, circulation issues, arthritis, and the common cold [16]. Cinnamic acid is found in cinnamon oil. It can also be readily oxidized from benzaldehyde by the gentle heating of cinnamaldehyde [10]. Cinnamic acid and benzoic acid are structurally similar compounds classified as hydroxycinnamic acid and hydroxybenzoic acid, respectively [17]. The antioxidant capacity of cinnamic acids is greater than that observed in benzoic acid homologous counterparts [18].

Cinnamon bark has been reported as a successful anti-arthritic agent because of its anti-inflammatory, pain relieving, and immunoregulatory effects [19]. Its anti-inflammatory activity is attributed to procyanidin oligomers found in the bark [20]. Water-soluble cinnamon bark extract has been reported to regulate immune function in vitro and to prevent and treat inflammatory diseases [21–23].

In the present study, we investigated the efficacy of cinnamaldehyde in an AR rat model. For this study we utilized four groups of rats: (1) a healthy control group, (2) AR rats given no treatment, (3) AR rats treated with Azelastine HCl, and (4) AR rats treated with cinnamaldehyde.

2. Material and methods

This study was conducted at Experimental Studies Center of Eskişehir Osmangazi University. All animals were treated in compliance with the principles of the Declaration of Helsinki.

2.1. Animal subjects

Twenty-eight healthy (190–220 g) female Wistar albino rats were used in this study. The experimental protocol was reviewed and approved by the Committee of Ethics of Osmangazi University, the Center of Medical and Surgical Experiments. All animal procedures were performed in accordance with the approved protocol.

All rats were housed under the same conditions in a temperature- and humidity-controlled room (20 ± 1 °C, 50 ± 10% relative humidity) under a 14–16 h light/dark cycle. Tap water and standard feed were provided on a regular basis.

2.2. Experimental design

Twenty-eight female Wistar albino rats were divided randomly into four groups ($n = 7$):

1. Group 1 (Control).
2. Group 2 (AR with no treatment; AR + NoTr). These rats had AR but did not receive treatment.
3. Group 3 (AR + Azelastine HCl; AR + Aze). These rats had AR and were treated with Azelastine HCl (antihistamine) for 7 days starting on day 21.
4. Group 4 (AR + cinnamaldehyde; AR + Cin), These rats had AR and were treated with cinnamaldehyde for 7 days starting on day 21.

2.3. Methods

2.3.1. Sensitization procedure for developing an AR rat model

The sensitizing solution was prepared by dissolving 0.3 mg ovalbumin (OVA) (Sigma, St. Louis, MO, USA) into 1 mL saline using 30 mg aluminum hydroxide (40 mg/mL) as an adjuvant. Rats in Groups 2 (AR + NoTr), 3 (AR + Aze), and 4 (AR + Cin) were injected intraperitoneally every other day for 14 days (days 1, 3, 5, 7, 9, 11, and 13) for a total of seven injections per rat. The rats in Group 1 (Control) were given 1 mL saline plus 30 mg aluminum hydroxide intraperitoneally on these same days. On day 14 following sensitization, rats in Groups 2, 3, and 4 were treated with 25 μL 2% OVA-saline solution in the form of intranasal drops on each side of the nose, once a day for 14 days. Group 1 (control) was given intranasal drops containing saline only [24–27].

2.3.2. Measurement of total IgE

On day 28, total IgE was measured in the blood of all rats. Blood was withdrawn (1 mL) and centrifuged for 20 min at 3000 rpm. Supernatant was removed, and the sample was stored at −20 °C until further analysis. Serum IgE levels were measured using a commercially available rat IgE ELISA kit (SunReed Biotechnology Co. Ltd., China) according to the manufacturer's instructions. Result values of this assay are expressed in KU/L.

2.3.3. Symptoms of AR

Symptoms of AR including sneezing, nose rubbing, eye lacrimation, and difficulty breathing (nasal congestion) were observed and scored over a 30-min period. Sneezing was characterized by an explosive expiration immediately after a deep inhalation [28] and was scored on a scale of 0–3. Nose rubbing was characterized by external perinasal scratching with either one or both of the rat's forelimbs [28]. Nose rubbing was scored on a scale of 0–3. Eye lacrimation was scored on the following scale: 0 (No lacrimation), 1+ (hazy eyes), 2+ (lacrimation), and 3+ (lacrimation and the onset of conjunctivitis) [29]. Nasal congestion/obstruction was evaluated on the following scale: 0 (No obstruction), 1+ (impaired inspiration), 2+ (nasal inflammation), and 3+ (severe breathing impairment) [29].

2.3.4. Azelastine HCl treatment (Group 3)

Group 3 was treated with an Azelastine HCl drop in each nostril, once a day for 7 days. Azelastine HCl treatment was given on day 21 and continued for 7 days. Intranasal Azelastine HCl treatment was administered 1 h prior to intranasal OVA application.

2.3.5. Cinnamadehyde treatment (Group 4)

Group 4 was treated with 20 μL cinnamaldehyde (dissolved in distilled water (20 mg/mL)) in each nostril, twice a day for 7 days. Cinnamaldehyde treatment was given on day 21 and continued for