

# Rosmarinic Acid as a Novel Agent in the Treatment of Allergies and Asthma\*

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## ABSTRACT

Rosmarinic acid, a caffeic acid ester and a component of several members of the *Lamiaceae* family including *Rosmarinus officinalis*, *Perilla* spp., and *Salvia officinalis*, has antioxidant and anti-inflammatory effects and is used for the treatment of asthma and reactive airway diseases, allergic disorders such as allergic rhinitis, otitis media, chemical sensitivity and multiple allergen reactivity. Rosmarinic acid can be used alone or in combination with other agents such as antioxidants, essential fatty acid supplements and other plant derived products. Rosmarinic acid can be administered orally and no adverse drug interactions have been reported. Nausea or mild stomach upset has been reported in sensitive patients in association with its oral intake and it is therefore recommended that Rosmarinic acid be ingested with food. Rosmarinic acid has shown free radical scavenging ability and suppression of allergic immunoglobulin and inflammatory responses of polymorphonuclear leukocytes, which may underlie its effectiveness in the treatment of allergic disorders, as demonstrated in clinical trials. Rosmarinic acid is a valuable agent for the treatment of allergic conditions, which is of importance considering the recent increase in the incidence of allergies, asthma and lung diseases associated with airborne pollutants.

**Keywords:** Asthma; Allergy; Antioxidant; Anti-inflammatory; Plant derived product; Rosmarinic acid

## CLINICAL IMPLICATIONS

Rosmarinic acid is a naturally occurring plant compound that reduces inflammation and allergic responses and is therefore indicated in the treatment of asthma and allergies. Rosmarinic acid can be combined with other herbs in the management of acute asthmatic episodes and is appropriate for long-term use to reduce allergic airway reactivity.

## PRIMARY INDICATIONS

Asthma and reactive airway diseases, allergic disorders such as allergic rhinitis, serious otitis media, chemical sensitivity, and multiple allergen reactivity.

## ADJUNCTIVE OR STAND ALONE TREATMENT

May be either adjunctive or stand alone.

## BIOACTIVE CONSTITUENTS

150 mg rosmarinic acid per capsule.

## CAPSULE DOSE

A minimum of 150 mg *twice per day* and a maximum of 4 or 5 times this amount.

## TIME TO CLINICAL EFFICACY

A minimum of 4 weeks.

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### **CLINICAL IMPLICATIONS (CONTINUED)**

#### **LAB TESTS TO ASSESS EFFICACY**

Eosinophil count when elevated, nasal swabs for eosinophils.

#### **SYNERGISTIC COMBINATION**

Combines well with antioxidant vitamins, essential fatty acid supplements, and other herbs specific to the individual patient.

#### **SIDE EFFECTS**

Those with gastric ulcers or sensitive digestive systems may experience nausea, irritation, or mild stomach upset at the higher doses; consume with food to reduce this potential reaction.

#### **PROVEN DRUG INTERACTION**

None documented.

## DISCUSSION

*Rosmarinus officinalis* L. (common name, rosemary) is a woody herb, native to Mediterranean regions. It has been used in traditional medicine for many centuries, for respiratory disorders, depression, renal colic, and hair loss. Culpepper's Herbal recommends rosemary especially for conditions affecting the mind, for maladies of the eye, stomach and joints due to effects of cold, and for coughs. Rosemary was traditionally thought to dispel negative thoughts, and is used in aromatherapy for anxiety.

Rosmarinic acid is an ester of caffeic acid present in several members of the *Lamiaceae* family including *Rosmarinus officinalis*, *Perilla* spp., and *Salvia officinalis* among others (Fig. 1). These plants have been traditionally used to treat upper respiratory and allergic symptoms. Rosmarinic acid is one of the more abundant caffeic esters occurring in plants, and becomes active in humans when it is auto-oxidized.<sup>1</sup>

Rosmarinic acid is well absorbed from the gastrointestinal tract.<sup>2</sup> It is readily assimilated in humans by all major organ systems, with higher concentrations found in the lungs.<sup>3</sup> This may explain why it shows higher efficacy in the treatment of asthma and respiratory allergies than in other types of allergic responses. It has also shown promise as an effective treatment for pulmonary eosinophilia.<sup>4</sup>

### ROSMARINIC ACID DISPLAYS NUMEROUS ANTI-INFLAMMATORY EFFECTS

Numerous antioxidant and anti-inflammatory effects have been reported for Rosmarinic acid,<sup>5-7</sup>

which may contribute to its anti-allergy activity. Rosmarinic acid has demonstrated free radical scavenging ability against superoxide anions and hydroxyl radicals.<sup>8</sup> Additionally, animal studies have shown that Rosmarinic acid suppresses the allergic immunoglobulin response and inflammatory responses of polymorphonuclear leukocytes.<sup>9</sup> All of these actions are putative mechanisms for Rosmarinic acid's anti-inflammatory effect.

### PLANTS THAT CONTAIN ROSMARINIC ACID TEND TO HAVE ANTI-ALLERGY EFFECTS

Individual herbs known to be high in Rosmarinic acid also have anti-inflammatory properties. *Rosmarinus* is a powerful antioxidant,<sup>10, 11</sup> and *Perilla frutescens* extracts and several *Salvia* species that contain Rosmarinic acid have antioxidant and anti-inflammatory effects including inhibition of lipoxygenase.<sup>12-16</sup> Although the combined total of the chemical constituents in each plant contributes to its medicinal effects, Rosmarinic acid is increasingly being identified as a major anti-inflammatory and immune modulating substance (Fig. 2).

*Perilla frutescens* is both a popular culinary garnish and part of the Asian herbal medicine tradition, with much of the research emanating from Japan and Korea. *Perilla* has been used traditionally for allergies and as an antidote against allergic reactions triggered by the consumption of seafood and shellfish.<sup>17</sup> *Perilla frutescens* has also been used for the treatment of bronchial asthma. The anti-inflammatory activity of *Perilla* was demonstrated in an animal model in which a *Perilla* decoction was

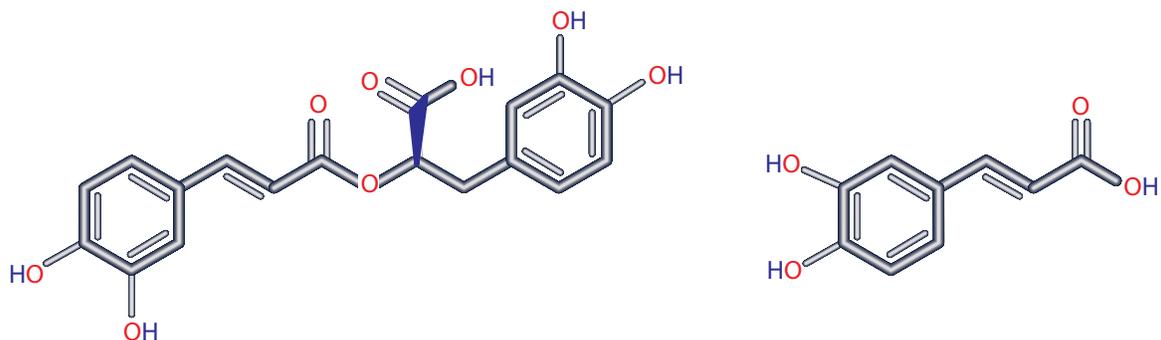
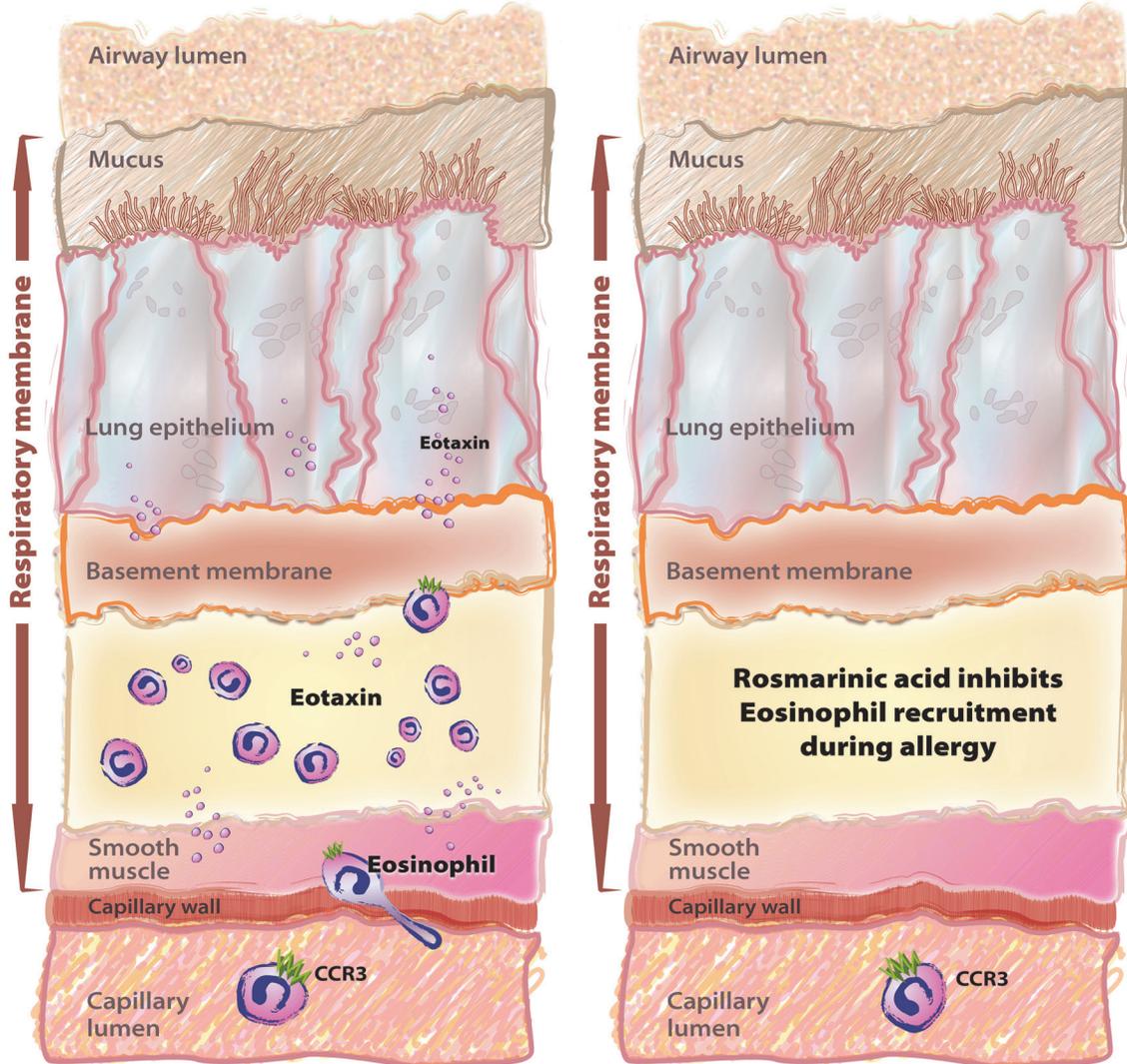


Figure 1: Rosmarinic acid (left); caffeic acid (right).

## ANTI-INFLAMMATORY EFFECTS OF ROSMARINIC ACID



**Figure 2: Anti-inflammatory effects of Rosmarinic acid. Left: Eosinophils infiltrating respiratory submucosa, capillaries and smooth muscle. Right: Eosinophils infiltration is reduced under the influence of Rosmarinic acid.**  
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effective in blocking the passive cutaneous anaphylaxis (PCA)-reaction, reducing the inflammatory reaction in the injured animal's skin compared to untreated control animals.<sup>17</sup>

### Rosmarinic Acid for Respiratory Allergies and Asthma

Airborne pollutants have been implicated in the increasing incidence of allergies, asthma, and lung diseases in the general population and especially in children.<sup>17</sup> Previous work in animals has

demonstrated that intratracheal instillation of diesel exhaust particles will generate reactive oxygen species (ROS).<sup>18</sup> In one study, pre-exposure oral supplementation with Rosmarinic acid prevented inflammation caused by diesel exhaust.<sup>19</sup> The authors provided evidence of reduced pro-inflammatory proteins, decreased neutrophil infiltration, and less lung parenchymal and interstitial edema in animals treated with Rosmarinic acid.

Dust mites are another pervasive and potent instigator of allergy and asthma symptoms. One mouse model of

allergic asthma uses tracheal tissue that has been sensitized to dust mites. This model reproducibly causes eosinophilic inflammation and measurable changes in interleukin and eotaxin levels. Eotaxin, found in a variety of mucosal tissues, is a chemokine that regulates and activates eosinophils. Mice pretreated with *Perilla* extract containing a high concentration of Rosmarinic acid exhibited only a blunted inflammatory response.<sup>20</sup> Likewise, eosinophils, interleukins, and eotaxin levels were proportionally lower in mice treated with Rosmarinic acid.

## HUMAN CLINICAL TRIALS ON ROSMARINIC ACID

Takano and colleagues conducted a 21-day, randomized, double-blind, clinical trial in which various doses of a Rosmarinic acid-enriched *Perilla* extract were compared with placebo in the treatment of allergic conjunctivitis.<sup>21</sup> Study subjects received the enriched extract at 200 mg per day or 50 mg per day, or placebo. Symptoms were recorded in a daily log along with periodic nasal lavage. There was a dose-dependent decrease in subject-reported symptoms including itchy nose, itchy eyes, and watery eyes. The treatment groups also had significantly lower neutrophil and eosinophil levels by nasal lavage. In another study, the same group administered Rosmarinic acid to subjects with seasonal allergic rhinitis and examined cytokine concentrations from nasal cells obtained by lavage. Again, the treatment groups had decreased neutrophil and eosinophil counts compared to the placebo group.<sup>22</sup>

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## SUMMARY

The antioxidant and anti-inflammatory effects of Rosmarinic acid (and plants high in this compound) make it a valuable tool in the treatment of allergic conditions, especially respiratory allergies. *In vitro* and *in vivo* studies along with clinical trials support the use of Rosmarinic acid in the prevention and treatment of asthma and allergy. Furthermore, herbs that contain Rosmarinic acid have a long history of safe use in alternative and traditional therapies.

## DISCLOSURE OF INTERESTS

Dr. Stansbury has nothing to disclose.

## REVIEW ESSAY

Many nutrients and herbs that have not been the subject of randomized controlled studies are used regularly by clinicians. They have also been used traditionally for hundreds, sometimes thousands of years. Review Essays contain the opinions of professionals and experts in the fields of nutritional and botanical medicine on how to most effectively use herbs and nutrients in clinical practice. The dosages recommended are based on clinical experience. Side effects that are described in “Unsubstantiated Theoretical Concerns” have not been seen in clinical practice or clinical studies but are speculative based on, for example, possible mechanisms of action.

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