ภาคผนวก ก.

งานวิจัยที่สนับสนุนคุณสมบัติของ Quercetin

Regulation of IL-1-induced selective IL-6 release from human Mast-cells and inhibition by quercetin

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Abstract:

1. Mast-cells are involved in allergic reactions, but also in innate immunity and inflammation. Crosslinkage of Mast-cell Fc immunoglobulin E receptors (FceRI) by multivalent antigen triggers secretion of granule-stored mediators, as well as de novo synthesis of cytokines, including interleukin(IL)-6.
2. We showed recently that the proinflammatory cytokine IL-1 stimulates human leukemic Mast-cells (HMC-1) and human umbilical cord blood-derived cultured Mast-cells (hCBMCs) to release newly synthesized IL-6 without tryptase in the absence of degranulation.

3. Here, we investigated several signal-transduction pathways activated by IL-1 leading to IL-6 production by HMC-1 and hCBMCs.
4. We also investigated the effect of the flavonol quercetin that was recently shown to strongly inhibit IL-6 secretion in response to allergic stimulation from hCBMCs.
5. IL-1 stimulated p38, but did not activate extracellular signal-regulated kinase (ERK) or c-jun N-terminal kinase (JNK); it also did not activate protein kinase C(PKC) isozymes a, b, m and z,except for PKC-y, which was phosphorylated.
6. The p38 inhibitor SB203580 and the PKCinhibitors Calphostin Cand Go 6976 completely inhibited IL-1-induced IL-6 production.
7. Quercetin 1–100 mM inhibited IL-1-induced IL-6 secretion, p38 and PKC-y phosphorylation in a dose-dependent manner.
8. These results indicate that IL-1-stimulated IL-6 production from human Mast-cells is regulated by Biochemical pathways distinct from IgE-induced degranulation and that quercetin can block both IL-6 secretion and two key signal transduction steps involved.

Inhibitory effect of quercetin on tryptase and interleukin-6 release, and histidine decarboxylase mRNA transcription by human Mast-cell-1 cell line

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Abstract:

Mast-cells are involved in inflammatory processes and in allergic reactions where immunologic stimulation leads to degranulation and generation of numerous cytokines and inflammatory mediators. Mast-cells have been proposed as an immune gate to the brain, as well as sensors of environmental and emotional stress, and are likely involved in neuropathologic processes such as multiple sclerosis. Among Mast-cell products, the protease tryptase could be associated with neurodegenerative

processes through the activation of specific receptors (PARs) expressed in the brain, while interleukin (IL)-6 likely causes neurodegeneration and exacerbates dysfunction induced by other cytokines; or it could have a protective effect against demyelinisation. In this report we show that quercetin, a natural compound able to act as an inhibitor of Mast-cell secretion, causes a decrease in the release of tryptase and IL-6 and the down-regulation of histidine decarboxylase (HDC) mRNA from human Mast-cell (HMC)-1 cells. As quercetin dramatically inhibits Mast-cell tryptase and IL-6 release and HDC mRNA transcription by HMC-1 cell line, these results nominate quercetin as a therapeutical compound in association with other therapeutical molecules for neurological diseases mediated by Mast-cell degranulation.

Inhibitory Effect of Quercetin on Tryptase and MCP-1 Chemokine Release, and Histidine Decarboxylase mRNA Transcription by Human Mast-cell-1 Cell Line

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Abstract:

Mast-cells are important in reactions of allergic disease and are also involved in a variety of neuroinflammatory diseases. Mast-cells can be immunologically activated by IgE through their Fc receptors, as well as by neuropeptides and cytokines to secrete mediators. Here we used a human Mast-cell-1 (HMC-1) cell line cultured and treated with a physiological activator, anti-IgE, and a nonphysiological activator, calcium ionophore A23187, for tryptase and MCP-1 generation and transcription of histidine decarboxylase. We used quercetin, a potent antioxidant, cytoprotective and anti-inflammatory compound capable of inhibiting Histamine and some cytokines released from several cell types, as an inhibitor of immunological and nonimmunological stimulus for Mast-cells. In this study quercetin inhibits, in a dose-response manner, tryptase and

MCP-1. Moreover, using RT-PCR quercetin inhibited the transcription of histidine decarboxylase, the rate-limiting enzyme responsible for the generation of Histamine from histidine, and MCP-1. Our data suggest that quercetin is an important and good candidate for reducing the release of pro-inflammatory Mast-cell mediators activated by physiological and nonphysiological stimulators.

Histamine release from the cultured mouse Mast-cell line PT 18 in response to immunologic and non-immunologic stimuli

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Abstract:

Cultured mouse Mast-cells that are dependent on spleen-derived factors for their proliferation and maintenance have been shown rapidly to release Histamine in response to immunologic stimuli, concanavalin A, and ionophores A23187 and Br-x537A. These cells did not, however, release Histamine when treated with compound 48/80 or adenosine 5′-triphosphate. Immunologically mediated Histamine release was inhibited by theophylline and quercetin, but not by disodium cromoglycate. The results presented here are discussed in terms of the possible relationship of this cell line to mucosal Mast-cells.

Quercetin—The Anti-Allergy Bioflavonoid

http://www.immunesupport.com/92fal004.htm

Every spring, summer and fall millions of Americans sneeze, wheeze, drip, and sniffle their way through a world filled with trillions of airborne pollen, dust, and smoke particles. Over-the-counter anti-allergy drugs (antihistamines) tend to leave their users either

sleepy or over-stimulated. Fortunately, modern nutritional science now offers a highly effective, natural and nontoxic remedy for allergies: the bioflavonoid quercetin.

Quercetin, a "cousin" of the more well-known bioflavonoid rutin, is one of a thousand or so members of the bioflavonoid family. This is a group of coloring pigments widely found throughout the plant kingdom, where they also provide plants with antioxidant protection against environmental stresses. Natural diets high in vegetables, fruit, sprouts, and whole grains typically provide a total of 1,000 to 2,000 mg. a day of a broad range of flavonoids. Blue-green algae are the usual source of quercetin, but it's also available as a food supplement.

Allergies and asthma are inflammatory conditions usually triggered by air- or food-borne pollens and chemicals called "allergens." After these allergens are absorbed into the blood (through the lungs, skin, or intestines), they cause the B cells (white blood cells) of allergy-sufferers to produce billions of molecules of the allergic antibody IgE. The IgE molecules then travel through the bloodstream until they combine to with mast cells or basophils. Mast cells (which line many blood vessels) and basophils (a type of white blood cell circulating in the bloodstream) are the main storage sites for histamine and serotonin. The IgE allergic antibody then causes the cell membranes of the mast cells/basophils to become "leaky, " allowing their storage load of histamine and serotonin to pour into the surrounding blood and tissues. The IgE-released histamine and serotonin then produce the familiar allergic symptoms of runny, swollen nose; blocked sinuses; itchy eyes; skin blotches; coughing and wheezing; etc.

Quercetin to the rescue! Quercetin has a strong affinity for mast cells and basophils. It tends to stabilize their cell membranes, preventing them from spilling their pro-inflammatory, allergy-symptom-causing load of histamine/serotonin into the surrounding blood and tissue in response to the IgE antibody. And without the release of these potent inflammatory mediators, the familiar misery of allergies simply will not occur, even

though you've inhaled the pollen, animal hair, or whatever normally triggers allergy attacks.

Asthma is an allergic inflammation involving the lungs. During an asthma attack (which can be triggered by air- or food-borne pollen, dust, animal hair, chemicals, etc.), the millions of tiny air sacs within the lungs are constricted, seriously impairing breathing and causing a feeling of tightness in the chest. In addition to IgE-released histamine, the primary biochemical cause of the asthmatic symptoms is a group of fatty acid derivatives called leukotrienes (LTs). These asthma-causing LTs are made from arachidonic acid (a key fatty acid constituent of many cell membranes) by the action of two enzymes - phospholipase A2 and lipoxygenase. Quercetin is known to be a powerful inhibitor of both these enzymes. Thus it prevents the formation of asthma-causing LTs, even when the IgE antibody (formed in response to inhaled or swallowed allergens) is present in the lungs to stimulate LT Production and release. Since quercetin suppresses the release and/or production of the two primary inflammatory mediators–histamine and leukotrienes–that cause the actual symptoms of asthma, its potential benefit in the prevention and treatment of asthma is evident.

Quercetin is a safe, nontoxic substance. A report by I. Hirono et al in Cancer Letters (1981), for example, found no evidence of toxicity or carcinogenicity in rats, even when quercetin made up 10 percent of their total dietary intake.

Unfortunately, quercetin is barely soluble in water, so poor dietary absorption may limit its efficacy. Because of this, Murray, N.D., has suggested that quercetin be taken in combination with bromelain to improve its absorption. Bromelain is a natural, protein-digesting enzyme derived from pineapples. It has been used "to increase absorption of compounds, including antibiotics. Also, bromelain has powerful anti-inflammatory properties that synergize with quercetin. Bromelain inhibits several other common inflammatory mediators, including bradykinin and fibrin. It's widely used in sports

medicine to reduce the pain and swelling of bruises, sprains, muscle tears, etc., for this reason.

As a clinical nutritionist I have had numerous occasions to use quercetin on allergy and asthma suffers. About 1,000 to 2,000 mg. a day, divided into three to six doses, is sufficient to control most cases of allergy and many cases of asthma. I have remained virtually allergy and asthma free for several years through daily use of quercetin, and finding it much more effective for this purpose than other bioflavonoids.

Activated Quercetin - help your allergy and sinus problems

http://vitanetonline.com/forums/1/Thread/85

Most of us like to stroll through the countryside. Or play with our pets. Or eat our favorite foods. Or just stop and smell the beautiful flowers. But when our bodily systems are at odds with the natural world, these simple pleasures can be difficult to enjoy. That's why the nutrition experts at Source Naturals created ACTIVATED QUERCETIN: a truly hypoallergenic formula developed so we all can enjoy the pleasures of nature.

Quercetin: A Unique Bioflavonoid Quercetin is a unique bioflavonoid that has been extensively studied by researchers over the past 30 years. Bioflavonoids - first discovered by Nobel Prize Laureate Albert Szent-Györgyi in the 1930's - occur as pigments in plants, where they usually are found in close association with vitamin C. Together, bioflavonoids and vitamin C provide antioxidant protection, helping plants withstand harsh variations in wind, rainfall, temperature, and sunlight. Bioflavonoids also can be important to our optimal health - but they cannot be manufactured by our bodies.

Quercetin is no stranger to the human diet: for example, onions may contain up to 6% quercetin (dry weight). As a food supplement, quercetin is hypoallergenic, containing no citrus, wheat, corn, or other common allergens.

Histamine and Leukotriene Inhibition: Helping Us Enjoy the Natural World

Quercetin has a strong affinity for mast cells, the body's main storage unit for histamines. Like many other bioflavonoids, it has the ability to stabilize cell membranes, preventing histamines from spilling out of mast cells into the bloodstream and surrounding tissues. Also, quercetin helps inhibit the action of two enzymes - phospholipase A2 and lipoxygenase - which act on arachidonic acid (a key fatty acid constituent of many cell membranes) to create leukotrienes. By inhibiting the release of histamines and leukotrienes into our bloodstreams, quercetin can leave us free to enjoy the natural world.

Activated for Absorption

Quercetin's main disadvantage is that it is barely soluble in water, and therefore difficult for the body to absorb. Without biochemical help, its beneficial properties may be of very limited use to our bodies. There are lots of quercetin products on the market, but they won't do much good if the quercetin is not activated for use by the body. Source Naturals combines its quercetin with bromelain, an enzyme derived from pineapple that is known to increase the body's ability to absorb various substances. Bromelain also is known to have many of the same histamineand leukotriene-inhibiting properties as quercetin, so they enhance each others' performance. Source Naturals ACTIVATED QUERCETIN contains vitamin C in a non-acidic form, magnesium ascorbate. Studies suggest that vitamin C has a synergistic relationship with quercetin, which improves quercetin's use by the body. Since the acidic form of vitamin C (ascorbic acid) can create mild stomach irritation, and since quercetin is best taken on an empty stomach to maximize absorption, a pH-buffered form of vitamin C such as magnesium ascorbate is preferable.

Combined Excellence

Source Naturals ACTIVATED QUERCETIN is a state-of-the-art quercetin complex. With 333 mg of quercetin in each tablet, and key additional ingredients to maximize quercetin's absorption and beneficial properties, ACTIVATED QUERCETIN is a potent formula. It gives you more help - so you can enjoy nature again. Source Naturals ACTIVATED QUERCETIN is available in 50, 100 and 200-tablet bottles.

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Natural Relief from Seasonal Allergies

Every summer for the past ten years, 34-year-old Peter Vernoff has experienced the misery of hayfever. He was resigned to living with the sneezing, itchy eyes, runny nose and post-nasal drip, but when his symptoms worsened last year, Peter called on a holistic doctor for help. Also known as seasonal allergic rhinitis, hayfever is a condition that is characterized by sneezing, runny nose and itchy, teary eyes upon exposure to an allergen, in Peter's case, ragweed pollen. When pollen particles are inhaled, they become trapped in the mucous layer of the nasal passages and form allergens. This causes the immune system to respond and results in the release of enormous amounts of substances known as IgE's, white blood cells called eosinophils and inflammatory cells such as histamine, prostaglandins and leukotrienes.Peter's holistic doctor

recommended that he take the supplements quercetin and nettle leaf. He also suggested reducing consumption of foods that aggravate his symptoms and trying nasal washes.

QuercetinThe supplement quercetin is a promising treatment to control inflammation by reducing the release of histamine and other mediators of allergic reactions from cells. Quercetin is believed to work by stabilizing cell membranes so they are less reactive to allergens. Adding the supplemental enzyme bromelain increases the amount of quercetin absorbed in the digestive tract. Side effects are rare and include nausea, headache and tingling in the hands and feet.

Nettle Leaf In a double-blind, randomized study during the peak season for allergic rhinitis, an extract of the herb nettle leaf (Urtica dioica) was compared to a placebo. Ninety eight participants were given 1300 mg capsules of nettle leaf or placebo and were advised to take two capsules when symptoms began and continue for seven days. Overall assessment ratings of nettle leaf were higher than placebo, and patients reported a slight reduction in symptoms of hayfever, including sneezing and itchy eyes. This is the only research study that has been conducted on nettle leaf for allergic rhinitis, however, it has a long history of traditional use for allergies.

Food Intolerance Some researchers suggest that people who react to pollens may also have a hypersensitivity to certain foods. For example, several studies have found that people allergic to grass pollens also reacted to tomatoes, peanuts, wheat, apple, carrot, celery, peach, melon, eggs and pork. To find out which foods aggravate symptoms of allergic rhinitis in a particular individual, an elimination and challenge diet is recommended. This diet involves the removal of suspected foods from the diet for at least a week followed by systematic re-introduction of foods in order to isolate the foods that may aggravate certain symptoms.

Nasal Wash A nasal wash can help to remove inhaled pollen from the nose and prevent attachment to the mucous lining of the nose. To make a solution add a 1/4 teaspoon of salt to one cup of warm water. Use this solution to rinse the nostrils.Bend the head

forward, keeping the nostrils lower than the throat to prevent excessive salt water from draining to the back of the throat.

Other Treatments Homeopathy, acupuncture and massage are other therapies that are used to manage allergic rhinitis

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