Quercetin SAP

Science-based bioflavonoid for allergy and inflammation management

Quercetin is a bioflavonoid found in onions, apples, black tea, and grapefruit. Quercetin has antiallergic, antioxidant, and anti-inflammatory activity. Mast cells contribute to the inflammatory process in allergic reactions, where immunologic stimulation leads to degranulation of the mast cell as well as the generation of numerous cytokines and inflammatory mediators. Quercetin is an effective treatment option for allergies, as it has been shown to inhibit mast-cell secretions, and it has the ability to downregulate histamine production via inhibition of the enzyme histidine decarboxylase (HDC) mRNA from human mast cells. Quercetin also causes a decrease in the release of IL-6 and tryptase, and is known to inhibit phospholipase A_2 and 5-lipoxygenase, thereby reducing synthesis of leukotrienes and the series-2 prostaglandins via the arachidonic-acid pathway. The anti-inflammatory properties of quercetin were explored in a double-blind, placebo-controlled study on men with chronic prostatitis syndrome. The study found that after one month of treatment, 67% of men in the treatment group reported at least a 25% improvement in their pain levels.

Bromelain is a proteolytic enzyme derived from the stem of the pineapple plant. Bromelain has been found to be a mucolytic agent effective in respiratory disorders, and functions as an anti-inflammatory agent. Bromelain counteracts the fibrin and kinin pathways, which stimulate plasmin. Plasmin blocks endogenous arachidonic-acid mobilization and reduces prostaglandin synthesis, which reduces localized inflammation and edema. This is thought to be the mechanism by which bromelain helps reduce symptoms of allergic rhinitis. Bromelain may also enhance the effectiveness of quercetin.

ACTIVE INGREDIENTS

Serving Size: 1 Capsule — **Servings: 60**

	Amount Per Serving	% Daily Value
Quercetin	500 mg	**
Bromelain (*Ananas comosus*), 2400 GDU/g [3,600,000 FCC PU]	100 mg	**

** Daily value not yet established

This product is non-GMO and vegan friendly.

Contains no: Gluten, soy, wheat, eggs, dairy, yeast, citrus, preservatives, artificial flavour or colour, starch, or sugar.

WARNING: Take caution for use in patients with pineapple allergies.

DIRECTIONS FOR USE

Adults: Take 1 capsule twice daily with food in divided doses or as directed by your healthcare practitioner. Consult a healthcare practitioner for use beyond 4 weeks.

INDICATION

Quercetin SAP:

- Is an effective treatment for mild/moderate allergic reactions. It has been shown to prevent histamine release and reduce systemic inflammation, and therefore is a good proactive therapy for allergy treatment and prevention.*
- Can be used to treat chronic asthma symptoms.*
- Has anti-inflammatory properties, and can be used to treat men with chronic pelvic pain syndrome/chronic prostatitis.*

PURITY, CLEANLINESS, AND STABILITY

All ingredients listed for all **Quercetin SAP** lot numbers have been tested by a third-party laboratory for identity, potency, and purity.

*** These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.**

Scientific Advisory Panel (SAP): adding nutraceutical research to achieve optimum health

NFH®

351, Rue Joseph-Carrier, Vaudreuil-Dorion, Quebec, J7V 5V5
T 1 866 510 3123 • F 1 866 510 3130 • nfh.ca

For healthcare professional use only.

ALLERGIES AND MAST CELLS

The IgE receptor plays a key role in inducing an allergic reaction. When a mast cell is exposed to an antigen, it binds to the IgE receptor and causes degranulation, leukotriene and prostaglandin secretion, and cytokine production.[1] While mast cells are found throughout the body, they are found in high concentrations in connective tissue of the respiratory tract and nasal mucosa, and in blood vessels.[2] Degranulation of mast cells accounts for almost 50% of symptoms of nasal rhinitis through the release of histamine.[2] This degranulation also leads to symptoms that can include nasal congestion, sneezing, itching, inflammation, conjunctivitis, hives, throat irritation, vasodilation, increased capillary permeability, and smooth-muscle contraction. Allergy symptoms can be caused by a variety of sources such as environmental sources, foods, medications, and metabolic conditions. Studies on allergy sufferers demonstrate that during symptoms, there is a decline in the ability to perform daily activities and a measurable decline in physical and mental health status.[2] Typical treatments of allergies include antihistamines, decongestants, anticholinergic agents, and corticosteroid drug therapy, alone or in combination; these can lead to adverse side effects including sedation, impaired learning/memory, and cardiac arrhythmias.[2]

QUERCETIN FOR ALLERGIES

Quercetin is an effective treatment option for allergies, as it has been shown to inhibit mast-cell secretion and has the ability to downregulate histidine decarboxylase (HDC) mRNA from human mast cells.[3] Quercetin inhibits the inflammatory process that is regulated by an increased release in neutrophils. The release of neutrophils leads to the destabilization of mast cells and their subsequent release of histamine and leukotrienes.[2] By preventing the release of neutrophils, quercetin is therefore able to add stability to the mast-cell membrane, to help prevent degranulation and subsequent allergy symptoms. A placebo-controlled study performed by Hirano et al. (2009), in which subjects received 100 mg/d quercetin, demonstrated a reduction in allergic symptoms including congestion, lacrimation and itching, and a reduction in use of other allergy medications when compared to controls.[4]

QUERCETIN FOR ASTHMA

In a mouse model, quercetin was dosed between 3 and 10 mg/kg and worked in a dose-dependent manner to inhibit eosinophil recruitment to the bronchoalveolar lavage fluid, and also significantly reduced both IL5 and IL4 levels. Quercetin also reduced P-selectin expression and the mucus production in the lung.[5] These findings suggest the potential of therapeutic treatment of inflammatory airway diseases using quercetin.[5]

QUERCETIN FOR CHRONIC PROSTATITIS

In a double-blind, placebo-controlled study by Shoskes et al. (1999), male subjects with chronic pelvic pain were randomly assigned to either placebo group or to receive 500 mg of quercetin twice a day.[6] Pain was then evaluated before the study commenced and after 1 month, using the NIH chronic prostatitis symptom score. 67% of patients taking quercetin had a statistically significant improvement in symptoms of at least 25%.[6] An unblinded follow-up arm of this study was also performed where participants received quercetin with bromelain and papain for one month, and 82% of these patients demonstrated an improvement in symptoms of at least 25%.[6]

A separate randomized, double-blind, placebo-controlled trial was also performed to test the efficacy of quercetin in men with chronic prostatitis (CP). This study assessed 30 men with CP to receive quercetin, 500 mg twice daily, or the placebo pill for 1 month.[7] Significant change in the NIH-CPSI score was observed in the quercetin group (p = 0.003) versus the placebo group, who had an insignificant mean improvement in the NIH-CPSI score.[7] These 2 trials indicate that quercetin is a viable treatment option for men suffering from chronic prostatitis.

BROMELAIN

Bromelain has been found to be a mucolytic agent in respiratory disorders, and works as an anti-inflammatory. Bromelain counteracts the fibrin and kinin pathways, which stimulates plasmin. Plasmin blocks endogenous arachidonic acid by prostaglandins, which reduces localized edema.[2] Bromelain also has a long-term effect of inhibiting the firm adhesion of leukocytes to blood vessels at the site of inflammation, which also reduces edema.[9] A study performed by Secor et al. (2005) dosed mice with 2 g/kg or 6 g/kg of bromelain twice a day for 4 d and resulted in attenuated development of allergic airway disease while altering $CD4^+$ to $CD8^+$ T-lymphocyte populations.[8] The reduction in allergic airway disease outcomes suggests that bromelain may have similar effects in the treatment of human asthma and hypersensitivity disorders.[9] Bromelain has also shown the ability to enhance the absorption and therefore the effectiveness of quercetin.[2, 6]

SAFETY

Both bromelain and quercetin have an excellent safety profile, with minimal toxicity pictures. Bromelain demonstrates very low toxicity with an LD_{50} greater than 10 g/kg.[10] Due to the efficacy of bromelain after oral administration, its safety and lack of undesired side effects, it has high compliance among patients.[11] Since bromelain is derived from the stem of pineapple, caution must be taken in patients with pineapple allergy. Caution should also be taken in patients using heparin, because in the study by Grabovac et al. (2006), evidence was found that heparin and bromelain form stable complexes leading to a significantly improved uptake of heparin, which could have an impact on blood-thinning potential.[12] Quercetin has an LD_{50} of 159 mg/kg in a mice model orally before reaching toxicity.[13]

REFERENCES

1. Takahashi, K. "Interaction between the intestinal immune system and commensal bacteria and its effect on the regulation of allergic reactions." *Bioscience, Biotechnology, and Biochemistry* Vol. 74, No. 4 (2010): 691–695.
2. Thornhill, S.M. and A.M. Kelly. "Natural treatment of perennial allergic rhinitis." *Alternative Medicine Review* Vol. 5, No. 5 (2000): 448–454.
3. Kempuraj, D., et al. "Inhibitory effect of quercetin on tryptase and interleukin-6 release, and histidine decarboxylase mRNA transcription by human mast cell-1 cell line." *Clinical and Experimental Medicine* Vol. 6, No. 4 (2006): 150–156.
4. Hirano, T., et al. "Preventative effect of a flavonoid, enzymatically modified isoquercitrin on ocular symptoms of Japanese cedar pollinosis." *Allergology International* Vol. 58, No. 3 (2009): 373–382.
5. Rogerio, A.P., et al. "Anti-inflammatory effect of quercetin-loaded microemulsion in the airways allergic inflammatory model in mice." *Pharmacological Research* Vol. 61, No. 4 (2010): 288–297.
6. Shoskes, D.A., et al. "Quercetin in men with category III chronic prostatitis: a preliminary prospective, double-blind, placebo-controlled trial." *Urology* Vol. 54, No. 6 (1999): 960–963.
7. Capodice, J.L., et al. "Complementary and alternative medicine for chronic prostatitis/chronic pelvic pain syndrome." *Evidence-based complementary and alternative medicine* Vol. 2, No. 4 (2005): 495–501.
8. Secor, E.R. Jr, et al. "Bromelain exerts anti-inflammatory effects in an ovalbumin-induced murine model of allergic airway disease." *Cellular Immunology* Vol. 237, No. 1 (2005): 68–75.
9. Fitzhugh, D.J., et al. "Bromelain treatment decreases neutrophil migration to sites of inflammation." *Clinical Immunology* Vol. 128, No. 1 (2008): 66–74.
10. Kelly, G.S. "Bromelain: A literature review and discussion of its therapeutic applications." *Alternative Medicine Review* Vol. 1, No. 4 (1996): 243–257.
11. Maurer, H.R. "Bromelain: biochemistry, pharmacology and medical use." *Cellular and Molecular Life Sciences* Vol. 58, No. 9 (2001): 1234–1245.
12. Grabovac, V. and A. Bernkop-Schnürch. "Improvement of the intestinal membrane permeability of low molecular weight heparin by complexation with stem bromelain." *International Journal of Pharmaceutics* Vol. 326, No. 1–2 (2006): 153–159.
13. MDS data sheet for quercetin • https://fscimage.fishersci.com/msds/56284.htm

Quercetin SAP

*Science-based bioflavonoid for allergy and inflammation management**

INDICATION SPECIFIC DOSAGE SUMMARY BASED ON HUMAN CLINICAL RESEARCH#

#Please note these suggestions are guidelines based on the clinical studies. Evidence for efficacy and safety have been qualitatively (study quality in terms of study design, sample size, appropriate methods of analysis, use of appropriate placebo/control, bias) assessed and have been rated using a 5 star ★ rating classification.

*** These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.**

Indication	Suggested Dosage	Supporting evidence and study outcomes	Study design	Outcomes measures/ selection criteria for studies	Safety	Evidence quality rating
Pulmonary Diseases						
SARS-Cov-2 infection[1]	1 capsule/day	Reduced the hospitalization period*	Randomized open label control study, n=60, dose = 1000 mg/day for 1 week. Patients in the intervention group received quercetin in addition to remdesivir or favipiravir	Peripheral blood samples, serum levels of interleukin 1 beta, tumor necrosis factor alpha (TNF α), and interleukin-6 cytokines	No adverse events were reported	★★★
COPD and URTI[2,3]	2 capsules/ day	Lowered severity of URTI*	2 Randomised, double-blind, placebo-controlled, single-centre dose-escalation studies, n=1012, avg dose = 1250 mg/day for 1-12 weeks	Wisconsin upper respiratory symptom survey, total plasma quercetin and its primary conjugates, COPD assessment test	Adverse events were gastro-esophageal reflux disease, stomach upset, breathlessness, chest congestion, headache, and nausea	★★★★
Oxidative Stress						
Inflammation in sarcoidosis[4]	2 capsules/ day	Reduced markers of oxidative stress and inflammation*	Double-blind intervention study, n=18, dose = 2000 mg/day	Forced expiratory volume, forced vital capacity and diffuse capacity for carbon monoxide, plasma antioxidant status, vitamin C, uric acid, total glutathione, TNF-α, interleukin-8, and interleukin-6.	No adverse events were reported	★★
Exercise in humans[5]	2 capsules/ day	Improved oxidative stress*	Randomized, crossover, intervention study, n=14, dose = 1000 mg/day for 2 weeks.	Hemolysis assay, glutathione homeostasis, thiobarbituric acid reactive substances, intracellular superoxide dismutase, catalase and glutathione peroxidase activities	No adverse events were reported	★★
Muscular Function						
Muscle Damage[6,7]	2 capsules/ day	Improved muscle weakness and enhanced recovery*	2 Randomized, double-blind, crossover studies, n=24, avg dose = 1000 mg/ day for 2 weeks.	Neuromuscular tests, maximal voluntary isometric contractions, force–velocity relationship task, creatine kinase, interleukin-6, insulin-like growth factor (IGF-1 & IGF-II) levels	No adverse events were reported	★★★
Neuromuscular function[8]	2 capsules/ day	Accelerated the recovery of neuromuscular function*	Double-blind, placebo-controlled, crossover study, n=16, dose = 1000 mg/day for 2 weeks	Neuromuscular test, maximal voluntary isometric contraction, and force-velocity relationship	No adverse events were reported	★★★
Cardiovascular Health						
MI[9]	1 capsule/day	Enhanced total antioxidant capacity and improved the insecurity dimension of quality of life*	Randomized double-blind, placebo-controlled trial, n=88, dose = 500 mg/day for 8 weeks	Body weight, BMI, body fat percentage, muscle mass percentage, visceral fat and blood pressure, 2-day food recall questionnaire, quality of life assessment, myocardial infarction and dimensional assessment scale	No adverse events were reported	★★★
Hypertension[10]	1 capsule/day	Reduced systolic blood pressure and plasma, oxidized low-density lipoprotein concentrations*	Randomized, double-blind, placebo-controlled, crossover study, n=41, dose = 730 mg/day for 4 weeks	Blood pressure measurement, blood lipid, glucose, urine collection, indices of oxidative stress, urinary isoprostane measurement, dietary analysis	No adverse events were reported	★★★

Women's Health						
Metabolic and Hormonal Parameters (PCOS)[11, 12]	2 capsules/ day	Significant changes in lowering major contributors of PCOS*	2 Randomized, double-blind, placebo-controlled trials, n = 79, avg dose = 1000 mg/day for 12 weeks	Glucose homeostasis, circulatory testosterone, luteinizing hormone, sex hormone-binding globulin, and anthropometric measurements, fasting serum levels of total adiponectin, high-molecular-weight (HMW) adiponectin	No adverse effects were reported	★★★★
Rheumatoid Arthritis[13]	1 capsule/day	Reduced clinical symptoms, and pain*	Double-blind, placebo-controlled randomized clinical trial, n=50, dose = 500 mg/day for 8 weeks.	Physician global assessment, disease activity score–28, validated HAQ, plasma hs-TNFα	No adverse events were reported	★★★★
Men's Health						
Pre-hyperuricaemic males[14]	1 capsule/day	Lowered plasma uric acid levels*	Randomized, double-blinded, placebo-controlled, cross-over trial, n=22, dose = 500 mg/day for 4 weeks.	Plasma glucose level, uric acid in plasma and urine samples	No adverse events were reported	★★★
Prostatitis[15]	1 capsule/day	Significant symptomatic reductions* In the open-label study with 17 patients who received a supplement containing quercetin, bromelain, and papain, 82% had at least a 25% improvement in symptom score*	Randomized double-blinded, placebo-controlled trial, n=30, dose = 500 mg/day for 4 weeks In a follow-up unblinded, open-label study, 17 additional men received a supplement containing quercetin, bromelain, and papain (amounts unknown) to enhance bioflavonoid absorption for 4 weeks	Chronic prostatitis symptom score	No adverse events were reported	★★ ★★ (For the open-label follow up study)
Thalassemia						
Iron overload and inflammation[16]	1 capsule/day	Removed excess iron, ferritin, hs-CRP, transferrin saturation, and increased transferrin*	Randomized placebo-controlled trial, n=84, dose = 500 mg/day for 12 weeks	TNF-α hemoglobin, serum iron, ferritin, transferrin, total iron binding capacity, transferrin saturation, and high sensitivity C-reactive protein	Some gastro-intestinal events were reported	★★★
Antiviral						
Chronic Hepatitis C[17]	1 capsule/day	Decrease in hepatitis C virus*	Phase 1 dose escalation study, n=30, dose = 250-5000 mg/day for 4 weeks	Aspartate aminotransferase (AST) and alanine aminotransferase (ALT), Alkaline phosphate, total bilirubin, direct bilirubin, prothrombin time, partial thromboplastin time, international normalized ratio, hepatitis C viral load, and cholesterol panel	No adverse events were reported	★★

References:

1. Mojtaba et al. "The therapeutic efficacy of quercetin in combination with antiviral drugs in hospitalized COVID-19 patients: A randomized controlled trial." *Eur J Pharmacol*. (2022 Jan 5): 914-174615.
2. Serena A. Heinz, et al. "Quercetin supplementation and upper respiratory tract infection: A randomized community clinical trial." *Pharmacol Res*. Vol. 42, No. 3 (2010 Sep): 62-237.
3. Meilan K. et al. "Randomized clinical trial to determine the safety of quercetin supplementation in patients with chronic obstructive pulmonary disease." *BMJ Open Respir Res*. No. 1 (2020 Feb): 7-e000392.
4. Agnes W. Boots, et al. "Quercetin reduces markers of oxidative stress and inflammation in sarcoidosis." *Clin Nutr*. Vol. 12, No. 4 (2011 Aug): 30-506.
5. Duranti G., et al. "Chronic consumption of quercetin reduces erythrocytes oxidative damage: Evaluation at resting and after eccentric exercise in humans." *Nutr Res*. Vol. 81 (2018 Feb): 50-73.
6. Ilenia Bazzucchi., et al. "The effects of quercetin supplementation on eccentric exercise-induced muscle damage." *Nutrients*. No. 1 (2019 Jan 21): 11-205.
7. Paolo Sgrò., et al. "Quercetin modulates IGF-I and IGF-II levels after eccentric exercise-induced muscle-damage: A placebo-controlled study." *Front Endocrinol (Lausanne)*. (2021 Nov 3): 12-745959.
8. Ilenia Bazzucch., et al. "Quercetin supplementation improves neuromuscular function recovery from muscle damage." *Nutrients*. No. 9 (2020 Sep 17): 12-2850.
9. Fereshteh Dehghani., et al. "Effects of quercetin supplementation on inflammatory factors and quality of life in post-myocardial infarction patients: A double blind, placebo-controlled, randomized clinical trial." *Phytother Res*. Vol. 2098, No. 4 (2021 Apr): 35-2085.
10. Randi L. Edwards, et al. "Quercetin reduces blood pressure in hypertensive subjects." *J Nutr*. Vol. 11, No. 11 (2007 Nov): 137-2405.
11. Masoud Khorshidi., et al. "The effects of quercetin supplementation on metabolic and hormonal parameters as well as plasma concentration and gene expression of resistin in overweight or obese women with polycystic ovary syndrome." *Phytother Res*. Vol. 2289, No. 11 (2018 Nov): 32-2282.
12. Rezvan N., et al. "Effects of quercetin on adiponectin-mediated insulin sensitivity in polycystic ovary syndrome: A randomized placebo-controlled double-blind clinical trial." *Horm Metab Res*. Vol. 121, No. 2 (2017 Feb): 49-115.
13. Fatemeh Javadi, et al. "The effect of quercetin on inflammatory factors and clinical symptoms in women with rheumatoid arthritis: A double-blind, randomized controlled trial." *J Am Coll Nutr*. Vol. 15, No. 1 (2017 Jan): 36-9.
14. Shu, Y. & Williamson, G. "Quercetin lowers plasma uric acid in pre-hyperuricaemic males: a randomized, double-blinded, placebo-controlled, cross-over trial." *Br J Nutr*. Vol. 6, No. 5 (2016 Mar 14): 115-800.
15. Daniel A. Shoskes, et al. "Quercetin in men with category III chronic prostatitis: a preliminary prospective, double-blind, placebo-controlled trial." *Urology*. Vol. 3, No. 6 (1999 Dec): 54-960.
16. Zohreh Sajadi Hezaveh, et al. "The effect of quercetin on iron overload and inflammation in β-thalassemia major patients: A double-blind randomized clinical trial." *Complement Ther Med*. Vol. 28 (2019 Oct): 46-24.
17. Lu N.T., et al. "A phase I dose escalation study demonstrates quercetin safety and explores potential for bioflavonoid antivirals in patients with chronic hepatitis C." *Phytother Res*. Vol. 8, No. 1 (2016 Jan): 30-160.