

Case Report

Evaluation of Quercetin Phytosome™ and Zinc in Supporting Subjects with Chronic Allergic and Non-Allergic Rhinitis

Paolo Gamba*

Department of Otorhinolaryngology-Head and Neck Surgery LAB of Clinical and Instrumental Vestibology Poliambulanza Foundation Hospital, Italy

***Corresponding author:** Gamba P, Department of Otorhinolaryngology-Head and Neck Surgery LAB of Clinical and Instrumental Vestibology, Poliambulanza Foundation Hospital, Italy.

Email: paolo-gamba@libero.it

Received: November 27, 2024; **Accepted:** December 17, 2024; **Published:** December 24, 2024**Abstract**

The aim of this study is to evaluate the possible benefit of Quercimimun (quercetin Phytosome™, a quercetin formulated as phospholipid Phytosome™ and zinc), in subjects with Chronic Allergic and Non-allergic Rhinitis, in order to alleviate symptoms. All enrolled subjects were supplemented with Quercimimun, 2 tablets/day for 60 days. The retrospective anamnestic and clinical-instrumental analysis of 36 enrolled subjects led to the subdivision of 3 groups: 12 mild chronic allergic rhinitis (according to ARIA), 12 vasomotor non allergic rhinitis, and 12 chronic drugs induced rhinitis (decongestive nasal therapy abuse).

Monitoring was carried out at baseline and after 60 days of supplementation. The statistical evaluation of symptoms such as nasal obstruction, rhinorrhea, sneezing was carried out by associating a score according to the severity of the symptoms. Quercimimun was effective in alleviating symptoms after 60 days supplementation, confirming the beneficial properties of quercetin, proposing its use as a support aid in nasal-sinus disorders, especially of allergic origin.

Keywords: Rhinitis; Quercetin; Phytosome**Introduction**

Allergic Rhinitis (AR) should not be considered as an organ pathology, it should be interpreted as an immune-mediated systemic disease that shares common pathophysiological mechanisms with other allergic pathologies, such as asthma, allergic conjunctivitis, food allergies and atopic dermatitis, all of which recognize a type 2 immunopathological mechanism. The worldwide prevalence of rhinitis can be estimated by about 30% [1,2]. Although in most cases rhinitis is not a serious disease, it negatively affects social life at work and at school. Chronic Allergic Rhinitis, according to the Allergic Rhinitis and its Impact on Asthma guidelines [3], is classified based on symptoms duration: Intermittent when the symptoms last less than 4 days a week, or less than 4 weeks; when the symptoms occur for more than 4 days or for more than 4 weeks then the rhinitis is persistent [4,5]. Based on the symptoms, it can be divided into Mild and Moderate/Severe, when there is an alteration in daily activities. From the literature it can be seen that rhinitis and asthma in allergic subjects constitute different clinical aspects of a single immune-mediated disorder of the respiratory system. It is estimated that approximately 85% of subjects with allergic asthma also have chronic rhinitis [6,7]. A significant portion of subjects with allergic rhinitis manage themselves with OTC (Over-The-Counter) drugs and do not consult their doctors, so they fall into a condition of uncontrolled

rhinitis, Sever Chronic Upper Airways Disease [8,9]. In subjects suffering from seasonal or perennial rhinitis with moderate/severe symptoms, it is recommended the association of topical corticosteroid and antihistaminic, or topical corticosteroids alone [10]. Vasomotor non-allergic rhinitis, characterized by an abnormal dilation of the blood vessels of the nasal mucosa, which can create a marked nasal obstruction, was caused by non-allergic non-infectious triggers, such as strong odors, humidity, temperature changes, barotraumatic pressure, alcohol exposure [11]. The pathophysiologic explanation behind that rhinitis type is still not yet well understood, although the most known theories are the following: autonomic sino-nasal imbalance, nociceptive nerve dysfunction, neurogenic inflammatory reflex [12]. A third type of rhinitis, called chronic drugs induced rhinitis is due to excessive and prolonged use of decongestant drugs, such as phenylephrine or oxymethazoline, that led to a persistent nasal constriction, altered vascular permeability and edema [13]. The main symptoms of Allergic and Non-Allergic Chronic Rhinitis are nasal obstruction, watery rhinorrhea, sneezing and nasal itching. Often there may be concomitant ocular symptoms, anosmia and sometimes also epistaxis. Natural substances, like polyphenols, can be of support to the rhinitis management [14]. The most widespread polyphenols in nature are flavonoids. The flavonoid quercetin

shows antihistamine activity, reducing the secretion of histamine by the mast cells and inhibiting the production of IgE, responsible for allergic symptoms [15]. Quercetin inhibits tyrosine kinase, an enzyme that activates macrophages, which among many activities also produce pro-inflammatory cytokines. It has been described that the optimized form of quercetin, formulated with phospholipids according to Phytosome™ technology, supplemented for 30 days, significantly ameliorated symptoms in asthmatic subjects [16], and that a preventive administration to healthy subjects reduced the allergy symptoms induced by histamine injection [17]. Quercetin act also as zinc ionophores, transporting cations across the plasma membrane. Zinc is an important element for the correct functioning of the immune system and the protection of cells from oxidative stress [3]. The incidence of respiratory infections was reduced by zinc supplementation [18]. Quercetin from *Sophora Japonica*, in association with phospholipids according to Phytosome technology, and in presence of zinc (Quercimmun™), was utilized in the present study to evaluate its possible benefit in subjects with Chronic Allergic and Non-Allergic Rhinitis.

Methods

Population

36 subjects (19:M;17:F), aged between 18 and 71 years, were enrolled and were supplemented by Quercimmun™, 2 tablets/day for 60 days. The retrospective anamnestic and clinical-instrumental analysis led to the subdivision of the 36 subjects enrolled into 3 groups: 12 mild chronic allergic rhinitis (according to ARIA), 12 vasomotor non-allergic rhinitis, and 12 chronic drugs-induced rhinitis (decongestive nasaltherapy abuse). The group chronic allergic rhinitis (seasonal moderate-severe) simultaneously was treated with budesonide nasal spray 2 puffs/day/100 µg in association with Desloratadine 5 mg, 1 tablet/day. The evaluation of symptoms (nasal obstruction, rhinorrhea, sneezing) was carried out by associating a score according to severity (grade: 0 absent; 1: mild; 2: moderate; 3 severe). Monitoring was carried out at baseline (T0), and at time 1 (T60) after 60 days of supplementation.

Supplement

Quercimmun™ tablets (Scharper, SpA), containing 250 mg Quercetin phospholipids formulated by the Phytosome™ technique (Indena, SpA), and 5 mg of zinc, were administered twice a day for 60 days.

Statistical Analysis

Data were initially tested for normality using the D'Agostino and Pearson test. As they were not normally distributed, data were then analyzed by Wilcoxon test.

Results

A progressive reduction in the scores can be seen from the baseline visit (T0) to the control after 60 days (T60) of supplementation in subjects with Allergic Rhinitis (Figure 1), non-allergic vasomotory rhinitis (Figure 2) and Chronic Drugs-induced Rhinitis (Figure 3); parameters evaluated are nasal obstruction (A), rhinorrhea (B) and sneezing (C). The present study finds that subjects had a significant clinical improvement in nasal obstruction and rhinorrhea in all the

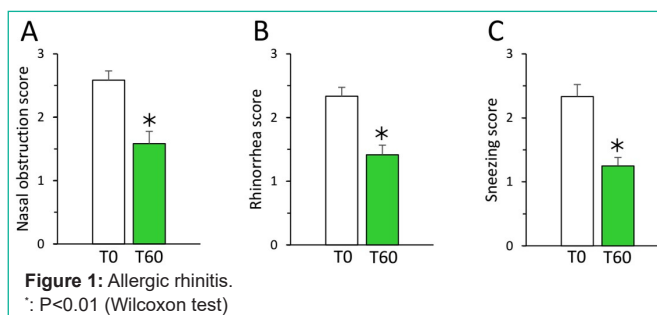


Figure 1: Allergic rhinitis. *: P<0.01 (Wilcoxon test)

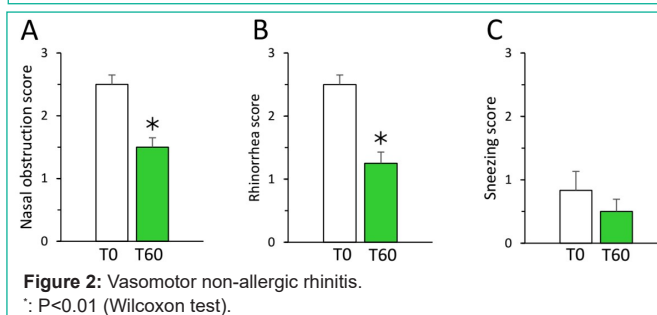


Figure 2: Vasomotor non-allergic rhinitis. *: P<0.01 (Wilcoxon test).

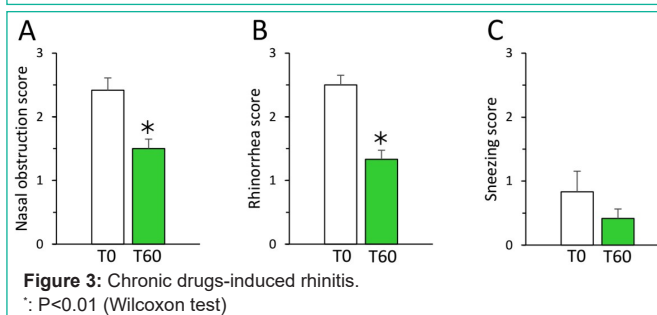


Figure 3: Chronic drugs-induced rhinitis. *: P<0.01 (Wilcoxon test)

three rhinitis types, while sneezing were significantly reduced only in allergic rhinitis. No side effects occurred during all the study.

Discussion

Different types of rhinitis were described in literature, and can be classified as allergic, vasomotor and chronic drugs induced rhinitis, as discussed in the Introduction. Pharmacological approach mainly utilizes oral antihistamines and/or nasal corticosteroids. Quercetin belongs to the family of flavonoids, of vegetal extraction with antihistamine activity, reduces the secretion of histamine by the mast cells and inhibits the production of IgE, responsible for allergic symptoms [19,20]. Quercetin has proven to be a valid natural aid with anti-inflammatory, anti-histaminic and anti-oxidant action, proposing its use as a therapeutic aid in nasal-sinus pathologies, especially of allergic origin [20-23]. Recent studies have underlined how in subjects with RA it is common to find dysbiosis, i.e. a microbiota alteration both at a respiratory and enteric level [24]. This concept is the basis of the use of natural substances that can re-establish a condition of eubiosis, and quercetin was shown able to ameliorate dysbiosis [25]. In order to overcome the low absorption of quercetin, formulation studies by using phospholipid Phytosome™ technique allowed to obtain a highly significant improvement in absorption after oral supplementation to human healthy volunteers [26]. Quercetin Phytosome™ has demonstrated no interaction with platelet, oral anti-coagulant and anti-diabetic drugs [27]. Previous

studies using quercetin Phytosome™ showed a significant reduction of daytime and nighttime symptoms, decreasing the use of inhalers and improving the rhinitis score [16]. Another study in subjects with allergic symptoms of pollinosis, not requiring drug treatment, demonstrated that in the first and fourth week after starting of taking quercetin Phytosome™, allergic symptoms such as itchy eyes, sneezing, nasal secretions and sleep disturbances significantly improved compared to the placebo group. Furthermore, based on the responses of the Visual Analogue Scale (VAS), the quality of life of these subjects is significantly improved [20]. Zinc is a fundamental trace element playing crucial roles in cellular metabolism. It acts by binding a wide range of proteins, thus affecting a broad spectrum of biological processes, which include cell division, growth and differentiation. In addition, zinc has extensive roles in both the adaptive (specific) and the innate (non-specific) immune response at multiple levels, including gene expression as well as differentiation and development of immune cells that either affects the cells [28]. On the basis of those evidence, in the present study we have utilized quercetin Phytosome™ in association with zinc.

Conclusion

The results of our study confirm the data present in the literature relating to the activity of quercetin, proposing its use as an aid in nasal-sinus forms. The improvement in symptoms observed after 60 days supplementation, confirms that Quercimmun is effective and safe as an adjuvant support of allergic and vasomotor rhinitis, and also in chronic drug-induced rhinitis. While the improvement in nasal obstruction and rhinorrhea was detected in all the three rhinitis types, sneezing was significantly reduced only in allergic rhinitis. The reasons for that difference could be investigated in a future study. These promising results, however, must be considered preliminary, given the absence of a control group, not foreseen by the study design, and require further confirmation through randomized controlled trials with adequate numbers.

Author Statements

Acknowledgement

We would like to express our gratitude to Dr. Paola Misiano for her valuable editorial support and Dr. Mauro A.M Carai for statistical analysis.

References

- Savouré M, Bousquet J, Jaakkola JJK, Jaakkola MS, Jacquemin B, Nadif R. Worldwide prevalence of rhinitis in adults: A review of definitions and temporal evolution. *Clin Transl Allergy*. 2022; 12: e12130.
- Pawankar R. Allergic diseases and asthma: a global public health concern and a call to action. *World Allergy Organ J*. 2014; 7: 12.
- Passalacqua G, Cecchi L, Canonica G, Lombardi C. ARIA (Allergic Rhinitis and its Impact on Asthma). 2019.
- Brožek JL, Bousquet J, Agache I, Agarwal A, Bachert C, Bosnic-Anticevich S, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines-2016 revision. *J Allergy Clin Immunol*. 2017; 140: 950-8.
- Bousquet J, Van Cauwenberge P, Bachert C, Canonica GW, Demoly P, Durham SR, et al. Requirements for medications commonly used in the treatment of allergic rhinitis. *European Academy of Allergy and Clinical Immunology (EAACI), Allergic Rhinitis and its Impact on Asthma (ARIA), Allergy*. 2003; 58: 192-7.
- lordache A, Balica NC, Horhat ID, Morar R, Tischer AA, Milcu AI, et al. A Review Regarding the Connections between Allergic Rhinitis and Asthma - Epidemiology, Diagnosis and Treatment. *Curr Health Sci J*. 2023; 49: 5-18.
- Leynaert B, Neukirch F, Demoly P, Bousquet J. Epidemiologic evidence for asthma and rhinitis comorbidity. *J Allergy Clin Immunol*. 2000; 106: S201-5.
- Ciprandi G, Ricca V, Paola F, Alessandra B, Riccio AM, Milanese M, et al. Duration of antiinflammatory and symptomatic effects after suspension of intranasal corticosteroid in persistent allergic rhinitis. *Eur Ann Allergy Clin Immunol*. 2004; 36: 63-6.
- Trincianti C, Tosca MA, Ciprandi G. Updates in the diagnosis and practical management of allergic rhinitis. *Expert Rev Clin Pharmacol*. 2023; 16: 669-76.
- Linton S, Hossenbaccus L, Ellis AK. Evidence-based use of antihistamines for treatment of allergic conditions. *Ann Allergy Asthma Immunol*. 2023; 131: 412-20.
- Pattanaik D, Lieberman P. Vasomotor rhinitis. *Curr Allergy Asthma Rep*. 2010; 10: 84-91.
- Baraniuk JN. Pathogenic mechanisms of idiopathic nonallergic rhinitis. *World Allergy Organ J*. 2009; 2: 106-14.
- Birinci M, Ozdemir D, Pusuroglu M, Sevim Ö, Yemiş T, Cihan SN, et al. Rhinitis medicamentosa and substance addiction. *Eur Arch Otorhinolaryngol*. 2024; 281: 5255-9.
- Dębińska A, Sozańska B. Dietary Polyphenols-Natural Bioactive Compounds with Potential for Preventing and Treating Some Allergic Conditions. *Nutrients*. 2023; 15: 4823.
- Gamba P, Lombardi C. Eosinophil fungal rhinosinusitis caused by *Fusarium* infection secondary to odontogenic maxillary sinus disease: when collaboration between otolaryngologist and allergologist leads to the correct diagnosis and therapy. *Eur Ann Allergy Clin Immunol*. 2017; 49: 138-42.
- Cesarone MR, Belcaro G, Hu S, Dugall M, Hosoi M, Ledda A, et al. Supplementary prevention and management of asthma with quercetin phytosome: a pilot registry. *Minerva Med*. 2019; 110: 524-9.
- Belcaro G, Cesarone MR, Scipione C, Scipione V, Dugall M, Hu S, et al. Quercetin Phytosome reduces the wheal response to histamine injection. *ESPERIENZE DERMATOLOGICHE - DERMATOLOGICAL EXPERIENCES-MINERVA MEDICA*. 2020; 22: 5-9.
- Skalny AV, Rink L, Ajsuvakova OP, Aschner M, Gritsenko VA, Alekseenko SI, et al. Zinc and respiratory tract infections: Perspectives for COVID-19 (Review). *Int J Mol Med*. 2020; 46: 17-26.
- Gani F, Lombardi C, Bonizzoni G, Rolla G, Brussino L, Landi M, et al. The Characteristics of Severe Chronic Upper-Airway Disease (SCUAD) in Patients with Allergic Rhinitis: A Real-Life Multicenter Cross-Sectional Italian Study. *Int Arch Allergy Immunol*. 2019; 178: 333-7.
- Yamada S, Shirai M, Inaba Y, Takara T. Effects of repeated oral intake of a quercetin-containing supplement on allergic reaction: a randomized, placebo-controlled, double-blind parallel-group study. *Eur Rev Med Pharmacol Sci*. 2022; 26: 4331-45.
- Meltzer E, Ratner P, Bachert C, Carr W, Berger W, Canonica GW, et al. Clinically relevant effect of a new intranasal therapy (MP29-02) in allergic rhinitis assessed by responder analysis. *Int Arch Allergy Immunol*. 2013; 161: 369-77.
- Lohia S, Schlosser RJ, Soler ZM. Impact of intranasal corticosteroids on asthma outcomes in allergic rhinitis: a meta-analysis. *Allergy*. 2013; 68: 569-79.
- Moriconi P, Marinelli A. Rinite allergica e stagionalità. *ARGOMENTI DI ACTA OTORHINOLARYNGOLOGICA ITALICA*. 2020: 8-12.
- Hu Y, Zhang R, Li J, Wang H, Wang M, Ren Q, et al. Association Between Gut and Nasal Microbiota and Allergic Rhinitis: A Systematic Review. *J Asthma Allergy*. 2024; 17: 633-51.

25. Zhao L, Zhu X, Xia M, Li J, Guo AY, Zhu Y, et al. Quercetin Ameliorates Gut Microbiota Dysbiosis That Drives Hypothalamic Damage and Hepatic Lipogenesis in Monosodium Glutamate-Induced Abdominal Obesity. *Front Nutr.* 2021; 8: 671353.
26. Riva A, Ronchi M, Petrangolini G, Bosisio S, Allegrini P. Improved Oral Absorption of Quercetin from Quercetin Phytosome®, a New Delivery System Based on Food Grade Lecithin. *Eur J Drug Metab Pharmacokinet.* 2019; 44: 169-77.
27. Riva A, Corti A, Belcaro G, Cesarone MR, Dugall M, Vinciguerra G, et al. Interaction study between antiplatelet agents, anticoagulants, diabetic therapy and a novel delivery form of quercetin. *Minerva Cardioangiol.* 2019; 67: 79-83.
28. Grüngreiff K, Reinhold D, Wedemeyer H. The role of zinc in liver cirrhosis. *Ann Hepatol.* 2016; 15: 7-16.