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Clinical Evidence and Formulation Value of an NVTIA Quercetin-Eucalyptus Oil Layered Respiratory Support System

Jabar Yassine*, Gregg L. Semenza, Liam O'Connor

World Food Supplement Association, New York, USA

* Corresponding Author: info@wfsas.org

Abstract

Background: Respiratory-support compositions that aim to reduce cough, sputum burden, airway irritation, and post-inflammatory discomfort often fail in practice because volatile ingredients are lost during storage, enzyme components are inactivated in gastric acid, and multi-ingredient formulas disperse poorly in vivo. Methods: We examined a seven-ingredient NVTIA composition containing quercetin, eucalyptus oil, bromelain, dihydromyricetin, perillaldehyde, icariin, and ultra-low-molecular-weight sodium hyaluronate. We summarized the formulation-level dataset associated with this composition and then searched public clinical literature through March 2026 for randomized or controlled human studies and systematic reviews relevant to quercetin, cineole/eucalyptus, bromelain, hyaluronan, and Perilla-derived respiratory or airway-related outcomes. Results: The formulation-level dataset showed bromelain activity retention of 98.1%-98.5% after 2 h in simulated gastric-acid conditions versus 6.8% in a simple comparator, and 6-month total active retention of 95.8%-96.3% at 25 °C versus 32.5% in comparator material. Among public human studies, cineole showed the strongest direct respiratory signal: symptom scores improved significantly in acute rhinosinusitis and acute bronchitis, and 6-month concomitant therapy reduced COPD exacerbation burden while improving asthma-related multi-criteria outcomes. Quercetin was safely tolerated up to 2000 mg/day in COPD, and a later pilot phase II study reported reductions in inflammatory and oxidative stress markers, but broad symptom efficacy remains inconsistent across populations. Perilla-derived clinical evidence supported improvement in allergic rhinoconjunctivitis, especially when paired with quercetin in pediatric preventive use. Bromelain evidence in sinus disease remained suggestive but methodologically uneven, and inhaled hyaluronan studies supported mucociliary and airway-support concepts without directly validating oral sodium hyaluronate. Conclusions: Taken together, we believe the layered delivery concept is formulation-rational and clinically plausible, but no completed human trial currently verifies the full seven-ingredient finished composition itself. A registered randomized controlled trial of the final product remains necessary.

Keywords

Quercetin; eucalyptus oil; cineole; bromelain; hyaluronan; respiratory support; cough; rhinosinusitis; COPD; asthma.

1. Introduction

We increasingly encounter respiratory-support products positioned around cough relief, sputum reduction, throat comfort, or "lung protection," yet the gap between formulation ambition and human evidence remains wide. In multi-component systems, volatile terpenes may be lost during manufacturing or storage, enzymes may be rapidly inactivated by gastric acid, and polyphenols often show suboptimal dispersibility or unstable exposure profiles after

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oral administration. These formulation weaknesses help explain why many ostensibly sophisticated products do not translate into reproducible clinical performance.

The present composition combines seven active directions: quercetin, eucalyptus oil, bromelain, dihydromyricetin, perillaldehyde, icariin, and ultra-low-molecular-weight sodium hyaluronate. Rather than functioning as a simple physical blend, it is organized into a three-phase layered delivery architecture consisting of enteric-protective microspheres, nano mixed micelles, and sustained-release microcapsules. In our view, that architecture is the central scientific value of the composition because it explicitly addresses acid sensitivity, volatility loss, and release timing.

Instead of presenting hypothetical clinical outcomes, we chose a more rigorous path. We retained the composition-specific formulation data and matched them with published human evidence that is mechanistically or clinically relevant to airway symptoms, cough, rhinosinusitis, asthma, COPD, and allergic upper-airway inflammation. By doing so, we aim to produce a manuscript that is publishable as an evidence-based clinical review while remaining faithful to what is and is not already known.

2. Composition Logic and Evaluation Framework

The composition distributes bromelain into enteric-protective microspheres, flavonoid-type components into nano mixed micelles, and eucalyptus-oil-related volatile fractions into sustained-release microcapsules. This design is intended to protect acid-sensitive components, improve the dispersion of poorly soluble ingredients, and extend the residence time of volatile actives. At the same time, the inclusion of quercetin, dihydromyricetin, icariin, and sodium hyaluronate suggests a broader aim: not only symptom relief, but also airway-surface support, anti-inflammatory modulation, and improved tolerance.

For the clinical-evidence section, we prioritized PubMed-indexed randomized or controlled human studies and systematic reviews. We included studies if they assessed respiratory symptoms, cough, rhinosinusitis, asthma, COPD, allergic rhinoconjunctivitis, or airway-related inflammatory endpoints that could reasonably inform the translational value of the composition.

3. Retained Formulation-Level Results

Table 1. Retained formulation metrics associated with the composition [1].

Metric	Embodiment 1	Embodiment 2	Embodiment 3	Comparator
Bromelain encapsulation efficiency	97.2%	95.5%	96.8%	No relevant index
Flavonoid-component encapsulation efficiency	92.6%	90.8%	91.5%	No relevant index
Volatile-component encapsulation efficiency	94.5%	92.3%	93.8%	No relevant index
Bromelain activity retained after 2 h in gastric acid	98.5%	98.1%	98.3%	6.8%
Total active-component retention after 6 months at 25 °C	96.3%	95.8%	96.1%	32.5%

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The retained formulation dataset indicates two immediate strengths. First, bromelain protection in acidic conditions is nearly complete in all three embodiments and is sharply superior to the non-structured comparator. Second, total active retention after six months at 25 °C remains above 95% for all embodiments, whereas comparator retention declines to 32.5% [1]. For a composition that includes volatile eucalyptus-oil fractions and acid-labile enzyme activity, these two performance domains are not cosmetic; they are central to whether the formula can plausibly retain biological function until administration.

4. Published Human Clinical Evidence

Table 2. Quercetin- and Perilla-related human studies relevant to airway and upper-airway inflammation.

Component / study	Population and design	Intervention	Main findings	Interpretation
Quercetin phase I COPD safety trial [2]	COPD; randomized, dose-escalation, placebo-controlled phase I	500-2000 mg/day for 1 week	Safely tolerated up to 2000 mg/day; no study-drug-related severe adverse events	Supports tolerability of the quercetin axis
Quercetin phase II COPD biomarker trial [3]	14 COPD patients with CRP > 3 mg/L; pilot randomized study	2000 mg/day for 6 months	Reduced BAL IL-8, IL-1β, 8-isoprostane and serum SP-D; symptom trend improved	Supports anti-inflammatory plausibility
Community URTI trial [4]	1002 adults; randomized community clinical trial	500 or 1000 mg/day for 12 weeks	No overall URTI benefit in the full cohort; benefit only in fitter older subgroup	Efficacy is population-dependent
Intensive-exercise URTI model [5]	40 cyclists; randomized placebo-controlled trial	Quercetin around intensified exercise	Post-exercise URTI incidence: 1/20 vs 9/20 in placebo	Suggests benefit under stress-related immune challenge
Perilla rosmarinic-acid trial [6]	29 adults with seasonal allergic rhinoconjunctivitis; randomized placebo-controlled	21 days, 50 mg or 200 mg/day	Improved itchy nose, watery/itchy eyes, total symptoms; reduced neutrophils/eosinophils in nasal lavage	Supports upper-airway anti-allergic activity
Quercetin-Perilla pediatric preventive study [7]	128 children with allergic rhinoconjunctivitis; multicenter randomized study	Continued nutraceutical use after pharmacologic phase	Risk of exacerbation halved (HR 0.54); fewer rescue-medication days; no clinically relevant adverse event	Supports the quercetin+Perilla pairing

The quercetin literature is mixed but clinically meaningful. In a phase I dose-escalation COPD trial, quercetin was safely tolerated up to 2000 mg/day without study-drug-related severe adverse events [2]. A later pilot phase II study in COPD patients with elevated C-reactive protein found significant reductions in bronchoalveolar lavage IL-8, IL-1β, 8-isoprostane, and serum surfactant protein-D after six months of treatment, while patient-reported symptoms trended downward [3]. These data do not yet prove symptom efficacy, but they provide a credible signal for airway inflammatory modulation.

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By contrast, efficacy signals in broader community infection settings are less consistent. In a 1002-participant randomized community trial, quercetin supplementation did not significantly reduce overall upper respiratory tract infection outcomes in the full study population, although a fitter middle-aged and older subgroup benefited with fewer sick days and lower severity [4]. In a smaller exercise-stress model, quercetin reduced post-exercise URTI incidence in cyclists, with illness reported in 1 of 20 participants in the quercetin arm versus 9 of 20 in placebo [5]. Taken together, we interpret quercetin as biologically active and clinically promising, but not yet uniformly effective across heterogeneous respiratory contexts.

Perilla-related evidence strengthens the upper-airway and anti-allergic dimension of the composition. In a randomized placebo-controlled trial, rosmarinic-acid-enriched Perilla frutescens extract improved itchy nose, watery eyes, itchy eyes, and total symptom response rates in seasonal allergic rhinoconjunctivitis, while also lowering neutrophil and eosinophil counts in nasal lavage fluid [6].

A later multicenter randomized pediatric study of a quercetin-Perilla-vitamin D3 nutraceutical reported that continued use halved the risk of allergic-rhinoconjunctivitis exacerbation (hazard ratio 0.54), reduced exacerbation burden, and lowered rescue-medication use without clinically relevant adverse events [7]. Although this evidence does not validate the present finished composition directly, it supports the logic of combining quercetin with Perilla-derived anti-allergic signaling in airway-focused formulations.

Among all public ingredients-related studies, cineole/eucalyptus demonstrates the clearest and most repeatable direct respiratory benefit. In acute nonpurulent rhinosinusitis, a 152-patient double-blind placebo-controlled trial showed symptom-sum-score reductions from a shared baseline of 15.6 to 6.9 at day 4 and 3.0 at day 7 in the cineole group, compared with 12.2 and 9.2 in placebo [8].

In acute bronchitis, a 242-patient double-blind placebo-controlled trial found significantly faster improvement in Bronchitis Sum Score after four days of cineole, with the strongest single-item signal seen in cough-fit frequency ($p = 0.0001$) [9]. In stable COPD, six-month concomitant therapy lowered exacerbation frequency, duration, and severity while also improving lung function, dyspnea, and quality of life relative to placebo [10]. A similarly designed six-month asthma trial showed significantly greater improvement in multi-criteria outcomes with cineole ($p = 0.0027$) [11].

At the evidence-synthesis level, a 2022 systematic review and meta-analysis of six randomized trials involving 1,857 participants concluded that eucalyptus products improved or resolved overall cough symptoms versus placebo (RR 1.45, 95% CI 1.26-1.67) and reduced cough frequency, although the magnitude of benefit was modest and several studies used combination formulas rather than isolated eucalyptus [12]. Even with that limitation, we regard eucalyptus/cineole as the strongest clinically validated axis inside the present composition.

Bromelain is plausible from both a formulation and symptomatic perspective, especially given the strong gastric protection seen in the retained formulation dataset [1]. However, the human respiratory literature is older and less uniform than that for cineole. A systematic review of rhinosinusitis trials found that three randomized studies of bromelain reported positive findings and that meta-analysis of two acute-sinusitis trials suggested symptom benefit [13].

A broader 2023 systematic review and meta-analysis across clinical indications concluded that bromelain may be effective against sinusitis and did not reveal major health risks, although study heterogeneity remained substantial [14]. We therefore view bromelain as a supportive rather than decisive clinical pillar: scientifically defensible, potentially useful for mucus-related and sinus-related symptom complexes, but still under-validated by modern respiratory trial standards.

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Table 3. Eucalyptus/cineole, bromelain, and hyaluronan-related evidence relevant to respiratory translation.

Evidence axis	Population and design	Intervention	Main findings	Interpretation
Cineole in acute rhinosinusitis [8]	152 patients; double-blind placebo-controlled trial	200 mg three times daily for 7 days	Symptom score fell from 15.6 to 6.9 (day 4) and 3.0 (day 7) vs 12.2 and 9.2 in placebo	Strong direct evidence for upper-airway symptom relief
Cineole in acute bronchitis [9]	242 patients; double-blind placebo-controlled trial	200 mg three times daily for 10 days	Bronchitis Sum Score improved faster; cough-fit frequency improved strongly ($p = 0.0001$)	Supports cough and mucus-related symptom benefit
Cineole in stable COPD [10]	242 patients; double-blind placebo-controlled multicenter trial	200 mg three times daily for 6 months	Lower frequency, duration, and severity of exacerbations; better dyspnea, QoL, and lung function	Most clinically persuasive evidence in chronic airway disease
Cineole in asthma [11]	247 patients; double-blind placebo-controlled multicenter trial	200 mg three times daily for 6 months	Multiple-criteria improvement significant vs placebo ($p = 0.0027$)	Extends relevance beyond COPD
Eucalyptus cough meta-analysis [12]	6 RCTs, 1857 participants	Eucalyptus products vs placebo	Overall cough improvement/resolution RR 1.45; cough frequency reduced; effect modest	Confirms signal but also its limitations
Bromelain sinusitis evidence [13,14]	Systematic reviews of randomized and clinical studies	Oral bromelain across sinusitis-related studies	Suggestive symptom benefit in sinusitis; modern evidence heterogeneous but no major health risks reported	Supportive rather than decisive clinical pillar
Aerosolized hyaluronan in COPD [15,16]	Pilot randomized studies in COPD / alpha-1 antiprotease deficiency COPD	Inhaled HA for 2-4 weeks	Well tolerated; desmosine/isodesmosine biomarkers declined	Supports airway-surface and matrix-protection rationale
HMW hyaluronan in AECOPD [17]	41 patients; randomized placebo-controlled pilot study	Inhaled HMW-HA during severe AECOPD requiring NIPPV	Shorter time to liberation from non-invasive ventilation and shorter hospital stay	Supports mucociliary and acute-support relevance, but route mismatch remains

Hyaluronan-related evidence supports airway-surface and mucociliary concepts, but route differences matter. In a 2017 pilot COPD trial, aerosolized hyaluronan was well tolerated and was associated with progressive reductions in desmosine/isodesmosine biomarkers of elastin degradation [15]. A 28-day study in alpha-1 antiprotease deficiency COPD likewise reported no

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significant safety concerns and showed biomarker improvement consistent with reduced ongoing lung elastic-fiber injury [16].

More directly, a 2021 randomized placebo-controlled pilot study in acute COPD exacerbation found that inhaled high-molecular-weight hyaluronan shortened time to liberation from non-invasive ventilation and reduced hospital stay [17]. We consider these studies important because they support the general airway-surface rationale of hyaluronan. Nevertheless, inhaled hyaluronan cannot be treated as a direct proxy for oral ultra-low-molecular-weight sodium hyaluronate. The route, molecular size, and pharmacodynamic context differ materially.

5. Evidence Gaps and Translational Priorities

Table 4. Components that still require direct respiratory clinical validation.

Ingredient with current evidence gap	Status of human respiratory evidence	How we interpret its role in the formula	Priority for future validation
Dihydromyricetin	No comparable randomized human respiratory trial identified in our search	May broaden antioxidant and stress-response coverage	Needs direct human airway data
Perillaldehyde	No eligible human respiratory efficacy trial identified	May contribute volatile anti-inflammatory and sensory effects	Needs controlled symptom studies
Icariin	No comparable human respiratory clinical trial identified	Potential anti-inflammatory breadth remains mechanistic	Needs target-population validation
Oral ultra-low-molecular-weight sodium hyaluronate	Human respiratory evidence available mainly for inhaled HA, not oral ULMW-HA	Supports airway-surface concept but route equivalence is unproven	Requires route-specific pharmacodynamic confirmation

Our search did not identify comparable human respiratory trials for dihydromyricetin, perillaldehyde, or icariin as individual oral components in the same evidentiary class as the studies summarized above. At present, those three ingredients contribute more to mechanistic breadth than to clinically verified respiratory outcomes. That does not negate their possible value, but it does mean that future validation of the finished composition should not rely on cineole and quercetin alone while assuming the rest of the formula is already clinically settled.

6. Discussion

When we weigh the entire evidence chain, the composition appears strongest in three areas. First, the layered delivery system clearly improves pre-administration integrity for acid-sensitive and volatile ingredients. Second, cineole-centered human data provide a real, repeated clinical signal across rhinosinusitis, bronchitis, COPD, and asthma. Third, quercetin and Perilla-related data support an anti-inflammatory and anti-allergic upper-airway rationale that may complement the more symptom-driven cineole signal.

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The weakest point remains full-product validation. No published randomized clinical trial currently demonstrates that the complete seven-ingredient composition itself improves cough burden, sputum burden, LCQ score, SGRQ score, CAT score, exacerbation rate, or spirometric endpoints. For that reason, we believe the next step should be a registered, double-blind, comparator-controlled study in a clearly defined target population, such as chronic productive cough, recurrent pollution-related airway irritation, or stable COPD with chronic sputum burden.

A sensible modern trial should measure symptom trajectories early and late. For symptom-dominant populations, cough frequency, sputum burden, night-time awakening, and patient-reported throat or chest comfort are relevant. For chronic airway disease populations, CAT, SGRQ, rescue-medication use, exacerbations, CRP, IL-8-related biomarkers, and selected lung-function endpoints would help distinguish whether the product is acting mainly as a symptom reliever, an anti-inflammatory adjunct, or both.

7. Conclusion

We conclude that the NVTIA layered respiratory support system has a stronger scientific basis than a simple multi-herb blend. The formulation-level evidence shows that it protects bromelain and preserves active components during storage, and the published clinical literature provides the clearest support for cineole/eucalyptus, moderate support for quercetin and Perilla-related anti-allergic signaling, suggestive support for bromelain in sinus-related disease, and concept-level support for hyaluronan in airway-surface management. What is still missing is the decisive step: a rigorous human trial of the final finished composition.

References

[1] NVTIA quercetin-eucalyptus-oil layered respiratory support composition. Formulation dossier and associated figures. 2026.

[2] Han MK, Barreto TA, Martinez FJ, Comstock AT, Sajjan US. Randomised clinical trial to determine the safety of quercetin supplementation in patients with chronic obstructive pulmonary disease. BMJ Open Respir Res. 2020;7:e000392. doi:10.1136/bmjresp-2018-000392.

[3] Patel S, Marchetti N, Ganjian H, Yu D, Kelsen SG, Criner GJ, Sajjan US. Effect of oral treatment with quercetin on inflammatory and oxidative stress markers in patients with chronic obstructive pulmonary disease. Pharmacol Res Nat Prod. 2025;7:100252. doi:10.1016/j.prenap.2025.100252.

[4] Heinz SA, Henson DA, Austin MD, Jin F, Nieman DC. Quercetin supplementation and upper respiratory tract infection: a randomized community clinical trial. Pharmacol Res. 2010;62(3):237-242. doi:10.1016/j.phrs.2010.05.001.

[5] Nieman DC, Henson DA, Gross SJ, Jenkins DP, Davis JM, Murphy EA, et al. Quercetin reduces illness but not immune perturbations after intensive exercise. Med Sci Sports Exerc. 2007;39(9):1561-1569. doi:10.1249/mss.0b013e318076b566.

[6] Takano H, Osakabe N, Sanbongi C, Yanagisawa R, Inoue K, Yasuda A, et al. Extract of Perilla frutescens enriched for rosmarinic acid, a polyphenolic phytochemical, inhibits seasonal allergic rhinoconjunctivitis in humans. Exp Biol Med (Maywood). 2004;229(3):247-254. doi:10.1177/153537020422900305.

[7] Marseglia GL, Licari A, Leonardi S, Papale M, Zicari AM, Schiavi L, Ciprandi G, Italian Study Group on Pediatric Allergic Rhinoconjunctivitis. A polycentric, randomized, parallel-group, study on Lertal®, a multicomponent nutraceutical, as preventive treatment in children with allergic rhinoconjunctivitis: phase II. Ital J Pediatr. 2019;45(1):84. doi:10.1186/s13052-019-0678-y.

[8] Kehrl W, Sonnemann U, Dethlefsen U. Therapy for acute nonpurulent rhinosinusitis with cineole: results of a double-blind, randomized, placebo-controlled trial. Laryngoscope. 2004;114(4):738-742. doi:10.1097/00005537-200404000-00027.

ISSN: 2710-0588

[9] Fischer J, Dethlefsen U. Efficacy of cineole in patients suffering from acute bronchitis: a placebo-controlled double-blind trial. Cough. 2013;9(1):25. doi:10.1186/1745-9974-9-25.

[10] Worth H, Schacher C, Dethlefsen U. Concomitant therapy with cineole (eucalyptole) reduces exacerbations in COPD: a placebo-controlled double-blind trial. Respir Res. 2009; 10(1): 69. doi:10.1186/1465-9921-10-69.

[11] Worth H, Dethlefsen U. Patients with asthma benefit from concomitant therapy with cineole: a placebo-controlled, double-blind trial. J Asthma. 2012; 49(8): 849-853. doi:10.3109/02770903.2012.717657.

[12] Her L, Kanjanasilp J, Chaiyakunapruk N, Sawangjit R. Efficacy and Safety of Eucalyptus for Relieving Cough: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. J Integr Complement Med. 2022;28(3):218-226. doi:10.1089/jicm.2021.0226.

[13] Guo R, Canter PH, Ernst E. Herbal medicines for the treatment of rhinosinusitis: a systematic review. Otolaryngol Head Neck Surg. 2006;135(4):496-506. doi:10.1016/j.otohns.2006.06.1254.

[14] Leelakanok N, Petchsomrit A, Janurai T, Saechan C, Sunsandee N. Efficacy and safety of bromelain: a systematic review and meta-analysis. Nutr Health. 2023; 29(3): 479-503. doi:10.1177/02601060231173732.

[15] Cantor J, Ma S, Turino G. A pilot clinical trial to determine the safety and efficacy of aerosolized hyaluronan as a treatment for COPD. Int J Chron Obstruct Pulmon Dis. 2017;12:2747-2752. doi:10.2147/COPD.S142156.

[16] Cantor JO, Ma S, Liu X, Campos MA, Strange C, Stocks JM, et al. A 28-day clinical trial of aerosolized hyaluronan in alpha-1 antiprotease deficiency COPD using desmosine as a surrogate marker for drug efficacy. Respir Med. 2021;182:106402. doi:10.1016/j.rmed.2021.106402.

[17] Galdi F, Pedone C, McGee CA, George M, Rice AB, Hussain SS, et al. Inhaled high molecular weight hyaluronan ameliorates respiratory failure in acute COPD exacerbation: a pilot study. Respir Res. 2021;22(1):30. doi:10.1186/s12931-020-01610-x.