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**Research Article** 

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# Rupatadine and Ginkgo Biloba: A Potential Synergia Concept for Neuroprotective, Antioxidant and Anti-Inflammatory Actions in Otorhinolaryngology

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#### Abstract

Otorhinolaryngologic (ENT) disorders, including allergic rhinitis, chronic rhinosinusitis, and inner ear diseases, frequently involve complex inflammatory and vascular mechanisms. Rupatadine, a second-generation  $H_1$ -antihistamine with additional platelet-activating factor (PAF) receptor antagonism, has demonstrated efficacy in allergic airway conditions by addressing both histamine- and PAF-mediated inflammation. Ginkgo biloba, a herbal extract rich in ginkgolides, also exhibits PAF antagonism, alongside antioxidant and microcirculatory-enhancing properties, making it relevant to neurotologic and vascular ENT conditions. This narrative review synthesizes human clinical evidence from the past decade, exploring the individual and potential combined therapeutic effects of rupatadine and Ginkgo biloba in ENT pathologies. Clinical studies support rupatadine's role in allergic rhinitis and inflammation-driven sinus disease, while Ginkgo has shown benefit in sudden hearing loss, tinnitus, and vertigo associated with vascular compromise. The concept of synergy—where co-administration targets multiple pathogenic pathways more effectively than monotherapy—is explored, particularly in conditions at the intersection of allergy, inflammation, and vascular dysfunction. While current evidence for combination therapy remains theoretical, the overlapping pharmacodynamics of these agents suggest a promising complementary approach. Future research, including controlled clinical trials, is warranted to evaluate the safety, efficacy, and optimal use of this potential synergy in ENT care.

Keywords: Rupatadine; Ginkgo biloba; Allergic rhinitis; Tinnitus; PAF receptor; ENT; Synergy; SSNHL; Otorhinolaryngology

#### Introduction

Otorhinolaryngologic (ENT) disorders such as allergic rhinitis, chronic rhinosinusitis, and inner ear diseases often involve complex inflammatory and vascular mechanisms [1]. Rupatadine is a modern second-generation H<sub>1</sub>-antihistamine with additional platelet-activating factor (PAF) receptor antagonist activity, approved for allergic conditions like rhinitis [1, 2]. Ginkgo biloba, a medicinal plant extract, has multifaceted pharmacological effects including PAF receptor antagonism via ginkgolide components (table 1), antioxidant properties, and enhancement

of microcirculatory blood flow [3]. Given these overlapping antiinflammatory and vasoactive actions, there is growing interest in their potential combined benefits. This narrative review examines human clinical evidence from the last decade on rupatadine and Ginkgo biloba, focusing on common actions in ENT-related pathologies and exploring possible synergy in conditions such as allergic rhinitis, chronic rhinosinusitis, hearing loss, and vestibular disorders. Each section integrates recent clinical studies to provide an up-to-date perspective.



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Table 1: Complementary Mechanisms of Action.

Complementary Mechanisms of Action	
Rupatadine	Ginkgo biloba
Dual antihistamine (H1 receptor antagonist) and PAF (platelet-activating factor) antagonist	Contains flavonoids and terpenoids with antioxidant properties
Reduces nasal congestion, sneezing, and rhinorrhea	Improves microcirculation in the inner ear and nasal mucosa
Decreases in inflammatory mediators in allergic rhinitis	Modulates neurotransmitter systems potentially beneficial in tinnitus
Minimal sedative effects compared to first- generation antihistamines	May reduce vertigo symptoms through vestibular system effects

#### Pharmacological Actions of Rupatadine

Rupatadine is distinguished by its dual pharmacological targets: it potently blocks histamine H<sub>1</sub> receptors and concurrently antagonizes PAF receptors [1]. This dual mechanism is clinically significant in allergic airway disease; histamine drives acute allergic symptoms, while PAF contributes to vascular permeability and inflammation in the nasal mucosa. In patients with allergic rhinitis, rupatadine's PAF-blocking capability provides additive relief of nasal congestion and rhinorrhea beyond what traditional antihistamines achieve. A meta-analysis pooling 10 randomized trials (>2500 patients) confirmed that rupatadine significantly improves allergic rhino conjunctivitis symptoms (including nasal blockage and ocular itching) compared to placebo. Correspondingly, a large Phase III trial in seasonal allergic rhinitis demonstrated that rupatadine 10mg and 20mg once daily were superior to placebo in reducing total nasal symptom scores and improving ocular symptoms over 2 weeks Patients treated with rupatadine showed marked decreases in sneezing, rhinorrhea, and congestion, reflecting its broad anti-allergic efficacy [2].

Beyond symptom control, rupatadine exhibits anti-inflammatory activity at the cellular level relevant to chronic ENT inflammation. In vitro and clinical studies show that rupatadine inhibits mast cell degranulation and the release of pro-inflammatory cytokines (e.g. IL-5, IL-8, TNF- $\alpha$ ) from immune cells. It also reduces eosinophil and neutrophil chemotaxis to inflammatory sites [1]. These effects suggest a capacity to modulate the persistent inflammation seen in conditions like chronic rhinosinusitis with allergic features. Indeed, while H<sub>1</sub>-antihistamines are not first-line therapy for non-allergic sinusitis, patients with coexisting allergies may benefit from rupatadine's anti-allergic and anti-PAF actions [4]. By blocking PAF, rupatadine uniquely addresses a mediator implicated in nasal edema and congestion. A crossover trial illustrated this PAF-related benefit: allergic rhinitis patients pretreated with rupatadine had significantly blunted nasal congestion responses to PAF challenge, whereas an H<sub>1</sub>-blocker without PAF activity (levocetirizine) failed to prevent symptoms [1]. This finding underscores rupatadine's dual mechanism translating into tangible clinical advantages in upper airway inflammation.

Clinically, rupatadine is well tolerated, with a safety profile comparable to other second-generation antihistamines [5]. Short-term studies report mild sedation ( $\sim$ 7% incidence) as the most

common side effect, with no serious adverse events observed at doses up to 20mg daily [5]. Importantly, long-term data over 52 weeks in patients with perennial allergic rhinitis showed no significant safety concerns: no cardiac arrhythmia, no significant laboratory changes, and no treatment-related serious events. Only mild to moderate adverse events (such as headache or drowsiness) were noted in a minority, without necessitating discontinuation. This favorable long-term safety supports the chronic use of rupatadine in persistent ENT allergic disorders. Overall, rupatadine's pharmacological profile – dual receptor blockade with resultant symptom relief and anti-inflammatory effects – makes it a valuable therapeutic agent in ENT allergy management [1].

#### Pharmacological Actions of Ginkgo biloba

Ginkgo biloba leaf extract (most commonly the standardized EGb 761) exerts a broad spectrum of biological effects that are pertinent to neurotologic and rhinologic conditions. A hallmark of Ginkgo's action is its content of unique terpene lactones (ginkgolides A, B, C) which are natural antagonists of the platelet-activating factor receptor [6]. Ginkgolide B in particular binds competitively to PAF receptors on inflammatory and vascular cells, thereby inhibiting PAF-mediated pathways [3]. This PAF antagonism can reduce platelet aggregation, vascular permeability, and leukocyte activation, mechanisms relevant to inner ear microcirculation and nasal mucosal inflammation. In addition, Ginkgo's flavonoid constituents provide significant antioxidant effects, scavenging free radicals and protecting tissues from oxidative damage [6]. These antioxidant and anti-inflammatory properties have been shown to modulate cytokine signaling (for example, down-regulating NF-κB and pro-inflammatory interleukins in ischemic and inflammatory models). By promoting a shift from pro-inflammatory to antiinflammatory phenotypes in immune cells, Ginkgo may exert a neuroprotective effect in the central and peripheral nervous system [3]. Such effects suggest potential benefits in cochlear or vestibular disorders where inflammation and oxidative stress contribute to pathology.

Clinically, Ginkgo biloba has been evaluated as a therapy in several ENT-related conditions, especially those involving cochleovestibular dysfunction and vascular compromise. In sudden sensorineural hearing loss (SSNHL), where impaired inner ear blood flow and inflammation are implicated, Ginkgo has been used as an adjunct to standard steroid therapy [7]. A randomized

controlled trial (RCT) in patients with idiopathic SSNHL added intravenous Ginkgo extract (EGb761) to systemic corticosteroids and found a significant improvement in speech discrimination scores compared to steroids alone. Although pure-tone hearing thresholds did not differ significantly, the combined treatment enhanced auditory speech clarity, suggesting a neurofunctional benefit [7]. More recently, a 2021 study of Ginkgo diterpene lactone in SSNHL reported that supplementing standard therapy with oral ginkgolide improved overall hearing recovery rates, especially in profound hearing loss cases [8]. These human trials support Ginkgo's role in improving inner ear perfusion and neuronal recovery in acute hearing loss, aligning with its known vasodilatory and neuroprotective actions.

Ginkgo biloba has also been studied for tinnitus [6], a condition often linked to cochlear neurodegeneration and microcirculatory deficits. In a 90-day RCT, Ginkgo extract (EGb761) therapy led to significant improvement in tinnitus loudness and severity scores in patients with chronic tinnitus and hearing loss [9]. Patients receiving Ginkgo reported reduced subjective tinnitus handicap, an effect comparable to that of sound therapy with hearing aids [9]. Notably, Ginkgo's efficacy was observed regardless of tinnitus duration, indicating its potential to aid even longstanding cases. While some larger meta-analyses have found mixed results on Ginkgo for tinnitus in general populations, this targeted trial in patients with coexistent hearing impairment suggests a tangible benefit when vascular/neurotrophic support is needed. Beyond the ear, Ginkgo's circulatory and anti-inflammatory effects have relevance in vestibular disorders. Vertigo due to vertebrobasilar insufficiency (a vascular cause) or peripheral vestibulopathy has been treated with Ginkgo in clinical studies. A meta-analysis in 2023 encompassing 25 RCTs (1209 patients) concluded that adding Ginkgo biloba to conventional treatment significantly improved vertigo symptoms in patients with vertebrobasilar ischemic vertigo and cervical vertigo, performing on par with the standard antivertigo drug betahistine [10]. Patients experienced reduced dizziness severity and disability, while Ginkgo demonstrated a favorable safety profile (fewer adverse events than betahistine in some trials). However, the same analysis noted Ginkgo was not effective for purely mechanical vestibular disorders like benign paroxysmal positional vertigo, underscoring that its benefits are most pronounced when vascular or inflammatory factors underline the vertigo.

 Table 2: Theoretical Synergistic Mechanisms.

In summary, Ginkgo biloba exerts multiple pharmacologic effects of interest to ENT clinicians: it antagonizes PAF-driven inflammation, improves microvascular blood flow, and protects against oxidative neuronal injury [3]. These actions have translated into clinical improvements in select scenarios of inner ear hypoperfusion (hearing loss, vascular tinnitus, vertigo from circulatory insufficiency) [7]. Ginkgo is generally well tolerated in these studies, with side effects comparable to placebo and no serious safety signals reported in doses up to 240mg/day of extract [10]. Such evidence provides a rationale for considering Ginkgo as an adjunct therapy in ENT conditions where its unique mechanism can complement standard treatments.

## Potential Synergy between Rupatadine and Ginkgo biloba in ENT Pathologies

Given the overlapping and complementary actions of rupatadine and Ginkgo biloba, a potential synergy could be envisioned in managing complex ENT pathologies (Table 2). Both agents share the ability to antagonize platelet-activating factor, a mediator implicated in allergic inflammation and microvascular dysfunction [3]. Rupatadine already leverages this mechanism to alleviate nasal congestion and inflammatory cell activation in allergic rhinitis [1]. Ginkgo's ginkgolides could reinforce PAF inhibition, possibly providing additional control of vascular leakage and edema in the nasal mucosa. In theory, co-administering Ginkgo with rupatadine in allergic rhinitis or chronic rhinosinusitis might lead to a complete blockade of inflammatory pathways (histamine, PAF, cytokines) than either alone. Notably, PAF is considered a key driver of nasal obstruction in allergies, and blocking PAF alongside histamine has been postulated to improve symptoms synergistically. While Ginkgo is not an established allergy treatment, its PAF-antagonist property and anti-inflammatory effects (e.g. NF-κB inhibition) could augment rupatadine's efficacy in refractory cases of allergic rhinitis or in chronic rhinosinusitis with allergic comorbidity. This combined approach has not yet been tested in clinical trials, so its true benefit remains hypothetical. However, the concept aligns with a strategy of blocking multiple inflammatory mediators - an approach supported by evidence in other inflammatory disorders [3]. Future studies in patients with difficult-to-control nasal inflammation (for instance, allergic rhinitis with nasal polyps or local eosinophilic inflammation) could explore whether adding Ginkgo to rupatadine or standard therapy yields incremental improvements in congestion, polyp size, or mucosal healing.

### Theoretical Synergistic Mechanisms

#### . Complementary Anti-inflammatory

Rupatadine blocks histamine and PAF receptors, while Ginkgo biloba inhibits pro-inflammatory cytokines and reactive oxygen species, potentially creating a broader anti-inflammatory effect [1, 3].

#### 2. Enhanced Microcirculation Pathways

Ginkgo's vasoregulatory effects combined with Rupatadine's PAF antagonism may improve cochlear blood flow more effectively than either agent alone [6, 8].

#### 3. Neuroprotection

The combination may provide superior protection against excitotoxicity and oxidative stress in auditory neurons and hair cells [7, 9, 10].

### 4. Reduced Side Effects

Lower doses of each drug might be used in combination, potentially reducing the risk of adverse effects while maintaining therapeutic efficacy [5, 10, 11].

Synergy may also be relevant in otologic conditions, particularly those at the interface of allergy, immunity, and vascular supply. Inner ear disorders such as Meniere's disease and some forms of sudden hearing loss are thought to involve both immunologic factors and microvascular compromise in the cochlea or vestibular apparatus. Rupatadine could address an allergic or histamine-mediated component - for example, some Meniere's patients experience allergy triggers or coexistent allergic rhinitis that can exacerbate Eustachian tube dysfunction and inner ear fluid dysregulation [4]. By controlling systemic and local allergic responses, rupatadine might reduce episodes of eustachian edema or attacks precipitated by allergens. Ginkgo, on the other hand, would target the vascular and neural aspects by improving inner ear blood flow and protecting against oxidative injury to auditory hair cells and neurons [7]. In sudden sensorineural hearing loss, a condition sometimes associated with cochlear ischemia and possibly immune-mediated damage, one could speculate that combining rupatadine's anti-inflammatory effects with Ginkgo's microcirculatory enhancement might offer a broader therapeutic coverage [8]. For instance, rupatadine might mitigate any underlying inflammatory or allergic contributions (such as immune complex deposition or mast cell activation in the inner ear), while Ginkgo facilitates recovery of cochlear perfusion and protects neural function. Although this is an extrapolation, it parallels combination approaches in other fields (e.g. adding anti-PAF Ginkgo to steroids in SSNHL showed improved speech outcomes [7]). Thus, a rupatadine-Ginkgo combination could be hypothesized as an ENT-tailored variant of multi-modal therapy addressing both immune and vascular factors.

Vestibular disorders present another arena for possible synergy. Patients with chronic vestibular syndrome may have multifactorial etiologies - for example, age-related vestibular decline compounded by microvascular insufficiency and chronic inflammation. Ginkgo alone has shown efficacy in vascular vertigo and dizziness [10]. If allergic inflammation or histaminergic overstimulation (as seen in motion sickness or vestibular migraine) plays a role, rupatadine could contribute by stabilizing mast cells and blocking H<sub>1</ sub> receptors, potentially reducing vertigo-related nausea or vestibular hypersensitivity [1]. Both drugs also have mild anxiolytic or neurotrophic benefits - rupatadine by improving sleep and reducing allergic discomfort, and Ginkgo by improving cognitive function and mood in some reports - which might together improve the quality of life in patients with tinnitus or vestibular disorders that often cause anxiety [9]. It is conceivable that in a patient with, say, persistent tinnitus with an anxiety component and microcirculatory deficits, rupatadine could alleviate any occult allergic contribution (like concurrent allergic rhinitis that can worsen middle ear pressure or tinnitus perception) while Ginkgo directly acts on the auditory system. Indeed, a trial combining Ginkgo with standard sound therapy for tinnitus indicated that the dual treatment was effective in reducing tinnitus severity [9]. Although that study did not include rupatadine, it exemplifies how Ginkgo can be paired with another modality to achieve symptomatic improvement.

In proposing synergy, it must be emphasized that direct clinical evidence for using rupatadine and Ginkgo together in ENT diseases is lacking to date. The rationale is built on their individual evidence bases and mechanistic complementarity. Any combined use at present would be experimental, and careful attention to safety would be required (for example, monitoring for potential pharmacodynamic interactions such as additive platelet inhibition, although rupatadine has minimal effect on coagulation) [5]. Fortunately, both agents have shown good safety profiles independently in long-term studies, which is encouraging for future trials of combination therapy [10]. Research is needed to determine optimal dosing, timing, and patient selection for such combination approaches. Small pilot studies could be designed in conditions like allergic rhinitis with comorbid tinnitus, or refractory chronic rhinosinusitis, to test whether adding Ginkgo to standard care (including rupatadine if allergy is present) yields objective improvements (e.g. better nasal airflow, improved hearing thresholds, or reduced dizziness handicap). Until such data emerge, any synergy between rupatadine and Ginkgo remains a scientifically intriguing hypothesis grounded in their shared antiinflammatory and vaso modulatory actions [1].

#### **Discussion**

Pharmaceutical synergy refers to the interaction of two or more drugs that produce a combined effect greater than the sum of their individual effects. This concept is particularly valuable in clinical practice, especially in managing complex conditions such as those encountered in otolaryngology (ENT). One of the primary benefits of pharmaceutical synergy is enhanced efficacy. When drugs act on different but complementary biological pathways, they can more effectively address the multifaceted nature of diseases. For instance, in allergic rhinitis, combining an antihistamine with a vasodilator or anti-inflammatory agent [11] can offer more comprehensive symptom relief than either drug alone (Example: combining an antihistamine-Rupatadine with a vasodilator- Ginkgo biloba might more thoroughly address the multifactorial nature of allergic rhinitis). Another significant advantage of synergy is the ability to use lower doses of each drug while still achieving therapeutic goals. This dose reduction can decrease the likelihood of dose-dependent side effects, thereby improving the overall safety of the treatment regimen. In conditions that require long-term management, such as chronic rhinosinusitis or vestibular disorders, this approach becomes particularly beneficial.

Pharmaceutical synergy can also help reduce the development of drug resistance or tolerance [12], a concern especially relevant with long-term use of antibiotics or corticosteroids. By attacking a condition from multiple angles, the body is less likely to adapt in a way that diminishes the effectiveness of treatment. Additionally, synergy allows for a broader spectrum of therapeutic action. For example, combining a drug that targets inflammation with one that improves vascular function or provides neuroprotection—such as Rupatadine and Ginkgo biloba in the context of Meniere's disease—can yield more comprehensive benefits. The overall

impact of such combinations is improved patient outcomes. Patients may experience better symptom control, faster recovery, and an enhanced quality of life. In some cases, the effectiveness of synergistic treatments can also lead to cost savings by reducing the need for additional medications, repeat doctor visits, or invasive procedures. Thus, pharmaceutical synergy not only optimizes therapeutic effectiveness and safety [13] but also contributes to more holistic and patient-centered care. Other examples of pharmaceutical synergy have shown that by integrating various agents with pharmacological treatments it has the potential to enhance clinical outcomes by promoting better treatment adherence [14].

Rupatadine and Ginkgo biloba represent an intersection of pharmaceutical and phytotherapeutic management strategies in ENT practice. This review highlights that both agents, despite originating from different medical traditions, converge on common pathophysiological targets relevant to allergic and neurotologic disorders. Rupatadine has established itself over the past decade as an effective and safe therapy for allergic rhinitis, offering dual inhibition of histamine and PAF-driven inflammation Its role in ENT extends logically to any condition with an allergic component, and emerging understanding of PAF's importance in nasal congestion has reinforced rupatadine's added value over single-action antihistamines [1]. Meanwhile, Ginkgo biloba extract has transitioned from an alternative remedy to a subject of rigorous clinical investigation in hearing and balance disorders. Contemporary trials in sudden deafness, tinnitus, and vertigo underscore Ginkgo's potential to improve microvascular circulation and modulate neuroinflammation in the ear [7]. These studies, drawn from the last ten years, bring clinical relevance and credibility to Ginkgo's use in ENT conditions that earlier anecdotal uses lacked. We now have a clearer picture that Ginkgo can produce measurable benefits (e.g. better speech discrimination, reduced vertigo severity) in specific patient populations.

Bridging these two therapeutic agents, the concept of synergy arises from the recognition that ENT disorders often do not have a single pathogenic pathway. Allergic rhinitis and chronic rhinosinusitis, for example, involve a cascade of immune mediators (histamine, leukotrienes, PAF, cytokines) and tissue responses (edema, mucus hypersecretion) [4]. A single modality treatment may not fully control such a multifaceted process. Rupatadine's broad anti-allergic profile makes it a valuable backbone therapy; however, there are inflammatory aspects (oxidative stress, microvascular dysfunction) that rupatadine does not directly address [3]. Here, Ginkgo's supplementary actions could fill the gap. The discussion of synergy is timely, given the growing interest in integrative medicine approaches within ENT - combining pharmacologic efficacy with supportive herbal interventions. Notably, a 2023 meta-analysis advocates for Ginkgo's inclusion in standard vertigo treatment, reflecting a shift toward evidence-based integration of herbal extracts in mainstream care [15].

However, important caveats emerged in our review. While mechanistic overlaps suggest potential synergy, one must avoid over-extrapolation. For instance, blocking PAF is beneficial in allergic rhinitis, but simply adding another PAF blocker (Ginkgo) to rupatadine might yield diminishing returns unless the second agent adds a distinct effect. Ginkgo's distinct contributions likely lie in areas rupatadine is weaker: enhancing vascular perfusion and providing neuroprotection. Clinical scenarios that might benefit from a combined approach would be those straddling allergy and ischemia – for example, an elderly patient with both allergic rhinitis and presbycusis (age-related hearing loss) who experiences chronic dizziness. Such a patient might gain from rupatadine relieving nasal inflammation (improving eustachian tube function) and Ginkgo improving inner ear blood flow, theoretically reducing dizziness and hearing fluctuations. Without direct clinical trials, these remain suppositions. Yet, they are grounded in the pharmacology and pathophysiology outlined in current literature.

An area of concern in combined use would be safety and interactions. Both rupatadine and Ginkgo are generally well tolerated on their own, but Ginkgo is known to have mild antiplatelet activity due to PAF antagonism and can interact with anticoagulants. Rupatadine has not shown significant bleeding risk, but its combination with Ginkgo should be approached cautiously in patients at risk for bleeding until studied. Furthermore, Ginkgo's influence on cytochrome P450 enzymes could theoretically affect rupatadine metabolism, although no such interaction has been documented specifically [2]. The discussion of synergy must therefore also emphasize that physicians should await evidence before routinely recommending this combination, and if used, it should be in a monitored, research setting.

Although the concept of drug additivity and the foundation for assessing drug synergy were introduced in the early 20th century [16], and widely used mathematical models to quantify synergy were developed in subsequent decades [17], the need for highthroughput screening methods to efficiently identify synergistic drug combinations remains essential [18]. Our review identifies a direction for future research: clinical trials that deliberately combine an antihistamine/PAF blocker with a neurovascular modulator in ENT diseases. The past decade provided robust data on each agent separately. The next step is to design studies that test their combination in well-defined clinical settings. Given the excellent safety profiles observed (even in long-term rupatadine use for one year and high-dose Ginkgo trials) [10], such combination trials are feasible. They would answer whether the theoretical benefits translate into superior patient outcomes or not. In vitro studies on combined anti-inflammatory effects using nasal epithelial cell cultures, animal models (Guinea pig models) of allergic rhinitis and tinnitus to assess synergistic effects and Clinical Trials (Phase II RCTs) comparing monotherapy vs. combination in refractory ENT patients are necessary not only to validate preclinical findings but also to determine the minimal effective doses of combined agents required to achieve synergistic effects and optimize treatment duration [19]. Subgroup analyses (age, pathology severity, comorbidities) will further assist the individualization of the treatment.

#### Conclusion

In summary, while rupatadine and Ginkgo biloba each improve aspects of ENT disease pathology, it is the careful scientific exploration of their combined use that will ultimately determine the viability of a synergistic approach in clinical practice. Rupatadine and Ginkgo biloba emerge as complementary allies in the realm of ENT therapeutics – one a rigorously tested anti-allergic drug, the other a time-honored herbal extract with modern clinical validation. Over the last decade, rupatadine's dual antagonism of histamine and PAF has proven efficacious in relieving the burdens of allergic rhinitis and related inflammatory conditions, while Ginkgo's vascular and neuroprotective effects have been harnessed to improve hearing and balance disorders. The convergence of their actions offers a tantalizing prospect: a synergistic strategy that addresses both immunologic and microvascular dimensions of complex ENT diseases. Although direct evidence for combined use is still lacking, the scientific rationale is compelling. Rupatadine can quell the storm of allergic inflammation, and Ginkgo can fortify the neural and circulatory environment - together potentially offering holistic relief where single therapies fall short. To move from promise to practice, well-designed clinical trials are imperative. The data reviewed here lay the groundwork, highlighting that both agents are effective and well tolerated in their domains. An eloquent synergy between rupatadine and Ginkgo biloba could represent a new frontier in ENT care, one that exemplifies the integration of pharmaceutical precision with phytotherapeutic breadth. With cautious optimism and a call for further research, we envision that uniting these therapies may one day enhance outcomes for patients suffering from intricate ailments of the ears, nose, and throat.

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#### **Conflict of Interest Disclosure Statement**

No Conflict of Interest to mention.

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