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CAPSAICIN AS A PROMISING TREATMENT FOR NASO-RESPIRATORY DISEASES: A COMPREHENSIVE REVIEW

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ABSTRACT: Background: Capsaicin, a bioactive compound derived from the dried fruit of the Solanaceae family, is widely recognized for its therapeutic potential. Its mechanism of action involves interaction with TRPV1 receptors, leading to analgesic effects and modulation of neurogenic inflammation. **Objective:** This review explores the therapeutic applications of capsaicin, particularly its role in treating non-allergic rhinitis, neuropathic pain, and inflammatory conditions. It also highlights its potential in preventing pneumonia and cluster headaches. **Methods:** A comprehensive review of existing clinical studies and randomized controlled trials (RCTs) observational studies, and systematic reviews, Randomised placebo-controlled, double blind study, Clinical case series with pre-post outcome assessment was conducted to evaluate capsaicin's efficacy, and mechanisms of action. Special emphasis was placed on intranasal formulations and their impact on nasal sensory nerve Fibers. **Results:** Capsaicin has demonstrated significant benefits in reducing nasal symptoms, improving nasal airflow, and alleviating neuropathic pain. Repeated nasal applications have been shown to provide prolonged relief for idiopathic rhinitis, while intranasal capsaicin has been effective in cluster headache prevention. Studies indicate that capsaicin treatment is generally well tolerated, with minimal long-term adverse effects. **Conclusion:** Capsaicin is a promising therapeutic agent with diverse clinical applications. While its effectiveness in symptom relief is well-documented, further research is needed to optimize dosing regimens, explore alternative TRPV1-targeting compounds, and assess long-term safety. Capsaicin-based treatments offer a valuable approach to managing chronic conditions, paving the way for future pharmaceutical advancements.

INTRODUCTION: The primary ingredient that gives chili peppers their fiery flavor is capsaicin, an alkaloid that comes from the Capsicum plant family and is especially concentrated around the seeds.

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It causes a burning sensation at first by binding to TRPV1 (vanilloid) receptors on sensory neurons. Later, it depletes substance P, a neuropeptide implicated in pain signaling, which results in desensitization and a reduction in pain sensitivity.

Capsaicin is a member of the vanilloid family of chemicals, which has a polar amide group that contributes to its biological activity, a hydrophobic tail, and a benzene ring. With the chemical formula $C_{18}H_{27}NO_3$, a molecular mass of 305.41 g/mol, and a melting point of 62–65°C, it is a colorless, fat-soluble, and hydrophobic substance.

Because capsaicin is hydrophobic, it cannot dissolve in water and needs to be dissolved in alcohol or organic solvents for its use in topical formulations at concentrations of 0.025% or 0.075% [1, 2].

Capsaicin, derived from the dried fruit of the Solanaceae family, is well-known for its therapeutic effects, such as pain relief, enhanced circulation, and digestive benefits. It has shown potential in treating neuropathic pain, inflammation, and conditions like non-allergic rhinitis [3], pain management [4], arthritis, and sinus infections by interacting with TRPV1 receptors and reducing substance P levels [5], and in preventing pneumonia [6]. Topical capsaicin is commonly used to treat neuralgias and psoriasis, while intranasal formulations like Sinus Buster have been effective in managing non-allergic rhinitis. Repeated doses of capsaicin initially cause pain but later result in analgesia [7]. Several studies have shown the use of intranasal capsaicin for preventing cluster headaches [8]. Research suggests that intranasal capsaicin targets sensory nerve fibers, reducing reflex responses without causing long-term side effects [9]. Additionally, studies indicate that capsaicin can significantly alleviate symptoms of idiopathic rhinitis (IR) for extended periods, with multiple nasal applications within a short time offering long-lasting relief. When symptoms return, retreatment has proven effective. Although capsaicin is generally considered safe, alternative plant-based compounds and synthetic drugs targeting TRPV1 are being investigated to develop safer and more effective treatments for IR [10].

TABLE 1: "CAPSAICIN ALSO EXHIBITS A BROAD SPECTRUM OF ANTIBACTERIAL, ANTI-MICROBIAL AND THERAPEUTIC PROPERTIES, AS SUMMARIZED IN TABLE 1 [2]

Bacteria	Diseases/Concerns	Mechanism of Action	Key Findings
Staphylococcus aureus (e.g., MRSA)	Food poisoning, skin infections, pneumonia, bacterial endocarditis	Affects cellular viability, suppresses toxin production, reduces inflammation	Potent action with partial-to-total bactericidal effects; Redghost pepper effective even at 1:16 dilution; alleviates inflammation in staphylococcal pneumonia.
Group A Hemolytic Streptococci	Pharyngitis, skin infections, toxic shock syndrome	Reduces biofilm formation, epithelial adhesion, and hemolytic activity	Decreases invasiveness and hemolytic activity; bactericidal action noted, especially against *S. pyogenes* and *S. mutans.*
Enterococcus species (e.g., VRE)	Nosocomial infections	Inhibits growth; MIC higher due to possible nutrient use of capsaicin	Dihydrocapsaicin shows lower MIC values and selective bactericidal effects.
Listeria monocytogenes	Foodborne illnesses, meningitis, complications in pregnancy	Exhibits bactericidal or bacteriostatic action depending on the extract used	Ghost pepper Red extract effective even at 1:16 dilution.
Bacillus species	Anthrax, food borne illnesses	Inhibits growth at higher MIC	Effective against *B. subtilis*; limited susceptibility in *B. thuringiensis*.
Vibrio cholerae	Cholera	Reduces toxin release by modulating gene transcription (e.g., txA, tcpA, toxT genes)	Effective across serogroups and biotypes, including resistant strains.
Acinetobacter baumannii	Pulmonary infections, septicaemia	Effective in synergy with colistin; reduces colistin MIC in combinatory use	Effective at 64 µg/mL; no direct action against colistin-resistant strains but strong synergy with colistin.
Helicobacter pylori	Gastric ulcer, gastric cancer	Not specified	Displays increased resistance to conventional antibiotics (e.g., clarithromycin); synergistic potential not yet elaborated here.
Salmonella typhimurium	Foodborne illnesses; commonly found in poultry, eggs, and dairy products; poses global health risks.	Capsaicin exhibits protein-inhibiting qualities; plant extract (*Capsicum Chinese*) is more effective.	Capsaicin shows partial bactericidal effects and prevents infection of Vero cells.

Escherichia coli	Opportunistic infections, especially in immune-compromised individuals; includes six major pathogenic types.	Capsaicin slows growth and has inhibitory effects, depending on the strain and capsaicin source.	*Roja Bhut* capsaicin is more effective than *Noga Bhut*. Inhibitory effects observed for E. coli O157:H7.
Klebsiella pneumoniae	Nosocomial infections; severe pathologies and high resistance, even to last-line antibiotics.	Capsaicin inhibits bacterial growth. Nanofiber formulations enhance antibacterial effects.	Capsaicin and gold nanoparticle nanofibers inhibit growth, including *Klebsiella rhinoscleromatis*.
Proteus species	Urinary tract infections (e.g., cystitis, pyelonephritis); complications like urinary stones and catheter obstruction.	Capsaicin is effective against some species but not others; resistance linked to surface polysaccharide secretion.	Effective against *P. mirabilis*. *P. vulgaris* resists effects due to elongation and protective secretion mechanisms.
Pseudomonas aeruginosa	Nosocomial and systemic infections; affects cystic fibrosis and COPD patients.	Capsaicin reduces production of biofilm-related compounds and inhibits growth in colonies.	High MIC for capsaicin. Reduces production of rhamnolipids, phenazine, and quinolone, essential for biofilm formation.

TABLE 2: ANTI-FUNGAL ACTIVITY OF CAPSAICIN

Fungal Pathogen	Diseases/Concerns	Mechanism of Action	Key Findings
Candida albicans	Oral candidiasis, vaginal candidiasis, systemic infections (life-threatening in some cases), especially in hospital settings.	Prevents ergo sterol biosynthesis in the cell wall, altering cell shape and integrity.	Capsaicin showed significant inhibitory properties, killing yeast cells at 1:4 and 1:8 dilutions and partially inhibiting at higher dilutions. Reduced biofilm by 70–89%. Enhanced fluconazole action, potentially preventing drug resistance.
Candida glabrata	Biomass and biofilm formation associated with infections.	Similar to *C. albicans*, with greater susceptibility to capsaicin.	Lower MIC (187.5 µg/mL) compared to *C. albicans* (1500 µg/mL). Reduced hemolysis and biofilm-formation capacity significantly.
Candida tropicalis	Infections involving biofilm formation.	Similar to *C. albicans*.	Demonstrated high susceptibility to capsaicin.
Aspergillus parasiticus	Produces aflatoxins causing carcinogenesis, mutagenesis, and teratogenesis. Prevalent in soil due to climate change.	Capsaicin interferes with spore germination and aflatoxin production by suppressing genes (*aflM*, *aflR*, *aflS*, and *aflD*).	Capsaicin in chitosan-lipid nanoparticles showed good antifungal effects with reduced toxicity. Inhibited fungal growth, spore germination, and aflatoxin production. Potential use as an eco-friendly, non-synthetic fungicide.
Aspergillus flavus	Similar concerns as *A. parasiticus* with aflatoxin production leading to severe health impacts.	Similar to *A. parasiticus*.	Promising antifungal effects with capsaicin-based formulations.

TABLE 3: ANTI PARASITIC ACTIVITY OF CAPSAICIN

Parasite	Disease	Mechanism of Action	Key Findings
Toxoplasma gondii	Toxoplasmosis (affects retina, CNS, newborns)	Inhibits proliferation of tachyzoites and interferes with parasite's gene transcription and pathways.	- Capsaicin inhibits proliferation of *T. gondii* in Be Wo cells. - Enhanced effect with pyrimethamine and sulfadiazine.
Trypanosoma cruzi	Chagas Disease	Affects trypomastigotes (more than epimastigotes), possibly targets the parasite at nanomolar levels.	- Capsaicin more potent than benznidazole. - Potential for oral administration.

Chronic cough (CC), defined as a cough persisting for over eight weeks, significantly impacts patients' quality of life [11], with 10–20% of cases being refractory chronic cough (RCC), unresponsive to standard medical therapies**.** RCC often stems from hypersensitivity of airway sensory neurons, particularly TRPV1 receptors, a condition termed cough hypersensitivity syndrome (CHS).

Behavioural Cough Suppression Therapy (BCST) has demonstrated effectiveness in managing RCC by reducing cough sensitivity through neuroplasticity. However, severely hypersensitive patients often struggle with BCST. Recent studies explored the use of aerosolized capsaicin, a safe and adjustable cough stimulant, in conjunction with BCST to gradually desensitize cough reflexes. This innovative approach has shown promise for RCC patients resistant to traditional BCST methods [1].

Capsaicin has also demonstrated potential in treating chronic conditions like non-allergic rhinitis, pain, and irritable bowel syndrome (IBS) by reducing hypersensitivity and alleviating symptoms. Moreover, recent studies suggest that it may even aid in cancer prevention [12]. In respiratory research, capsaicin-induced reflex cough has been used to assess airway sensitivity, proving beneficial for patients with weak voluntary cough, as it triggers stronger coughs to help clear secretions. However, its effectiveness in certain patient populations, such as those with impaired reflexes or reduced responsiveness, requires further investigation [13, 14].

Idiopathic rhinitis (IR), a subtype of non-allergic non-infectious rhinitis (NANIR), affects 5% of the population and is characterized by nasal hyperreactivity (NHR) triggered by environmental factors. This condition is linked to the over-expression of TRPV1 channels and neuropeptides like substance P. Capsaicin treatment has shown potential in reducing nasal symptoms and hyperreactivity by targeting TRPV1 pathways. A study that explored capsaicin's neural effects on nasal mucosa emphasized its therapeutic potential for IR by highlighting factors like age, gender, and symptoms affecting treatment outcomes [15].

Chronic obstructive pulmonary disease (COPD) and asthma share common symptoms, such as coughing, wheezing, and shortness of breath, yet differ in their nature COPD involves irreversible airflow limitation caused by exposure to harmful particles, while asthma is reversible and treatable. Some patients may experience overlapping symptoms of both conditions. Capsaicin, by activating TRPV1 receptors, induces cough and bronchoconstriction, aiding in diagnosing bronchial hypersensitivity and exploring therapeutic options for COPD and asthma [16]. Patients with asthma, particularly those experiencing chronic cough, often exhibit increased sensitivity to capsaicin. Sensitivity is measured using a C5 test, which assesses the concentration of capsaicin required to induce five or more coughs. Research shows that some asthma patients, especially those with non-atopic or type 2-low asthma, have heightened sensitivity to capsaicin, although findings remain inconsistent across different studies [17].

Capsaicin's ability to desensitize sensory C-fibers in the nasal lining has been demonstrated to alleviate symptoms in IR patients. Earlier studies involved frequent intranasal capsaicin applications every second or third day for a week, which, despite being effective, was inconvenient for regular clinical use. Recent trials have tested simplified regimens, such as delivering five doses in a single day, which proved both effective and convenient, offering symptom relief lasting up to nine months without significant safety concerns [18]. Additionally, capsaicin stimulates glandular secretions, such as total protein and lactoferrin, in the nasal airways without impacting vascular permeability. Repeated exposure reduces symptoms through tachyphylaxis, highlighting its central nervous system-mediated effects [19].

Methods: This review was conducted to analyse the efficacy of capsaicin in treating chronic cough and respiratory conditions by evaluating various clinical and preclinical studies. The methodology involved the following steps:

Literature Search Strategy: A comprehensive literature search was conducted using electronic databases, including PubMed, Scopus, Web of Science, and Google Scholar, covering articles published between [1990-2024]. The search terms used were:

"Capsaicin inhalation challenge AND cough sensitivity"

- "Capsaicin therapeutic application"
- "Capsaicin AND chronic cough"
- "Capsaicin AND respiratory therapy"
- "Capsaicin nasal spray AND safety"

- "Capsaicin in Naso-respiratory disorder"

Inclusion Criteria:

- Clinical or preclinical studies investigating the therapeutic effects of capsaicin on cough or respiratory conditions.
- Studies evaluating cough sensitivity, airway resistance, and lung function after capsaicin exposure.
- Randomized controlled trials (RCTs), observational studies, and systematic reviews, Randomised, placebo- controlled, double blind study, Clinical case series with pre-post outcome assessment,.
- Articles published in peer-reviewed journals in English.

Exclusion Criteria:

- Studies that focused solely on capsaicin's effects outside the respiratory system.
- Animal studies unless they provided translational insights for human application.
- Non-peer-reviewed sources (e.g., conference abstracts, editorials, unpublished data).

Data Extraction and Analysis: The following key data were extracted from each included study:

- Study design (RCT, observational, case-control, preclinical).
- Sample size and characteristics of participants (age, gender, condition).
- Dosage and administration of capsaicin.
- Primary and secondary outcomes (cough sensitivity, lung function, quality of life).
- Safety and adverse events.

A comparative analysis was performed to evaluate the consistency of findings across different studies.

Quality Assessment: The methodological quality of the selected studies was assessed using:

- Cochrane Risk of Bias Tool (for RCTs).
- Newcastle-Ottawa Scale (NOS) (for observational studies).
- Studies with high risk of bias or poor methodology were excluded or discussed with limitations.

Target Conditions: Several studies have investigated the therapeutic applications of capsaicin in respiratory and nasal conditions. Capsaicin has been shown to significantly reduce nasal hyperreactivity in non-allergic rhinitis [20, 21, 22] and improve nasal sensitivity in idiopathic rhinitis cases [23, 24, 18, 15]. It also plays a role in managing chronic cough by decreasing chronic cough sensitivity [25]. In addition, research suggests its potential in reducing inflammation in nasal polyposis [26] and sinonasal polyposis [27].

Studies exploring capsaicin's impact on pneumonia highlight its possible respiratory benefits [6]. Moreover, it has demonstrated effectiveness in relieving symptoms of vasomotor rhinitis by reducing nasal overactivity [28, 29]. Furthermore, a comparative analysis of capsaicin with other pharmacological agents provides insights into its relative efficacy as a treatment option [4].

RESULTS AND DISCUSSION:

TABLE 4: SUMMARY OF LITERATURE REVIEW

First author, year of publication	Target Condition	Study Design	Sample Size	Capsaicin Delivery Method	Key Findings
Zebda, 2020[20]	Non-Allergic Rhinitis	Randomised, placebo- controlled, double blind study	22 patients	Intranasal application (mucosal atomiser)	The treatment group demonstrated a tendency for better outcomes.
Lacroix, 1991[21]	Non-Allergic	Clinical case series with pre-post	20 patients	Nasal spray	Capsaicin treatment led to a decrease in nasal vascular

	Rhinitis	outcome assessment and healthy control group			responses, subjective nasal symptoms, and CGRP-LI content, with approximately a 50% reduction in subjective symptoms for all patients
Riechelmann, 1993 [22]	Non-Allergic Rhinitis	Clinical case series with pre-post outcome assessment	27 patients	Intranasal nebulised capsaicin inhalation	The results for nasal symptoms and treatment success were inconsistent, with no statistically significant outcomes. However, after treatment, reflex cough sensitivity improved, as higher concentrations of capsaicin were needed to trigger a cough.
Ciabatti, 2009[23]	idiopathic rhinitis	4-group randomised controlled trial (3 groups with different capsaicin doses, 1 placebo group)	208 patients	Capsicum oleous nasal spray	The group receiving 4 µg/puff showed a significant reduction in nasal symptoms compared to the placebo, while the two other intervention groups did not experience similar improvements.
VanGerven, 2017[15]	idiopathic rhinitis	Randomised, placebo- controlled, double blind study	33 patients	Intranasal application of capsaicin	The treatment group exhibited a notable decrease in nasal symptoms and self-reported improvement, along with a significant rise in the threshold for nasal mucosal potential recordings.
Van Rijswijk, 2003[18]	idiopathic rhinitis	Randomised, placebo- controlled, double blind study	30 patients	Intranasal application (metered nasal spray)	The intervention group demonstrated a tendency for better outcomes
Van Gerven, 2014[24]	idiopathic rhinitis	Clinical case series with pre-post outcome assessment	14 patients	Intranasal application of capsaicin	Patients experienced a notable decrease in nasal symptoms and a positive trend in self-reported improvement.
Slovarp, 2019[25]	Unexplained chronic cough	Case series with pre-post outcome assessment	5 healthy volunteer	Inhalations	After treatment, reflex cough sensitivity increased, meaning higher doses of capsaicin were needed to trigger a cough.
Ewa Ternesten 2014[13]	Chronic cough	randomized, double-blind, placebo-controlled crossover trial	46 Patient	Each soft capsule contained one dose corresponding to 0.4 mg of capsaicin	Capsaicin helped reduce cough sensitivity and improved symptoms in patients with mild chronic cough
Zheng, 2000[26]	Nasal Polyposis	Randomised, placebo- controlled, double blind study	51 patients	Intranasal cotton pellet soaked with capsaicin applied to both nostrils.	The treatment group exhibited significant improvements in self-reported NAR and clinical staging of polyposis, with no difference between groups in rhinorrhoea.
Baudoin, 2000[27]	sinonasal polyposis	Clinical case series with pre-post outcome assessment	9 patients	Intranasal spray	Four weeks post-treatment, there were notable improvements in major symptom scores, endoscopy scores, and mean NSAV, while ECP levels showed a tendency to increase following capsaicin treatment.
Jinnouchi, 2020[6]	Pneumonia	Clinical case series with retrospective control period	29 patients.	Capsaicin ointment applied to the	The incidence of pneumonia was significantly lower during the 6-month treatment period compared

				external auditory canal.	to the 6 months prior
Wolf, 1995[28]	Vasomotor rhinitis	Clinical case series with pre-post outcome assessment	123 patients	Topical application to both nasal cavities	Self-reported symptoms showed improvement in 50% to 66% of patients, with enhanced nasal flow and increased sensitivity to capsaicin.
Marabini, 1991[29]	Vasomotor rhinitis	Clinical case series with pre-post outcome assessment	20 patients	Nasal spray	Subjective symptoms were reduced by about 50% in all patients.

DISCUSSION: Capsaicin has been widely investigated for its potential therapeutic benefits in various upper and lower respiratory conditions. The reviewed studies provide valuable insights into its effectiveness, mode of delivery, and clinical outcomes.

Capsaicin in Non-Allergic Rhinitis: Multiple studies [20, 21, 22] have assessed capsaicin's role in managing non-allergic rhinitis. Results suggest that intranasal capsaicin application may reduce nasal vascular responses and subjective symptoms [20]. reported a positive trend in symptom improvement, while Lacroix (1991) found a 50% reduction in subjective symptoms. However, Riechelmann (1993) observed mixed findings, with no statistically significant results, indicating variability in treatment efficacy across studies.

Capsaicin in Idiopathic Rhinitis: In Studies examined capsaicin for idiopathic rhinitis [15, 18, 23, 24], most findings support its effectiveness in reducing nasal symptoms and improving patient-reported outcomes. Ciabatti (2009) highlighted that a specific dose (4 μg/puff) was more effective than lower doses or placebo. Van Gerven (2017) and Van Rijswijk (2003) reported a significant increase in nasal symptom relief and mucosal sensitivity thresholds, reinforcing capsaicin's potential as a therapeutic option.

Capsaicin in Chronic Cough and Unexplained Chronic Cough: The use of capsaicin in chronic cough has been explored in both clinical trials and case series. Slovarp (2019) found that inhaled capsaicin improved reflex cough sensitivity. A more robust study by Ternesten (2014) in a randomized, placebo-controlled trial showed that oral capsaicin capsules increased cough thresholds and improved symptoms in patients with mild chronic cough. However, it did not significantly reduce overall cough frequency compared to placebo. These findings suggest that while capsaicin modulates cough sensitivity, its clinical benefit may be limited to specific subgroups of patients [13, 25].

Capsaicin in Nasal Polyposis and Sinonasal Polyposis: Studies by Zheng (2000) and Baudoin (2000) investigated capsaicin's role in nasal and sinonasal polyposis. Zheng (2000) reported significant improvements in nasal airflow resistance (NAR) and polyposis staging after treatment with intranasal capsaicin. Baudoin (2000) found similar benefits, with improvements in symptom scores and endoscopic findings. However, ECP levels showed a trend towards increase, which may suggest inflammatory changes post-treatment. These findings indicate that capsaicin may be beneficial in managing nasal polyps, though further research is needed [26, 27].

Capsaicin in Pneumonia: Jinnouchi (2020) provided an interesting perspective on capsaicin's potential in preventing pneumonia. The study found that the application of capsaicin ointment to the external auditory canal significantly reduced pneumonia incidence over six months. This novel approach suggests capsaicin's role in modulating airway reflexes to prevent aspiration-related pneumonia, warranting further exploration [6].

Capsaicin in Vasomotor Rhinitis: Wolf (1995) and Marabini (1991) evaluated capsaicin for vasomotor rhinitis, with both studies reporting symptomatic relief in a significant proportion of patients.

Self-reported symptoms improved in 50–66% of patients, while nasal sensitivity and airflow improved post-treatment. These findings indicate that capsaicin may serve as an alternative treatment for vasomotor rhinitis, though individual response variability remains a challenge [28, 29].

Overall Interpretation and Future Directions: The reviewed studies consistently support capsaicin's role in modulating sensory nerve function to alleviate symptoms in various respiratory conditions. However, its effectiveness varies based on the condition, dosage, and delivery method. While intranasal capsaicin appears effective for rhinitis and polyposis, oral and inhaled forms show mixed results in chronic cough. The variability in outcomes highlights the need for standardized dosing regimens and larger, well-designed trials to identify patient subgroups most likely to benefit from capsaicin therapy. Additionally, novel applications, such as pneumonia prevention, present exciting areas for future research.

TABLE 5: HERE'S ANOTHER COMPARISON OF THE THREE STUDIES SUMMARIZED IN ONE TABLE [9]

Outcome	Study 1: Capsaicin vs. Placebo for Nasal Symptoms	Study 2: Capsaicin vs. Budesonide for Nasal Obstruction	Study 3: 5 Capsaicin Treatments in 1 Day vs. Daily Capsaicin for 5 Days for Smell Testing
Intervention	Capsaicin (various doses) vs. Placebo	Capsaicin vs. Budesonide	5Capsaicin Treatments in 1 Day vs. Daily Capsaicin for 5 Days
Outcome Measure	Nasal symptom score, symptom resolution	Nasal obstruction response, aggregate relief score	Smell testing (University of Pennsylvania Smell Identification Test)
Relative Effect	Capsaicin improved symptoms more than placebo	Capsaicin showed slightly better response, but not significantly	5 treatments in 1 day showed slightly better smell sensation than 5 daily treatments
Sample Size (Studies)	24 (1 RCT)	40 (1 study)	30 (1 study)
Follow-up Period	36 weeks	4 weeks	12 weeks
Key Findings	- Mean nasal symptom score lower in capsaicin group (3.52 lower)- More symptom resolution in capsaicin group (RR 3.17)	- Higher response to capsaicin in terms of nasal obstruction relief (RR 1.11)- Higher aggregate relief score in capsaicin group	Capsaicin treatment in 1 day improved smell sensation more than daily capsaicin treatment for 5 days
Quality of Evidence (GRADE)	Moderate	Low	Moderate
Treatment-related Adverse Events	Not reported	Not reported	Not reported
Study Population	Non-allergic rhinitis	Patients with nasal obstruction	Patients with non-allergic rhinitis
Comments	Capsaicin showed significant improvement in nasal symptoms.	The difference in response was not very large, but capsaicin had a slightly better outcome.	Capsaicin in 1 day treatment had a small benefit over daily treatment.

Summary of Comparison:

- Capsaicin consistently showed positive outcomes across studies, with some variations in the specific symptoms it improved (nasal obstruction, aggregate relief, or smell sensation).
- In Study 1, capsaicin was notably better than placebo in overall nasal symptoms and symptom resolution, with moderate evidence.
- Study 2 showed a slightly better response for capsaicin in terms of nasal obstruction relief, but the results were not statistically significant (low evidence).
- In Study 3, a single-day treatment of 5 capsaicin doses showed slightly better results than the daily 5-day treatment for improving smell sensation, with moderate evidence.

Future Outcomes:

Advanced Formulations: Lipid-based delivery (liposomes, nano emulsions) to reduce irritation and enhance bioavailability.

Standardized Dosing & Safety: Large-scale clinical trials to establish optimal dosage and long-term safety.

Expanded Applications: Potential use in asthma, post-viral cough, and respiratory infections.

Commercialization: Development of capsaicin-based nasal sprays for chronic rhinitis and cough relief.

CONCLUSION: Capsaicin has demonstrated significant potential in treating various conditions, particularly non-allergic rhinitis, neuropathic pain, and inflammatory disorders. Its ability to interact with TRPV1 receptors and reduce substance P levels contributes to its analgesic and therapeutic effects. Intranasal capsaicin treatments have shown effectiveness in alleviating rhinitis symptoms, improving nasal airflow, and reducing reflex responses without long-term adverse effects. Additionally, studies suggest its role in preventing pneumonia and cluster headaches.

Despite its promising benefits, further research is needed to optimize dosing regimens, assess long-term safety, and explore alternative TRPV1-targeting compounds for enhanced efficacy. Capsaicin remains a valuable therapeutic option, with repeated applications providing prolonged symptom relief. Its potential in clinical settings continues to expand, making it a promising candidate for future pharmaceutical developments

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