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ANTITUSSIVE PHARMACOTHERAPY IN ACUTE COUGH: EFFICACY, SAFETY, AND CURRENT CLINICAL EVIDENCE

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ABSTRACT

Background: Acute viral cough is one of the most frequent reasons for primary-care consultation, yet evidence for commonly used antitussive agents varies widely. This review synthesizes current data on the pathophysiology, efficacy, safety, and clinical recommendations guiding antitussive pharmacotherapy.
Methods: This review synthesizes current evidence on antitussive pharmacotherapy in acute cough in adults and children. A narrative review of eligible publications indexed in PubMed, Scopus, and Google Scholar from 2013–2025 was conducted, prioritizing systematic reviews, randomized controlled trials, pharmacovigilance studies, and clinical guidelines. Search terms included "acute cough", "antitussive", "dextromethorphan", "codeine", "hydrocodone", "levodropropizine", "butamirate", "benzonatate", "ivy leaf", "Pelargonium sidoides", and "honey". Relevant studies were screened and qualitatively analyzed.
Results: Acute viral cough arises from inflammatory sensitization of airway sensory pathways and heightened brainstem cough-reflex responsiveness. Opioid antitussives demonstrate limited symptomatic benefit and present substantial safety concerns, particularly in pediatric populations. Centrally acting non-opioid agents, such as dextromethorphan, show modest and inconsistent efficacy with dose-dependent toxicity. Peripherally acting antitussives—notably levodropropizine—exhibit more consistent reductions in cough severity with favorable tolerability. Complementary agents, including ivy leaf extract, Pelargonium sidoides, and honey in children over one year, offer modest symptomatic benefit with strong safety profiles. Contemporary guidelines consistently discourage routine antitussive use and emphasize the self-limiting nature of acute viral cough.
Conclusion: Evidence supports a cautious, symptom-targeted approach to pharmacologic therapy in acute viral cough, prioritizing safety and reserving antitussives for selected clinical scenarios.

KEYWORDS

Acute Cough, Antitussive, Dextromethorphan, Codeine, Levodropropizine, Butamirate

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1. Introduction

Acute cough — defined as cough lasting less than three weeks — remains one of the most common symptoms prompting healthcare consultation worldwide (Birring et al., 2019; Murgia, 2020; Vittorakis et al., 2024). It is mostly caused by acute respiratory viral infections—particularly rhinovirus, influenza, respiratory syncytial virus (RSV), and seasonal coronaviruses (Petat et al., 2025). These infections are typically self-limited (Kandiwa et al., 2022), yet patients annually seek symptomatic pharmacologic relief in antitussives. Although several antitussive drugs with different mechanisms have been introduced over the years, only a few provide reliable and safe relief for patients. (Birring et al., 2019)

The objective of this review is therefore to evaluate the current evidence regarding the efficacy and safety of antitussive pharmacotherapy in adults and children with acute cough.

2. Pathophysiology of Acute Cough

2.1 Cough Reflex: Sensory Pathway and Brainstem Integration

Acute cough is initiated by activation of airway sensory receptors embedded in the larynx, trachea, and bronchi. These receptors include mechanosensitive Aδ-fibers and chemosensitive C-fibers, whose terminals lie just beneath the airway epithelium. Their afferent signals travel primarily through the **vagus nerve** to the **cough center in the medulla**, where they are integrated with cortical inputs responsible for voluntary modulation of cough (Amos et al., 2022; Andrani et al., 2018). As described in CHEST's global pathophysiology review, this neural network relies on nodose-derived Aδ fibers (rapidly adapting mechanoreceptors) and jugular-derived C-fibers detecting chemical and inflammatory stimuli (Lee et al., 2021, Sykes et al., 2021). The brainstem pattern generator then coordinates the characteristic inspiratory, compressive, and expulsive phases of cough.

2.2 Brainstem Cough Center and Motor Output

Once processed in the medulla, efferent signals are transmitted via the phrenic, spinal motor, and laryngeal nerves to respiratory and laryngeal muscles. This produces the three-step motor sequence: deep inspiration, glottic closure with intrathoracic pressure build-up, and rapid expiratory airflow (Amos et al., 2022; Naqvi et al., 2023). The CHEST expert panel highlights that even though cough is often reflexive, cortical regulation enables suppression or voluntary initiation, demonstrating that cough operates as a brainstem reflex modulated by higher centers (Lee et al., 2021).

2.3 Viral Inflammation and Sensory Nerve Sensitization

In acute respiratory infections, viral pathogens and the resulting immune response increase the sensitivity of vagal afferents. As detailed in the review on infectious pathways to cough, viral inflammation produces a surge of inflammatory mediators—including bradykinin, leukotrienes, prostaglandins, type I and II interferons, ATP, and other inflammatory cytokines—that activate ionotropic and metabotropic receptors on airway sensory neurons, thereby enhancing cough reflex sensitivity (Naqvi et al., 2023). These mediators lower the activation threshold of C-fibers, resulting in heightened cough responsiveness to otherwise mild stimuli. CHEST guidelines also emphasize that viral inflammation promotes **cough hypersensitivity**, increasing both the frequency and severity of cough during acute illness (Lee et al., 2021).

Summary

In acute cough, the pathophysiology reflects a tightly coordinated reflex arc involving peripheral vagal receptors, brainstem integration, and efferent motor pathways. Viral infections amplify this reflex by increasing inflammatory mediator release, which sensitizes airway sensory neurons and lowers the cough threshold. These mechanisms, evidenced across multiple physiologic and guideline-based sources, form the foundation for understanding both symptom generation and the rationale for targeted antitussive interventions.

3.Overview of Antitussive Drug Classes

3.1. Opioid Antitussives

Opioid antitussives represent the oldest class of centrally acting cough suppressants. **Codeine**, a μ-opioid receptor agonist, exerts its antitussive effect through suppression of the medullary cough center (Singu & Verbeeck, 2021). Although codeine-containing formulations remain in use, multiple reviews show that evidence for their antitussive efficacy in acute, short-duration cough is weak, with several trials demonstrating no clear benefit over placebo (Singu & Verbeeck, 2021; Lam et al., 2021) These findings are reinforced by pediatric and general-population antitussive reviews, which note that many countries have restricted or discouraged codeine use for cough due to **poor evidence of clinical effectiveness** in viral upper respiratory infections (Lam et al., 2021). **Hydrocodone**, another centrally acting opioid, has a stronger antitussive and analgesic profile than codeine. However, observational data show that hydrocodone-containing cough syrups are primarily used in chronic or severe conditions, rather than routine acute cough, reflecting lack of evidence for benefit in uncomplicated, self-limiting viral illness (Sloan et al., 2019).

Therefore, opioid antitussives, including codeine, have little clinical evidence supporting their antitussive efficacy and therefore should not be considered first-line options (Singu & Verbeeck, 2021).

3.2. Non-Opioid Centrally Acting Antitussives

Non-opioid centrally acting antitussives are a mechanistically distinct class designed to suppress the cough reflex without μ-opioid receptor activity. **Dextromethorphan** is the most widely used agent in this category (Oh et al., 2023) and acts through NMDA receptor antagonism and sigma-1 receptor agonism (Oh et al., 2023, McCarthy et al., 2023). File-based clinical data, including a randomized phase-IV comparison, show that dextromethorphan reduces cough frequency and severity, although the magnitude of benefit is moderate (Ghosh, 2019). A multicenter observational study confirms its widespread use in acute cough formulations across Europe and North America, indicating its continued clinical relevance despite variable effect sizes across trials (Lam et al., 2021). **Butamirate** is a centrally acting, non-opioid antitussive widely used in European clinical practice. Evidence summarized in pharmacologic reviews indicates that it improves cough severity and overall symptom scores in adults with acute upper-airway irritation, without engaging opioid receptor pathways (Singu & Verbeeck, 2021).

3.3. Peripherally Acting Antitussives

Peripherally acting antitussives constitute a pharmacologic class that reduces cough by modulating airway sensory pathways rather than suppressing central cough-generation circuits. **Levodropropizine** is the best-characterized representative of this group and acts through inhibition of peripheral sensory C-fiber activation, a mechanism highlighted across mechanistic and clinical reports (Nayar et al., 2025). Because C-fiber afferents are primary mediators of cough initiation in response to chemical and mechanical stimuli, targeting these pathways provides a physiologically coherent therapeutic approach in non-productive and irritative acute cough (Nayar et al., 2025). European clinical analyses document that levodropropizine has been evaluated in multiple adult studies involving acute and subacute cough, including upper-respiratory infection–associated cough. Across these trials, levodropropizine produced clinically meaningful reductions in cough frequency, cough severity, and nocturnal disturbance, with corresponding improvements in sleep continuity and patient-reported symptom burden (Prasanna et al., 2023).

Evidence synthesized in the same European review describes symptom relief across a spectrum of acute cough presentations, suggesting that levodropropizine's therapeutic effect is maintained in the presence of viral inflammation and airway irritation (Prasanna et al., 2023). Its sensory-modulating mechanism differentiates it from centrally acting antitussives, and available evaluations consistently demonstrate improvements in both daytime and nighttime cough without involvement of opioid receptor pathways (Nayar et al., 2025; Prasanna et al., 2023).

Benzonatate is a peripherally acting antitussive whose clinical effectiveness in acute cough remains poorly supported by contemporary evidence (Rahurkar et al., 2025). Unlike levodropropizine, which has been evaluated across multiple controlled trials, benzonatate's efficacy data are limited, and no high-quality randomized studies assessing its benefit in acute viral cough are available (Ebell et al., 2025; Rahurkar et al., 2025). Real-world prescribing data show that benzonatate use has increased substantially, with U.S. ambulatory-care analyses demonstrating that prescribing rates more than tripled between 2003 and 2018 (Yang et al., 2022). However, effectiveness findings do not mirror this rise in use: in a 718-patient prospective cohort of adults with acute cough, benzonatate did **not reduce cough duration or severity**, indicating a lack of observable clinical benefit in routine care (Ebell et al., 2025). Complementary evidence from safety-oriented reviews notes that high-quality efficacy trials are scarce, with only a small number of studies available and no compelling demonstration of superiority over symptomatic care alone (Rahurkar et al., 2025). As a result, benzonatate occupies an uncertain position within peripherally acting antitussives, with increasing utilization despite limited evidence supporting its therapeutic effectiveness in acute cough.

3.4. Herbal and Complementary Agents

Complementary therapies are frequently used for symptomatic cough management, particularly in primary care settings, and several plant-derived formulations have been investigated for their antitussive properties. **Ivy-leaf extract** has demonstrated efficacy in acute respiratory tract infections, with randomized placebo-controlled trials showing reductions in cough severity and improvements in overall symptom burden (Völp et al., 2022). **Pelargonium sidoides** has also been evaluated in controlled clinical settings, with evidence from randomized trials indicating symptomatic benefit in acute bronchitis and upper-airway infections (NICE, 2019). **Honey** remains the most consistently supported complementary agent, with controlled trials and evidence syntheses demonstrating reductions in cough frequency, improved nocturnal symptoms, and overall symptomatic relief in upper-respiratory infections (Abuelgasim et al., 2021; Murgia et al., 2021; NICE, 2019). Real-world treatment-pattern data show that herbal and natural preparations continue to be widely used in common cough formulations (Prasanna et al., 2023). Although evidence quality varies—particularly for ivy-leaf and *Pelargonium* preparations—current reviews characterize their benefits as modest but clinically relevant for short-term relief of mild acute cough, with a smaller evidence base compared to conventional pharmaceutical antitussives (Singu & Verbeeck, 2021).

4. Comparative Efficacy

Comparative evidence across antitussive classes highlights clear differences in symptomatic effectiveness for acute cough. **Opioid antitussives**, particularly codeine, demonstrate **limited and inconsistent clinical benefit**, with several controlled evaluations showing no meaningful superiority over placebo in short-duration viral upper-respiratory infections (Thirion, 2019). Pediatric and general-population analyses similarly note that opioid formulations provide **poorly substantiated symptomatic relief**, contributing to reduced clinical use and regulatory caution in many settings (Lam et al., 2021). Evidence

regarding hydrocodone in acute cough is sparse; available data relate primarily to pediatric toxicity and highlight safety concerns rather than demonstrable antitussive efficacy (Diantini et al., 2024).

In contrast, **non-opioid centrally acting agents** such as dextromethorphan show **variable efficacy** across studies. Adult randomized trials report no significant improvement in cough outcomes when compared with usual care in acute bronchitis (Llor et al., 2022), whereas pediatric controlled data document reductions in objective cough counts, indicating age-dependent differences in treatment response (Meeves et al., 2023). Clinical summaries categorize the overall efficacy of centrally acting agents in uncomplicated acute cough as modest and inconsistent (Thirion, 2019).

By comparison, **peripherally acting agents**, particularly levodropropizine, display **more consistent symptomatic relief**. Meta-analytic evidence demonstrates that levodropropizine provides significantly greater improvement in cough severity and nocturnal symptoms than centrally acting agents, including codeine and dextromethorphan (Zanasi et al., 2015). Mechanistic and clinical reviews reinforce these findings, describing reproducible benefits in acute and subacute cough linked to upper-respiratory tract infections and irritative etiologies (Nayar et al., 2025; Prasanna et al., 2023).

Taken together, the available evidence indicates that **peripherally acting antitussives—most notably levodropropizine—exhibit greater and more consistent efficacy** in acute cough when compared with both opioid and non-opioid centrally acting agents. Centrally acting antitussives provide **limited and heterogeneous benefits**, whereas opioid agents offer **minimal therapeutic advantage** and carry a substantially higher safety burden. As a result, peripherally acting agents appear to occupy the most evidence-supported position among pharmacologic options for short-term symptomatic management of acute cough.

5. Safety Profile of Antitussive Agents

5.1. Safety of Opioid Antitussives

Opioid antitussives—primarily **codeine** and **hydrocodone**—are associated with clinically significant safety risks that outweigh their limited effectiveness in acute cough (Renny et al., 2022, Singu & Verbeeck, 2021). **Codeine** is subject to wide inter-individual metabolic variability due to CYP2D6 polymorphisms, resulting in unpredictable conversion to morphine and a corresponding risk of **respiratory depression**, particularly in ultra-rapid metabolizers (Singu & Verbeeck, 2021). Regulatory safety reviews document **substantial pediatric harm**, including **serious adverse events and deaths**, most attributed to opioid-induced respiratory depression following administration of codeine-containing antitussives to children (Medsafe Pharmacovigilance Team, 2018)

These risks have prompted extensive policy action. Restrictions by major regulatory bodies state that **codeine-containing cough medicines must not be used in children under 12 years**, with additional warnings applied to adolescents with risk factors for hypoventilation (Medsafe Pharmacovigilance Team, 2018). Population analyses further demonstrate declining codeine prescribing following implementation of these restrictions, reflecting growing clinical recognition of its unfavorable safety profile (Renny et al., 2022).

Additional pharmacologic analyses demonstrate that codeine has a narrow therapeutic margin, with opioid-related adverse effects—including respiratory depression, sedation, and misuse potential—documented in reviews of over-the-counter opioid preparations (Sobczak & Goryński, 2020). Furthermore, contemporary analyses note that the **risk–benefit balance for codeine in cough is negative**, citing limited evidence of efficacy combined with dose-dependent toxicity (Singu & Verbeeck, 2021).

Hydrocodone, another opioid antitussive used primarily in combination preparations, demonstrates similar safety concerns. A benefit–risk review of hydrocodone/chlorpheniramine products identified multiple serious pediatric adverse events, including **fatal cases**, largely linked to overdose or respiratory suppression (Sloan et al., 2019). Additional pediatric case data from the same safety assessment describe clinically significant respiratory and central nervous system depression following therapeutic or supratherapeutic hydrocodone exposure (Sloan et al., 2019). Prescribing-trend analyses following FDA safety communications also show that hydrocodone-containing cough and cold medicines lack evidence of efficacy for acute cough and pose **meaningful risks of respiratory depression, sedation, and accidental ingestion** (Chua & Conti, 2021).

5.2 Safety of Non-Opioid Centrally Acting Antitussives

Dextromethorphan is generally considered safer than opioid antitussives at therapeutic doses; however, its safety profile remains strongly dose-dependent (Colom Gordillo et al., 2022; Summerlin & Eiland, 2025). Clinical evaluations indicate that standard doses are typically well tolerated, with mild central nervous system effects—most commonly dizziness or drowsiness—reported during appropriate use (Summerlin & Eiland, 2025). At higher exposures, toxicity is mediated in part by dextrorphan-induced NMDA receptor antagonism, a mechanism implicated in the neuropsychiatric manifestations observed during acute dextromethorphan-induced psychosis (Zaremba et al., 2023).

Toxicology and poison-center data consistently demonstrate that supratherapeutic or recreational ingestion produces significant autonomic and CNS disturbances, including tachycardia, agitation, ataxia, hallucinations, dissociation, and, in severe cases, coma or toxic psychosis (Colom Gordillo et al., 2022; Zaremba et al., 2023). High-dose exposure can precipitate acute psychotic episodes through combined NMDA and sigma-1 receptor activation, as documented in clinical case analyses (Zaremba et al., 2023). Misuse is particularly prevalent among adolescents, where intentional high-dose ingestion substantially increases the risk of severe toxicity (Summerlin & Eiland, 2025).

Pharmacologic interactions further narrow the safety margin. Co-administration with serotonergic medications—including SSRIs and MAO inhibitors—carries a documented risk of serotonin syndrome, reflecting the drug's serotonergic effects at elevated exposures (Summerlin & Eiland, 2025).

Despite these concerns, a controlled adult study confirms that **therapeutic single doses are generally safe**. A randomized scintigraphic trial of dextromethorphan-containing cold products reported no serious adverse events in healthy volunteers, supporting the overall tolerability of standard dosing regimens (Mallefet et al., 2022). Nonetheless, both toxicology and pharmacovigilance reviews emphasize that overdose, drug interactions, and intentional misuse significantly reduce the safety margin and account for the majority of clinically significant adverse events (Colom Gordillo et al., 2022; Summerlin & Eiland, 2025).

Butamirate has been shown to be well tolerated in adult populations, with adverse events reported as infrequent and generally mild—most commonly headache, nausea, and somnolence—and with no serious safety signals observed in controlled trials (Faruqi et al., 2014). Complementary pediatric observational findings similarly describe good tolerability, with no reports of respiratory depression, sedation, cognitive impairment, or drug dependence, and no indications of severe toxicity during routine clinical use (Rashitova et al., 2020). Collectively, these data indicate that butamirate is well tolerated and lacks the central nervous system and respiratory risks associated with opioid antitussives, supporting its use for short-term symptomatic relief of dry cough (Faruqi et al., 2014; Rashitova et al., 2020).

5.3 Safety of Peripherally Acting Antitussives

Levodropropizine, a peripherally acting non-opioid antitussive, is described in contemporary reviews as having a more favorable safety profile than centrally acting agents, owing to its peripheral mechanism and minimal central nervous system involvement (Nayar et al., 2025; Shirsat et al., 2023). Clinical evidence further indicates that the drug is generally well tolerated, with a low incidence of treatment-emergent adverse effects in adult populations (Lee et al., 2022; Shirsat et al., 2023). In a randomized comparative trial in adults with chronic cough, levodropropizine was associated with significantly fewer treatment-related adverse events than codeine, reflecting a more favorable tolerability profile. Reported adverse effects were mild—primarily drowsiness, constipation, and headache—and occurred less frequently than in the codeine group.Importantly, no serious adverse events or treatment discontinuations attributable to levodropropizine were observed during the two-week treatment period (Lee et al., 2022).

These findings are consistent with controlled pharmacokinetic data in healthy adults, where levodropropizine demonstrated **good overall tolerability** and **no clinically significant elevations** in hepatic toxicity markers—including ALT, AST, and γ-GTP—across monitored dosing intervals (Jang et al., 2024). Only transient mild nausea was reported, supporting its favorable acute safety profile in first-in-human exposure (Jang et al., 2024).

Review-level assessments further corroborate these trial findings. Contemporary pharmacologic analyses describe levodropropizine as a **non-opioid agent with minimal central nervous system burden**, noting the absence of CNS depression or sedation traditionally associated with centrally acting antitussives (Shirsat et al., 2023; Nayar et al., 2025). These reviews also highlight its **favorable tolerability across age groups**, reflecting long-standing clinical use in European and Asian practice settings without documented serious toxicity at therapeutic dosing (Shirsat et al., 2023; Nayar et al., 2025).

Benzonatate, though non-opioid, presents a distinct set of safety concerns. Pediatric pharmacovigilance data identify 4,689 exposure cases from 2010–2018, with 80% involving single-substance ingestion and the highest unintentional exposure burden occurring in children aged 0–5 years (Kim et al., 2022). Serious outcomes—including CNS depression, seizures, and fatal events—were documented in both accidental and intentional ingestions, with intentional misuse increasing among adolescents (Kim et al., 2022). Parallel real-world analyses show benzonatate to be a **high-impact safety concern**: despite widespread use, only nine safety studies exist, while nearly **50 serious adverse events** (including seizures, arrhythmias, and deaths) have been reported in national surveillance systems (Rahurkar et al., 2025).

Case-based evidence further underscores its narrow safety margin. Therapeutic-use case series describe acute neuromuscular reactions such as **benzonatate-associated neck stiffness** (Era et al., 2022), while overdose reports document **rapid cardiovascular collapse and cardiac arrest** after ingestion of fewer than 30 capsules (Jin et al., 2019).

Despite these risks, U.S. ambulatory-care data show benzonatate prescribing has **more than tripled** since 2003 (Yang et al., 2022). Evidence from a 718-patient prospective cohort further indicates **no reduction in cough duration or severity** with benzonatate use (Ebell et al., 2025), reinforcing concerns about limited clinical benefit relative to safety liabilities.

5.4 Safety of Ivy Leaf, Honey, and Pelargonium Extracts

Ivy leaf extract demonstrates a favorable safety profile across regulatory assessments, clinical trials, and observational data. European regulatory evaluations describe adverse reactions as uncommon and generally mild, with no indication of serious toxicity during routine use (EMA, 2017). In controlled clinical studies, including those examining EA 575 in acute bronchitis, adverse events were infrequent and non-serious (Kardos et al., 2025). Large-scale pediatric observational data also support good tolerability; in more than 5,000 children treated with ivy-leaf preparations, no serious adverse reactions were identified (Olszanecka-Glinianowicz et al., 2020). Furthermore, a systematic review of randomized and observational studies concluded that ivy extract was consistently well tolerated, with no serious drug-related harms reported (Sierocinski et al., 2021).

Honey, commonly used to relieve acute cough in children, shows a similarly reassuring safety profile. A recent systematic review of randomized trials reported no severe adverse events associated with honey, with only occasional mild gastrointestinal symptoms noted across studies involving children older than one year (Kuitunen & Renko, 2023).

Pelargonium sidoides extract (EPs 7630) is well studied, with safety evaluated in numerous clinical and post-marketing settings. Clinical trial data comprising more than 10,000 adults and children show adverse-event rates comparable to placebo and no evidence of hepatic injury, as liver enzyme values remained within normal ranges across studies (Matthys et al., 2013). Regulatory guidance notes that Pelargonium sidoides extract is generally well tolerated, but the EMA also reports that cases of hepatotoxicity and hepatitis have occurred and advises discontinuation of treatment if signs of liver dysfunction appear (EMA, 2024). Pediatric-oriented analyses also report an absence of serious adverse reactions in clinical use and emphasize that safety conclusions apply specifically to standardized medicinal formulations (Baraniak & Kania-Dobrowolska, 2020).

Taken together, the evidence indicates that ivy leaf preparations, honey, and Pelargonium sidoides extract exhibit a favorable tolerability profile, with **no documented serious toxicity at therapeutic doses** in adults or children across the available clinical and regulatory literature.

6. Current Clinical Guidelines on Antitussive Use in Acute Cough

Current clinical guidance on the management of acute viral cough is informed by several authoritative sources, including the CHEST Expert Panel Report on acute cough associated with the common cold (Malesker et al., 2017), Canadian primary-care therapeutic recommendations summarised in contemporary international evaluations (Winck et al., 2025), systematic assessments of global acute-cough guidelines published between 2006 and 2019 (Thirion et al., 2019), and primary-care practice guidance from the Best Practice Advocacy Centre New Zealand (Best Practice Advocacy Centre New Zealand, 2023). Collectively, these sources constitute the principal evidence-based reference framework for current clinical practice.

Although all guidelines address symptomatic relief, they differ substantially in scope and the strength of their recommendations regarding antitussives. The CHEST Expert Panel adopts a restrictive stance, recommending against the use of over-the-counter antitussive and cough–cold medications for acute viral cough in adults and children due to insufficient evidence of clinical benefit and concerns related to opioid

safety in individuals younger than 18 years (Malesker et al., 2017). Canadian primary-care–oriented analyses summarised in international guideline evaluations similarly conclude that antitussives have limited evidence of benefit and emphasise caution in pediatric populations, reflecting broad restrictions on their use in young children (Winck et al., 2025). Systematic cross-national evaluations highlight further variation: while most guidelines do not recommend pharmacologic suppression of acute viral cough, methodological quality differs and some guidelines assign greater importance to non-pharmacologic options such as menthol preparations (Winck et al., 2025). Complementing these findings, Thirion et al. (2019) emphasise that symptomatic care forms the cornerstone of primary-care management and note that commonly used antitussive agents have poor or inconclusive evidence of effectiveness in uncomplicated acute cough, contributing to recommendations against their use in children and cautious, limited use in adults. In contrast, bpacnz guidance diverges slightly by acknowledging potential symptomatic benefit from selected complementary therapies—most notably honey in children older than one year and ivy leaf extract—while maintaining that conventional antitussives provide little to no demonstrable benefit and should not be used in children under six years (Best Practice Advocacy Centre New Zealand, 2023).

Despite these differences, several consistent themes emerge. All guidelines characterise acute viral cough as a self-limiting condition for which antitussive pharmacotherapy has limited evidence of efficacy. All emphasise safety concerns in pediatric populations, particularly regarding opioid antitussives. None recommend antitussives as first-line therapy for uncomplicated acute viral cough. The main differences relate to the degree to which selective, symptom-driven use may be considered in adults and whether complementary therapies are incorporated into management recommendations. Overall, contemporary guidance indicates that routine antitussive use is not supported by current evidence, although narrowly defined symptomatic use may be considered under specific clinical circumstances.

7. Discussion

Across pharmacologic classes, evidence consistently shows that opioid antitussives—particularly codeine and hydrocodone—offer limited symptomatic benefit in acute viral cough and carry meaningful safety risks, especially in children and adolescents. Regulatory reviews and clinical assessments document respiratory depression, variable metabolism, and lack of demonstrable efficacy, supporting strong recommendations against their use in routine acute cough management (Medsafe Pharmacovigilance Team, 2018; Sloan et al., 2019; Singu & Verbeeck, 2021). Non-opioid centrally acting agents such as dextromethorphan provide modest and inconsistent symptomatic benefit across age groups, with multiple pediatric and adult studies demonstrating no clear superiority over placebo; in addition, toxicity is clearly dose-dependent and increases substantially at supratherapeutic exposures (Lam et al., 2021; Oh et al., 2023)

Peripherally acting antitussives—particularly levodropropizine—demonstrate more consistent symptom reduction, with evidence showing improvements in cough severity, nocturnal symptoms, and patient-reported outcomes across viral and irritative cough presentations. These benefits occur alongside a favorable safety profile, minimal central nervous system involvement, and no documented serious toxicity at therapeutic doses (Nayar et al., 2025; Lee et al., 2022; Jang et al., 2024). Herbal and complementary therapies, including ivy leaf extract, honey, and Pelargonium sidoides, also exhibit favorable tolerability and modest symptomatic benefit, with high-quality safety data available for several formulations (EMA, 2017; Kardos et al., 2025; Kuitunen & Renko, 2023; Matthys et al., 2013).

Contemporary clinical guidelines echo these findings. The CHEST Expert Panel recommends against OTC antitussives due to insufficient evidence and opioid-related harm (Malesker et al., 2017). International guideline evaluations similarly report that most recommendations do not support pharmacologic suppression of acute viral cough and emphasize the self-limiting nature of the condition (Winck et al., 2025). Primary-care guidance, including bpacnz, advises against antitussive use—particularly in children under six—while acknowledging limited roles for honey and ivy leaf extract in selected cases (Best Practice Advocacy Centre New Zealand, 2023). Thirion et al. (2019) further reinforce that symptomatic care remains central and that widely used antitussives have poor or inconclusive evidence of benefit.

8. Conclusions

Acute viral cough is a self-limiting condition driven by transient inflammatory sensitisation of airway sensory pathways, yet it remains a frequent cause of clinical consultation. Across available evidence, opioid antitussives offer minimal symptomatic benefit and carry significant safety concerns, supporting strong restrictions on their use. Non-opioid centrally acting agents provide modest and inconsistent relief, whereas peripherally acting options—particularly levodropropizine—demonstrate more consistent improvements in cough severity and nocturnal symptoms with favorable tolerability.

Complementary therapies such as ivy leaf extract, Pelargonium sidoides, and honey in children over one year show modest benefit and good safety profiles, though evidence depth varies. Major guidelines consistently agree that **routine antitussive use is not supported for uncomplicated acute viral cough.** Instead, treatment should focus on symptomatic care, with selective pharmacologic use reserved for clearly defined circumstances and guided by safety considerations

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