International Journal of Scientific Research in Engineering and Management (IJSREM)
Volume: 09 Issue: 11 | Nov - 2025 SJIF Rating: 8.586 ISSN: 2582-3930

Pharmacology of Cough Suppressant: Herbal Vs Modern Drug

Vaishnavi Vijay Jambhulkar*, Miss. Kiran S. Langhe[1], Sunil Baban Rathod[2] , Shraddha Dadabhau Bhor[3] , Jyotiraditya Bapurao Pawar[4]

Sahakar Maharshi Kisanrao Varal Patil College of Pharmacy Nighoj , Maharashtra (414306)

Abstract

Cough is a protective reflex. Its main function is to clear the airways. Chronic cough represents a continuous challenge mainly for primary care. The investigation of cough is mainly based on its duration as it determines its possible causes or diseases, narrowing down the differential diagnosis, although there is always a significant overlap. Acute cough is defined as being less than 3 weeks in duration and is mainly caused by infections or potential life-threatening diseases. Sub-acute cough lasts between 3 and 8 weeks and is usually postinfectious. Chronic cough that exceeds 8 weeks in duration, is a diagnostic challenge as its etiology includes a wide range of causes. The main investigation-based approach depends on the presence or absence of radiological based abnormalities. When cough persists despite detailed evaluation and guideline-based treatment, the patient may suffer from chronic refractory cough. In the last, the main challenge Is to develop pharmaceutical interventions for either improvement or/and elimination of its intensity. In this review we suggest a stepwise approach for the investigation of cough.

Keywords : Cough suppressants , Phytotherapy , Safety profile, Natural remedies, Respiratory disorders, Traditional medicine

Introduction

Cough is an important protective reflex in adults. It is an innate immunity mechanism that clears the airways from mucus, noxious agents, and pathogens. Cough represents a common symptom for medical assessment mainly in the primary care setting. In a retrospective study of 200000 patients in the UK, approximately 18% of the total population was assessed by a primary health care physician for a condition related to cough, acute or chronic(1). A metaanalysis of 90 studies showed that the overall prevalence of chronic cough was 9.6% worldwide, with higher rates in Oceania (18.1%), Europe (12.7%) and America (11%) compared to Asia (4.4%) and Africa (2.3%)(2). Another study of 10032 patients in specialized cough clinics showed that chronic cough was more common in females aged between the 5th and 7th decade(3). Chronic cough is reported by patients at a rate ranging from 10% to 38% (4). It is more common in smokers and is related to environmental conditions as its prevalence increases with the mean annual concentration of nitrogen dioxide, total suspended particulates and particulates less than 10 μm in diameter in the atmosphere(5). Several population studies have shown an increase in the prevalence of chronic cough worldwide due to increase in conditions and diseases such as bronchiectasis, asthma, GERD, upper airway cough syndrome, low income, smoking, occupation exposure to dust/fumes, low vegetable intake and abdominal obesity(6).

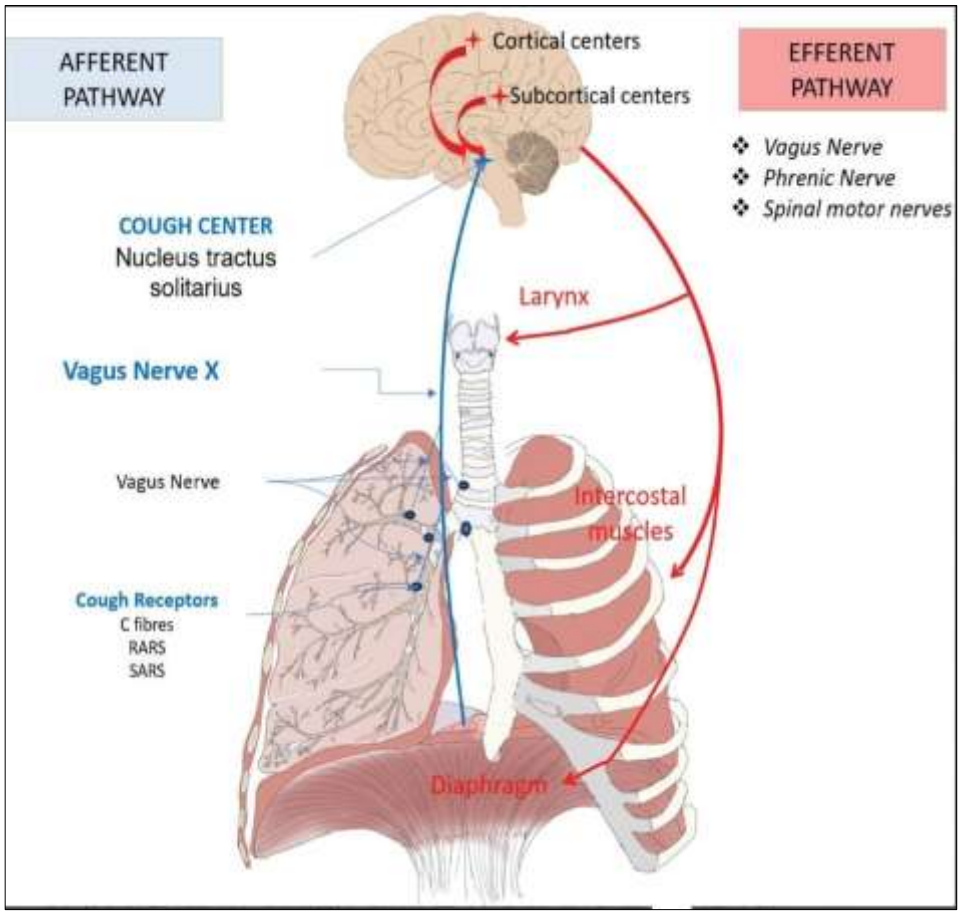

Figure 1. Physiology of cough (RARS: rapidly adapting receptors, SARS: slowly adapting receptors)

Understanding the Cough Reflex and Therapeutic Targets

The cough reflex serves as a vital protective mechanism involving complex neurophysiological pathways from peripheral sensory receptors to central processing centers in the brainstem. Cough-sensitive sensory fibers, including rapidly adapting receptors (RARs), slowly adapting receptors (SARs), and C-fibers, detect mechanical, chemical, and inflammatory stimuli in the respiratory tract. These signals travel through the vagus nerve to the nucleus tractus solitarius in the medulla oblongata, which functions as the primary cough center coordinating the motor response[7].

Modern understanding of cough pathophysiology has revealed that different types of cough may have varying sensitivities to antitussive interventions. Research demonstrates that cough induced from upper airway disorders shows reduced sensitivity to traditional opioid-based suppressants compared to lower airway pathology[8]. This finding has significant implications for therapeutic selection, as it suggests that the anatomical origin of cough influences treatment responsiveness.

The complexity of the cough reflex"explains why both herbal and modern therapeutic approaches can be effective through different mechanisms. While synthetic drugs typically target specific receptors or pathways, herbal remedies often provide multi-target effects that address various components of the cough reflex simultaneously.

Modern Antitussive Drug Pharmacology

Centrally Acting Opioid Suppressants

Codeine remains the archetypal centrally acting antitussive, despite growing questions about its clinical efficacy[9]. The drug functions as a prodrug, requiring metabolic conversion to morphine via the cytochrome P450 2D6 (CYP2D6) enzyme system to exert its therapeutic effects[10]. This conversion process creates significant inter-individual variability in response, with ultra-rapid metabolizers at risk for toxicity and poor metabolizers experiencing reduced efficacy[11].

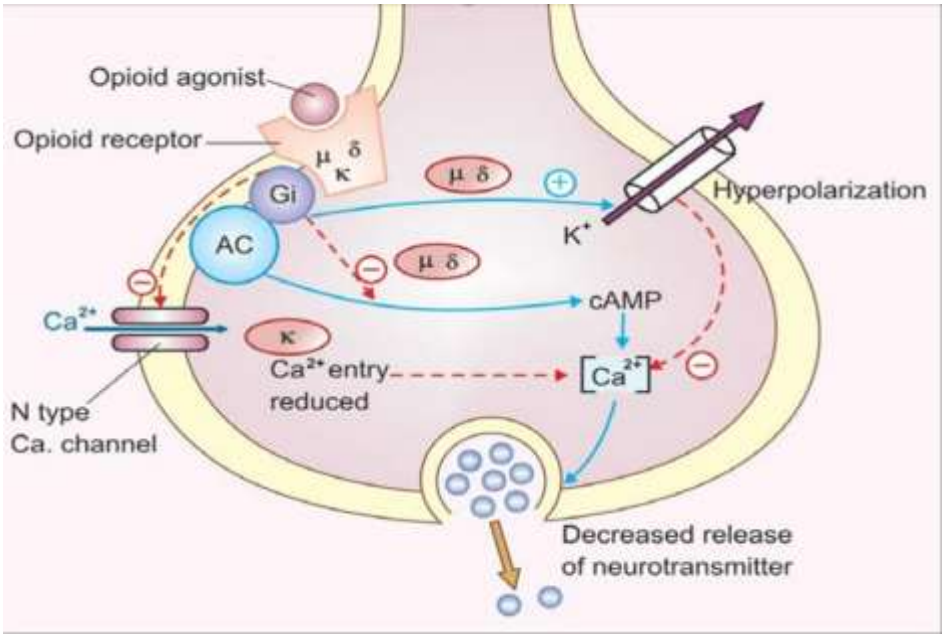

Figure 2. Mechanism of Codeine's antitussive action

The mechanism of codeine's antitussive action primarily involves mu-opioid receptor activation in the brainstem cough center. These receptors modulate neurotransmitter release through G-protein coupled signaling pathways, ultimately inhibiting glutamatergic transmission at the level of the nucleus tractus solitarius[7]. Clinical studies demonstrate that codeine can suppress cough by 50-100% in animal models, though human studies show more variable results[8].

Recent systematic reviews reveal important limitations in codeine's clinical efficacy. Multiple studies indicate that codeine at doses of 50mg fails to suppress cough effectively in patients with upper respiratory tract infections, while showing greater effectiveness in lower airway conditions such as chronic bronchitis[8,9]. This differential efficacy pattern suggests that the type and location of cough stimuli significantly influence treatment response.

Safety concerns surrounding codeine have led to significant regulatory restrictions. The FDA issued black box warnings regarding respiratory depression and death in pediatric patients, particularly those who are CYP2D6 ultra-rapid metabolizers[10]. These safety issues have prompted many countries to restrict or eliminate codeine use in children under 12 years of age[11].

Non-Opioid Central Suppressants

Dextromethorphan represents the most widely used non-opioid antitussive, with a fundamentally different mechanism of action compared to opioid-based drugs[12]. Unlike codeine, dextromethorphan functions as a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist and sigma-1 receptor agonist, avoiding the opioid-related side effects while maintaining antitussive efficacy[13].

The pharmacokinetics of dextromethorphan reveal favorable absorption characteristics, with oral bioavailability reaching peak plasma concentrations within 2-3 hours. The drug undergoes extensive first-pass metabolism through CYP2D6 and CYP3A4 pathways, producing the active metabolite dextrorphan, which contributes significantly to the overall antitussive effect[14].

Clinical trials consistently demonstrate dextromethorphan's superiority over placebo in suppressing experimentally induced cough. Meta-analyses of citric acid challenge studies show significant cough suppression lasting up to 24 hours following administration. The drug's antitussive potency in adults approaches that of codeine while avoiding respiratory depression, sedation, and dependence potential[15].

Safety profiles for dextromethorphan are generally favorable when used at therapeutic doses. The most common adverse effects include mild neurological symptoms such as dizziness, drowsiness, and gastrointestinal upset[16]. However, abuse potential exists at supratherapeutic doses, where the drug can produce dissociative effects similar to ketamine[16].

Peripheral Antitussives

Levodropropizine represents an important class of peripheral antitussives that target sensory pathways outside the central nervous system[17]. This drug inhibits cough reflex activation by modulating C-fiber activity in vagal sensory pathways, providing effective cough suppression without central nervous system effects[18].

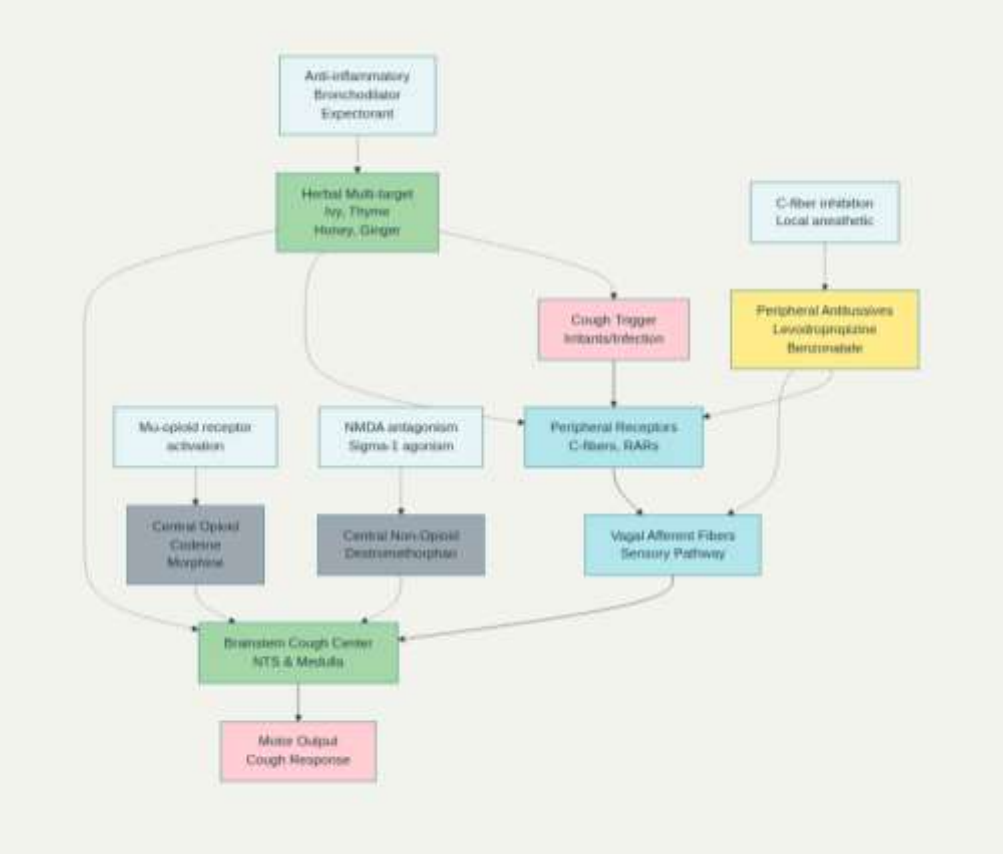

Figure 3. The Cough Reflex Pathway and Sites of Drug Action

Clinical evidence demonstrates levodropropizine's superiority over traditional central antitussives in several important outcomes. Comparative studies show significantly greater cough severity reduction compared to dextromethorphan, with faster onset of therapeutic benefit[17]. The drug exhibits particular efficacy in chronic bronchitis patients, with 75% of subjects showing meaningful symptom improvement[17].

The safety profile of levodropropizine represents a significant advantage over centrally acting alternatives. The drug causes minimal systemic side effects due to its peripheral mechanism of action, with negligible potential for respiratory depression, sedation, or dependence[17]. This favorable safety profile makes levodropropizine particularly suitable for pediatric populations and patients with respiratory compromise

Herbal Antitussive Pharmacology

Traditional Single-Plant Remedies

Herbal cough suppressants encompass a vast array of plant-based preparations with diverse mechanisms of action. Unlike synthetic drugs that typically target single pathways, herbal remedies often provide multi-target therapeutic effects through complex phytochemical compositions[19].

Honey represents one of the most extensively studied natural antitussives, with clinical evidence supporting its effectiveness in reducing cough frequency and severity[20,21]. The mechanism involves multiple pathways including antimicrobial effects, anti-inflammatory properties, and direct soothing action on irritated mucous membranes. Clinical trials demonstrate honey's superiority over placebo and equivalence to dextromethorphan in reducing nighttime cough in children[21].

Ginger (Zingiber officinale) exhibits potent anti-inflammatory and bronchodilatory properties through its active compounds gingerols and shogaols. Traditional preparations involve decoctions or combinations with other herbs to enhance therapeutic

effects. The anti-inflammatory mechanisms help reduce airway irritation while the warming properties promote expectoration[22].

Turmeric (Curcuma longa) provides antitussive effects through its active compound curcumin, which demonstrates powerful anti-inflammatory and antioxidant properties. Clinical applications typically involve combination with warm milk or honey to enhance bioavailability and provide additional soothing effects[22].

Complex Herbal Formulations

Ivy leaf (Hedera helix) extracts have gained significant attention as evidence-based herbal antitussives. Systematic reviews of clinical trials involving ivy preparations demonstrate consistent efficacy in reducing cough frequency and severity[23]. The active compounds include saponins, particularly hederacoside C and α-hederin, which exhibit expectorant, bronchodilatory, and anti-inflammatory properties[24].

Clinical trials comparing ivy extract with conventional treatments show favorable outcomes. A large randomized controlled trial (n=325) demonstrated that ivy extract EA 575 was non-inferior to combination treatments containing ivy/thyme and thyme/primrose extracts, while showing superior efficacy compared to the ivy/thyme combination. These findings challenge the assumption that herbal combinations necessarily provide greater therapeutic benefit than single-extract preparations[24] .

Traditional Chinese Medicine (TCM) formulations represent sophisticated multi-herb approaches to cough treatment. Systematic reviews of TCM for chronic cough encompassing 80 randomized controlled trials with 7,573 patients demonstrate significant improvements in cough severity and quality of life measures[25,26]. The most commonly used formulation, Zhisou-san, contains multiple herbs including Platycodon grandiflorus, Glycyrrhiza glabra, and Aster tataricus, which provide synergistic anti-inflammatory, expectorant, and bronchodilatory effects[25].

Phytochemical Mechanisms

The therapeutic effects of herbal antitussives derive from diverse phytochemical compounds that target multiple pathways simultaneously. Flavonoids such as quercetin, found in many medicinal plants including Adhatoda vasica and Psidium guajava, demonstrate anti-inflammatory and antimicrobial properties that help address underlying causes of cough[27].

Alkaloids present in plants like Adhatoda vasica contain vasicine, which exhibits bronchodilatory and expectorant properties[27]. Essential oils from plants such as eucalyptus and peppermint provide direct antimicrobial effects against respiratory pathogens while also producing local anesthetic effects that reduce cough sensitivity.

The multi-target nature of herbal antitussives may explain their clinical effectiveness despite lower concentrations of individual active compounds compared to synthetic drugs. This "shotgun approach" allows herbal preparations to address multiple aspects of the cough reflex simultaneously, potentially providing more comprehensive symptom relief[28].

Comparative Clinical Evidence and Efficacy

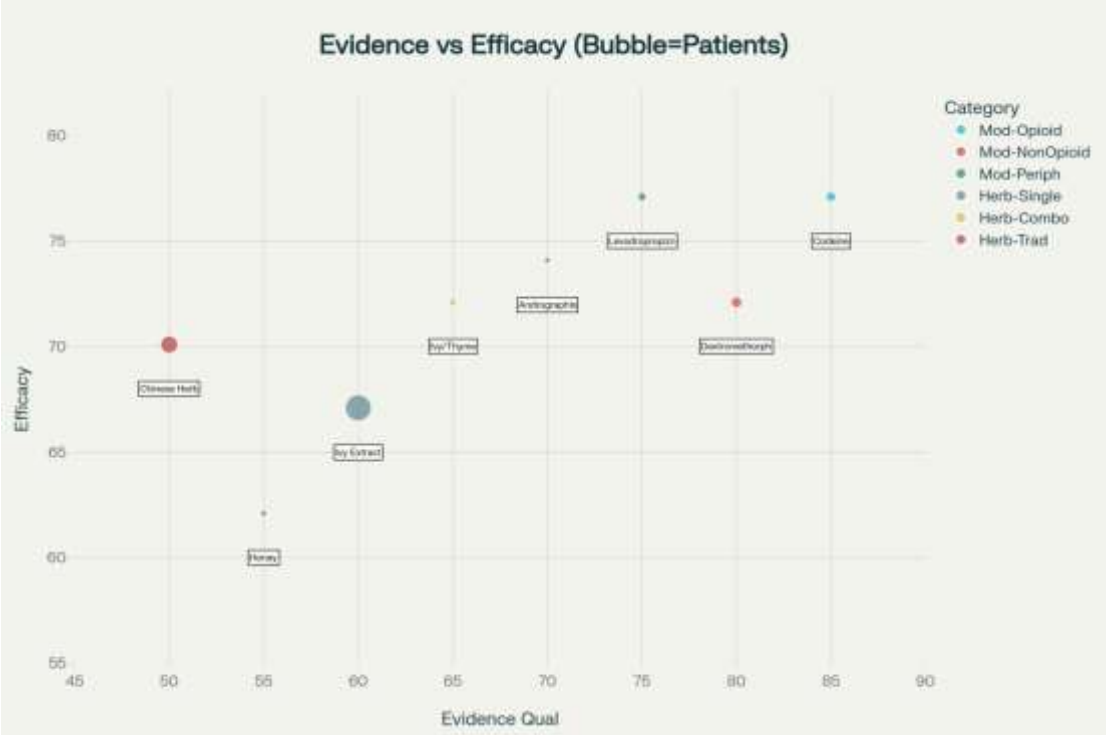

Figure 4. Comparative Clinical Evidence and Efficacy

Systematic reviews comparing herbal and synthetic antitussives reveal important differences in evidence quality and clinical outcomes. A comprehensive meta-analysis of herbal medicines for cough, encompassing 34 randomized controlled trials with 7,083 participants, found strong evidence supporting Andrographis paniculata and ivy/primrose/thyme combinations, with moderate evidence for Pelargonium sidoides[29].

Direct comparative studies between herbal and conventional treatments show mixed results depending on the specific preparations and outcome measures evaluated. When herbal medicines are used as add-on therapy to conventional medications, systematic reviews demonstrate significant improvements in cough severity, quality of life measures, and reduced recurrence rates[30]. However, when used as monotherapy, herbal treatments show inconsistent results across different cough severity rating scales[31].

The quality of clinical evidence varies significantly between herbal and synthetic antitussives. Modern pharmaceutical agents generally benefit from more rigorous clinical trial designs, larger sample sizes, and standardized outcome measures[32]. In contrast, herbal medicine studies often suffer from methodological limitations including inadequate blinding, heterogeneous preparations, and inconsistent outcome reporting[33].

Despite these limitations, several herbal preparations demonstrate clinical effectiveness comparable to synthetic drugs. Ivy leaf extracts show efficacy similar to or superior to conventional antitussives in head-to-head comparisons[34]. Chinese herbal medicine combinations demonstrate significant improvements in validated cough-specific quality of life measures[35].

Safety Profiles and Adverse Effects

Modern Drug Safety Concerns

Synthetic antitussive drugs carry significant safety considerations that limit their clinical utility. Opioid-based suppressants like codeine present risks of respiratory depression, particularly in pediatric populations and individuals with genetic polymorphisms affecting drug metabolism[36]. The FDA has issued specific warnings against codeine use in children under 18 years following tonsillectomy due to fatal respiratory depression cases[37].

Central nervous system effects represent another major concern with synthetic antitussives. Dextromethorphan can cause sedation, confusion, and at higher doses, dissociative effects that have led to recreational abuse[38]. Drug interactions with monoamine oxidase inhibitors can result in serious serotonin syndrome[39].

Peripheral antitussives like levodropropizine demonstrate superior safety profiles with minimal systemic effects[40]. However, these newer agents have limited long-term safety data and may not be available in all markets[41].

Herbal Medicine Safety Considerations

The perception that herbal medicines are inherently safer than synthetic drugs is misleading and potentially dangerous[42]. Systematic reviews of herbal medicine adverse effects reveal significant safety concerns with certain preparations. Serious adverse effects including liver damage, kidney toxicity, and even death have been reported with specific herbal products[43].

Plant misidentification and adulteration represent major safety risks in herbal medicine. Cases of "Chinese herbs nephropathy" caused by substitution of Aristolochia fangchi for Stephania tetrandra resulted in severe kidney damage and urothelial cancer in over 100 patients[44]. Such incidents highlight the importance of proper plant identification and quality control in herbal preparations.

Common adverse effects of herbal antitussives include gastrointestinal upset, allergic reactions, and skin sensitivity[45]. While generally milder than synthetic drug reactions, herbal medicines can still cause clinically significant adverse effects, particularly with prolonged use or in susceptible individuals[46].

Drug-herb interactions represent an underappreciated safety concern. Herbal preparations can affect the metabolism and efficacy of conventional medications through various mechanisms including cytochrome P450 enzyme modulation[47]. Patients using both herbal and synthetic medications require careful monitoring for potential interactions.

Regulatory Frameworks and Quality Control

Pharmaceutical Drug Regulation

Modern antitussive drugs undergo rigorous regulatory oversight through agencies like the FDA, ensuring standardized composition, proven efficacy, and defined safety profiles[48]. The drug development process requires extensive preclinical testing followed by three phases of human clinical trials before marketing approval[49].

The regulatory framework includes post-marketing surveillance systems that monitor adverse effects and drug interactions[50]. This comprehensive approach provides healthcare providers with detailed information about drug properties, appropriate dosing, contraindications, and expected side effects[51].

Controlled substance scheduling for opioid-based antitussives like codeine ensures appropriate prescribing practices while preventing diversion and abuse[52]. These regulatory controls balance therapeutic access with public health protection.

Herbal Medicine Regulation

Herbal medicines face significantly less regulatory oversight in most jurisdictions, often being classified as dietary supplements rather than pharmaceutical products[53]. This regulatory gap results in variable product quality, inconsistent labeling, and limited safety monitoring[54].

The lack of standardization in herbal preparations creates significant challenges for healthcare providers and patients. Products may contain varying concentrations of active compounds, adulterants, or contaminants that affect both efficacy and safety[55]. Some herbal products contain undeclared pharmaceutical ingredients that can cause unexpected adverse effects[56].

Recent regulatory initiatives aim to improve herbal medicine quality and safety through good manufacturing practices and standardized testing requirements[57]. However, implementation remains inconsistent across different countries and regions.

Economic Considerations and Healthcare Impact

Cost-effectiveness analyses reveal important differences between herbal and synthetic antitussive therapies. Herbal preparations generally offer lower acquisition costs, making them attractive options for patients with limited healthcare access or insurance coverage[58]. However, the variable quality and efficacy of herbal products may result in treatment failures requiring additional medical interventions.

Modern pharmaceutical antitussives typically have higher upfront costs but provide standardized, predictable therapeutic effect[59]. The controlled manufacturing processes and regulatory oversight justify higher prices while potentially reducing overall healthcare costs through more reliable symptom relief[60].

Healthcare system impacts differ significantly between the two approaches. Synthetic drugs require physician prescriptions and professional monitoring, increasing healthcare utilization but ensuring appropriate use[61]. Herbal medicines' over-the-counter availability reduces healthcare burden but may lead to inappropriate self-treatment or delayed medical attention for serious conditions.

Future Directions and Research Opportunities

The field of antitussive therapy is evolving toward more personalized and targeted approaches. Pharmacogenomic testing for CYP2D6 polymorphisms may optimize codeine dosing and reduce adverse effects in appropriate patients[62]. Similarly, understanding genetic variations in cough sensitivity could guide therapy selection.

Novel drug delivery systems offer opportunities to enhance both herbal and synthetic antitussive efficacy while minimizing systemic exposure. Inhaled formulations, sustained-release preparations, and targeted delivery mechanisms represent promising developments[63].

Integration of herbal and synthetic approaches may provide optimal therapeutic outcomes. Combination therapies that leverage the multi-target effects of herbal medicines with the potent, specific actions of synthetic drugs warrant further investigation[64].

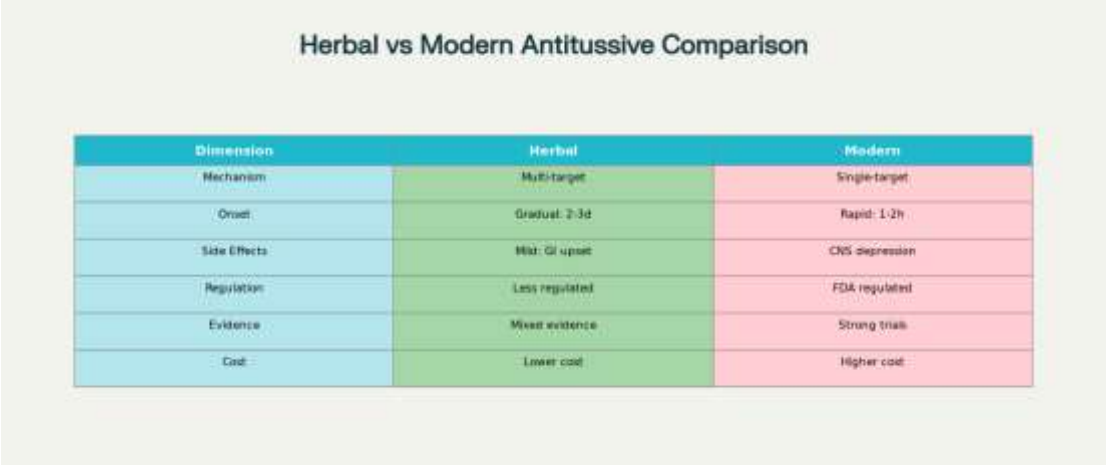

Figure 5 . Comparison of Herbal vs Modern Antitussive

Standardization efforts in herbal medicine research, including the development of validated extraction methods, biomarker identification, and standardized clinical trial protocols, will improve the quality of evidence supporting herbal antitussives[65]. Large-scale, well-designed randomized controlled trials comparing herbal and synthetic treatments directly would provide crucial evidence for clinical decision-making[66].

Conclusion

The pharmacology of cough suppressants reveals a complex landscape where herbal and modern drug therapies offer distinct advantages and limitations. Modern pharmaceutical agents provide potent, targeted effects through well-characterized mechanisms involving opioid receptors, NMDA antagonism, or peripheral sensory modulation. These drugs benefit from rigorous clinical testing and regulatory oversight but carry significant safety concerns including respiratory depression, dependence potential, and drug interactions.

Herbal antitussives offer multi-target therapeutic effects through complex phytochemical compositions, generally with milder side effect profiles and lower costs. However, they suffer from variable quality, inconsistent efficacy, and limited regulatory oversight. The clinical evidence supporting herbal treatments, while growing, remains less robust than that available for synthetic drugs.

The optimal approach to cough management likely involves individualized treatment selection based on patient characteristics, cough etiology, and risk factors. Healthcare providers must balance the proven efficacy and standardized quality of synthetic drugs against their safety risks, while considering herbal alternatives for patients seeking natural therapies or those intolerant of conventional medications.

Future research should focus on developing better integration between herbal and synthetic approaches, improving standardization of herbal preparations, and conducting high-quality comparative effectiveness studies. This evidence-based evolution will ultimately provide patients and healthcare providers with clearer guidance for optimal cough management strategies.

References

1) Holden SE, Morice A, Birring SS, et al. Cough presentation in primary care and the identification of chronic cough: a need for diagnostic clarity? Curr Med Res Opin. 2020;36(1):139-150. doi:10.1080/03007995.2019.1673716 CrossRef Google Scholar

2) Morice AH, Jakes AD, Faruqi S, et al. A worldwide survey of chronic cough: a manifestation of enhanced somatosensory response. Eur Respir J. 2014;44(5):1149-1155. doi:10.1183/09031936.00217813 CrossRef Google Scholar

3) Everett CF, Kastelik JA, Thompson RH, Morice AH. Chronic persistent cough in the community: a questionnaire survey. Cough. 2007;3:5. doi:10.1186/1745-9974-3-5 CrossRef Google Scholar

4) Chung KF, Pavord ID. Prevalence, pathogenesis, and causes of chronic cough. Lancet. 2008;371(9621):1364-1374. doi:10.1016/S0140-6736(08)60595-4 CrossRef Google Scholar

5) Zemp E, Elsasser S, Schindler C, et al. Long-term ambient air pollution and respiratory symptoms in adults (SAPALDIA study). The SAPALDIA Team. Am J Respir Crit Care Med. 1999;159(4):1257-1266. doi:10.1164/ajrccm.159.4.9807052 CrossRef Google Scholar

6) Yang X, Chung KF, Huang K. Worldwide prevalence, risk factors and burden of chronic cough in the general population: a narrative review. J Thorac Dis. 2023;15(4):2300-2313. doi:10.21037/jtd-22-1435 CrossRef Google Scholar

7) Chang AB. The physiology of cough. Paediatr Respir Rev. 2006;7(1):2-8. doi:10.1016/j.prrv.2005.11.009 CrossRef Google Scholar

8) Antitussive Drugs—Past, Present, and Future. PMC. 2013.

9) Current and future centrally acting antitussives. PMC. 2006.

10) Cough Suppressant and Pharmacologic Protussive Therapy. PMC. 2005.

11) Antitussive Agent - an overview. ScienceDirect Topics.

12) Review of Traditional and Phytochemical Compounds in Herbal Cough Treatments. Sage Journals. 2025

13) Herbal vs. Synthetic: The Drug Comparison. IJRPR.

14) Codeine - StatPearls. NCBI Bookshelf. 2024.

15) Central and peripheral mechanisms of narcotic antitussives. PMC. 2007.

16) Efficacy and Safety of a Single Ivy Extract Versus Two. PMC. 2025.

17) Exploration of the Use of Traditional Herbs to Overcome Cough. PMC. 2025.

18) Herbal versus synthetic drugs; beliefs and facts – PMC. 2014.

19) Antitussives - an overview. ScienceDirect.

20) Dextromethorphan – Wikipedia.

21) Levodropropizine for children and adolescents with acute post-viral cough: an evidence-based choice. Minerva Medica. 2024.

22) 7 Ayurvedic Home Remedies for Cough and Cold. Metropolis India. 2025.

23) Systematic Review of Clinical Trials Assessing the Effectiveness of Ivy Leaf (Hedera Helix) for Acute Upper Respiratory Tract Infections. Wiley. 2010.

24) Clinical Efficacy and Safety of Chinese Herbal Medicine Auxiliary Therapy for Childhood Cough Variant Asthma: A Systematic Review and Meta-analysis of 20 Randomized Controlled Trials. J-STAGE. 2016.

25) Introduction to Pharmacokinetics: Four Steps in a Drug's Journey Through the Body. Genomind. 2025.

26) The best natural cough remedies. Medanta. 2022.

27) Antitussives: Drug Class, Uses, Side Effects, Drug Names. RxList. 2021.

28) Comprehensive evidence-based review on European antitussives. BMJ Open Respiratory Research. 2016.

29) Adverse effects of herbal medicines: an overview. PMC. 2012.

30) Herbal Remedies: Adverse Effects and Drug Interactions. AAFP. 1999.

31) Clinical Toxicology of OTC Cough and Cold Pediatric Medications: A Narrative Review. PMC. 2024.

32) Should You Give Kids Medicine for Coughs and Colds? FDA. 2024.

33) Pathophysiology, conventional treatments, and evidence-based herbal remedies of hair loss with a systematic review of controlled clinical trials. Springer. 2025.

34) Clinical Evaluation of Kofsap-Sf Cough Syrup for Persistent Cough. JAIMS. 2025.

35) Medicinal plant phytochemical extracts for cough remedy. Google Patents. 2021.

36) Matthys H., Bleicher B., Bleicher U. "Dextromethorphan and codeine: objective assessment of antitussive activity in patients with chronic cough." J Int Med Res. 1983;11(2):92-100.

37) "Assessment of the Antitussive Efficacy of Codeine in Cough Associated with Common Cold." Journal of Pharmacy and Pharmacology. 1997;49(10):1045-1049.

38) "Comparison of the antitussive effects of codeine phosphate 20 mg, dextromethorphan 30 mg and noscapine 30 mg using citric acid-induced cough in normal subjects."

39) "Objectivation of the effect of antitussive agents using tussometry in patients with chronic cough." (noscapine, dextromethorphan, dihydrocodeine, codeine)

40) "Levodropropizine: A promising peripherally acting antitussive agent." Indian J Immunol Respir Med. — discusses non-opioid approaches.

41) Pharmacological Aspects of Over-the-Counter Opioid Drugs Misuse (includes codeine, dextromethorphan) — mechanisms, side effects.

42) "Evaluation of antitussive activity of formulations with herbal extracts in sulphur dioxide (SO2) induced cough model in mice" (uses codeine as positive control) — gives idea of how modern and herbal are compared in animal models.

43) "Herbal Medicine for Cough: a Systematic Review and Meta-Analysis." (Cough as symptom of upper respiratory tract infections) — includes herbs like Pelargonium sidoides, Echinacea, Andrographis paniculata, etc.

44) "Herbal medicine for adult patients with cough variant asthma: A systematic review and meta-analysis."

45) "Herbal polysaccharides and cough reflex." (Adhatoda vasica, Withania somnifera, Glycyrrhiza glabra) — mechanism, potency vs codeine etc.

46)"Understanding the molecular basis of herbal medicines for cough variant asthma under the guidance of traditional herbal theories."

47)"A Literature Review on Herbs used in Cough Medication." Scholars Academic Journal of Pharmacy. 2022 — catalogues active herbals, traditional use.

48)"Natural products for chronic cough: Text mining the East Asian historical literature for future therapeutics."

49)Codeine vs dextromethorphan kinetic and effect study: "Dextromethorphan and codeine: comparison of plasma kinetics and antitussive effects."

50)Safety, regulatory warnings around codeine especially in children; also non-opioid vs opioid side effect profiles. (from "Levodropropizine: A promising …" and "Pharmacological aspects … misuse")

51)"Cough: A protective reflex and herbal therapies." Romanian Journal of Rhinology. 2024 — looks at herbs + safety profiles.

52)The SO_2-induced cough model (herbal vs codeine).

53)The study of herbal polysaccharides reducing cough reflex in guinea pigs.

54)"Front Pharmacol. 2023: Herbal medicine for the treatment of chronic cough: a systematic review and meta-analysis."

55)"Future prospects of cough treatment; Herbal medicines vs Modern drugs." IJPSR. 2015.

56)"Literature-based Comparative Study between Herbal and Synthetic Mucolytics" — mucolytics are part of expectorant side of cough pharmacology.

57)Phadtare DG, Khan FA, Vidhate PV, Warule B et al. "Formulation And Evaluation of Herbal Cough Syrup Using Limonia acidissima." J Neonatal Surg. 2025.

58)Pratikeswar Panda & Arpita Sahu. "Formulation and Evaluation of Herbal Cough Syrup." Asian Journal of Pharmaceutical Research and Development. 2023.

59)"A literature review on herbs used in cough medication" (Manoj Kumar, Shweta Parihar).

60)The power of herbs in treatment of chronic cough — licorice, thyme etc.

61)"Cough Suppressant Herbal Drugs: A Review." International Journal of Pharmaceutical Science Invention. 2016. (as cited in some studies)

62)Studies of traditional formulae like Suhuang for cough variant asthma.

63)Reports of pharmacodynamics of herbal extract combinations vs modern antitussives in mice/hybrid models (like the SO_2 model)

64)"Natural products used historically in East Asia for chronic cough" (text mining historical lit)

65)Comparative evidence of quality-of-life effects in RCTs of herbal medicines vs montelukast/placebo etc for cough variant asthma.

66)Yang X, Chung KF, Huang K. Worldwide prevalence, risk factors and burden of chronic cough in the general population: a narrative review. J Thorac Dis. 2023;15(4):2300-2313. doi:10.21037/jtd-22-1435 CrossRef Google Scholar.