

RECENT ADVANCES IN PHYTOTHERAPY OF COUGH

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ABSTRACT: Cough is a protective reflex response induced by various irritants or infectious agents associated with respiratory diseases and tries to remove foreign particles and secretions from the bronchi and bronchioles of the airway. However, prolonged cough itself results in pathological consequences associated with physical strain on lungs tissue. Hence the cough response needs to be suppressed essential by using various cough syrups along with anti-allergic drugs. The side-effects associated with the available and frequently used therapeutic strategies against Cough has become a major limitation. Recently, the use of natural products has got tremendous attention globally owing to their minimal adverse outcomes. Some medicinal plants are potential source of therapeutically active substances with high-antitussive activity and minimum adverse effects. The current review is intended to describe the conventional and herbal management of cough and to provide an insight of herbs possessing antitussive activity based on the biochemical, ethno-botanic characteristics. The plant research with the focus on identifying the novel bioactive compounds may remarkably contribute to the development of equally more effective and harmless herbal formulations.

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Key words: Cough, medicinal plants, anti-tussive activity, respiratory disorders, upper respiratory infection

INTRODUCTION

Cough is a protective reflex in the form of violent exhalation by which irritant materials are expelled out from the airways (1). Noisy expulsion of air from lungs at once is known as cough (2). This helps the man to adopt the changes that are occurring in the environment. Pathological reflex is important and is a sign of serious illness. Cough is usually seen in postnasal-drip syndrome, asthma, gastroesophageal reflux disease, chronic bronchitis, bronchiectasis, bronchogenic carcinoma, carcinomatosis, sarcoidosis and left ventricular failure. Cough is one of the most commonly reported symptoms in patients seeking medical advice and people expend lot of money for the treatment of cough. Various antitussive agents which are frequently used to treat clinical conditions belongs to group of narcotic analgesics, in

which the narcotic dose is higher than antitussive dose. Side effects like the depression of respiratory center, inhibition of ciliary activity, decreased secretion in the bronchioles, increased sputum viscosity, decreased expectoration, constipation and hypotension act as a limitation to the therapy (3-5). Medicinal plants are the oldest form of the healthcare products familiar to mankind and constitute the integral part of modern civilization (4) and are predominantly used in the indigenous or alternative system of medicine (6-7). They are commonly employed in different systems of medicine e.g. Ayurvedic, Homoeopathic, naturopathic, Oriental and Native American Indian medicine, etc. WHO reports indicate that nearly three fourth of the herbal drugs correlated directly with their traditional uses in native culture. Medicinal plants are reservoirs of curative elements used

by a large population in all over the world for the treatment of various diseases including antitussive activity as they are safe and devoid of side effects. Medicinal plants contain bioactive chemical substances in their roots, leaves, stems, flowers and bark. These bioactive substances have led to the discovery of new drugs. Thus this review is intended to describe the conventional and herbal management of cough and to provide an insight of herbs possessing antitussive activity based on the biochemical, ethnobotanical and some chemical reports that will help the pharmaceuticals and researchers to formulate the effective antitussive medicine for the management of cough.

DIFFERENTIAL DIAGNOSIS

Chronic cough can be differentiated from other diseases (Fig 1).

Etiology

Cough is frequently found in the pulmonary conditions causing chronic dyspnea. However, patients with pure emphysema, thoracic wall deformities and pleural fibrosis, as well as those with no pulmonary causes of dyspnea, may not have associated cough. Additional causes of chronic cough are bronchogenic carcinoma, benign endotracheal tumors, chronic granulomatous diseases, tuberculosis, sarcoidosis, fungal diseases, lung abscess, primary ciliary dyskinesia, asthma, angiotensin-converting enzyme inhibitor use, bronchiectasis, upper airway cough syndrome, gastroesophageal reflux disease, chronic bronchitis, post infectious cough, no asthmatic eosinophilic bronchitis, irritant, arteriovenous malformation, laryngopharyngeal reflux, bronchiolitis, aspiration, bronchogenic carcinoma, persistent pneumonia, chronic interstitial lung disease, chronic asthma, irritation of external auditory meatus, gastroesophageal reflux disease, pertussis, foreign body (young children), cystic fibrosis, congenital abnormalities, immune deficiencies and

environmental exposure (8-9).

Adverse symptoms associated with cough Physical symptoms include lethargy, sleep deprivation, chest pain, vomiting, headache, hoarse voice and incontinence.

Psychological symptoms include frustration, fear of serious illness, embarrassment, anxiety and depression. Social symptoms include interrupted meals, interrupted telephone calls, interference with work, avoidance of social events, fear of public places and relationship tensions (10).

Potentially serious lung disorders with chronic cough

These include interstitial lung disease, cystic fibrosis, primary ciliary disorders, immune deficiencies, tuberculosis, protracted bacterial bronchitis, retained inhaled foreign body and recurrent pulmonary aspiration (11).

TREATMENT

Eliminate irritant exposure such as tobacco smoke, occupational agents and discontinue ACE inhibitor and beta blockers. Antihistamine and decongestant are given in common cold. Bronchodilators are prescribed in asthma. Potential targets for anti-tussive drugs are GABA-B receptors, opioid receptors, inflammatory and immunological mediators, ORL1 receptors, acid-sensing ion channels. GABA-B receptors, purine receptors, glycine receptors e.g. local anesthetics, tachykinin receptors, ORL1 receptors, 5-HT receptors, opioid receptors, glutamate receptors, neurokinin receptors, peripheral sensory nerve endings antagonists, BK and BKca receptors and vanilloid receptors (12). Bronchodilators are prescribed to the patient where a physician considers that a person has constrictions of bronchus. These drugs cause dilatation of bronchus. These drugs are sympathomimetics and stimulate beta receptors. Salbutamol and terbutaline are commonly prescribed to treat bronchial asthma and cough. These medicines are used to relieve the symptoms of cough associated with constriction of bronchus. These drugs are prescribed as inhalation or in pill form (13). Beta-adrenergic receptor agonists (beta-

agonists) are also bronchodilator because they cause dilatation of bronchus. Relaxation of bronchus occurs due to these drugs. These drugs inhibit release of bronchoconstrictor agents that cause bronchoconstriction and are cause of cough. Smucny et al (2001) reported that beta2-agonists are effective for treatment of acute cough in patients without underlying pulmonary disease (14). Anticholinergic agents are prescribed for chronic obstructive pulmonary diseases. These drugs cause relaxation of lung muscles and facilitate the breathing mechanism. As a result, cough is suppressed. However side effects like depression of respiratory center, inhibition of ciliary activity, decreased secretion in the bronchioles, increased sputum viscosity, decreased expectoration, constipation and hypotension acts as a limitation to the therapy (3).

List of Medicinal Plants

Anogeissus latifolia
(Combretaceae),
Aristolochia indica
(Aristolochiaceae), *Barleria prionitis* (Acanthaceae),
Bauhinia racemosa
(Caesalpiniaceae), *Butea monosperma*
(Papilionaceae), *Calotropis procera* (Asclepiadaceae),
Capparis decidua
(Capparaceae), *Cassia tora*
(Caesalpiniaceae), *Celosia argentea* (Amaranthaceae),
Clerodendrum multiflorum
(Verbenaceae), *Curcuma longa* (Zingiberaceae),
Cynodon dactylon (Poaceae),
Datura innoxia
(Solanaceae), *Emblica officinalis*
(Euphorbiaceae),
Euphorbia hirta
(Euphorbiaceae), *Ficus racemosa* (Moraceae),
Gmelina arborea

(Verbenaceae),
Hemidesmus indicus
(Asclepiadaceae), *Holarrhena antidysenterica* (Apocynaceae),
Holostemma annulare
(Asclepiadaceae), *Lawsonia inermis* (Lythraceae),
Leptadenia reticulata
(Asclepiadaceae), *Leucas cephalotus* (Lamiaceae),
Madhuca indica
(Sapotaceae),
Maerua oblongifolia (Capparaceae),
Mimosa hamata (Mimosaceae),
Neuracanthus sphaerostachyus
(Acanthaceae),
Pergularia daemia (Asclepiadaceae),
Punica granatum (Punicaceae),
Pupalia lappacea
(Amaranthaceae), *Solanum indicum* (Solanaceae),
Sphaeranthus indicus
(Asteraceae), *Tecoma undulata* (Bignoniaceae),
Terminalia arjuna
(Combretaceae), *Terminalia bellirica* (Combretaceae),
Terminalia crenulata
(Combretaceae),
Trachyspermum ammi
(Apiaceae), *Tylophora indica*
(Asclepiadaceae), *Uraria picta* (Papilionaceae),
Urginea indica (Liliaceae),
Vitex negundo (Verbenaceae),
Zingiber officinale (Zingiberaceae) (15)

Herbal treatment of cough

Adhatoda vasica

Adhatoda vasica belongs to family Acanthaceae. Parts used are leaves, roots, flowers and bark. Its chemical constituents are adhatodic acid, alkaloids, essential oils, vasicine, vasinol and volatile odorous principle (17-18). It is used in inflammation, body aches, cough, chronic bronchitis and sore throat (19). Pharmacological activity is

bronchodilator, anti-asthmatic and anti-ulcer (20). Dhuley *et al* (1999)., reported the antitussive effect of *Adhatoda vasica* extract. Extract of *Adhatoda vasica* exhibited significant antitussive activity in electrically and mechanically induced cough in the guinea pig. *Adhatoda vasica* extract was given orally and its activity was comparable to codeine (21).

Althaea officinalis

Althaea officinalis belongs to family Malvaceae. Parts used are roots and leaves. Its chemical constituents are salicylic acid, fatty acid, sterol, lecithin, asparagine, scopoletin, tannins, flavonoids and mucilages (22). Pharmacological activity is demulcent, digestive, diuretic, emollient, anti-inflammatory and antibacterial (23). It is used in gastritis, peptic ulcers, colitis, enteritis, cystitis, varicose veins, varicose ulcers, lung problems, intestinal pain, kidney diseases, gangrene, open wounds, burns, diarrhea, dysentery and vaginal infections (24). The root of *Althaea officinalis* contains rhamnogalacturonan that is involved in suppression of cough. Rhamnogalacturonan has antispasmodic activity. Cough suppression efficacy of rhamnogalacturonan is due to 5-hydroxytryptamine 2 serotonergic receptors (25).

Ananas comosus

Ananas comosus belongs to family Bromeliaceae. Parts used are fruits and roots. Its chemical constituents are vitamin C, ash, bromelain and ergosterol peroxide. It is used in sore throat, fatigue, venereal diseases, jaundice, palpitation and cancer (26). Pharmacological activity is anti-inflammatory, sedative, diuretic, aperients, purgative, anthelmintic, refrigerant, anti-bilious, cardiogenic, nutritive, emmenagogue, anti-scorbutic, digestive and uterotonic (27). Braun *et al* (2005)., reported therapeutic use, efficiency and safety of the proteolytic pineapple enzyme Bromelain-POS in children with acute sinusitis and cough (28). A study was conducted to investigate the efficacy of the combination of honey and *Ananas*

comosus extract (Bromelin®) in comparison with honey alone in the treatment of an irritative cough. This was randomized, double-blind, pragmatic, parallel group study involving the children between the age of 2 and 15 years. Marked improvement was observed in patients treated with a combination of honey and *Ananas comosus* extract (Bromelin®) as compared to honey alone. No side effects were observed in both groups. It indicates that *Ananas comosus* extract has a therapeutic effect on the characteristics of cough and mucus (29).

Andrographis paniculata

Andrographis paniculata belongs to family Acanthaceae. The whole plant is used to treat cough. Its chemical constituents are andrographolide, apigenin and kalmeghin (30). It is prescribed in anorexia, flatulence, general debility, cholera, dyspepsia, jaundice, diarrhea, influenza and dengue fever (31). Pharmacological activity is antimalarial, stomachic, anthelmintic, alterative, astringent, antidiabetic, cholagogue, hepatoprotective and anti-nociceptive (32). Coon *et al* (2004)., reviewed the efficacy of *Andrographis paniculata* in the treatment of upper respiratory tract infections. Systemic review of the efficacy of *A. paniculata* was conducted. Seven double blind clinical trials involving 896 patients met the inclusion criteria for efficacy evaluation of

A. paniculata. At least 3 scores were found out of a maximum of 5. Overall, the data concluded that

A. paniculata is better than placebo in reducing symptoms of infections involving upper respiratory tract. Least side effects were observed in patients by use of *A. paniculata*. The systematic review indicated that *A. paniculata* may be efficacious and safe in the management of uncomplicated upper respiratory tract infections (33).

Echinacea angustifolia

Echinacea angustifolia belongs to family

Asteraceae. Parts used are roots. Its chemical constituents are cichoric acid, alkylamide, polysaccharide, phenol, caftaric acid, echinosides and phenyl propanoid (34). It is used for gonorrhea, syphilis, indigestion, worm infections, skin infections, carbuncles, abscesses, gangrene, bacterial infections and cancer (35). Pharmacological activities are a blood purifier, immunostimulator, laxative, anti-asthmatic and antioxidant (36). Minetti *et al* (2011)., reported the efficacy of *Echinacea angustifolia* in recurrent upper respiratory tract infections during the pediatric age. In this study, herbal compounds containing *Echinacea angustifolia*, beta-glucan e zinc (Imoviral® Junior), acerola (Vitamin C) and arabinogalactan, was administered to 37 children suffering from otitis media or recurrent pharyngotonsillitis. The frequency of inflammatory episodes such as otitis media or tonsillitis was more during 6 months before administration of drug but was significantly less during 6 months following initiation of treatment. After treatment completion, the improvement was observed in 77% children. Improvement in life quality was also observed in patients treated with the herbal compound. This study showed that herbal compound containing zinc, arabinogalactan, vitamin c, beta glucan and echinacea improve the life quality in children suffering from recurrent otitis media or pharyngotonsillitis (37).

Matricaria chamomilla

Matricaria chamomilla belongs to family Asteraceae. Flowers are used to treat cough. Its chemical constituents are tryptophan, salicylates, glycosides, coumarines, beta

heteroside, chamillin, matricin and chamazulin (38). Pharmacological activity is relaxant, sedative, anti-inflammatory, febrifuge, antispasmodic, carminative, antiseptic, vulnerary, digestive, anti-allergic, anti-fungal and anti-tussive (39). It is used in stress related problems, anxiety, tension, insomnia, fever, indigestion, colitis, diarrhea, peptic ulcer, headache, cystitis, conjunctivitis, eczema, asthma, rhinitis and cough (40).

Thymus serpyllum

Thymus serpyllum Linn belongs to family Labiateae. The whole plant is used as the anti-tussive agent. Its chemical constituents are zingiberene, carvacrol, thymol, alcohols, terpenes, p-cymene and essential oils containing phenols (41). Pharmacological activity is anti-asthmatic, tonic and anticancer (42). It is used in stomach trouble, fever and whooping cough (43). Arshad and Bibi (2012)., reported the ethnomedicinal use of this plant in cough (44).

CONCLUSION

Medicinal plants being prescribed globally by Unani physicians bear promising therapeutic potentials to manage a variety of cough. The current review was focused to document the authentic data on medicinal plants with scientifically proven therapeutic potential against cough and respiratory disorders. However, elucidation of precise mode-of-action of active constituents present in listed medicinal plants may further flourish the current understanding of such plant-based therapeutic modalities.

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Table 1: Plants proved as anti-tussive agents						
Family	Country	Parts used	Uses	Animal	Extract type	Dose and References
Malvaceae	Germany	Roots	Bronchitis and cough	Cats	Complex extract	80 and 100mg/kg (45)
Asparagaceae	India	Roots	Cough	Mice	Methanolic extract	200 and 400 mg/kg (46)
Saxifragaceae	India	Rhizome	Pulmonary infection, cough and fever	Mice	Methanolic extract	300 mg/kg (p.o.) (47)
Leguminosae	India	Leaves	Cough, constipation	Mice	Methanolic extract	400 mg/kg and 600 mg/kg (p.o.) (48)
Iridaceae	Iran	Petals and stigma	Cough	Guinea pig	Ethanollic extract	100- (49)
Caryophyllaceae	India	Leaves	Cough	Mice	Methanolic extract	(50)
Onagraceae	India	Leaves	Cough	Mice	Methanolic extract	200 and 400 mg/kg (51)
Labiatae	India	Whole plant	Cough, dermatosis, conjunctivitis	Mice	Methanolic extract	400 mg/kg (52)
Labiatae	India	Leaves	Anti-obesity, anti-diabetic	Mice	Methanolic extract	100, 200, 300 mg/kg (53)
Rubiaceae	Slovakia	Whole plant	Cough	Cats	Ethanollic extract	200 mg/kg (54)
Passifloraceae	India	Leaves	Insomnia, asthma, nerve pain	Mice	Methanolic extract	100 and 200 mg/kg (55)
Boraginaceae	India	Roots	Joint pain, fever, cough		Methanolic extract	200 mg/kg (56)
Asteraceae	India	Whole plant	Fever, cancer, cough	Mice	Aqueous extract	100, 200 mg/kg (57)

Plant Name
<i>Althaea officinalis</i> Linn.
<i>Asparagus racemosus</i>
<i>Bergenia ciliata</i>
<i>Cassia fistula</i>
<i>Crocus sativus</i>
<i>Drymaria cordata</i> Willd
<i>Jussiaea suffruticosa</i> Linn
<i>Leucas lavandulaefolia</i>
<i>Lagerstroemia parviflora</i>
<i>Pederia foetida</i>
<i>Passiflora incarnate</i>
<i>Trichodesma indicum</i>
<i>Xanthium strumarium</i>

