Plants in Respiratory Disorders II- Antitussives, A Review

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This work was carried out in collaboration between all authors. Authors SKA, IIJ and GO contributed to the chemistry, ethnopharmacology and biological studies in this review and also collaborated in all facets of the work-literature search, collection of data, ChemDraw, referencing and collectively made inputs to the lay-out and design. All authors read through and approved the final manuscript for publication.

ABSTRACT

Aim of This Review: Antitussives, more familiarly known as cough suppressants, are usually taken to suppress dry, irritating and patient-disturbing coughs. This review is an attempt to bring together some of the common medicinal plants traditionally used to manage respiratory disorders other than asthma. The review includes some information on traditional use of the plants as it relates to respiratory disorders, some chemistry and pharmacology in an attempt to ascertain their chemical composition and biological values, and so justify their uses.

Study Approach: Information on the above was sourced from published articles and reviews on the subject available from various data bases and journals. Thirty-three medicinal plants drawn from twenty-two plant families were reviewed along with two natural products honey which always serve as vehicle for many plant medicines and bile.

Findings: Table 1 gives a list of thirty-three plants used locally as antitussives. The various plant parts utilized in remedies include all the parts of the plant. The biochemistry and medicinal...
significance of tannins, terpenoids and essential oil components are now better appreciated in the management of respiratory disorders.

**Conclusion:** Herbal antitussives not only suppress coughs, they always attempt to remove the respiratory disorders causing the coughs and thus make patients healthier. The use of medicinal plants remains a universal phenomenon; this review justifies the need for polyherbal formulations for use in the management of respiratory disorders.

**Keywords:** Respiratory disorders-cough suppressants/antitussives; expectorants; medicinal plants; ethnopharmacology; phytochemistry; pharmacology.

1. **INTRODUCTION**

Respiratory disorders are considered in this review to include the common cold, pneumonia, bronchitis, tuberculosis, hiccough and cough apart from asthma considered earlier in our earlier submission. Antitussives are commonly taken to suppress coughs arising from these disorders.

Bronchitis which may be acute or chronic, has been described as an inflammation of the mucous membranes of the bronchi (airways). Symptoms of acute bronchitis include the development of a cough and this may be accompanied with or without sputum. It is believed that 90% of acute bronchitis is caused by viruses and 10% by bacteria. Chronic coughs also cause a recurrent injury to the airways and may be caused by inhaled irritants [1].

The common cold is a viral infection of the upper respiratory tract and the most commonly implicated virus is a rhinovirus (30-80%); others include influenza viruses (10-15%), adenoviruses (5%), human coronavirus (~15%), human parainfluenza viruses etc. More than 200 virus strains are implicated in the cause of the common cold and the rhinoviruses are believed to be the most common. When accompanied with a cough, the cough is usually mild compared to that which usually accompany influenza, hence justifying the common cold caused by influenza viruses. It is believed that the symptoms of the common cold can be cured [1].

Pneumonia has also been described as an inflammatory condition of the lung, affecting the air sacks and usually caused by infections mainly with the bacterium *Streptococcus pneumoniae* and viruses. Its symptoms include a cough, fever and difficulty in breathing [1].

Tuberculosis, MTB, or TB (*Tubercle bacillus*), is an infectious disease caused by various strains of mycobacteria usually *Mycobacterium tuberculosis*. Tuberculosis typically attacks the lungs (known as pulmonary tuberculosis). Tuberculosis spreads through the air when people with an active TB infectious cough sneeze or otherwise transmit respiratory fluids through the air [1].

The underlying symptom for all these respiratory diseases (or disorders) is cough. What then is cough? Cough has been described as a protective reflex mechanism that removes foreign materials and secretions from the bronchi and bronchioles of the airways (foreign objects, catarrhs of the respiratory system, etc.) [2]. Cough appears fundamental to all the manifestations of the respiratory disorders identified earlier.

2. **HERBAL THERAPY FOR RESPIRATORY DISEASES**

Many medicinal plants have been identified as capable of treating respiratory disorders. The herbal remedies are now known as cough suppressants, expectorants, mucolytics, sympathomimetics and nasal decongestants. Some of these remedies behave as anti-inflammatory agents, anti-cough drugs, some act to smoothen the lungs and others to stimulate the heart and mind and for some, a combination of many actions. For instance, as Martindale [3] puts it, nasal congestion is frequently a symptom of conditions such as rhinitis, the treatment of which can include the use of antihistamines, sympathomimetics, corticosteroids, antimuscarinics and cromoglycate or nedocromil.

From the fore-going, respiratory disorders may be caused by bacteria, viruses and fungi. Examples include respiratory viruses that are known to be associated with the development of respiratory disease from childhood. Parainfluenza virus and respiratory syncytial virus (RSV) for example, are known to cause bronchitis early in life. These disease conditions and other respiratory infections are effectively treated by the use of plants with constituents
possessing strong antibacterial, antiviral and antifungal properties.

3. MEDICINAL PLANTS USED AS ANTITUSSIVES

3.1 Lannea acida A. Rich Anacardiaceae

*Lannea* species are traditionally used in folk medicine as natural healing remedies with therapeutic effects such as prevention of inflammation disorders like asthma, inflammatory bowel disease, pulmonary diseases and other oral diseases [4]. Other species found useful locally are *Lannea schimperi* (A. Rich) Engl. and *Lannea welwitschi*.

The bark contains irisolidone, 7-methyltectorigenin, 3, 4-dihydroxy-7, 8 (2', 2'dimethylchromeno)-6-γ, γ-dimethylallyllavonol and 6, 7-(2", 2"-dimethylchromeno)-8-γ, γ-dimethylallyllavonone [5].

*Lannea* species have demonstrated antibacterial, anti-inflammatory and antioxidant activities and lipoxygenase inhibition activities and these are associated with polyphenol contents of the plant [6].

The effect of hydro-alcoholic extract of *L. acida* against *Mycobacterium tuberculosis H₃₇Rv* activities was assessed. The percentage of inhibition of *Mycobacterium tuberculosis* proliferation was respectively 77.6 and 36.8% at 1.2 and 0.6 mgML⁻¹ of extract. The study concluded that the stem bark EtOH/H₂O-(70%v/v) extract might contain potential antibacterial and immune-stimulating agents for clinical use [7].

3.2 Dennetia tripetala Barker F., Annonaceae (Pepper fruit, Peppermint)

*D. tripetala* fruit is used traditionally as a remedy for fevers, cough, toothache, nausea etc. and the fruits are commonly eaten as spice or stimulant [8].

The root furnished dennetine (2, 6-dimethoxychromene), 3 phenanthrene alkaloids-uvariopsine, stephenanthrine, argentiine and vanillin; the fruit essential oil gave 2-phenylnitroethane (72.41%), linalool (18.0%) and (6E) - nerolidol (4.51%), α-cymene, β-ocimene, copaene, α-farnesene, caryophyllene and its oxide, eudesmol [9,10].

The essential oil and phenolic acid extracts inhibited the growth of food-borne microorganisms and the rot-causing fungus *Sclerotium rolfsii* and other fungi. Besides, flavonoid glycosides exerted antioxidant and antimicrobial properties as well. The fruit essential oil was found to possess significant antinociceptive, muscle relaxant and anti-inflammatory effects in the animals used. The implication of these results are that the plant can be used to manage fevers, pain and be of value in respiratory disorders caused by bacteria [8,11].

3.3 Uvaria chamae P. Beauv, Annonaceae (Finger root, Bush Banana)

*Uvaria chamae* is used traditionally in the treatment of fevers, wounds, sores and yellow fever. It is listed as an anti-asthmatic plant in Nigeria [12,13].

*U. chamae* contains flavonoids- pinocembrin, pinostrobin, chamaneatin 5-methyl ether etc., and an essential oil [13].

*U. chamae* has shown significant antimicrobial properties and 1-Nitro-2-phenylethane and linalool isolated from it have demonstrated antibacterial and anti-inflammatory properties. Nitro-2-phenylethane showed anti-inflammatory, antinociceptive, anticycadi and brine shrimp lethality effects while linalool showed anti-inflammatory, antinociceptive and antimicrobial effects [13,14].
3.4 *Cocos nucifera* Linn, Arecales (Coconut, Coco, Tree of Life, Coconu-of-the-beach)

Coconut is used traditionally to treat many health problems including asthma, bronchitis, colds, cough, dysentery, ear ache, fever, flu, sore throat, tooth ache, tuberculosis, typhoid, ulcers, wounds [15,16]. *C. nucifera* was listed as a component of anti-asthmatic medication [12]. An aqueous extract of the fresh husk fibre is used for oral asthma treatment.

Coconut fiber (mesocarp) ethanol extract contains phenols, tannin, flavonoids- catechin and quercetin; the liquid albumen contains vitamin C, L-arginine, α-tocopherol, lauric acid and vitamins, enzymes and plant hormones and the leaves-skimmiiwallin and its isomer and lupeol methylether [16].

Coconut oil was found to be antiviral, antibacterial and antifungal. Husk fiber extract showed antibacterial and antifungal properties. Potential biocomponents for antimicrobial activity were tocopherol, cycloartenol, palmitoleyl alcohol and β-sitosterol. Aqueous crude extracts of the husk fiber showed strong anti-inflammatory properties as shown in the formalin test and the subcutaneous air pouch model. The extracts (50, or 100 mg/kg) significantly inhibited (p<0.05) the time that animals spent licking their formalin-injected paws and reduced inflammation induced by subcutaneous carrageenan injection by reducing cell migration, extravasation of protein and TNF-α production [16].

3.5 *Gongronema latifolium* Benth et Hook, Asclepiadaceae (Amaranth Globe)

G. *latifolium* is traditionally used as a leafy vegetable and to treat cough, viral hepatitis, diarrhoea and other microbial infections. An anti-diarrhoeal, antitussive and an anti-asthmatic plant, the plant extract has been used to treat fowl cough [12,17].

Leaf extract gave four pregnane glycosides, related to marsdenin and fatty acids [18-19].

Investigations were carried out on the antitussive properties of *G. latifolium* extracts against *S. aureus* tracheal infection in 7 week old broilers [17]. The authors found that the number of aerobic bacteria in the trachea was reduced from 36 x 10^4 cfu/ml of viscera suspension to 8 x 10^2 cfu/ml within 3 weeks of drug application. In addition, the number of pleura-pneumonia-like organisms was reduced within 2 weeks and was totally eliminated by 3 weeks of drug application. It was concluded that the ability of the extract to reduce the number of aerobic bacteria and totally eliminate the pleura-pneumonia-like organisms at particular times confirmed its antibacterial nature.
3.6 *Crassocephalum crepidioides* (Benth) S. Moore (Asteraceae)

*C. crepidioides* (Syn. *C. rabens*) is reputed in ethnomedicine for the management of respiratory problems such as asthma. It is a well-known anti-inflammatory food supplement/vegetable for the elderly [20].

*C. crepidioides* leaf contains an essential oil, the constituents of which vary with the location and time of collection [20,21]. Other constituents are flavonoids, pyrrolizidine alkaloids-Jacobine I and Jacoline 2, and a chemopreventive galactolipid [22].

Hou et al. [22] isolated a bioactive galactolipid, 1,2-di-0-α-linolenoyl-3-0-β-galactopyranosyl-sn-glycerol and showed it to be a very potent anti-inflammatory agent. The bioactive glicerolglycolipid was found in vitro and in vivo to be a potent nitric oxide (NO) scavenger, showing cytotoxic effects. The presence of antimicrobial oil constituents with flavonoids, also antibacterial phenolic compounds and this galactolipid working in synergy in *C. crepidioides* may serve to find an explanation for its use in respiratory disorders.

3.7 *Crescentia cujete* Linn, Bignoniaceae (Calabash tree)

*C. cujete* pulp syrup is used in folk medicine to treat chest and respiratory tract disorders, asthma and cough, dysentery and stomachache. [23,24].

Fruits afford iridoids and their glycosides, the Sarcocarp furnishes terpenoids, benzoic acid and derivatives, D-allitol and ergostadiene derivatives. Other constituents of the plant are crescentins I- V and crescentosides A, B and C, apart from lapachones and naphthol derivatives reported [25].

Antibacterial activity of the aqueous and alcoholic extracts of *C. cujete* stem bark and leaves was investigated against multidrug resistant (MDR) isolates DKU-156 and JAL-1236 of *M. tuberculosis* as well as the fast growing pathogen *M. fortuitum* (TMC-1529) [26]. The susceptible strain *M. tuberculosis* H$_3$$_7$$_H$_4$ was used as control. All the extracts were potent and showed inhibitory effects on all the strains of *Mycobacterium tuberculosis* used. Four morphologically distinct endophytic fungi were isolated and identified from *C. cujete*. The fungal extracts which analyzed for aspirin and diethyl phthalate as the major constituents showed a strong growth inhibitory effect against bacterial human pathogens [23].

3.8 *Kigelia africana* (Lam) Benth, Bignoniaceae (Sausage Tree, Cucumber Tree, African Sausage Tree)

*K. africana* is widely used in folk medicine in the treatment of bacterial, amoebic and fungal infections, respiratory disorders, pneumonia, etc. It is listed as an anti-asthmatic plant [12,27,28].

Fruit contains iridoids, flavonoids, kigelinone, isopinnatal, dehydro-α-lapachol and p-coumaric acid, The stem contains kigelinone, isopinnatal and iridoids etc. [27,28].

Plant is antiprotozoal, antibacterial, antifungal, analgesic and anti-inflammatory. Compounds with antibacterial activity were kigelinone, isopinnatal, dehydro-α-lapachol, lapachol, p-coumaric acid, ferulic acid and palmitic acid. Verminoside was found to be more active than the standard drug while specioside showed activities comparable to metronidazole [29].

The stem bark ethanol extract showed antimycobacterium activity, while the fruit polar extract showed anti-inflammatory and analgesic activities due to its content of verminoside. Verminoside caused significant anti-inflammatory effects inhibiting iNOS expression and NO release in the LPS-induced macrophage cell line [27,29].
3.9 **Bixa orellana** L. Bixaceae (Anatto, Annato)

*B. orellana* is used in traditional medicine of many cultures of the world to treat respiratory and pulmonary disorders—cold, cough, bronchitis [30], and for the prevention and treatment of asthma, allergy, skin problems and urinary infections (oral and topical) etc. [31].

*Bixa orellana* has furnished many constituents in the leaf, seeds and roots—carotenoids, terpenoids and terpenes, volatile oil and flavonoids [30,31].

Anatto extract exhibited antimicrobial activity against strains of *Clostridium perfringens* and *C. botulinum* [32]. The leaf, flower and seeds extracts also showed a broad spectrum of antimicrobial activity [31].

3.10 **Ananas comosus** Linn., Bromeliaceae (Pipeapple)

*A. comosus* is used traditionally in indigestion and to clear bronchial passages in those suffering from pneumonia, sinusitis, cold and bronchitis [33].

*A. comosus* contains minerals and vitamins, phenolic compounds and esters [34].

*A. comosus* fruit contains a proteolytic enzyme, bromelain which digests food by breaking down protein. On an empty stomach, *A. comosus* has anti-inflammatory properties. The stem and fruit of *A. comosus* contain bromelain and plenty of vitamin C which have been found to suppress coughs and loosen mucus. It was shown that sinusitis, burns, skin rashes also benefit from ingestion of bromelain [33].

3.11 **Canarium schweinfurthii** Engl. Burseraceae (Bush Plum)

*C. schweinfurthii* is used traditionally for managing chest pains, pulmonary affections, coughs, *Mycobacterium tuberculosis*, asthma and gastritis; a decoction of the leaves, stem bark and rhizome is usually drunk [35,36].

Canarium species produce edible kernels and resins (oleoresins) used in food and medicines. Stem bark oleoresin and fruit contain phenolic aromatic compounds, oxygenated terpenes, lignans and triterpenes-spathulenol, viridiflorol, E-nerolidol [36,37].

The essential oil and leaf extracts showed strong antimycobacterium and antimicrobial properties generally [35,38]. The anti-inflammatory effects of the plant extracts and oil combined with the strong effect of the natural antimicrobials seem to be of value in the management of respiratory disorders.

3.12 **Dacryodes edulis** (G. Don) H. J. Lam, Burseraceae (African Pear, African Plum, Bush Butter, Bush Fruit Tree or Native Pear)

Different parts of *D. edulis* are used traditionally in folk medicine; bark decoction is taken as gargle and mouth wash and to treat tonsillites, twig may be chewed to manage cough and related respiratory disorders [39].

The stem bark gives flavonoids, methyl 3, 4, 5-trihydroxybenzoate, sitosterol 3-0-β-glucopyranoside and hydrocarbon monoterpenes and fatty acids [40-41].

*D. edulis* essential oil is antimicrobial, antioxidant and anti-inflammatory [41]. The presence of ascorbic acid, the flavonoid constituents and the essential oil, no doubt, will help to explain the use of *D. edulis* in treating cough and related symptoms.

3.13 **Carica papaya** Linn., Caricaceae (Papaya)

*C. papaya* ground seeds are used in traditional medicine as a substitute for pepper and papaya latex has been used to relieve whooping cough. Juice from *Citrus aurantifolia* fruit may be added to *Allium sativum* bulb extract and *Carica papaya* ground seed extract to manage tuberculosis. Papaya leaf when dried and cured is smoked by asthmatic persons [42,43].
C. papaya seeds contain fatty acids, alkaloids, benzylisothiocyanate, benzylglucosinate, glucotrapacolin, benzylthiourea, hentriacontane, carcin and the enzyme myrosin. The latex contains proteolytic enzymes. The juice contains fatty acids and lipids. Leaves are rich in flavonoids, alkaloids and carotenoid and hence possess medicinal values such as anti-inflammatory, antioxidant, anthelmintic and antibacterial [42]. The protein digesting enzymes and antioxidant nutrients in Papaya reduce inflammation and help to reduce the severity of adverse effect of asthma, arthritis and other respiratory disorders [42,44].

3.14 Chenopodium ambrosioides Linn, Chenopodiaceae (American wormseed, goosefoot)

C. ambrosioides is widely used as dietary condiment in folk medicine to treat catarrh, excessive mucus, bronchitis, pneumonia, asthma, tuberculosis, dysentery and diarrhea [45].

C. ambrosioides contains essential oil mainly (Z)- ascaridole (29.7%), isoascaridole and p-cymene (12.7), sterols- avenasterol, spinasterol and flavonoids [45-47].

C. ambrosioides showed strong analgesic, antifungal, antibacterial, anti-inflammatory, antioxidative and antiparasitic properties. The essential oil and its three main active ingredients- ascaridole, iso-ascaridole and p-cymene were formulated for treating gastritis, bronchitis and peptic ulcer caused by Helicobacter pylori [45,47].

3.15 Guiera senegalensis J. F. Gmel, Combretaceae (Sabara)

G. senegalensis leaf decoction is used in folk medicine to treat pulmonary and respiratory complaints, respiratory congestion, bronchitis, cough, rhinitis, microbial infections and cough. This plant was listed as an antitussive plant of India [2,48].

The plant contains flavonoids, alkaloids and tannins [49].

Leaves of G. senegalensis are beneficial as an antitussive [50,51]: the activity of the leaf was evaluated using the citric acid-evoked model in guinea pigs. The leaf decoction dose-dependently decreased the number of coughs as expected. The results were comparable with codeine phosphate at a dose of 10 mg/kg. An inhibition of 76.32% was noted [48].

3.16 Terminalia avicennioides Guill et Perr, Combretaceae

T. avicennioides is used traditionally in and around Nupeland, North Central Nigeria in the treatment of respiratory diseases particularly tuberculosis [52].

The plant contains triterpenoids and hydrolysable tannins-punicalagin, flavogallonic acid and terchebulin [52,53].

T. avicennioides ethanol and methanol extracts showed antifungal, antimicrobial and antimycobacterium activities [54]. The activity test was conducted on the isolated triterpenes and arjunicolic acid exhibited some moderate activity (MIC 156 μg/ml) when compared to the positive control. The above result justifies the use of the plant in treating blood sputum and cough in humans.

3.17 Terminalia glaucescens Planch ex Benth, Combretaceae

T. glaucescens occurs as one of the plants used traditionally in the management of asthma in Nigeria. [12].

T. glaucescens contains terpenoids, tannins sterols etc [53,55].

T. glaucescens was reported to be anti-dysenteric and strongly antimicrobial, helpful in the management of AIDS and in the management of E. coli-related infections [56]. Terminalin I, isolated from the plant was reported to exhibit activity against prolylendopeptidase (PEP); ellagic acid and derivatives have also shown significant antimicrobial activity [57]. These results justify the use of the plant in the treatment of bacterial, fungal and viral infections.

3.18 Terminalia ivorensis A. Chev., Combretaceae

T. ivorensis is widely used in traditional medicine in the treatment of bacterial infections, cold, sore throat, pneumonia, coughs, cutaneous infections, buccal and teeth infections, nose bleed, diarrhea and skin diseases [58,59].
T. ivorensis stem bark and heartwood yielded terpenoids, acids and tannins [53,61].

Recently Samuel et al. [61] isolated 2-(3,5-dihydroxyphenyl) benzofuran-5,6-diol as the bioactive antibacterial compound of T. ivorensis leaves. T. ivorensis was reported highly antibacterial [61]. Quattara et al. [59,60] evaluated the in vitro antifungal activity of trunk bark-extracts and the aqueous and hydroalcoholic stem bark extracts and found that the antifungal activity of T. ivorensis stem barks was better than for the standard drug, ketoconazole. These results have provided the basis for the use of the leaf and stem bark in the treatment of infections and other diseases of microbial origin.

3.19 Terminalia macroptera Guill et Perr. Combretaceae

Traditionally, T. macroptera has been used as an efficient antimicrobial remedy and the roots are sold in markets locally in West Africa. It is used against cough, pulmonary tuberculosis, hepatitis, pain and rheumatism [62].

T. macroptera stem bark contains terpenoids, tannins, ellagic acid and derivatives [53,62,63].

T. macroptera showed antibacterial properties. The isolated triterpenes were tested in a number of bio-assays-antibacterial, antifungal and anthelmintic [64]. It was found that all the compounds showed antimicrobial activities against B. subtilis (MIC 8-64 µg/mL).

![Chemical structures](image)

R=H, Argungenin  
R=β-D-Glc, Arjunglucoside  
R=CH3, Arjunic acid  
R=gallate, 23-O-galloyl-arjunolic acid

3.20 Alchornea laxiflora (Benth.) Pax and Hoffman, Euphorbiaceae

Leaf infusion is used in folklore medicine to treat fevers, malaria, inflammatory and infectious diseases [65].

The leaves of A. laxiflora contains flavonoids, β-sitosteryl-β-D-glucoside, quercetin disulphate derivatives and quercetin-3, 4-diacetate [66].

A. laxiflora leaf extract was evaluated for antibacterial and antifungal potential; the extract inhibited the growth of all the bacterial and 15 fungal isolates tested [65].

3.21 Bridelia ferruginea Benth, Euphorbiaceae

B. ferruginea is widely used for rheumatic pains, dysentery, diarrhea, thrush and buccal disorders, coughs, asthma, toothache [12,67].

B. ferruginea leaf contains flavonoids, n-hexadecanoic acid, octadecanoic acid l-icosanol, α-amyrin acetate and stearylaldehyde [67,68].

The plant is used for many disease conditions mostly for its antimicrobial, anti-inflammatory, antifungal, antiviral and its anti-oxidative properties [68].

3.22 Bridelia micrantha (Hochsl) Baill, Euphorbiaceae

B. micrantha is used in ethnomedicine for gastrointestinal ailments, painful joints, coughs, conjunctivitis, and bloody dysentery [67].

B. micrantha contains phenolic acids, ellagic acid; the flavonoid, delphinidin and triterpenes – friedelin and taraxerol.

B. micrantha has shown antioxidant, antimicrobial and anti-inflammatory properties. Its extracts were tested for antiviral effects. The n-BuOH fraction was the most active with an IC_{50} of 7.3 µg/ml. This justifies its use against respiratory disorders caused by infections [67].

3.23 Phyllanthus muellerianus (O. Ktze) Exell, Euphorbiaceae

P. muellerianus is used in ethnomedicine to treat cough. A decoction of the stem and leaves, or root only was listed as a medication for cough. [39].

The plant contains tannins, phenolic acids, quinic acids, flavonoids, triterpenes and essential oil [69,70].

P. muellerianus was reported to contain ellagitannins, phenolic acids, triterpenes and essential oil which showed strong antibacterial effects. Geraniin was found to be seven times
more potent as a pain reliever than aspirin or acetaminophen, it was also found to be effective for its antiulcerous properties and to protect the gastric tract. The antibacterial properties of the plant are beneficial in the treatment of disorders caused by infections.

3.24 Ocimum gratissimum Linn, Labiatae/Lamiaceae (Fever Plant of Sierra Leone, Tea Bush, Mosquito Plant)

O. gratissimum is used in folk medicine to treat pneumonia, cough, fever and other upper respiratory tract infections [71].

O. gratissimum contains an essential oil with many bio-active compounds [72,73].

All the parts of the plant have shown antiseptic, antibacterial, antioxidant and antifungal effects making the plant useful in treating disorders caused by infections [71,73]. The leaves have been used for coughs as the essential oil showed strong anti-inflammatory effects [73].

3.25 Hibiscus rosa-sinensis Linn, Malvaceae (Shoeflower, Tropical Hibiscus, Chiness Hibiscus)

A decoction of the leaf is traditionally used to suppress cough. The root decoction, flower and petal decoctions are taken in bronchial catarrh and cough [74].

The flower contains flavonoids and vitamins. The leafy stem contains sterolic and malvalic acids, carotene, fatty acids and their derivatives etc while petals contain flavonoids, cholesterol, catalase, sitosterol, etc. [75,76].

Plant shows anti-inflammatory, antibacterial, demulcent and expectorant properties; it also relaxes spasms and soothes irritated tissue [76]. The antitussive effect of the MeOH extract (200 mg/kg, p.o) was examined [77] in guinea pigs, codeine (5 mg/kg) was the reference drug. Codeine and the extract of H. rosa-sinensis significantly reduced the number of coughs compared to disease control group; this suggests the potential antitussive activity of both drugs.

3.26 Dissotis rotundifolia (SM) Triana, Melastomataceae

In Nigeria and Ghana, the dried leaves of D. rotundifolia are used for the treatment of common cold, conjunctivitis, cough, diarrhea, tuberculosis among other diseases [78]. The plant extract is a component of a commercial cough mixture known as “sirop de Dissotis” [79].

D. rotundifolia contains vitexin, orientin, iso-orientin and isovitexin; these compounds were also detected in the formulated product [80].
The EtOH and n-BuOH fractions of *D. rotundifolia* showed strong antioxidant and antibacterial properties [81]. This led to the isolation of the glycoflavones, which showed varied antimicrobial activities against the test organisms.

### 3.27 Eucalyptus camaldulensis Dehn, Myrtaceae

*E. camaldulensis* is used to treat gastrointestinal disorders, sore throat, cough, influenza, toothache, fevers and other bacterial infections of the respiratory and urinary tracts [82].

Leaf contains terpenoids, eucalyptanoic acid, essential oil and flavonoids [83].

Six strains of *H. pylori* were found susceptible to the leaf extract of *E. camaldulensis*. The essential oil showed strong antimicrobial and anti-tuberculosis activity. The leaf extract also inhibited four non-tuberculosis Mycobacteria species. Begum et al. [84] reported on the structure and spasmylic activity of eucalyptanoic acid from *E. camaldulensis*. These results justify the use of the plant in the treatment of infections associated with Mycobacteria and respiratory disorders [82,85].

### 3.28 Piper guineense Schum et Thonn, Piperaceae (West African Black Pepper, Ashanti Pepper)

*P. guineense* is used in many traditional formulations for the treatment of coughs, gastrointestinal disorders, bronchitis, toothache etc. [86-87].

*P. guineense* leaf, stem and berries furnished many bio-active compounds mainly amides and essential oil components [88].

Piperine, dihydropiperine, dihydropiperlongumine and dihydrocubebin showed antimicrobial activity against *Mycobacterium smegmatis* (ATCC 607) at a concentration of 100 µg/ml; piperine exhibited anti-microbial activity against *Candida albicans* (ATCC 12023) and dihydropiperine was active against *Klebsiella pneumonia* (ATCC 1003). The antimicrobial and antifungal effects of seed ethanol extract were also reported [89].

### 3.29 Citrus aurantifolia (Christm) Swingle, Rutaceae (Lime)

*C. aurantifolia* is used traditionally as an antiseptic, antibacterial, anthelmintic, tonic, anti-inflammatory, digestive and for coughs, sore throat and colds. Lime is a common ingredient of herbal potions incorporated/formulated for the treatment of tuberculosis and weight management diet [90,91]. *C. aurantifolia* fruit juice is often added to palm oil, sugar or honey to relieve cough traditionally.

*C. aurantifolia* contains coumarins, proteins and amino-acids, vitamins and flavonoids. 44 volatile compounds were identified from *C. aurantifolia* [92].

*C. aurantifolia* isolates were tested against *M. tuberculosis* H37Rv strain. Compounds found responsible for the antimycobacterial activity in lime were 5,8-Dimethoxypsoralen (Isopimpinellin) with MICs = 25-50 µg/ml, 5-geranyloxypsoralen (bergamottin) with MICs = 50 – 100 µg/ml, palmitic acid (MICs = 50 -100 µg/ml), Oleic acid(MICs = 100 µg/ml), 4-hexen-3-one (MICs = 50 – 100 µg/ml) and Citral (MICs = 50 µg/ml). The authors reported that Isopimpinellin possessed antimicrobial, spasmylic, cancer chemopreventive and vasorelaxing properties [92]. Flavonoids showed anti-inflammatory, anti-allergenic and antimicrobial properties. Quercetin was reported to have positive effects against allergies and inflammations and respiratory diseases. Ascorbic acid found in large amounts is a necessary anti-stress compound and protector against colds, chills and damp [91].

### 3.30 Trema orientalis (Linn) Blume, Ulmaceae (Waste Land Tree, Pigeon Wood Tree, Gunpowder Tree)

*T. orientalis* is widely used in folk medicine to treat many diseases including respiratory diseases-asthma, cough, bronchitis, pneumonia, sore throats, toothache [93,94].

The trunk and root barks furnished terpenoids, coumarins, tannins and flavonoids [94-97]. The leaf furnished tannins, simiarenone, trematol [98]. The aqueous and methanol root extracts showed antibacterial activity [99]. Occhiuto et al. [100] reported that the leaf extract induced contractions in isolated guinea pig ileum, effects were always concentration dependent. This result supports the traditional use of this drug as a remedy for cough and chest conditions in traditional medicine.
3.31 *Gmelina arborea* Roxb, Verbenaceae (Coomb Teak, Cashmeri Tree, Candhar Tree)

The fruits and leaves are used as carminative, in the treatment of asthma, bronchitis, sore throat, cough, rheumatism among other disorders in folk medicine. The roots are used as demulcent, stomachic, anti-inflammatory and tonic [101].

Leaf contains flavonoids, hentriacontanol, premnazole – an anti-inflammatory compound and iridoid glycosides – gmelinosides. Fruits contain butyric and tartaric acids, ceryl alcohol, gmelinol, arborone, arboreal and flavonoids [101,102].

Plant leaf and bark extracts showed antibacterial activities against pathogenic bacterial strains, while heartwood constituents – iridoid glycosides showed antifungal activity. Arboreal, (+) – paulownin, (+)-gmelinol, (+)- epieudesmin showed antifungal activity. Studies on *in vivo* antioxidant and vasodilating activities of *Gmelina arborea* leaf extracts showed that the extracts possessed bioactive compounds with antioxidant and vasorelaxant properties [103].

3.32 *Costus afer* Ker Gawl, Zingiberaceae (Twisted Ginger, Ginger Lily, Bush Cane, Spiral Ginger and Monkey Sugar cane)

Bush cane is used in traditional medicine in West Africa to treat inflammation, rheumatism, arthritis and cough [78]. The leaves are used also. Decoction of the leafy stem is used alone or inadmixture with the infusion or extract of *Bryophyllum pinnatum* leaf [104].

*C. afer* rhizome extract contains diosgenin, aferosides, dioscin, paraphillin C, flavonoids, essential oil and other bioactive compounds [105,106].

*C. afer* extracts showed antioxidant, anti-inflammatory, antibacterial and antifungal properties. Anyasor et al. [106], subjected the hexane, EtoAC and n-BuOH fractions of *C. afer*’s aqueous fraction to *in vitro* anti-inflammatory screening assays. The hexane fraction was the most potent, confirming the use of the plant in folklore medicine to treat inflammation and respiratory disorders.

3.33 *Curcuma aromatica* Salisb, Zingiberaceae

*C. aromatica* rhizomes are used in combination with astringents and aromatics for bruises, sprain, hiccough, bronchitis and cough [107].

The rhizomes contain curcuminoids, terpene derivatives and volatile oil [108].

*C. aromatica* EtOH extract was investigated for its antitussive effect on sulphur dioxide-induced cough model in mice. The extract exhibited significant antitussive activity in dose-dependent manner. Codeine phosphate was the reference compound. The EtOH extract (100 mg, 200 mg and 400 mg/kg, p.o) showed 68%, 74% and 79% of inhibition of cough with respect to control group [109]. *C. aromatica* oil has shown antimicrobial activity.
4. HONEY IN REMEDIES FOR RESPIRATORY DISORDERS

Honey is a sweet and flavorful natural food product that results from the harvest and processing of nectars or honeydews by honey bees. Honeydews are plant secretions and excretions of plant sucking insects [110].

Honey occurs formulated with various plant extracts and/or animal juices in various herbal remedies available for the treatment of asthma or cold or cough. For instance, a combination of a mixture of honey and snail juice in a 1:1 ratio in a cup of boiled water is known to help in the healing/treatment of asthma. The mixture soothes respiratory distress, sore throat and other symptoms of discomfort in the lungs. A mixture of honey (1 teaspoonful) and water, vinegar or bee pollen (1 teaspoonful) and lime juice in equal parts melted together by gentle heat is an excellent adjunct to cough mixture.

The composition and various characteristics of honey are influenced by floral source from which honeybees process their nectars. Darker honeys have been found to have higher concentration of polyphenols and so higher anti-oxidant and anti-inflammatory properties.

Honey has been reported to contain moisture (17.20%), dextrose (31.28%), maltose (7.31%), lactose (7.11%), levulose (38.19%), sucrose (1.31%), higher sugar (1.5%) and diastase (20.8%). Honey also contains vitamins, amino-acids, anti-oxidants- such as phenolic acids and flavonoids, pollen grains and enzymes (invertase, diastase, inulase) etc. A typical honey was analyzed to contain phenolic acid, syringic acid, quercetin, luteolin, 8-methoxy kaempferol, pinocembrin, isorhamnetin, kaempferol, chrysin, galantin; methyl syringate, leptosin, glyoxal, phenylacetic acid, 2-methoxybenzoic acid, phenyl lactic acid etc. [110].

Honey has inherent antibacterial activity. The ability of honey to reduce inflammation and cure infections, heal wounds, etc. has been attributed to its total composition and properties [111,112]. Honey has also been found to stimulate inflammatory cytokine production from monocytes [110,113].

5. CONCENTRATED BILE IN RESPIRATORY DISORDERS

There are about twenty different kinds of bile known and these include the common types-from pigs, sheep, chickens and cows. The main constituents of bile are bile salts-sodium glycocholate, sodium taurocholate, biliverdin, cholesterol and derivatives, lecithin and bile acids. Bile helps in the digestion of fat and for eliminating worn out red blood cells [114].

Bile is antibacterial and has the ability to inhibit most gram-positive bacteria. Bile acid and deoxybile acid are both antibacterial with the deoxy derivative exhibiting more antibacterial activity than garlic. Bile is an effective antitussive and expectorant. It inhibits smooth muscle contraction and has a choleric effect.

Bile is used in the treatment of chronic bronchitis, whooping cough, tuberculosis, jaundice, hepatitis and trachoma [114].

6. RESULTS

This is a review of thirty-three medicinal plants used traditionally as cough suppressants-antitussives (Table 1). Nine of these—Lannea acida, Crescentia cujete, Kigelia Africana, Canarium schweinfurthii, Chenopodium ambrosioides, Terminalia macroptera, Eucalyptus camaldulensis, Piper guineense and Citrus aurantifolia have exhibited antiMycobacterium activity, just as different parts of Lannea acida, Uvaria chamae, Cocos nucifera, Gongronema latifolium, Crassocephalum crepidioides, Crescentia cujete, Kigelia Africana, Bixa orellana, Canarium schweinfurthii, Carica papaya, Gmelina arborea etc. have been found from ethnopharmacological studies to be remedies for asthma and cough. Traditional practitioners may not be interested in this scientific classification as polyherbal formulations, have over the years, taken care of their interests.

Whereas synthetic products may not affect the underlying symptoms of diseases causing the coughs, plant antitussives, by their nature and composition, more often remove the causative agents of coughs and the coughs themselves, leaving the patient healthier.
<table>
<thead>
<tr>
<th>S/N</th>
<th>Plants names</th>
<th>Parts used</th>
<th>Mechanism of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Lannea acida</td>
<td>Stem bark</td>
<td>Anti-inflammatory, antibacterial, antifungal, lipoxygenase inhibitor, anti-Mycobacterium tuberculosis activity</td>
</tr>
<tr>
<td>2</td>
<td>Dennettia tripetala</td>
<td>Fruit</td>
<td>Antifungal, anti-inflammatory, muscle relaxant, antimicrobial</td>
</tr>
<tr>
<td>3</td>
<td>Uvaria chamae</td>
<td>Leaf oil, Stem</td>
<td>Strongly antibacterial, anti-inflammatory</td>
</tr>
<tr>
<td>4</td>
<td>Cocos nucifera</td>
<td>Fruit</td>
<td>Anti-inflammatory, antibacterial, demulcent mucolytic, antiviral and anti-histaminic</td>
</tr>
<tr>
<td>5</td>
<td>Gongronema latifolium</td>
<td>Leaf</td>
<td>Anti-inflammatory, antibacterial, expectorant, mucolytic, antitussive</td>
</tr>
<tr>
<td>6</td>
<td>Crassocephalum crepidioides</td>
<td>Aerial parts</td>
<td>Anti-inflammatory, antibacterial, mucolytic, antitussive, antihistaminic</td>
</tr>
<tr>
<td>7</td>
<td>Crescentia cujete</td>
<td>Pulp syrup, stem bark</td>
<td>Expectorant, antiviral, antibacterial, antifungal, showed anti Mycobacterium activity</td>
</tr>
<tr>
<td>8</td>
<td>Kigelia Africana</td>
<td>Fruit, stem bark</td>
<td>Anti-histaminic, antifungal, showed anti-Mycobacterium tuberculosis activity, anti-inflammatory, antibacterial</td>
</tr>
<tr>
<td>9</td>
<td>Bixa orellana</td>
<td>Leaf, Seeds</td>
<td>Anti-inflammatory, antibacterial, proven antitussive</td>
</tr>
<tr>
<td>10</td>
<td>Ananas comosus</td>
<td>Fruit</td>
<td>Mucokinetic, anti-inflammatory, proteolytic</td>
</tr>
<tr>
<td>11</td>
<td>Caranarium schweinfurthii</td>
<td>Leaf, stem, fruit</td>
<td>Anti-inflammatory, antibacterial, aromatic, demulcent; showed anti-Mycobacterium tuberculosis activity</td>
</tr>
<tr>
<td>12</td>
<td>Dacryodes edulis</td>
<td>Stem bark,</td>
<td>Antibacterial, anti-inflammatory and antiseptic</td>
</tr>
<tr>
<td>13</td>
<td>Carica papaya</td>
<td>Seed, latex, leaf</td>
<td>Anti-inflammatory, antibacterial, demulcent, anti-histaminic, proteolytic</td>
</tr>
<tr>
<td>14</td>
<td>Chenopodium ambrosioides</td>
<td>Plant essential oil</td>
<td>Mucokinetic, antifungal, anti-inflammatory, antibacterial, showed anti-Mycobacterium activity</td>
</tr>
<tr>
<td>15</td>
<td>Guiera senegalensis</td>
<td>Leaf</td>
<td>Mucokinetic, anti-inflammatory, antibacterial, antitussive</td>
</tr>
<tr>
<td>16</td>
<td>Terminalia avicennoides</td>
<td>Stem bark, root</td>
<td>Antibacterial, antifungal, showed anti-Mycobacterium tuberculosis activity, proven antitussive</td>
</tr>
<tr>
<td>17</td>
<td>Terminalia glaucescens</td>
<td>Stem bark</td>
<td>Strongly antimicrobial, anti-HIV AIDS</td>
</tr>
<tr>
<td>18</td>
<td>Terminalia ivorensis</td>
<td>Leaf, stem bark</td>
<td>Strongly antibacterial, antifungal</td>
</tr>
<tr>
<td>19</td>
<td>Terminalia macropera</td>
<td>Root, stem bark</td>
<td>Strongly antibacterial and antifungal, showed anti-Mycobacterium activity</td>
</tr>
<tr>
<td>20</td>
<td>Alchornea laxiflora</td>
<td>Leaf</td>
<td>Anti-inflammatory, antibacterial, antifungal</td>
</tr>
<tr>
<td>21</td>
<td>Bridelia ferruginea</td>
<td>Leaf</td>
<td>Anti-inflammatory, antimicrobial, antifungal, antiviral</td>
</tr>
<tr>
<td>22</td>
<td>Bridelia micrantha</td>
<td>Leaf</td>
<td>Antimicrobial, anti-inflammatory, anti-viral</td>
</tr>
<tr>
<td>23</td>
<td>Phyllanthus muellerianus</td>
<td>Stem, leaf</td>
<td>Strongly antibacterial, phenolic, anti-inflammatory, analgesic</td>
</tr>
<tr>
<td>24</td>
<td>Ocimum gratissimum</td>
<td>Aerial parts</td>
<td>Nasal decongestant, mucokinetic, anti-inflammatory, antibacterial, antiseptic, antifungal</td>
</tr>
<tr>
<td>25</td>
<td>Hibiscus rosa-sinensis</td>
<td>Root, aerial parts</td>
<td>Demulcent, anti-inflammatory, antibacterial, expectorant; proven antitussive</td>
</tr>
<tr>
<td>26</td>
<td>Dissotis rotundifolia</td>
<td>Leaf</td>
<td>Antibacterial, proven antitussive</td>
</tr>
</tbody>
</table>
S/N | Plants names | Parts used | Mechanism of action
--- | --- | --- | ---
27 | *Eucalyptus camadulensis* | Leaf | Antiseptic, antibacterial, strong *anti-Mycobacterium tuberculosis* activity, spasmylytic, proven antitussive
28 | *Piper guineense* | Aerial parts, fruit | Antimicrobial, antifungal; showed *anti-Mycobacterium tuberculosis* activity
29 | *Citrus aurantifolia* | Fruit | Antiseptic, antibacterial, anti-inflammatory, mucolytic, anti-allergic, showed *anti-Mycobacterium tuberculosis* activity
30 | *Trema orientalis* | Leaf, stem, root | Anti-inflammatory, antibacterial
31 | *Gmelina arborea* | Fruit, leaf, stem | Carminative, anti-inflammatory, antibacterial, antifungal, vasorelaxant activities, antitussive
32 | *Costus afer* | Leafy stem, rhizome | Anti-inflammatory, antibacterial, antifungal
33 | *Curcuma aromatic* | Rhizome | Proven antitussive, antimicrobial, anti-inflammatory, aromatic

7. CONCLUSIONS

The popular and effective herbal medications for cough known for a very long time are the leaf and root decoctions of *Althaea officinalis* (Marshmallow) which is believed can reduce inflammation, the leaf infusion or hot tea of *Hyssopus officinalis* (Hyssop) which is expectorant, and the pungent aromatic spices and hot remedies such as the fruit of *Dennettia tripetala* or *Zingiber officinale* rhizome. The antitussive potentials of plants may be enhanced with polyherbal formulations when the pungent spices are mixed with other plants for efficacy.

Very many of the plants reviewed are known to accumulate essential oils in their leaves, fruits, roots, flowers and stem barks. Essential oils are a complex mixture of hydrocarbons and their oxygenated derivatives and have been used in many formulated medicinal products all over the world since ancient times. Essential oils and their constituents are much valued because of their biological activities which include antimicrobial, analgesic, antifungal, anti-inflammatory etc. Citral and linalool, major constituents of *Cymbopogon citratus* have been found to relax bronchial smooth muscles, antagonize histamine- or acetylcholine-induced constriction, exert expectorant effect and relieve chronic bronchitis and hypersensitivity. Limonene, linalyl acetate and linalool were found to be responsible for the antymycoplasmal activity of *Citrus bergamia* essential oil, with linalool and limonene showing very high activity especially on *Mycoplasma pneumonia* (MIC values 0.015% and 0.03% resp [115]). *C. aurantium* leaf essential oil also exerted high antimicrobial activity and moderate activity against yeasts and fungi; linalool (43.2%-65.97%), linalyl acetate (0.77%-24.77%) and α-terpinol (9.29%-12.12%) occurred as the highest constituents [116].

Various plant essential oils have shown anti-inflammatory properties. It is speculated that the anti-inflammatory activity of essential oils may be the basis of their protective activity against gut inflammation diseases [117]. Polo studied [117] the effects of *C. aurantium* fruit peel essential oil on a gastric ulcer model system and found out that the oil significantly decreased the gastric lesion area by 76% compared to the control group at an oral dose of 250 mg/kg/day for 14 consecutive days. Limonene, a main compound of the essential oil gave same results in the same gastric ulcer model system. Bonamin et al. [118] has also demonstrated the protective activity of β-myrcene, another monoterpene constituent of *C. aurantium* oil, thus confirming the anti-inflammatory properties of the essential oil and its constituents.

Terpenoids and tannins, many of which have been isolated from the plants reviewed have exhibited anti-inflammatory, anti-allergic and other biological activities *in vitro* and *in vivo*; many mechanisms have to be proposed to explain these activities. Punicalagin and punicalin possessed anti-inflammatory activities [119]. Punicalagin also displayed a good antifungal activity [120] and, with terchebulin were responsible for the *in vitro* activity of *T. macroptera* against *Helicobacter pylori* [63]. Chebulinic acid showed a gastroprotective effect against ulcers induced by cold restraint, aspirin, alcohol and pyloric litigation-induced ulcer.
models. It significantly reduced free acidity, total acidity and upregulated mucin secretion [121]. Gallic acid present in many hydrolysable tannins exhibited strong antibacterial [122] and high antifungal activities [123], making these phytochemicals relevant in the management of respiratory disorders caused by infections.

Herbal antitussives not only suppress coughs, they always attempt to remove the respiratory disorders causing the coughs and thus make patients healthier. The use of medicinal plants remains a universal phenomenon; this review justifies the need for polyherbal formulations for use in the management of respiratory disorders.

Herbal products are receiving increasing attention all over the world for the management of respiratory disorders as these have shown expectorant, mucolytic, anti-inflammatory, sympathomimetic, nasal-decongestant, antibacterial, antiMycobacterium and antitussive activities.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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