Minor common disorders of the respiratory system can often be successfully treated with phytotherapy and it can be helpful as a supportive measure in more serious diseases, such as bronchitis, emphysema and pneumonia. For severe infections, antibiotic therapy may be needed and, although most antibiotics are natural products, their study is a separate issue and will not be dealt with here. However, for colds and flu-like virus infections, decongestants (e.g. menthol and eucalyptus), broncholytics and expectorants (including ipecacuanha, thyme and senega), demulcents (e.g. mallow), antibacterials and antivirals (e.g. linden and elder flowers, pelargonium) and immune system modulators (e.g. echinacea, andrographis) are popular and effective. Allergic conditions such as hay fever can be treated with butterbur, Petasites and, traditionally, a compound of garlic and echinacea is used for allergic and infective rhinitis. Asthma is becoming more prevalent for reasons as yet unknown, but is best treated aggressively with inhaled steroids and bronchodilators. Many bronchodilators are either of natural origin (e.g. theophylline and ephedrine) or have been developed from natural products. Although isolated ephedrine and pseudoephedrine are theoretically contraindicated in asthma because they can precipitate an attack, ephedra herb has a long history of use without apparent ill-effects; this is attributed to other constituents in the whole extract. Antimuscarinic drugs (e.g. atropine), which have bronchodilator effects and also dry up secretions, have largely been superseded by derivatives such as ipratropium. An important compound, sodium cromoglycate, is an anti-allergic drug developed from khellin, which stabilizes mast cells and is used in the form of an inhaler to treat asthma. Platelet-activating factor antagonists (e.g. the ginkgolides) have anti-allergic effects, which may be useful in asthma but are not yet employed clinically. Ginkgo is covered in Chapter 16. Leukotriene antagonists have recently been introduced for asthma therapy and, although no plant products are yet in use, there are several natural compounds (e.g. quercetin) with this property and they may become available in the future. Cough suppressants are very popular, although there is some controversy as to whether they are clinically effective. The most important antitussives are codeine and other opiate derivatives obtained from the opium poppy.

**BRONCHODILATORS AND DECONGESTANTS**

**SYSTEMIC DRUGS**

**EPHEDRA, EPHEDRA SPP. (EPHEDRAE HERBA)**

Ephedra, also known as Ma Huang (Ephedra sinica Stapf. and other species of the family Ephedraceae) is an ancient Chinese medicine, which is now used worldwide. It was the original source of ephedrine, a useful decongestant and bronchodilator. Traditionally, it is used to treat asthma and nasal congestion, in the form of nasal drops. Pseudoephedrine is now used more widely for respiratory congestion as it has fewer central nervous system (CNS) stimulatory properties. The plant has slender green stems, which are jointed in branches of about 20 tufts about 15 cm
long, and terminate in a sharp, recurved point. These are the medicinal part. The leaves are reduced to sheaths surrounding the stems.

**Constituents**

Alkaloids, up to about 3%, but widely varying; the major alkaloid is (–)-ephedrine (Fig. 16.1), together with many others. These include (+)-pseudoephedrine, norpseudoephedrine, ephedroxane, N-methylephedrine, maokonine, transtorine and the ephedradines A–D. Other components are catechin derivatives, and diterpenes, including ephedrannin A and mahuannin A, have been isolated from other species of *Ephedra*.

**Therapeutic uses and available evidence**

*Ephedra* has been used since ancient times in China for asthma and hay fever, as a bronchodilator, sympathomimetic, CNS and cardiac stimulant. Herbalists also use it to treat enuresis, allergies, narcolepsy and other disorders, and anti-inflammatory activity has been observed in extracts. Ephedrine is used in the form of elixirs and nasal drops, and has an additional use as a heart rate accelerator in the treatment of some types of bradycardia. Pseudoephedrine, the D-isomer of ephedrine produced by chemical synthesis, is usually the compound of choice for isolated alkaloid preparations. Ephedra herb, ephedrine and pseudoephedrine are all the subject of European Pharmacopoeia (Eur. Ph.) monographs. Ephedra herb is used as an anti-allergic agent; this is supported by evidence that it induces immunoglobulin A in Peyer’s patches and blocks complement activation by both the classical and alternative pathways.

**Toxicological risks**

The herb has been abused as a slimming aid, and an ergogenic aid in sports and athletics, but this is dangerous (Fleming 2008). For example, hypertension and other cardiovascular events, and a case of exacerbation of hepatitis, have been noted with high doses.

The absorption of ephedrine and pseudoephedrine is slower after ingestion of the herb than for isolated alkaloid preparations, and the other constituents, the ephedradins, mahuannins and maokonine, are mildly hypotensive; but both the herb and the isolated alkaloids should be avoided by hypertensive patients as well as in cases of thyrotoxicosis, narrow-angle glaucoma and urinary retention. Therapeutic doses of the herb are calculated to deliver up to 30 mg of the alkaloids, calculated as ephedrine.

**THEOPHYLLINE**

Although a natural xanthine, theophylline (Fig. 16.2), which is found in cocoa (*Theobroma cacao*), coffee (*Coffea* spp.) and tea (*Camellia sinensis*), is almost invariably used as the isolated compound. It is indicated in reversible airways obstruction, particularly in acute asthma. Because of the narrow margin between the therapeutic and the toxic dose, and the fact that the half-life is highly variable between patients, especially smokers and in heart failure or with concurrent administration of other drugs, care must be taken. The usual dose is 125–250 mg in adults, three times daily, and half of that in children. Side effects include tachycardia and palpitations, nausea and other gastrointestinal upsets. These can be reduced using sustained-release preparations, and this is the usual form of theophylline products.

**INHALATIONS**

Essential oil containing drugs are often used with aromatic compounds (especially camphor) as chest rubs, steam inhalations or nasal sprays, for their decongestant properties. They are particularly useful for infants, children, asthmatics and pregnant women for whom systemic decongestants may not be appropriate. They may also be used orally, in pastilles, lozenges, or ‘cough sweets’. Oils distilled from the aerial parts of members of the pine family...
[e.g. the common Pumilio (Alpine) pine (*Pinus mugo*), the European larch (*Larix decidua*) and the fir tree (*Abies* spp.)] and the Australian Myrtaceae (e.g. eucalyptus and tea-tree oil) are used frequently. These oils can also be used in steam baths.

**CAMPHOR**

Camphor (Fig. 16.3), a pure natural product, is derived from the Asian camphor tree (*Cinnamomum camphora* T. Nees & Eberm., Lauraceae). It is often combined with the essential oil containing drugs as an aromatic stimulant and decongestant.

Camphor has antiseptic, secretolytic and decongestant effects. Small doses were formerly taken internally for colds, diarrhoea and other complaints, but it is now used only externally.

**Toxicological risks**

Camphor has been in use for many years; however, ‘camphorated oil’ was recently taken off the market since, in large quantities, camphor may be absorbed through the skin causing systemic toxicity. Overdose causes vomiting, convulsions and palpitations, and can be fatal. However, when used externally in therapeutic doses it is generally well tolerated.

**EUCALYPTUS OIL, *EUCALYPTUS SPP.* (EUCALYPTI AETHEROLEUM)**

The blue gum tree, *Eucalyptus globulus* Labill., and other species (Myrtaceae) yield a highly characteristic oil which is widely used as a decongestant and solvent. The leaves are scimitar-shaped, 10–15 cm long and about 3 cm wide, shortly stalked and rounded at the base, with numerous transparent oil glands.

**Constituents**

The oil contains 1,8-cineole (eucalyptol; see Fig. 16.4) as the major component, with terpineol, α-pinene, p-cymene and small amounts of ledol, aromadendrene and viridoflorol, aldehydes, ketones and alcohols.

**Therapeutic uses and available evidence**

The oil is antiseptic, antispasmodic, expectorant, stimulant and insect repellent. It is a traditional Australian Aboriginal remedy for coughs, colds and bronchitis. It may be taken internally in small doses (0.05–0.2 ml), as an ingredient of cough mixtures, sweets and pastilles, or as an inhalation; it is applied externally in the form of a liniment, ointment or ‘vapour rub’. The leaf extract and oil have well-defined antiseptic effects against a variety of bacteria and yeasts. The oil is also insect-repellent and larvicideal, and is used in pharmaceutical products for these properties as well as for its antiseptic and flavouring properties in dentifrices and cosmetics. It is widely used in Menthol and Eucalyptus Inhalation BP for steam inhalation as a decongestant. Eucalyptus oil is irritant and, although safe as an inhalation, caution should be exercised when taken internally as fatalities have been reported.

**MENTHOL**

Menthol is a monoterpane (Fig. 16.4) extracted from mint oils, *Mentha* spp. (especially *M. arvensis*) or it can be made synthetically. Whole peppermint oil is used in herbal combinations to treat colds and influenza (as well as for colic, etc.; see Chapter 14), but isolated menthol is an effective decongestant used in nasal sprays and inhalers. Menthol can be irritant and toxic in overdose, but is generally well tolerated in normal usage.

**ANTI-ALLERGICS**

Most antihistamines are synthetic in origin and, although many flavonoids have anti-allergic properties, they are nowhere near as potent as, for example, cetirizine, desloratidine, fexofenadine or chlorpheniramine. Recently, however, an extract of the herbal drug butterbur (see below) was found
to be equivalent in activity to cetirizine. There is a problem with toxic alkaloids in this plant, which if present must be removed from the product; thus it is not suitable as a home remedy without expert advice. Smooth muscle relaxant drugs have been used widely in asthma, and one of these, khellin (used particularly in the Mediterranean region, and isolated from *Ammi visnaga*), was investigated as a lead compound for development. One derivative, sodium cromoglycate, was discovered to have antiallergic effects (see below).

**BUTTERBUR, *PETASITES HYBRIDUS* L.**

*Petasites hybridus* (syn. *P. vulgaris, Tussilago petasites, Compositae*) is a downy perennial, common in damp places throughout Europe, with very large heart-shaped leaves and lilac-pink brush-like flowers which occur in early spring before the leaves appear. The root and herb are used.

**Constituents**

Butterbur contains sesquiterpene lactones (eremophilinolides), including a series of petasins and iso-petasins, neopetasin, petasalin, furanopetasin, petasinolides A and B, and flavonoids including isoquer cetin glycosides. However, toxic pyrrolizidine alkaloids (senecionine, integerrimine, senkirkine, petasitine and neopetasitine) may be present, usually in higher concentrations in the root.

**Therapeutic uses and available evidence**

Butterbur is traditionally used as a remedy for asthma, colds, headaches and urinary tract disorders. It is used as an antihistamine for seasonal allergic rhinitis, and a recent randomized, double-blind comparative study using 125 patients over 2 weeks of treatment showed that butterbur extract is as potent as cetirizine. The anti-inflammatory activity is due mainly to the petasin content. Extracts inhibit leukotriene synthesis and are spas modyltic, and reduce allergic airway inflammation and AHR by inhibiting the production of the Th2 cytokines IL-4 and IL-5, and RANTES (Brattström et al 2010), thus supporting its use in asthma. Use as prophylactic treatment for migraine has also been suggested but further evidence of efficacy is needed (Agosti et al 2006). The usual dose is an extract equivalent to 5–7 g of herb or root. Internal use is not recommended unless the alkaloids are present in negligible amounts or have been removed from preparations, as is the case with the commercially available product, which is a ‘special extract’. Maximum intake of the alkaloids should be less than 1 µg daily for fewer than 6 weeks per year.

**KHELLA, *AMMI VISNAGA* (L.) LAM.**

Also known as the ‘toothpick plant’, as the woody pedicels can be used for this purpose, khella (*Apiaceae*) is an herbaceous annual reaching 1.5 m in height, with divided filiform leaves and typically umbelliferous flowers. The botanical drug is the fruits, which are very small, broadly ovoid and usually found as separate greyish-brown merocarps. The drug has a long history of use in the Middle East, especially Egypt, as an antispasmodic in renal colic, for asthma and as a coronary vasodilator for angina.

**Constituents**

Key active principles are furanocoumarins, the most important being khellin (Fig. 16.5), together with visnagin, visnadin and khellol glucoside.

**Therapeutic uses and available evidence**

Khellin, visnadin and visnagin are vasodilators, with calcium channel blocking and spasmodyltic activity. Khellin was the starting material for the development of several important semi-synthetic derivatives such as sodium cromoglycate, which is widely used as a prophylactic treatment for asthma, hay fever and other allergic conditions, often in the form of an inhaler or eyedrops. It was also the basis for the development of nifedipine (a calcium channel antagonist and vasodilator) used in heart disease, and amiodarone, a cardiac antiarrhythmic.

![Khellin](https://example.com/khellin.png)
EXpectorants AND mucolytics

The purpose of these drugs is to reduce the viscosity of mucus in the respiratory tract to enable expectoration of phlegm in cases of chest and throat infection. Frequently, essential oils are used with expectorant aromatic compounds such as camphor. Many expectorants are included in cough mixtures and, although efficacy is difficult to demonstrate, these products are very popular with patients in the absence of other treatments. All are used for coughs and colds, bronchitis and sinusitis, usually in conjunction with other decongestants, demulcents, analgesics and, occasionally, antibiotics. Some of these drugs contain essential oils and salicylates (e.g. poplar buds, thyme), and may also include the decongestants mentioned above (eucalyptus, menthol); others contain saponins (e.g. senega, ivy).

Balm of Gilead (Poplar Buds), Populus spp.

Poplar buds (from various Populus spp., including P. candidans Ait., P. gileadensis Rouleau, P. balsamifera L. and P. nigra L., Salicaceae) are collected in the spring before they open. P. gileadensis and P. nigra are cultivated in Europe; the others are North American. The buds of all species are similar, being about 2 cm long and 0.5 cm wide, with narrow, brown, overlapping scales; the inner scales are sticky and resinous. The bark of these species is also used.

Constituents

All contain the phenolic glycosides salicin (salicyl alcohol glucoside), populin (benzoyl salicin) and a volatile oil containing α-caryophyllene, with cineole, bisabolene and farnesene. Flavonoids (pinocembrin and pinobanksin) and, in P. nigra at least, lignans, based on isolariciresinol, have been isolated.

Therapeutic uses and available evidence

Balm of Gilead is an expectorant, stimulant, antipyretic and analgesic. It is a common ingredient of herbal cough mixtures, and also ointments used for rheumatic and other muscular pains. The phenolic glycosides (e.g. salicin) and the volatile oil constituents have antiseptic and expectorant activity. Little evidence is available for efficacy, but the drug has a long history of traditional use. The bark of poplar species is used in a similar way to willow bark, as an antirheumatic.

Balm of Gilead is generally non-toxic, except for patients who are allergic to salicylates. If excessive amounts of these drugs are taken, adverse effects such as stomach upset and tinnitus are possible, due to the salicylate content.

Thyme and Wild Thyme, Thymus vulgaris L. and Thymus serpyllum L. (Thymi Herba and Serpylli Herba)

Thymus vulgaris (known as garden or common thyme) and wild thyme (T. serpyllum, mother of thyme or serpyllum, Lamiaceae) are indigenous to Europe, especially the Mediterranean region, and are cultivated extensively. They are small, bushy herbs, with small, elliptical, greenish-grey, shortly stalked leaves. Those of thyme are up to about 6 mm long and 0.5–2 mm broad, with entire recurved margins. The leaves of wild thyme are a little broader and the margins are not recurved; it has leaves with long trichomes at the base. Microscopically, the herbs are similar; both having the characteristic Lamiaceous glandular trichomes; the rather subtle differences are described in the Eur. Ph. Both have a characteristic odour of thymol and are used as culinary herbs.

Constituents

The active principle is the volatile oil, which has the major constituent thymol, with lesser amounts of carvacrol, 1,8-cineole, borneol, thymol methyl ether and α-pinene. However, the flavonoids (apigenin, luteolin, thymonin, etc.) and the polyphenolic acids (labiatic, rosmarinic and caffic) are expected to contribute to the anti-inflammatory and antimicrobial effects.

Therapeutic uses and available evidence

Thyme, and oil of thyme, are carminative, antiseptic, antitussive, expectorant and spasmolytic, and, as such, are used for coughs, bronchitis, sinusitis, whooping cough and similar respiratory complaints. Most of the activity is thought to be due to the thymol, which is expectorant and highly antiseptic. Thymol and carvacrol are spasmolytic and the flavonoid fraction has a potent effect on
the smooth muscle of guinea pig trachea and ileum. Thymol (Fig. 24.1) is a popular ingredient of mouthwashes and dentifrices because of its antiseptic and deodorant properties. The oil may be taken internally in small doses of up to 0.3 ml, unless for use in a mouthwash, which is not intended to be swallowed in significant amounts. Thymol is irritant, and toxic in overdose, and should be used with care.

**SAGE, SALVIA OFFICINALIS L. (SALVIAE FOLIUM) AND SALVIA SPP.**

*Salvia officinalis* L. (syn. garden or red sage, Lamia-ceae) is indigenous to Europe, especially the Mediterranean region, and cultivated extensively. Spanish sage is *S. officinalis* subsp. *lavandulifolia* (Vahl) Gams; Greek sage is *S. triloba* L. fil. The leaves are stalked, 3–5 cm long and 1–2.5 cm broad, oblong or lanceolate and rounded at the base and at the apex. Sage has a strong, characteristic, odour. It is widely used as a culinary herb.

**Constituents**

Sage contains a volatile oil, with α- and β-thujone as the major components (usually about 50%), and cineole, borneol, camphor, 2-methyl-3-methylene-5-heptene and others. Spanish sage does not contain thujone; Greek sage contains only small amounts. Diterpene bitters picrosalvin (carnosol), carnosolic acid, abietane derivatives called royleanones, and flavonoids such as salvigenin, genkwanin, luteolin and derivatives are present, together with the polyphenolic acids salvianolic, rosmarinic and caffeic acids.

**Therapeutic uses and available evidence**

An infusion of sage is used as a gargle or mouthwash for pharyngitis, tonsillitis, sore gums, mouth ulcers and other similar disorders. Sage extracts and oil have been reported to be antimicrobial. The flavonoids and phenolic acid derivatives have antiviral and anti-inflammatory activity. Sage has a reputation for enhancing memory, and there is some clinical trial evidence (Scholey et al 2008), and the fact that it has anticholinesterase activity, to support this use.

**SENEGA, POLYGALA SENEGA L. (POLYGALAE RADIX)**

Senega (snake root, rattlesnake root, *Polygala senega* L., Polygalaceae) is native to the USA. In Chinese medicine, senega may also refer to *P. tenuifolia* Willd.; both species are used for similar purposes. The root is light yellowish-grey with a knotty crown, from which slender stems arise, bearing the remains of rudimentary leaves and buds at the base.

**Constituents**

The active constituents are triterpenoid saponins, the mixture generally known as ‘senegin’. These are based on the aglycones presenegenin, senegenin, hydroxysenegin, polygalacic acid and senegnic acid, including the E- and Z-senegins II, III and IV, E- and Z-senegasaponins a, b and c, and others.

**Therapeutic uses and available evidence**

Senega is used primarily for chronic bronchitis, catarrh, asthma and croup. The saponins are the active constituents, as with other mucolytic plant drugs, and senega is usually taken orally as an infusion. The saponins also have immunopotentiating activity to protein and viral antigens, and exhibit less toxicity than quillaia saponins. They are anti-inflammatory and antiseptic. Senega extracts, the senegasaponins and the senegins are hypoglycaemic in rodents, the senegasaponins are inhibitors of alcohol absorption, and the senegins also have anticancer and anti-angiogenic effects *in vitro* (Arai et al 2011). The dose is usually equivalent to 0.5–1 g of the powdered root.

The saponins are irritant and haemolytic, but taken orally do not appear to pose many problems. Nausea and vomiting are the most common side effects and, in view of the other pharmacological actions, care should be taken with senega when given in high doses or to sensitive individuals.

**IVY, HEDERA HELIX L. (HEDERAE FOLIUM)**

Ivy is a saponin-containing expectorant. It is a common European plant, found also in northern and eastern Asia and introduced into America. *Hedera helix* (Araliaceae) has dark green leathery leaves, shiny, with 3–4 triangular lobes. The berries are small, purplish-black and globular, with the calyx ring visible at the apex. Both leaves
and berries may be used as part of phytotherapeutic preparations. The berries are somewhat toxic if consumed.

**Constituents**

The actives are saponins based on oleanolic acid, bayogenin and hederagenin, including the hederosaponins (or hederosides) B, C and D, and α- and β-hederin, the polyyne falcarinol, and also flavonoids.

**Therapeutic uses and available evidence**

Ivy extracts are used in preparations for bronchitis and catarrh, as an expectorant. The saponins and sapogenins are the main active ingredients; they are expectorant and antifungal. Few clinical studies have been carried out, and further work is needed (Holzinger and Chenot 2011). One study showed that after 7 days of therapy with dried ivy leaf extract, 95% of patients showed improvement or healing of their symptoms, and it was safe and well-tolerated: the overall incidence of adverse events was 2.1%, mainly gastrointestinal disorders (Fazio et al 2009).

Both the saponin and the flavonoid fractions have spasmolytic effects.

A specific mode of action relevant for respiratory conditions of the saponins has been postulated: hederoside C (which is converted into α-hederin by esterases) as well as its aglucose hederagenin, acts on G protein-linked β₂-adrenergic receptors of epithelial lung cells, resulting ultimately in an indirect β₂-sympathomimetic effect (Hegener 2004). Ivy extracts are often used in cosmetic preparations to treat cellulite, with some success. Ivy saponins are being widely investigated for their antileishmanial, molluscicidal, antimutagenic, antithrombin and anticlastogenic effects. The usual therapeutic dose as an expectorant is 0.3 g of crude drug, or equivalent.

Like all saponin-containing drugs, ivy can be irritating and allergenic. These effects are also due at least in part to the falcarinol content.

**TOLU BALSAM, MYROXYLON BALSAMUM L. (BALSAMUM TOLUTANUM)**

The resin, which is collected from incisions in the bark and sapwood of Myroxylon balsamum (Fabaceae), is a light brown, fragrant, balsamic resin, softening when warm and becoming brittle when cold. It has a pleasant, sweetish, aromatic, vanilla-like odour.

**Constituents**

The main constituents of the balsam are cinnamic and benzoic acids, their esters such as benzyl benzoate and cinnamyl cinnamate, and esters with resin alcohols, including coniferyl and hydroconiferyl benzoates.

**Therapeutic uses and available evidence**

Balsam of tolu is expectorant, stimulant and antiseptic. It is used in cough mixtures and pastilles, and as a lozenge base. Although there is no modern clinical evidence, many balsams are used for similar purposes and generally agreed to have a useful therapeutic role as expectorants, antiseptics and demulcents. Balsam of tolu is an ingredient in Friar’s balsam, which is used as a steam inhalation and also as a protectant in skin formulations. The antimicrobial activity is due to the benzyl benzoate and benzyl cinnamate content.

Tolu balsam, like many other balsam resins, can cause allergic reactions.

**IPECACUANHA, CEPHAELIS IPECACUANHA A. RICH AND C. ACUMINATA KARSTEN (IPECACUANHAE RADIX)**

‘Ipecac’ is obtained from the root and rhizome of Cephaelis ipecacuanha and C. acuminata (Rubiaceae). Rio, Matto Grosso and Brazilian ipecac are used to describe C. ipecacuanha (syn. Psychotria ipecacuanha Stokes) and Cartagena, Nicaragua or Panama ipecac, C. acuminata. They are native to tropical central and south America and cultivated in southern Asia. C. ipecacuanha root is slender, twisted and reddish brown, up to about 4 mm in diameter, with a characteristic ringed appearance. C. acuminata is larger, with fewer annulations. The root can be identified microscopically by the characteristic tracheids and bordered pitted xylem vessels, and the needle crystals of calcium oxalate (see Eur. Ph.).

**Constituents**

Both species contain isoquinoline alkaloids as the active principles, usually about 2–3%. The most important are emetine (Fig. 16.6) and cephaeline, with psychotrine and some others.
Therapeutic uses and available evidence

Ipecac extract is an ingredient of many cough preparations, both elixirs and pastilles, because of its expectorant activity. It is also well known as an emetic and has been employed to induce vomiting in cases of drug overdose, particularly in children. This use is, however, highly controversial (Quang and Woolf 2000). The alkaloids are amoebicidal, but the emetic activity means that they are rarely used for this purpose. There is little clinical evidence for the use of ipecac as an expectorant but it has a long history of traditional use. Ipecacuanha Liquid Extract BP is given at a dose of 0.25–1 ml.

Ipecac causes vomiting in large doses and the alkaloids are cytotoxic.

COUGH SUPPRESSANTS

Cough is a reflex action and a symptom of other diseases such as asthma and colds due to ‘nasal drip’. Cough suppressants may be useful in some instances, but efficacy is not fully proven and if expectoration is required, for example to avoid sputum retention, they should not be used. They are not recommended for small children who are highly susceptible to respiratory depression caused by opiates. Codeine and semi-synthetic opiates such as dextromethorphan are the most common antitussives; in severe cases such as in lung cancer, stronger opiates such as methadone may be used.

CODEINE

Although found in opium (Papaver somniferum), codeine (Fig. 16.7) is usually used as the isolated alkaloid, in the form of a salt (usually phosphate) formulated as a linctus, at a dose of 5–10 mg 4-hourly, to treat cough. The dose for treating diarrhoea and pain is much higher (up to 240 mg daily in divided doses).

Codeine is sedating and constipating. In large doses it may cause respiratory depression and should not be used in hepatic or renal impairment. It is also liable to abuse and is available only on prescription in many countries.

GENERAL PHYTOMEDICINES USED IN Colds AND InFLUENZA

Some of these herbs have antiviral and anti-inflammatory activity, some are demulccent or stimulate the immune system, and many have several of these properties. They are often used in combination with other ingredients as herbal teas for the supportive or symptomatic therapy of respiratory disease.

DEMULCENTS AND EMOLLIENTS

Many herbal teas, made particularly from flowers and leaves, are used to obtain symptomatic relief from colds and influenza. Some are diaphoretic (induce sweating), some are anti-inflammatory and analgesic, others are mucilaginous and soothing, and many have some antiviral activity due to the polyphenolic constituents. They are used as a general supportive measure and are usually pleasant to take. As well as the plants discussed here, other botanical drugs rich in mucilage are also used for respiratory conditions, for example the lichen ‘Icelandic Moss’ from Cetraria islandica (L.) Ach. (Parmeliaceae).
COLTSFOOT, **TUSSILAGO FARFARA L.** (TUSSILAGO FOLIUM) EUPHORBIA COLEUS

Coltsfoot (Asteraceae) is a common wild plant in Britain and Europe, growing in damp places. The flowers appear in early spring before the leaves. The leaves are hoof-shaped, with angular teeth on the margins, green above and coated with matted, long white hairs on the lower surface. The flowers are bright yellow, with a characteristic scaly pedicel. Both the leaves and flowers are used medicinally.

**Constituents**

The main constituent is a mucilage composed of acidic polysaccharides, together with flavonoids, triterpenes and sterols. Pyrrolizidine alkaloids, including senkirkine, tussilagine and isotussilagine, may be present in variable amounts, usually very minor (about 0.015%) or absent, depending on source.

**Therapeutic uses and available evidence**

Coltsfoot is used for pulmonary complaints, irritating or spasmodic coughs, whooping cough, bronchitis, laryngitis and asthma. The polysaccharides are anti-inflammatory and immunostimulating, as well as demulcent, and the flavonoids also have anti-inflammatory and antispasmodic action.

The pyrrolizidine alkaloids are known to cause hepatotoxicity in rats fed daily on high doses, but not on daily low-dose regimens, and appear not to cause damage to human chromosomes *in vitro*. However, samples containing significant quantities of these alkaloids should not be used.

ELDERFLOWER AND ELDERBERRY (FRUIT), **SAMBUCUS NIGRA L.** (SAMBUCI FLOS, SAMBUCI FRUCTUS) EUPHORBIA COLEUS

*Sambucus nigra* (Adoxaceae or Sambucaceae), the Black or European elder (berry), is a common European hedge tree or shrub. The flowers appear in May as small, creamy-white, flat-topped umbel-like clusters and are followed by small, shiny, purplish-black berries. Most parts of the plant are used, but most commonly the flowers and berries, which are also used to make refreshing drinks and country-style wines. The berries should not be eaten raw as they contain lectins, which can cause gastrointestinal disturbances, but which are destroyed by heat. Related species are toxic (e.g. Danewort, *S. ebulus*).

**Constituents**

Triterpenes including ursolic and oleanolic acid derivatives, flavonoids (rutin, quercetin, nicotinfolin, hyperoside), and phenolic acids such as chlorogenic acid are the main actives. The flowers contain an essential oil.

**Therapeutic uses and available evidence**

Elder flowers are used as an infusion or herbal tea, and a mixture with peppermint is a traditional remedy for colds and influenza. They induce perspiration, which is thought to be beneficial in such cases. Recent studies show an *in vitro* activity against several strains of influenza virus, and a clinical study has also demonstrated a reduction in the duration of flu symptoms for the berries (see Vlachojannis et al 2010 for review). The effect was attributed to an increase in inflammatory cytokine production as well as a direct antiviral action. The usual dose is about 3 g of flowers infused with 150 ml of hot water, but is not critical. Elder flowers are non-toxic and no side effects have been reported. Both the berries and the flowers are used to make cordials which are taken medicinally for their reputed antioxidant and antiviral properties.

LINDEN FLOWERS, **TILIA SPP.** (TILIAE FLOS) EUPHORBIA COLEUS

Linden flowers (although called ‘lime flowers’ they are not related to lime fruit) are from *Tilia platyphyllos* Scop., *T. cordata* Mill. and their hybrid (Tiliaceae). They are ornamental trees native to Europe. The pedicel bears 3–6 yellowish-white, five-petalled, fragrant flowers on stalks half-joined to an oblong bract.

**Constituents**

The flowers contain volatile oil (linalool, germacrene, geraniol, 1,8-cineole, 2-phenyl ethanol and others), flavonoids (hesperidin, quercetin, astralagnin, tiliroside), a mucilage of arabinose, galactose and rhamnose polysaccharides, polyphenolics such as chlorogenic and caffeic acids, and GABA (γ-aminobenzoic acid).

**Therapeutic uses and available evidence**

Linden flowers are used for feverish colds, catarrh, coughs and influenza. They are used as herbal teas to induce diaphoresis (perspiration) like elder and
at a similar dose (see above). The polysaccharides are soothing and adhere to epithelial tissue, producing a demulcent effect. The other main use of the flowers is for nervous disorders; the extract is thought to act as an agonist for the peripheral benzodiazepine receptor. There is evidence that components of the aqueous extract of the flowers bind to GABA receptors in rat brain (an effect not due entirely to the GABA content of the extract) and mild sedative effects were confirmed using the elevated maze anxiety test in mice (Anesini 1999). Linden flowers are non-toxic and no side effects have been reported.

MALLOW FLOWER AND LEAVES, MALVA SYLVESTRIS L. (MALVAE FLOS AND MALVAE FOLIUM)

The common mallow (Malva sylvestris L., Malvaceae) is a wild plant indigenous to southern Europe but naturalized worldwide. The leaves are downy, with 5–7 lobes, and prominent veins on the under surface. The flowers are mauve, with darker veins; both are used for their mucilage content.

Constituents

The main constituents are mucilages, sulphated flavonol glycosides such as gossypin-3-sulphate, hypolaetinglucoside-30-sulphate and others, and anthocyanins (malvin, the diglucoside of malvidin, and delphinidin).

Therapeutic uses and available evidence

Mallow is a demulcent and pectoral. An infusion is used for colds and coughs, and the mucilage from the leaves is anti-inflammatory with anticomplement activity. Little clinical evidence is available but there is a long tradition of historical use. No adverse effects are known.

MARSHMALLOW LEAF AND ROOT, ALTHEA OFFICINALIS L. (ALTHAEAE FOLIUM, ALTHAEAE RADIX)

Both the leaves and the rootstock of the marshmallow (Malvaceae) are used as a demulcent, expectorant and emollient. The plant is a downy perennial reaching up to 2 m in height with leaves broadly ovate or cordate, 10–20 cm long and about 10 cm wide, with 3–7 rounded lobes, palmate veins and a crenate margin. The flowers are pink, five-petalled, up to 3 cm in diameter. The root as it appears in commerce is dried, fibrous, cream-white when peeled, deeply furrowed longitudinally and with some root scars. It is largely tasteless.

Constituents

Both rootstock and leaves are rich in mucilage, consisting of a number of polysaccharides (composed of L-rhamnose, D-galactose, D-galacturonic acid and D-glucuronic acid) and others. It also contains common flavonoids, especially derivatives of kaempferol and quercetin.

Therapeutic uses and available evidence

Both the leaves and root are used internally for coughs and bronchial complaints. Extracts of both are used occasionally for gastric and urinary inflammation in general, and for cystitis. They may be applied externally as a soothing poultice and vulnerary. The mucilages have proven biological activity, including the stimulation of phagocytosis in vitro. Antimicrobial and anti-inflammatory activities have also been documented. Several of the polysaccharides isolated from the roots have been found to have antitussive activity. The most common use of extracts of marshmallow root is in the making of confectionery.

PELARGONIUM, PELARGONIUM SIDOIDES DC AND P. RENIFORME CURT (PELARGONII RADIX)

Pelargonium is obtained from two southern African species, Pelargonium sidoides and P. reniforme (Geraniaceae) where the tubers, stems and root have been used for centuries to treat a range of infectious conditions.

Constituents

The main active components are hydrolysable tannins, (+)-catechin, gallic acid and methyl gallate, including a unique series of O-galloyl-C-glucosylflavones. Flavonoids including myricetin and quercetin-3-O-beta-d-glucoside, coumarins including scopoletin,
umckalin, 5,6,7-trimethoxycoumarin and 6,8-dihydroxy-5,7-dimethoxycoumarin, are present in both species. A series of benzopyranones has been isolated from *P. sidioides*, and the pelargoniins (a type of ellagitannin) and a diterpene, reniformin, have been found in *P. reniforme*.

**Therapeutic uses and available evidence**

In Germany, a standardized extract of *Pelargonium sidioides* (EPs* 7630, also known as Umckaloabo*) is registered by the Federal Institute for Drugs and Medical Devices (BfArM) for the indication 'acute bronchitis' and several randomized, double-blind, placebo-controlled clinical trials support its efficacy in adults and children (Agbabiaka et al 2008). The extract EPs* 7630 has multiple effects which are beneficial in respiratory infections, and include antiviral, antibacterial, immunomodulatory and cytoprotective effects. It also increases the frequency of ciliary beats, thus helping to remove pathogens for the upper respiratory tract, and inhibits the interaction between bacteria and host cells. A recent study has found that EPs* 7630 interferes with the replication of different respiratory viruses including seasonal influenza A virus strains, RSV, human coronavirus, parainfluenza virus and coxsackie virus (Michaelis et al 2011). This extract is also given to athletes to help strengthen the immune system, which can be compromised by extreme exercise, to protect against colds. A study in athletes submitted to intense physical activity found that *Pelargonium sidioides* increased the production of secretory immunoglobulin A in saliva, and decreased levels of both interleukin-15 and interleukin-6 in serum, suggesting a strong modulating influence on the immune response associated with the upper airway mucosa (Luna et al 2011).

**IMMUNOSTIMULANTS**

Immune stimulation is usually measured using parameters such as an increase in numbers of circulating immune cells, or enhanced phagocytosis after inoculation with a pathogen. It is notoriously difficult to substantiate claims for the prevention of disease, since very large clinical studies are needed for statistical validity, and these are difficult and expensive to perform. However, echinacea is taken widely and the use of an Oriental herb, astragalus, is increasing in the West for the same indications.

**ECHINACEA, ECHINACEA PALLIDA (NUTT.) BRITT., E. PURPUREA MOENCH AND E. ANGUSTIFOLIA (DC.) HELLE. (ECHINACEAE HERBA, RADIX)**

Members of the genus *Echinacea* (Asteraceae) are widely distributed in North America and have a long tradition of use, both by the American Indians and the settlers, who developed the first commercial preparations during the 19th century. Both aerial parts and secondary roots are used. The indigenous people used *E. pallida* in particular for a variety of illnesses, such as pain, inflammatory skin conditions and toothache. The three botanical species are used in the preparation of phytomedicines to 'prevent colds and other respiratory infections', as immunostimulants. The complex situation regarding species, quality of products made from them and method of production makes an assessment of the clinical efficacy very difficult. Echinacea is often combined with garlic, for the treatment of colds and allergic rhinitis.

** Constituents**

Numerous compounds have been identified, but the most pharmacologically relevant ones are not known. All species contain similar types of compounds, although not necessarily the same individual ones. The most important are the caffeic acid derivatives, including echinacoside (Fig. 16.8) (*E. pallida* root), cichoric acid (*E. purpurea* aerial parts) and others, and the alkylamides (found throughout the plant in all three species), which are a complex mixture of unsaturated fatty acid derivatives. Some have a diene or diyne structure (with two unsaturated and two triple unsaturated groups) or a tetrane structure (with four unsaturated groups) linked via an esteramide to a (2)-methylpropane or (2)-methylbutane residue.

![Echinacoside](Fig. 16.8)
Therapeutic uses and available evidence

Echinacea preparations are available both as traditional herbal medicinal products used to relieve the symptoms of the common cold and influenza type infections, but also as preparations with a well-established use. There is some evidence in the treatment and prevention of respiratory infections, but more limited evidence for slow healing wounds using topical applications. Clinical evidence for uses as an immunostimulant is available for some of the chemically characterised extracts. Overall a series of meta-analyses showed that Echinacea preparations seem to be efficacious both therapeutically (reducing symptoms and duration) and in terms of prophylaxis against the common cold (Shah et al 2007, Woelkart et al 2008). However, Echinacea preparations tested in clinical trials differ greatly. There is better evidence that preparations based on the aerial parts of E. purpurea might be effective for the early treatment of colds in adults but the results are not fully consistent. A mechanism of action has been postulated by Chicca et al (2009), suggesting that the alkylamides dodeca-2,4,8Z,10Z-tetraenoic acid isobutylamide (A1) and dodeca-2E,4E-dienoic acid isobutylamide (A2) bind to the cannabinoid-2-(CB2) receptor and are the main anti-inflammatory and immune-modulatory principles, acting in synergy. In addition, alkylamides potently inhibit LPS-induced inflammation in human whole blood and exert modulatory effects on cytokine expression, but these effects are not exclusively related to CB2 binding.

Echinacea appears to be safe, although allergic reactions have been reported. The risk of interactions seems to be very limited (Modarai et al 2007).

Constituents

Triterpenoid saponins, the astragalosides I–VIII, and their acetyl derivatives, agroastragalosides I–IV, astramembranins I and II and others; isoflavones including formononetin and kumatakenin, and polysaccharides known as astrogaloglucans.

ASTRAGALUS, ASTRAGALUS MEMBRANACEUS (FISCH.) BGE. (ASTRAGALI RADIX)

Astragalus membranaceus (Fabaceae) is an herbaceous perennial native to north-eastern China, central Mongolia and Siberia. The drug is known in Chinese medicine as Huang qi. The use of Astragalus root as a general tonic dates back to the legendary Chinese emperor Shen-Nong. The root consists of a long cylindrical tap root, which is internally yellowish in colour, but rootlets should be absent.

Constituents

The main actives are diterpenes, known as andrographolides, and consist of andrographolide and its many analogues, including neoandrographolide, isoandrographolide, 14-deoxyandrographolide, 14-deoxy-14,15-dehydroandrographolide, 3,19-isopropylideneandrographolide and 14-acetylandrographolide and many others. Flavonoids and polyphenols such as 7-O-methylwogonin, apigenin, onysilin and 3,4-dicaffeoylquinic acid are also present. An alkaloid, andrographine, and a series of sesquiterpene lactones, paniculides A, B, and C, are also present in the root.
Therapeutic uses and available evidence

Andrographis is most commonly used as an immune stimulant, but is also reputed to possess antihypotensive, antimicrobial, antithrombogenic, antiinflammatory and anticancer properties (www.thorne.com 2003). Andrographolide has been shown to have immunostimulatory activity, shown by an increase in proliferation of lymphocytes and production of interleukin-2, and the antiinflammatory activity has been demonstrated by an inhibition of NFB, nitric oxide, PGE2, IL-1β, IL-6, LTB4, TXB2 and histamine (Bao et al 2009, Chandrasekaran et al 2010). In one Chilean study, andrographis herb had a significant drying effect on the nasal secretions of cold sufferers who took 1,200 mg of the extract daily for 5 days (Cáceres et al 1999). A systematic review of the literature has suggested the herb alone (or in combination with Eleutherooccus) may be an appropriate treatment for uncomplicated acute upper respiratory tract infection (Poolsup et al 2004).

References


the common cold: a meta-analysis. 


Further reading

