Chapter 28
Arbuscular Mycorrhizal Fungi: Effects on Secondary Metabolite Production in Medicinal Plants

Devendra K. Pandey, Prabhjot Kaur, and Abhijit Dey

Abstract Medicinal plants are used by 80% of the world population for their primary health care. The medicinal value of plants is primarily attributed to the secondary metabolite content such as terpenoids, alkaloids, and phenolics. These compounds play a crucial role in plant defense, are merchandised valued for their therapeutic applications and ecological role, and are also used as flavoring agents. Arbuscular mycorrhizal fungi (AMF) or *Glomeromycota* is known to form a symbiotic relationship with many terrestrial plants. AM fungi–plant consortium enhanced the production of plant terpenoids, alkaloids, and phenolics, which are valuable to human health. The potential role of arbuscular mycorrhiza (AM) symbiosis in amplification of the secondary metabolite content has attained enormous recognition for sustainable cultivation of medicinally important crops. AMF–plant symbiosis not only improves the growth and nutrients but also exerts a synergistic effect on accumulation of bioactive compounds with medicinal importance. Current studies have also recognized AM-mediated modulation of morphology, biochemistry, and gene expression in medicinal as well as in the industrial important plants. This chapter provides an appraisal on contemporary finding in the area of AMF investigation with a marked emphasis on the yield of pharmaceutically important plant-derived secondary metabolites.

Keywords Secondary metabolites · Medicinal plants · Nutrient uptake · AM fungi

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28.1 Introduction

The use of medicinal plants as therapeutic agents against various diseases has been notable for thousands of years (Gopal 2001). The World Health Organization (WHO) appraises that more than 80% of global population utilize plants and plant products for their primary health care (Cordell 1995). There is a huge demand for traditional herbal medicine which has increased several folds globally during the recent past. The primary reason behind this boon is thought to be the introduction of traditional knowledge-based drugs like Taxol (anticancer), Artemisinin (antimalarial), Forskolin (antihypertensive) (Ghisalberti 1993), and many others in the Western market.

Fransworth et al. (1985) estimated that at least 119 compounds derived from 90 plant species are considerably significant drugs currently practiced in one or more countries and 77% of these are obtained mostly from botanicals used in traditional medicine. The traditional Chinese medicine (TCM), the Indian system of medicine (ISM), the Japanese Kampo, and African folklore are still practiced by major population of Asia and Africa. The botanical-based treatments have remained a major part of TCM, and even today it comprises approximately 50% of total drugs used in China. Of the 5500 medicinal plants used in TCM, about 300–500 are commonly used in day-to-day prescriptions (Corizier 1974). One such drug that has been used in China for the past hundreds of years is *Ephedra sinica* (Ma huang), the active principle of which is a potent sympathomimetic amine, ephedrine. This medicine in the form of various salts is now used in Western medicine to treat bronchial asthma.

The Indian system of medicine (ISM), mainly constituting of Ayurveda, Siddha, and Unani, is considered as one of the traditional system of medicine with thoroughly documented plant-based therapeutics. In India and abroad also, Ayurveda is being practiced by a vast population. In ISM, the remedies are primarily based on plants and plant products that usually work on the human system to boost immunity, resistance, and strength in order to cure the diseases (Swami Tirtha 1998). Some of the classical examples are as follows: (a) reserpine, an indole alkaloid as a potent antihypertensive and tranquilizing agent developed from the Indian medicinal plant *Rauwolfia serpentina* (Warrier et al. 1996), and (b) forskolin, a highly oxygenated labdane diterpenoid from the roots of Indian medicinal plant *Coleus forskohlii* exhibiting potent antihypertensive, antithrombotic, and positive ionotropic properties (Rastogi and Meharotra 1990). The Kampo system of medicine is practiced by a considerable population in Japan, where about 70% of physicians prescribe one or another Kampo formulations (Ishibashi 2002). Some of the bioactive isolates from the plants used in Japanese Kampo are baicalein (from *Scutellaria baicalensis*) (Huang 1999), glycyrrhizin (from *Glycyrrhiza uralensis*) (Tang and Eisenbrand 1992), and saikosaponin I (from *Bupleurum falcatum*) (Shibata et al. 1923).

In most of the African countries, up to 80% of population depends entirely on botanicals for therapeutics (Suzuki 2002; David 2000), many of which have been documented in the form of an African pharmacopeia issued by a scientific technical research commission of the organization of African Unity in 1984. A few promising drugs developed from African medicinal plants include (a) caffeine from the coffee tree *Coffea arabica* (from the highlands of southwest Ethiopia), a purine alkaloid exhibiting potent CNS activity and positive inotropic activity and activates lipolysis, and (b) ouabain (γ-strophanthin) isolated from *Strophanthus gratus* (from tropical West Africa) – a cardiac glycoside used to treat heart problems in acquits cardiac insufficiency (Hostettmann et al. 2000).

Due to the devoted work from the researchers, good proportion of promising drugs, numerous therapeutic leads, and many novel pharmacologically potent drugs have been developed from botanicals (Fig. 28.1) (Phillipson 1999). E. Merck, in the year 1826, manufactured an analgesic morphine, which was derived from opium poppy on commercial level, which was marked as the dawn of commercialization of plant-based drugs (Galbley and Thiericke 1999). Reserpine, the chief constituent from the roots of the Indian medicinal plant *R. serpentina*, introduced by CIBA (USA) in 1953 is another classical example of plant-derived drug. The following (Fig. 28.1) are the examples of plant-derived drugs which are under commercialization.

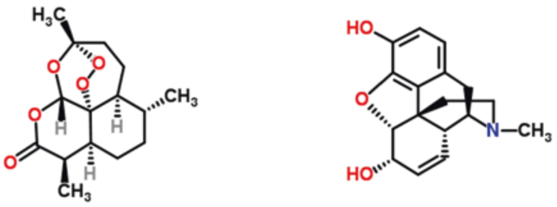
The widespread skepticism on synthetic medicines and worry of their usage due to adverse side effects such as toxicity, teratogenicity, and carcinogenicity which steered to the noticeable change in the status of herbal drugs as alternative medicine. The recent boon in the demand for herbal drugs is attributed to the introduction of promising plant-based drugs, viz., (1) Taxol (anticancer), (2) artemisinin (antimalarial), (3) forskolin (antihypertensive), etc. in the Western market. The present annual global market for herbal medicine is 62.0 billion US dollars. However, it is very sad to note the Indian share amounts to a meager 1%.

28.2 Plant Secondary Metabolites

According to Verpoorte (1999): "Secondary metabolites are compounds which act as a defensive role in the interaction of the organism with its environment for survival in the ecosystem and are restricted to particular taxonomic group". Three major secondary metabolites present in plants such as triterpenoids, alkaloids and phenolics.

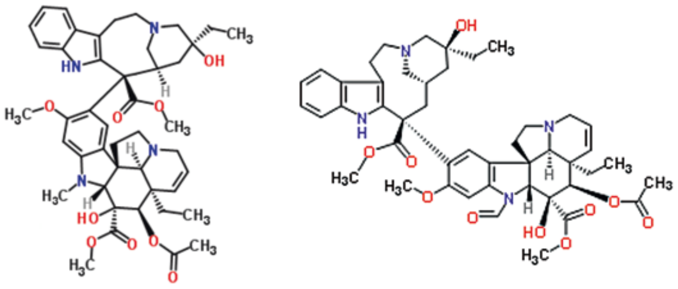
28.2.1 Terpenoids

Terpenoids or isoprenoids are the largest class of secondary metabolites represented by nearly 27,000 compounds. Triterpenoids are classified on the basis of number of isoprenoid units present in any terpenoidal compound. For example, the monoterpenes are made up of two isoprenoid units (citronellal in lemon and menthol from peppermint), sesquiterpenes are made up of three isoprenoid units (zingiberene and artemisinin), diterpenes are made up of four isoprenoid units (gibberellic acid), triterpenes are made up of six isoprenoid units (ursolic, oleanolic, and betulinic acid), and tetraterpenes are made up of eight isoprenoid units (lanosterol, stigmasterols, diosgenin, lupeol) (Gershenzon and Kreis 1999).



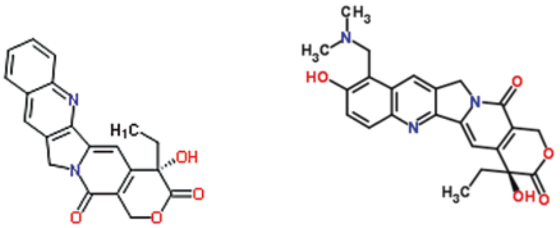
Artemisinin

Morphine



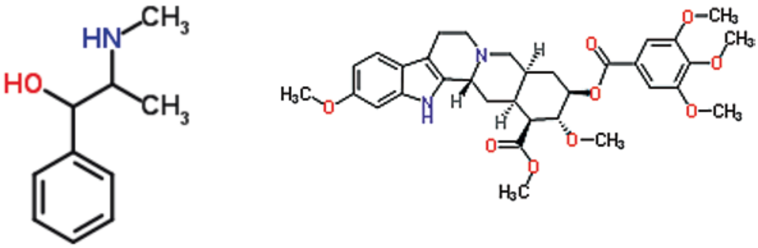
Vinblastine

Vincristine



Camptothecin

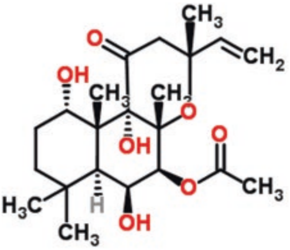
Topotecan (camptothecin derivatives)



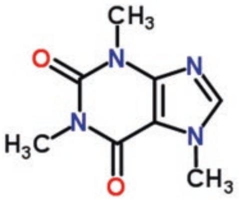
Ephedrine

Reserpine

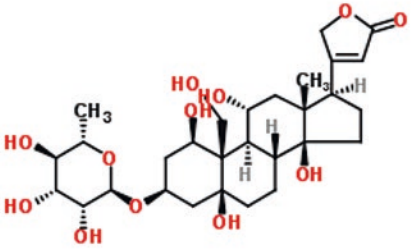
Fig. 28.1 Potent plant-based drugs derived from various traditional medicinal systems of the world



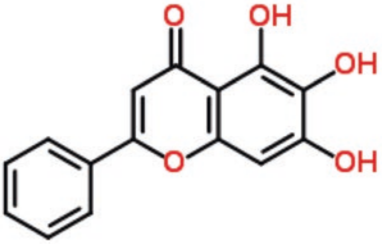
Forskolin



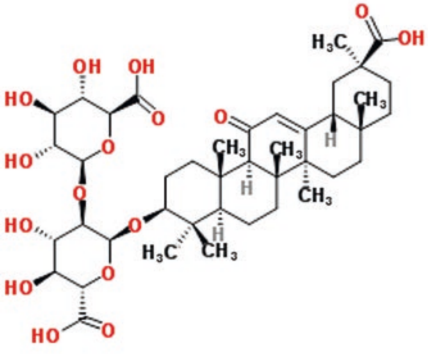
Caffine



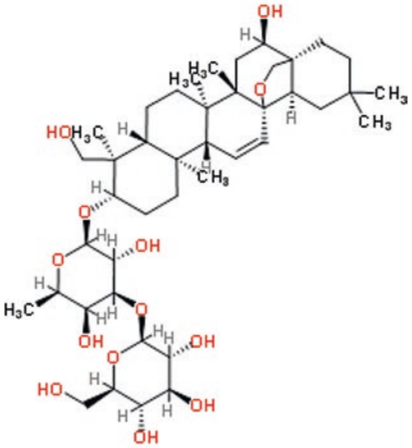
Ouabaine



baicalein



Glycyrrhizin



Saikosaponin

Fig. 28.1 (continued)

28.2.2 Alkaloids

The alkaloids contain nitrogen besides carbon, oxygen, and hydrogen, commonly as part of a cyclic system, and are numerous among plants with diverse pharmacological properties depending on the specific alkaloid structure. The well-known examples of potent alkaloids are reserpine, ajmaline, vincristine, colchicines, mescaline, nicotine, cocaine, and morphine. Alkaloid biosynthesis in plants is from amino acids, terpenes, and aromatic compounds (Herbert 2001).

28.2.3 Plant Phenolics

Phenolic compounds are comprised of carbon, hydrogen, and oxygen atoms arranged as an aromatic ring having a hydroxyl substituent. Among plant polyphenols, the flavonoids form the largest group followed by phenolic quinones, lignans, xanthones, coumarins, and monocyclic phenols (Croteau et al. 2000).

28.2.4 Transport, Storage, and Turnover of Plant Secondary Metabolites

The biosynthesis of secondary metabolites is restricted in plants to various compartments, and their accumulation, storage, and release occur in highly specialized organs or tissues such as in glands, bark, roots, stem, and flowers (Croteau et al. 2000). In the vacuole the high polar water-soluble compounds are generally accumulated (Wink 1999; Boller and Wiemken 1986), whereas low polar compounds are restricted in other parts of plants such as resin ducts, lactifers, glandular hairs, trichomes, thylakoid membranes, or the cuticle and defend plants from abiotic and biotic stress (Wiermann 1981). In the peppermint monoterpenes, essential oils are accumulated in glandular trichomes during the development of leaves (McGarvey and Croteau 1995).

28.3 Biotic and Abiotic Factors Influencing Accumulation of Secondary Metabolites

In order to become a key player at the global level and to provide efficacious herbal remedy to the society, it is absolutely necessary to consider certain regulatory aspects. The primary aspect is the identification of high bioactive secondary metabolite-producing plants. The collection of secondary metabolites in a plant species depends principally on (1) soil nature, (2) climatic condition, and (3) altitude.

Microbes also play a pivotal role in accumulation of secondary metabolites in herbal plants. Some important microbes such as plant growth-promoting rhizobacteria (PGPR) and *mycorrhiza* influence the bioactive phytochemical accumulation in herbal plants. Detailed investigation in this aspect will help in identifying the high-yielding plant source as well as will be useful in optimizing the parameters in which the medicinal plants may be cultivated under stringent and unfavorable conditions. Arbuscular mycorrhizal fungi (AM fungi) exist in mutually beneficial symbiotic coexistence with the higher land plants (Smith and Read 1997). Clark and Zeto (2000) and Augé (2001) have indicated that AMF improves plant nutrient assimilation specially phosphorus along with nitrogen, zinc, iron, and copper as well as water relations. Furthermore, AMF ameliorate cultivation condition and abiotic stresses (Jeffries et al. 2003) through high underground root biomass and improved absorption of soil nutrients and secretion of different enzymes by AMF colonized roots and/or hyphae (Marschner 1995; Smith and Read 1997).

28.3.1 Arbuscular Mycorrhizal Fungi (AMF)

AMF is symbiotic fungi that form a beneficial relation with the roots of a diverse group of terrestrial plants (Fig. 28.1). The AM fungi are classified under the order *Glomales* under the *Zygomycota* (Redecker et al. 2000), but currently it is moved to a new phylum, the *Glomeromycota* (Schüßler et al. 2001). These fungi are widespread soil-borne fungi, whose origin and occurrence have been established more than 450 million years (Redecker et al. 2000). AMF association with higher plants can be seen in temperate, tropical, and arctic regions but was found to be absent in waterlogged conditions (Smith and Read 1997). These fungi have a synergistic effect on plant growth performance in comparison with any microbes by an increase in biomass of the root system of the plant and also by enhancing the root surface area for absorption of minerals and water (Leake et al. 2004). Thus, it can be inferred that arbuscular mycorrhizal (AM) symbiosis with terrestrial plants is of significant utility in forest ecology, land reformation, improved growth, and better yield of plants in low-input systems (Sieverding et al. 1991).

28.3.2 Agronomic and Ecological Roles of AMF

The economically and medicinally important crops are known to be colonized by AMF (Sieverding et al. 1991). AMF improves the phosphorus nutrition by increasing the root biomass and surface area and by improving the P uptake (Koide 1991). AMF act as phosphate solubilizers by producing organic acids that increased the availability of insoluble mineral phosphates (Lapeyrie 1988) and enhanced the phosphorus uptake by host plants. Moreover, AMF also improves the uptake of macronutrients and micronutrients (Clark and Zeto 2000; Smith et al. 2004).

Marschner (1998) and Hodge and Campbell (2001) on their studies on mycorrhiza established that the better plant nutrition is dependent on (i) enhanced root surface via extra-radical hyphae that extend beyond root depletion zone, (ii) decomposition of organic substances, and (iii) enhanced microbial consortium in the rhizosphere zone.

Contemporary studies reveal that AMF is an ideal tool for sustainable agriculture, landscape resurrection, and horticulture via decomposition of organic material, seedling establishment, enhanced pathogenic resistance, herbivore tolerance, soil stability, heavy metal detoxification, water stresses/cold temperature resistance, and reducing desertification (Jeffries et al. 2003; Hart and Trevors 2005). The function of AMF to their hosts in nutrient suppressive soil (less P) environment is high whereas it is less under P-sufficient conditions (Koide and Schreiner 1992), and plant growth rates can be reduced by AM colonization when available P is present (Peng et al. 1993).

28.3.3 Mycorrhizal Association with Medicinal Plants

Inoculation of crop plants with AMF is known to enhance growth, nutritional, and secondary metabolite contents of many medicinally and industrially significant crops which is attributed to enhanced uptake of nutrients, production of growth-promoting factors, biotic and abiotic stress tolerance, and synergistic interaction with PGPR such as nitrogen-fixing rhizobacteria and PSB (Bagyaraj and Varma 1995; Rajan et al. 2000). Enhanced mineral nutrition, i.e., N, P, Fe, Cu, Zn, and B, helps in the synthesis of chlorophyll thus enhancing photosynthetic rate (Bian et al. 2001; Feng et al. 2002; Toussaint 2007). In addition, AMF inoculation on medicinal plants is responsible for reduction in the intensity of disease caused by bacterial and fungal pathogens by morphological modulations such as thickening of the cell wall, stronger vascular bundles, etc. Moreover AMF inoculation leads to physiological alterations in host such as enhanced levels of P, phenolics, sulfur-containing amino acids, etc. (Boby and Bagyaraj 2003).

AM fungi that have a symbiotic relationship with medicinal plants belong to several families of angiosperms and gymnosperms. AM fungi are associated with *Adhatoda vasica* and *Datura somnifera* (Wei and Wang 1989). Several authors reported symbiotic relation of AMF with plants that belong to Araliaceae such as *Panax ginseng* (Zhang et al. 1990; Xing et al. 2000, 2003; Li 2003a; Cho et al. 2009; Ren et al. 2007; Zhang et al. 2011). There were many plants that belong to Labiatae family having association with AMF such as *Salvia miltiorrhiza* (He et al. 2009a, b; Wang and He 2009; Ma et al. 2009; He et al. 2010; Meng and He 2011), *Schizonepeta tenuifolia* (Wei and Wang 1991), *Bupleurum scorzonerifolium* (Teng and He 2005), *Pogostemon cablin* (Arpana et al. 2008), *Coleus forskohlii* (Sailo and Bagyaraj 2005), *Salvia officinalis* (Nell et al. 2009), *Mentha arvensis* (Gupta et al. 2002; Karagiannidis et al. 2011), *Ocimum basilicum* (Copetta et al. 2006; Toussaint et al. 2007; Lee and Scagel 2009; Prasad et al. 2011; Rasouli-Sadaghianil et al. 2010), and *Origanum* sp. (Khaosaad et al. 2006; Morone Fortunato and Avato 2008; Karagiannidis et al. 2011). Mycorrhization was also observed in plants that belong to Umbelliferae such as *Anethum graveolens*, *Trachyspermum ammi* (Kapoor et al. 2002a), *Coriandrum sativum* (Kapoor et al. 2002b; Farahani et al. 2008), *Foeniculum vulgare* (Kapoor et al. 2004), and *Angelica dahurica* (Cao and Zhao 2007; Zhao et al. 2009; Zhao and He 2011). AMF was reported in several plants that belong to Liliaceae such as *Gloriosa superba* L. (Yadav et al. 2013; Pandey et al. 2014), *Aloe barbadensis* (Gong et al. 2002; Mamta et al. 2012; Pandey and Banik 2009; Burni et al. 2013), *Ophiopogon japonicus* (Pan et al. 2008), *Paris polyphylla var.* (Zhou et al. 2009, 2010), and *Allium sativum* (Borde et al. 2009). Several authors reported mycorrhizal plants belonging to Leguminosae such as *Pueraria lobata*, *Astragalus membranaceus*, *Glycyrrhiza inflata*, *Castanospermum australe*, and *Prosopis laevigata* (Wang et al. 2006; Liu and He 2008, 2009; He et al. 2009b; Liu et al. 2007; Abu-Zeyad et al. 1999; Rojas-Andrade et al. 2003). AMF reported in plants belong to the Asteraceae family (Binet et al. 2011; Asrar and Elhindi 2010; Jurkiewicz et al. 2010; Araim et al. 2009; Kapoor et al. 2007; Rapparini et al. 2008; Chaudhary et al. 2008; Awasthi et al. 2011; Huang et al. 2011; Guo et al. 2006; Zhang et al. 2010, 2011; Asrar and Elhindi 2010). AMF is also reported in *Forsythia suspense*, *Taxus chinensis var.*, *Pinellia ternata*, *Catharanthus roseus*, *Valeriana officinalis*, *Atractylodes macrocephala*, *Camptotheca acuminate*, *Coix lacryma-jobi var.*, *Ginkgo biloba*, and *Gentiana manshurica* (Wang et al. 1998, 2010; Qi et al. 2002, 2003; Zhang et al. 2004; Wu and Wei 2008; Li 2003b; Huang et al. 2003; Zhao et al. 2006, 2007; Yu et al. 2010; Lu and He 2005, 2008; Lu et al. 2008a, b, 2011; Ren et al. 2008; Chen et al. 2009a, b, 2010; Guo et al. 2010; Shen et al. 2011; Zubek et al. 2012; Rosa-Mera et al. 2011; Nell et al. 2010; Geneva et al. 2010) (Fig. 28.2 and Table 28.1).

28.3.4 Synergistic Effects of AMF on Secondary Metabolites Accumulation in Medicinal Plants

There is alteration in the secondary metabolite accumulation due to chemical and biological events taking place during the AMF–host interaction (Akiyama and Hayashi 2002; Allen et al. 1982; Barrios 2007; Cai et al. 2008). AMF is known to enhance contents of secondary metabolites such as terpenoids, alkaloids, and phenolics in many economically and industrially significant crops such as production of flavonoids, cyclohexanone derivatives and apocarotenoids, phytoalexins, phenolic compounds, triterpenoids, and glucosinolates in herbal, and medicinal important plants colonized by AMF has been reported (Gianinazzi et al. 2010; Hadwiger et al. 1986; Harris et al. 2001; Harrison, 1999; Heet al. 2009c; Huang et al. 2004; Janardhan and Abdul-Khaliq 1995, Jie et al. 2007; Loomis and Corteau 1972; Maier et al. 1999; Paterson and Simmonds 2003; Shah et al. 1980; Silva et al. 2008; Singh et al. 2013; Smith and Read 2008; Szakiel and Paczkoski 2011a, b; Toussaint et al.

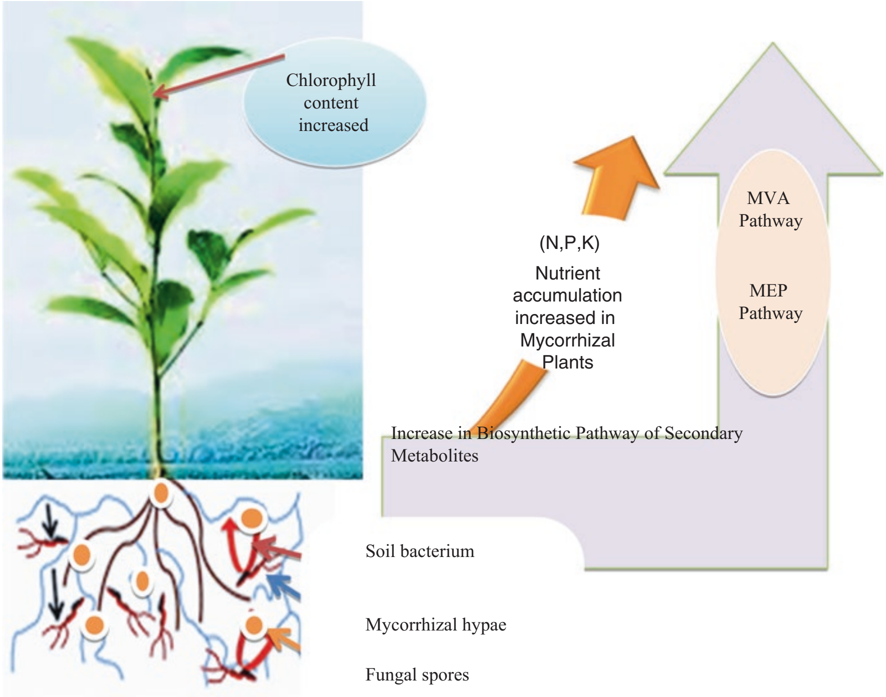


Fig. 28.2 Symbiotic association of AMF with plants

2004; Volpin et al. 1994; Wink 1997; Wu et al. 2010; Xiao et al. 2011; Yang et al. 2008; Zeng et al. 2007; Zubek et al. 2010, 2013).

28.3.4.1 Plant Terpenoid Accumulation Associated with AMF

The influence of mycorrhization on the terpenoid production in different plants has been presented in Table 28.2. The enhancements in triterpenoids are both qualitative and quantitative due to modifications in morphology of various aromatic plants due to (atractylol, anethole, thymol, artemisinin, stevioside, rebaudioside A, β-caryophyllene, p-cymene, geraniol, patchoulol, valerenic acid, and glycyrrhizic acid) in AMF-colonized plants (Kapoor et al. 2007; Mandal et al. 2013, 2015; Morone Fortunato and Avato 2008; Khaosaad et al. 2006; Lu et al. 2011; Farahani et al. 2008; Wei and Wang 1991; Arpana et al. 2008; Geneva et al. 2010; Liu et al. 2007; Jurkiewicz et al. 2010). Furthermore many researchers reported that increase in terpenoids (thymol, geraniol, anethol, forskolin) in aromatic and medicinal plants is due to P availability (Torelli et al. 2000; Kapoor et al. 2002a; Strack et al. 2003; Krishna et al. 2005; Sailo and Bagyaraj 2005; Bagheri et al. 2014; Guo et al. 2006; Zhang et al. 2010, 2011) and transcription of gene responsible for terpenoid

Table 28.1 Medicinal plants that have been investigated for AM effects

Species	Families	Major marker compounds	Medicinal value
Datura stramonium	*Solanaceae*	Hyoscyamine	Cures rheumatism, cough, relieving pain
Panax ginseng	Araliaceae	Ginsenosides	Immunodulatory, increase vigorness
Panax notoginseng	Araliaceae	Ginsenosides	Improves vital energy
Salvia miltiorrhiza	Labiatae	*Salvinorin*	Regularize menstruation, hepatoprotective
Schizonepeta tenuifolia	Labiatae	*Pulegone*, limonene, and menthofuran	Headache and improves digestion and cures vomiting
Bupleurum scorzonerifolium	Labiatae	Saikosaponin	Effective against cough and cold; regularize menstruation
			l
Pogostemon cablin	Labiatae	Pogostol	Cures cold and diarrhea
Coleus forskohlii	Labiatae	Forskolin	Antihypertensive and cures placebo, asthma, and glaucoma
Salvia officinalis	Labiatae	*Salvinorin*	Anti-inflammatory agent
Gloriosa superba L.	Liliaceae	Colchicine	Abortifacient, anti-gout, anticancer properties
Gentiana manshurica	Gentianaceae	Amarogentin, swertiamarin	Cures acute icterohepatitis, fever, and convulsions
Aloe barbadensis	Liliaceae	Barbaloin	Bactericidal effects and treat inflammation, improves immunity
Ophiopogon japonicas	Liliaceae	Ophiopojaponin	Cures cough and insomnia and digestive problem
Paris polyphylla var.	Liliaceae	Polyphyllin	Cures mouth ulcer
Allium sativum	Liliaceae	*Allicin*, ajoene	Cures hypertension, potent drugs for cardiovascular and immune systems
Ginkgo biloba	Ginkgoales	Ginkgolic acid, bilobalide	Cures hypertension
Coix lacryma-jobi var.	*Poaceae*	Palmitic, stearic, oleic, and linoleic acid	Cures diarrhea and lung problem
Camptotheca acuminata	Nyssaceae	Camptothecin and *piperine*	Potent drug against tumors
Atractylodes macrocephala	*Poaceae*	Astragaloside	Treatment of digestive disorders
Atractylodes lancea	Asteraceae	Astragaloside	Treatment of digestive disorders, rheumatism, cold, and nyctalopia
Artemisia annua	Asteraceae	Artemisinin	Cures malaria
Echinacea purpurea	Asteraceae	Cichoric acid	Potent antimicrobial and antiviral properties

(continued)

Table 28.1 (continued)

Species	Families	Major marker compounds	Medicinal value
Arnica montana	Asteraceae	*Helenalin* and chamissonolid	Effective against bruises, swellings, and mouth ulcers
Inula ensifolia	Asteraceae	Borneol, β-caryophyllene, p-cymene, and bornyl acetate	Potent anti-inflammatory and antiviral compound
Artemisia umbelliformis	Asteraceae	Artemisinin	Antimicrobial effect
Tagetes erecta		Carotenoids, scopoletin, ferulic acid	Cures inflammation, cold, and cough
Phellodendron amurense	Rutaceae	Nexrutine, quercetin, berberine	Treating digestive disorders
Phellodendron chinense	Rutaceae	Nexrutine, quercetin, berberine	Potent drug to cure dysentery
Citrus aurantium	Rutaceae	Limonin glucoside and phlorin	Potent digestive agent and improves appetite
Pueraria lobata	Leguminosae	Quercetin, tryptamine, apigenin 5-hydroxytryptamine	Cures fever and antioxidant activity
Astragalus membranaceus	Leguminosae	Astragaloside	Immunomodulatory and diabetes II
Glycyrrhiza inflata	Leguminosae	Glycyrrhizin	Cures throat problem
Castanospermum austral	Leguminosae	1-epilexine	Anti-HIV, diabetes II
Prosopis laevigata	Leguminosae	Juliflorine, patulitrin	Immunomodulatory
Mentha arvensis	Lamiaceae	Eucalyptol, terpinolene, linalool, pulegol, menthol, menthofuran, menthyl acetate	Cures fever, cough and cold
Ocimum basilicum	Lamiaceae	Eugenol, linalool	Fever, cold, and antivenom
Origanum sp.	Lamiaceae	Carvacrol, thymol, cosmocide, vicenin-2, rosmarinic acid	Improves appetite and stomach ailment
Origanum vulgare	Lamiaceae	Carvacrol, thymol, cosmocide, vicenin-2, rosmarinic acid	Cures digestive problems
Origanum onites	Lamiaceae	Carvacrol, thymol, cosmocide, vicenin-2, rosmarinic acid	Cures digestive problems
Coleus forskohlii	Lamiaceae	Forskolin	Anti-inflammatory activity
Forsythia suspense	*Oleaceae*	Phillyrin, pinoresinol, phillygenin, lariciresinol, and forsythiaside	Detoxification, cold and cough

(continued)

Table 28.1 (continued)

Species	Families	Major marker compounds	Medicinal value
Taxus chinensis var.	*Taxaceae*	10-deacetylbaccatin, baccatin III, cephalomannine and paclitaxel paclitaxel	Chemotherapy drug used to cure tumor and cancer
Pinellia ternate	*Araceae*	β-cubebene, atractylon, methyl eugenol, and δ-cadinene	Treating cough and vomiting
Anethum graveolens	Umbelliferae	Alpha-phellandrene, apiole, dill ether, limonene, geraniol	Cures flatulence, anti-spasm effect
Trachyspermum ammi	Umbelliferae	Thymol	Cures gaseous distention, cholera and diarrhea
Coriandrum sativum	Umbelliferae	Caffeic acid, chlorogenic acid, quercetin, kaempferol, rhamnetin, and apigenin	Improve appetite and cures analgesia, detoxifying
Foeniculum vulgare	Umbelliferae	Anethole, fenchone, and methyl chavicol	Promoting appetite and potent drug to cure digestive problem
Angelica dahurica	Umbelliferae	Ferulic acid and ligustilides	Treating headache, toothache, and nasosinusitis
Hypericum perforatum	Garcinia	Hypericin	Antimicrobial effect, diminishing inflammation
Catharanthus roseus	*Apocynaceae*	Vinblastine, vincristine, vindoline, and catharanthine	Antiproliferation and antitumor and anticancer effect
Valeriana officinalis	Valerianaceae	Valerenic acid	Sedatives and tranquilizers, treating insomnia
Hypericum perforatum,	Valerianaceae	Hypericin, naphthodianthron, and hyperforin	Antidepressant activity and potent anti-inflammatory properties, antispasmodic, analgesic, antiseptic, carminative, cholagogic, diaphoretic, and vasodilator properties

biosynthetic pathways (Floß et al. 2008; Mandal et al. 2014, 2015). Adams et al. (2004) investigated that composition of essential oil (EO) levels in Vetiver roots is altered in the presence of unidentified bacteria PGPR, and AMF were suggested to be involved in the modulation of essential oil (EO) accumulation. Copetta et al. (2006) and Freitas et al. (2004) reported that AM fungal root colonization enhances the essential oil content (linalool and geraniol, menthol, menthone, carvone, and pulegone) in *Ocimum basilicum* and *Mentha arvensis*, respectively. Moreover, many authors reported increase in terpenoids such as menthol, menthone, carvone, pulegone, carvacrol, and thymol in aromatic plants (Gupta et al. 2002; Karagiannidis et al. 2011; Khaosaad et al. 2006; Morone Fortunato and Avato 2008; Rasouli

Table 28.2 Effects of AM symbiosis on secondary metabolism of medicinal plants under the conditions of artificial inoculation

Secondary metabolite		Medicinal plant	AMF	Change in secondary metabolite
Terpene	–	*Schizo tenuifolia*	*G. epigae*, *G. mossae*	Significant enhancement
Terpene	Atractylol	*Atractylodes macrocephala*	*Glomus mosseae*	Significant increase
Terpene	Menthol, menthone, carvone, and pulegone	*Mentha arvensis*	*G. fasciculatum*, *G. etunicatum*, *G. lamellosum*	Significant enhancement
Terpene	Carvacrol, thymol	*Origanum* sp.	*G. mosseae*	Significant improvement
Terpene	Thymol	*Origanum vulgare*	*G. viscosum*	No change
Terpene	Linalool and geraniol	*Ocimum basilicum*	*Gigaspora margarita*, *Gigaspora rosea*	Significant increase
Terpene	Eugenol	*Ocimum sanctum*	*Glomus fasciculatum*	Relatively increased
Terpene	Anethole	*Anethum graveolens*	*G. macrocarpum*, *G. fasciculatum*	90% of the control
Terpene	Thymol	*Trachyspermum ammi*	*G. macrocarpum*, *G. fasciculatum*	72% of the control
Terpene	β-caryophyllene, p-cymene, geraniol	*Coriandrum sativum*	*Glomus hoi*	Significant improvement
Terpene	Anethol	*Foeniculum vulgare*	*G. macrocarpum*, *G. fasciculatum*	78% of the control
Terpene	Sesquiterpenes Artemisinin	*Artemisia annua*	*G. macrocarpum*, *G. fasciculatum*	Significant improvement
Terpene	Patchoulol	*Pogostemon cablin*	*A. laevis*, *G. mosseae*, *S. calaspora*	Significant improvement
Terpene	Atractylol	*Atractylodes lancea*	*G. mosseae*:*G. mosseae*, *G. aggregatum*, *G. versiforme*, *G. intraradices*	No change
Terpene	Menthol, menthone, carvone, and pulegone	*Mentha spicata*	*G. etunicatum*, *G. mosseae*	No change
Terpene	Thymol	*Trachyspermum ammi*	*G. fasciculatum*	51.21%
Terpene	Geraniol, linalool	*Coriandrum sativum*	*G. macrospermum*, *G. fasciculatum*	28% and 43% over control
Terpene	Anethol	*Foeniculum vulgare*	*G. macrospermum*, *G. fasciculatum*	Significant increase

(continued)

Table 28.2 (continued)

Secondary metabolite		Medicinal plant	AMF	Change in secondary metabolite
Terpene	Artemisinin	*Artemisia annua*	*G. macrospermum*, *G. fasciculatum*, *G. mosseae*, *G. versiforme*	15.2–32.8% over the control
Terpene	Sesquiterpene lactones	*Arnica montana*	*G. geosporum*, *G. constrictum*	Either increase or decrease
Terpene (triterpenoid)	Glycyrrhizic acid bornyl acetate, 1,8-cineole, α-thujones, β-thujones	*Glycyrrhiza inflata*	*G. mosseae*, *G. versiforme*	Significant increase
Triterpene saponins		*Dioscorea* spp.	*G. clarum*, *G. etunicatum*	42% over the control
Terpene	Valerenic acid	*Valeriana officinalis*	*G. intraradices*	Relative quantity increase
Terpene (diterpenoid)	Stevioside, rebaudioside-A	*Stevia rebaudiana*	*Rhizophagus fasciculatus*	Significant increase
		Stevia rebaudiana	*G. intraradices*	Upregulates genes for biosynthesis
Phenolics	Rosmarinic, caffeic acids	*Ocimum basilicum*	*G. caledonium*, *G. mosseae*	Significant increase
Phenolics		*Ocimum basilicum*	*Glomus intraradices*	No change
Phenolics	Diobulbinone	*Dioscorea* spp.	*G. clarum*, *G. etunicatum*	Significant increase
Phenolics	Phenolics	*Echinacea purpurea*	*Glomus intraradices*	Significant increase in roots
Phenolic acids	Caffeic, chlorogenic acid	*Arnica montana*	*G. geosporum*, *G. constrictum*,	Significant increase in roots
Phenolics	Caffeic acid	*Viola tricolor*	*Rhizophagus irregularis*	Significant influence
Phenolics			*Funneliformis mosseae*	No response
Phenolics	Salvianolic acid B	*Salvia miltiorrhiza*	*G. mosseae*, *G. aggregatum*	Significant increase
Phenolics	Gallic acid	*Libidibia ferrea*	*Claroideoglomus etunicatum*	21% over the control
Phenolics			*A. longula*	No response
Phenolics			*G. albida*	No response

(continued)

Table 28.2 (continued)

Secondary metabolite		Medicinal plant	AMF	Change in secondary metabolite
Phenolics	Rutin, quercetin, and kaempferol	*Catharanthus roseus*	*Glomus species*	Significant increase
Phenolics	Caffeic acid, rosmarinic acid, and luteolin	*Mentha spicata*	*G. etunicatum*, *G. mosseae*	Significant increase
Phenolics	Coumaric and ferulic acids	*Myracrodruon urundeuva*	*A. longula*	81.03%
Phenolics	Thymol derivative	*Inula ensifolia*	*G. intraradices*, *G. clarum*	Either increase or decrease
Phenolics	Gallic acid, chlorogenic acid, catechin, hydroxyl benzoic acid	*Valeriani jatamansi*	*G. intraradices*	Significant increase
Flavonoid		*Salvia miltiorrhiza,*	*G. mosseae*	Significant increase
Flavonoid		*Astragalus membranaceus*	*G. mosseae*	Significant increase
Flavonoid		*Myracrodruon urundeuva*	*A. longula*	57.5% over control
		Viola tricolor	*Rhizophagus irregularis*	Significant influence
Flavonoid	Imperatorin, total coumarins	*Angelica dahurica*	*Glomus species*	Significant increase
Flavonoid	Total phenolic, rosmarinic acid	*Salvia officinalis*	*G. mosseae*, *G. intraradices*	No change in leaves and roots
Flavonoid	Valerenic acid	*Valeriana officinalis*	*G. mosseae*, *G. intraradices*	Significant increase
Tannins		*Valeriana jatamansi*	*G. intraradices*	Significant increase
Alkaloid	Castanospermine	*Castanospermum australe*	*G. intraradices*, *G. margarita*	Significant improvement with *G. intraradices*
Alkaloid	Trigonelline	*Prosopis laevigata*	*G. rosea*	1.8-fold increase in roots
Alkaloid	Vinblastine alkaloid	*Catharanthus roseus*	*Glomus species*	Significant increase
Alkaloid	Hyoscine, hyoscyamine	*Datura stramonium*	*G. mosseae*, *G. epigaeum*	Significant increase

(continued)

Table 28.2 (continued)

Secondary metabolite		Medicinal plant	AMF	Change in secondary metabolite
Alkaloid	Berberine, jatrorrhizine, palmatine	*Phellodendron amurense*	*G. mosseae*, *G. etunicatum*,*G. versiforme*, *G. diaphanum*	Significant increase
Alkaloid	Berberine	*Phellodendron Chinese*	*A. laevis*, *A. mellea*	Significant increase in the tree bark
Alkaloid	Vindoline, vinblastine, vincristine, catharanthine, ajmalicine, and serpentine	*Catharanthus roseus*	*G. etunicatum* and *G. intraradices*	Significant increase
Alkaloid	Nicotine, anabasine, and nornicotine	*Nicotiana tabacum*	*G. etunicatum*, *G. intraradices*	Significant increase
Alkaloid	L-ephedrine, guanosine	*Pinellia ternate*	*G. intraradices*, *G. mosseae*	Significant increase in the tuber
Alkaloid	Camptothecin	*Camptotheca acuminate*	*A. mellea*, *G. intraradices*	Significant increase
Alkaloid	Forskolin	*Coleus forskohlii*	*A. laevis*, *G. monosporum*, *S. calospora*	Significant increase
	Alliin	*Allium sativum*	*G. fasciculatum*	Significant increase
Others	Hypericin, pseudohypericin	*Hypericum perforatum*	*G. intraradices*, *G. mosseae*	Significant increase
	Oleoresin	*Zingiber officinale*	*S. heterogama*, *G. decipiens*, *A. koskei*, *Entrophospora colombiana*	Significant increase

Sadaghianil et al. 2010; Chaudhary et al. 2008). Moreover, studies on anatomical and pharmacognosy suggested that enhanced production of essential oils was due to improvement in the number of glandular hairs in leaves in AM-inoculated plants (Guerrieri et al. 2004). Furthermore, plant growth regulator levels are also known to be amended in both arbuscule-containing cells and whole tissues of mycorrhizal plants (Allen et al. 1980).

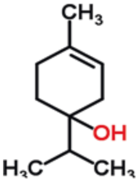
28.3.4.2 Plant Alkaloid Accumulation Associated with AMF

The effect of arbuscular mycorrhizae (AM) on accumulation and biosynthesis of alkaloids has been attributed to mycorrhization in various medicinal plants such as *Castanospermum australe* (Abu-Zeyad et al. 1999), *Catharanthus roseus* (Rosa-Mera et al. 2011; Andrade et al. 2013), *Datura stramonium* (Wei and Wang (1989), *Phellodendron amurense* (Fan et al. 2006), and *Camptotheca acuminate* (Zhao et al. 2006; Yu et al. 2010). Liu et al. (2007) investigated that enhanced production of alkaloid in medicinal plants are linked with the higher biomass production in AM-inoculated plants which are usually connected to the nutritional benefits of mycorrhization. AM fungi directly controlled the expression of different genes associated with the plant defense system, with consequences for whole-plant fitness and its response to biotic stresses (Pozo and Azco'n-Aguilar 2007; Fan et al. 2006; Zhou and Fan 2007). It was reported in many medicinal plants that mycorrhization enhances alkaloid contents such as ephedrine, camptothecin, and alliin (Guo et al. 2010; Zhao et al. 2006; Yu et al. 2010; Borde et al. 2009). Studies performed by El-Sayed and Verpoorte (2007) and Roepke et al. (2010) reported the improved production of several pharmacologically important monoterpene indole alkaloids (MIAs), such as vinblastine, vincristine, ajmalicine, vindoline, catharanthine, and serpentine in *Catharanthus roseus* and pyridine alkaloids (PAs) in *Nicotiana species*.

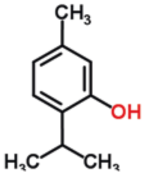
28.3.4.3 Plant Phenolic Accumulation Associated with AMF

The effect of AM on the production of phenolics in various plants has been summarized in Table 28.2. The enhancements of phenolics such as anthraquinone glycosides and flavanoids are both qualitative and quantitative (Araim et al. 2009; Silva et al. 2014; Rosa-Mera et al. 2011; Bagheri et al. 2014; De Sousa et al. 2013; He et al. 2009a, b, c; Meng and He 2011; Zhao et al. 2009; Zhao and He 2011; Nell et al. 2009). It was observed by many researchers that the enhancement of phenolics in medicinal plants was due to increase in the biomass of plants due to better nutrition and expression of genes related to the defense system of plants. Jurkiewicz et al. (2010) reported increase in the caffeic and chlorogenic acid in *Arnica Montana*. Furthermore there was improved production of phenolics in *Viola tricolor* (Zubek et al. 2015), *Salvia* spp. (Yang et al. 2017), and *Aloe vera* (Pandey and Banik 2009; Mamta et al. 2012). There were significant increases in the content of rosmarinic and caffeic acids (Jugran et al. 2015; Zubek et al. 2015; Jurkiewicz et al. 2010; Toussaint et al. 2007; Lee and Scagel 2009) and diobulbinone (Lu et al. 2015).

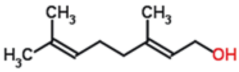
Structure of Secondary Metabolites Affected by AM



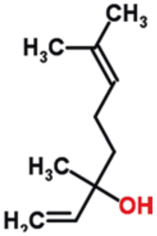
4-terpinenol



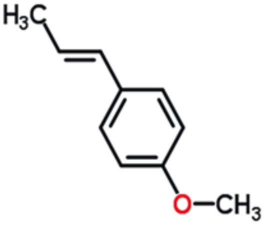
Thymol



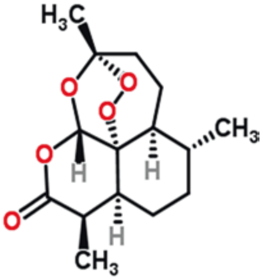
Geraniol



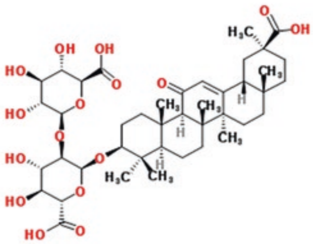
Linalool



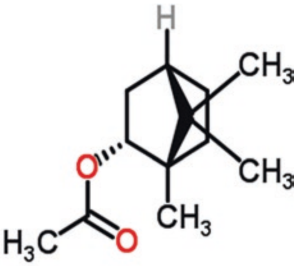
trans-Anethole



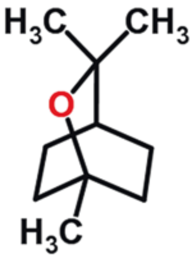
Artemisinin



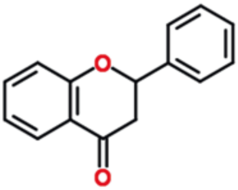
Glycyrrhizin



l-Bornyl acetate

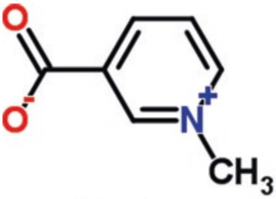


(±)-Eucalyptol

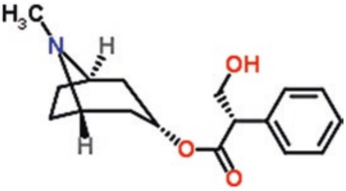


FLAVANONE

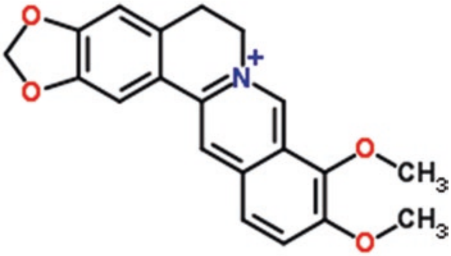
A. Triterpene



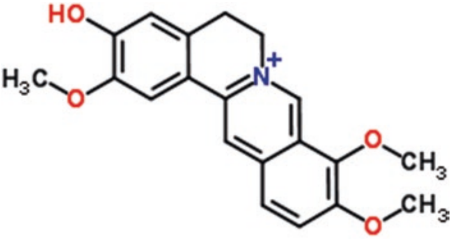
Trigonelline



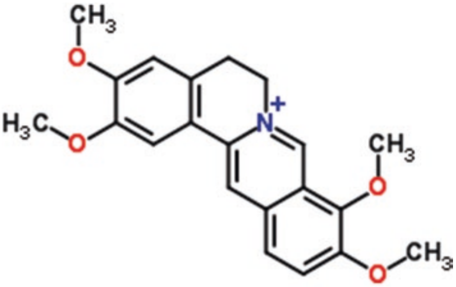
(S)-(-)-atropine



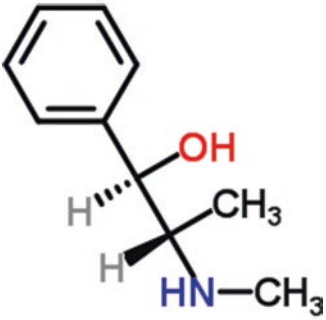
Jatrorrhizine



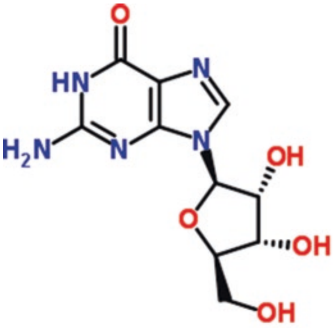
Berberine



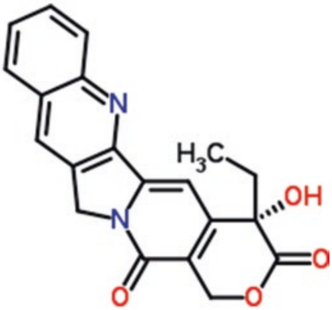
palmatine



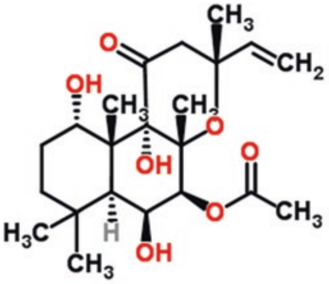
L-(-)-Ephedrine



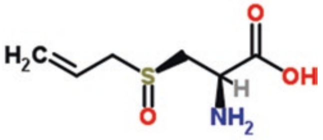
Guanosine



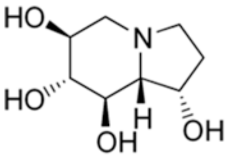
Camptothecin



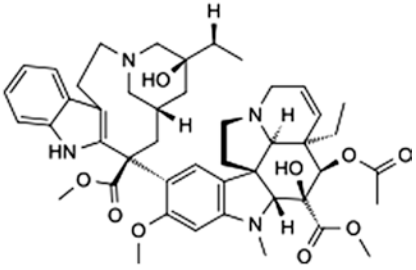
Forskolin



(+)-L-Alliin

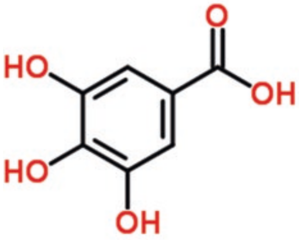


Castanospermine

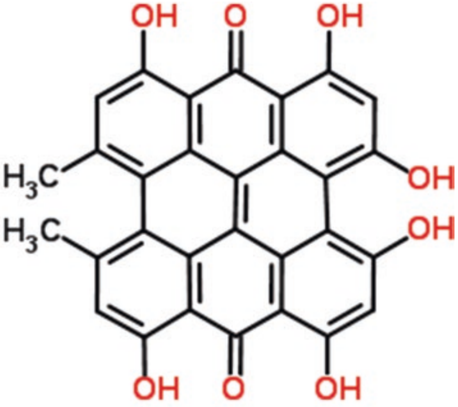


Vinblastine

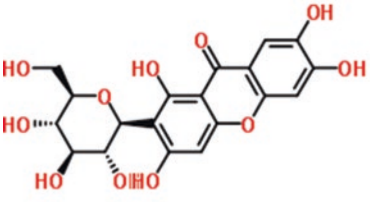
B. Alkaloids



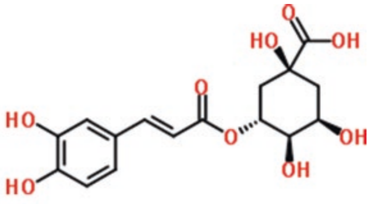
Gallic acid



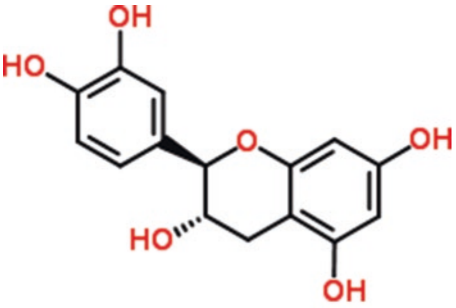
Hypericin



Mangiferin



Chlorogenic acid



D-(+)-Catechin

C. Flavanoids and Phenolic Compounds

28.4 Conclusion

Now it is well-established that symbiotic association between medicinal plants and AM fungi can be exploited for the enhanced production of plant secondary metabolites. These secondary metabolites not only play an important role in uplifting the defense system of plants but also can be used for curing human ailments. In production of herb-based materials, there is a need to implement mycorrhizal technology to explore the role of AM fungi in the cultivation of medicinal plants. Thus future research priorities should emphasize on (1) isolation, selection, and screening of promising and effective AM fungal strains which can be adapted to natural habitat where medicinal and aromatic plants have to be grown, (2) strategies for the production of seedlings of medicinal and aromatic plants with mycorrhiza, (3) intensive cultivation of medicinal plants and the production of medicinally important phytochemicals as well as plant parts rich in medicinally important compounds, and (4) strategies by which AM fungi modulate the contents of bioactive principles in medicinal plants.

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