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Review

Arnica montana L. – a plant of healing: review

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Abstract

Objectives *Arnica montana* is a widely used therapeutic plant used traditionally to treat various ailments. The objective of this study was to evaluate the botany, phytochemistry and ethnopharmacology along with special emphasis given on pharmacological activity of plant *A. montana.*

Key findings The plant extracts have been reported to possess antibacterial, anti-tumor, antioxidant, anti-inflammatory, antifungal and immunomodulatory activity. A wide range of chemical compounds including sesquiterpene lactones and their short-chain carbonic acid esters, flavonoids, carotenoids, essential oils, diterpenes, arnidiol, pyrrolizidine alkaloids, coumarins, phenolic acids, lignans and oligosaccharides, etc., are found in different parts of the plant.

Summary It has been scrutinized that extensive research has been carried out to explore the therapeutic potential of flowers of the plant. Therefore, investigations should be carried out to explore the therapeutic potential of other parts of the plant for better therapeutic utilization.

Introduction

Asteraceae, also known as the aster, daisy, composite or sunflower family, is one of the largest flowering plant family containing about 1600 genera and more than 23 000 species and 13 subfamilies.[1–3] Medicinally important compounds for curing various ailments are found in some genera, e.g. species of *Arnica, Centaurea granatensis Boiss., Conyza bonariensis and Senecio doronicum,* which are reported for the treatment of variety of ailments.[3] 'Asteraceae' name is give after one of the genus of this family, i.e. 'Aster', which is derived from the Greek word 'ἀστήρ' which means star that denotes its inflorescence. Synantherology is the name given to the study of this family. As its petals open in the morning and close in the evening, members of this family are also called 'Daisy', which is derived from English name: daegesege, which means 'day's eye'.[4] The plants of this family grow as annual and perennial herbs and shrubs, vines or trees in forests to high-altitude grasslands.[5] Characteristic inflorescences (flowers in dense heads with involucrum) and the calyx forming a pappus crowning the nut are found in this family.[6] *A. montana* (Asteraceae) is a high-altitude perennial plant indigenous to mountain slopes in Europe, northern Asia, Siberia and America also known as fall-kraut, leopard's bane, sneezewort and mountain tobacco[7] and had proved to be an important medicinal plant.[3]

Occurrence, botanical description and ethnopharmacology

Arnica montana is used since centuries in homoeopathic system of medicine. It is used for the treatment of 66 different pathological conditions, but frequently used for contusion, wounds, rheumatism and inflammation. In early medieval texts, the name '*Arnica*' was not referred anywhere. This name was given in 1533 by the St, Hildegard's 'Physica' editor which was further used in 16th century by Dalechamps, who thought it was derived from Greek word '*Ptarmika*' which means something that causes sneezing, and Haller and Linnaeus were the first people to use the name '*Arnica*' in both pharmacy and botany. In northern Spain, *Arnica montana L.* was named as: '*betónica de los montes*', '*tobaco de montana*', '*talpa*' or '*talpica*', and in 1785, the plant was successfully used in hospitals for the treatment of loss of vision that occurs without an apparent lesion affecting the eye also called as amaurosis.

The 32 species known as '*Arnica*' belong to six botanical families and five subgenera. Of this, 24 species are Asteraceae that belong to eight tribes as follows:

Anthemideae Cass. (Achillea ageratum L.).,
Astereae Cass. (Conyza bonariensis (L.) Cronquist),
Cardueae Cass. (Centaurea granatensis Boiss. ex DC.).,
Cichorieae Lam. & *DC. (Andryala integrifolia L., A. ragusina L., Crepis paludosa (L.) Moench, C. vesicaria L.* subsp. *taraxacifolia (Thuill.) Thell.* and *Hieracium* sp.*).*,
Doroniceae Panero (Doronicum carpetanum Boiss. & Reut. Ex Willk. & *Lange, D. grandiflorum Lam.* and *D. pardalianches L.).*,
Inulaeae Cass. (Chiliadenus glutinosus (L.) Fourr, Dittrichia vis- cosa (L.) Greuter, Inula britannica L., I. helenioides DC, I. helvetica
Weber, I. Montana L., I. salicina L., Asteriscus spinosus (L.) Sch. Bip., Pulicaria odora (L.) Rchb., and *P. paludosa Link.).*,
Madieae Jeps. (A. montana L.).,
Senecioneae Cass. (Senecio doronicum (L.) L., S. jacobaea L., and *S. pyrenaicus L.).*,[3] and the subgenera are Arctica, Andropurpurea, Austromontana, Montana and Chamissonis.[8] The flowers of the plant are traded by the following pharmaceutical trade names, i.e. *Arnica flos* (latin), *Fleur d* '*Arnica*' (Fr), *Flor de árnica* (Sp), *Arnikablüten* (Ge) and *Fiore de Arnica* (It), and the trade names for the dried roots are *Arnikawurzel* (Ge), *Arnicae radix* (latin), *Raiz de Arnica* (Sp) and *Racine d* '*Arnique*' (Fr). However, this species is considered endangered in different European countries like Bosnia-Herzegovina, Croatia, Slovenia, Germany and Lithuania, Luxembourg, Sweden, Romania, Balkans, Spain and Hungary, so in order to protect this species, its cultivation is increasing but its harvest is not allowed in most European countries including Italy.[9,10] The plant grows best at an altitude of 500–2500 m in less fertile meadows and on acidic soils in alpine meadows and peat bogs healthlands. *A. montana L.* (Asteraceae) is an herbaceous, perennial, 1–2 ft tall plant, with dark green basal, lower cauline leaves (obovate or elliptical to oblanceolate), hairy stems and bright yellow daisy-like ray flowers. The ray flowers' teeth size is as <1 mm long or between 1 and 2 mm long. The second flowers' diameter varies between 4.9 and 5.7 cm. The flowers appear in July and August with 1–7 flower heads.[9] The best harvesting time for the flowers including the calyx in the Northern Hemisphere is June–August; however, in central Otago, New Zealand, it is December–January and for the roots, it is in spring (April) and autumn (October). The fresh flowers are used to prepare tincture, or they may be dried before in warm shady area with proper air circulation to prepare tincture. Its fruit is like a seed with white or pale tan bristles and has a pappus of plumose. Seeds are of cylindrical shape. Plants are germinated by division from cuttings in the spring or by *A. montana* seed; however, seed germination is below 80% and may take about a month or as long as 2 years to germinate. Seeds are sown in the late summer by lightly covering them and spaced 30 cm apart. Plants may be grown indoor by sowing in pots at 13 °C for 1 year and then transplanting them outdoor after last frost. These are cut before flowering to keep stems short and after flowering to produce secondary bloom.

The plant possesses numerous medicinal activity. The flowers of the plant show greater medicinal value and are used as antiphlogistic, inotropic, antibiotic, anti-inflammatory, immunomodulatory, antiplatelet, uterotonic, antirheumatic and analgesic in febrile conditions.[11,59] Both oral administration of flowers in the form of fresh plant mother tincture and local external application in the form of cream, ointment or gel or in the form of wet poultice comprising of a solution that contains one tablespoon of *A. montana* tincture to a quarter litre of light warm water have been valued for curing osteoarthritis, alopecia and chronic venous insufficiency.[12] According to European pharmacopoeia (1809), *A. montana* tincture is produced from *A. montana* flowers with 0.04% sesquiterpene lactones expressed as dihydrohelenalin tiglate. The tincture contains one part of the drug in 10 parts of ethanol (60% (V/V) to 70% (V/V)). According to European Union, herbal preparation(s) containing *A. montana* are tincture (1 : 10) extracted with ethanol 70% v/v, tincture (1 : 5) extracted with ethanol 60% v/v and liquid extract (1 : 20) extracted with ethanol 50% m/m, mainly of flowers. Tincture is dried by evaporation, and the extract is incorporated in numerous herbal drug products.[12,13] *A. montana* has proved its worth as anti-inflammatory agent. *A. montana* extract (3–30%) when blended with one or more therapeutic or pharmaceutical agents, i.e. camphor, menthol, eucalyptus oil, mint oil, guaifenesin, topical analgesics, non-steroidal anti-inflammatory drugs or either transdermal opioid analgesics in a petroleum base or pluronic lecithin organogel, reduces inflammation.[14] Alam[15] reported that post-traumatic bruising of skin or post-surgery, postlaser treatment effects can be prevented by applying ointment containing *A. montana* (30–40%) in a petrolatum base to the affected area of the skin.

In Videki *et al.*, US patent No. 5043153, compositions are prepared for the treatment of parodonthopathy and in Marissal *et al.*, US patent No. 4684522, a cosmetic formulation possessing anticellulitis and slandering activity comprising of required content of extracts of various plants such as *Hedera haelix L.*, *A. montana L.* (containing glycols), *Aesculus hipocastanus* L., *Ruscus aculeatus L.*, extract containing saponins and kola nut extract containing caffeine has been reported.[16]

In another study, by Ayache *et al.*, US patent No. 4795638 revealed a cosmetic preparation for reducing or eliminating cellulite or fat build-up containing an oily base, a rubefacient (extracts of capsicum; nicotinic acid salts like triethanolamine nicotinate; nicotinic acid esters like

methyl, ethyl, hexyl, phenyl and benzyl nicitinate and alpha tocopherol nicotinate; nicotinyl alcohol and its organic acid esters like nicotinate and nicotinyl tartarate), one oil soluble plant extract of either climbing ivy, *A. montana*, marigold, rosemary, ginseng, sage, ruscus, Saint Johns wort, ulmaria, algae, a volatile polysiloxane and orthosiphon.[17] Paradise L. in US patent No. 5795573 A has concluded that homoeopathic topical anti-inflammatory preparations containing synergistic combination of extracts from *A. montana, Rhus toxicodendron* and *Aesculus hippocastanum* and *belladonna* can be used to treat muscular cramps, soreness and pain. In many inflammatory diseases in order to relieve pain or mask pain caused by kinins and kallakreins, it is desirable to promote healing and improve circulation to tissues nerves. US patent No. 5162037 to Whitson-Fischman discloses a homoeopathic mixture to treat pathogenic conditions of body containing one herb or herbal extract of *A. montana, Rhus Toxicum*, pineal gland and a magnetically permeable substance.[18] *Arnica* in combination with *Ruta graveolens, Aconitum napellus, Bellis perennis, Hamamelis virginiana, Hypericum perforatum, Calendula officinalis, Ledum palustre, Bryonia alba* is effective for treating inflammation.[19]

Recently, Bilia has reported that both the tincture and the dried extract of the plant are physically incompatible and unstable when formulated as semisolid formulations as well as contain very less content of sesquiterpene lactones. Therefore, he introduced a pioneering supercritical carbon dioxide extract, analysed by both HPLC and NMR spectroscopy containing 9.5%(w/w) of sesquiterpenes. It can be a good substitute for the topical semisolid preparations available in the market.[20] Roots of *A. montana* contain thymol, which is used for flavouring purposes, as antioxidant in foodstuffs and beverages and also as fungicide, preservative and insecticidal agent.[21,22] Roots of the plant are also used as bacteriostatic, antiphlogistic, choleretic and cholagogic due to presence of polyacetylenic compounds, phenol esters and phenolcarboxylic acids.[23] Alcoholic or isopropanolic extract of *A. montana* flowers in the form of liquid formulations such as syrups, tinctures and ointments is used for the treatment of cattle, sheep, horses, swine and goats for inflammation of udder, joints, tendons, skin; eczema and to cure wounds of mucous membrane and skin.[23] *A. montana* in combination with *Echinacea angustifolia, Eupatorium perfoliatum* and *Baptisia tinctoria* is used to treat upper respiratory infections.[24] Numerous homoeopathic preparations of the plant are available in the market such as Hyland's *Arnicated* hair oil, shampoo, *Arnica* ointment, *Arnica* tablets and pellets [6×, 12×, 30×, 30CH, 200CH], Hyland's *Arnica* spray as the plant possesses various activities. Bioactive constituents such as sesquiterpene lactones, i.e. helenalin an 11a,13-dihydohelenalin, phenolic acids and flavonoids, have been isolated by various chemical and pharmacological analyses of the plant which acts as anti-inflammatory agent, antioxidant, antiphlogistic, immunomodulatory and used to treat various ailments like osteoarthritis. Cosmetic, pharmaceutical and nutraceutical utility of *A. montana* ethanolic seed extract has been reported in combination with other plant active constituents or either alone. It has also been reported in literature that decoction, infusion or macerated extracts of *A. montana* flowers, leaves or aerial parts of the plant can be used to treat numerous ailments such as bowels ache, cough, contusion, cuts, haematoma, headache and rheumatism.[3]

As recognized in US Pat. No. 4569839, *A. montana* also has soothing and healing properties for the hair and skin. As taught in US Pat. No. 3832343 by Majoie *et al.*, perhaps the most common topical use for *A. montana* is in the treatment of haematomas as it prevents coagulation of blood. In US patent No. 4938960 to Ismail, extract of *A. montana* promotes blood circulation and is therefore used for treatment and protection of the skin on the theory that the *A. montana* will increase the action of the vitamin E in the composition.[25]

Phytochemistry

One hundred and fifty therapeutically active substances are present in *A. montana* plant, i.e. sesquiterpene lactones, i.e. helenalin,11a,13-dihydohelenalin and their short-chain carbonic acid esters (0.3–1% of dry weight in the flower heads, 0.1–0.5% in leaves), flavonoids (0.6–1.7%) by micellar electrokinetic capillary chromatography[26] in the form of flavonoid glycosides, flavonoid glucuronides and flavonoid aglycones; essential oils, composed thoroughly of fatty acids, thymol derivatives, monoterpenes and sesquiterpene. Other constituents of *A. montana* are carotenoids; diterpenes; arnidiol (a triterpene); pyrrolizidine alkaloids (tussilagine and isotussilagine)[27]; polyacetylenes; coumarins (umbelliferone and scopoletin); phenolic acids (chlorogenic acid, caffeic acid and cynarin, 1.0–2.2%)[26]; lignans; dicaffeoyl quinic derivatives (1,3- 3,5 and 4,5 dicaffeoyl quinic acids); and oligosaccharides.[22] It contains sesquiterpene lactones being metacryl, isobutyryl, tygloyl, methacryloyl, isovaleryl helenalin derivatives,[28] apigenin, luteolin, hispidulin, quercetin and kaempferol glycosides in high quantities. Phytochemical study of *A. montana* notifies that the nature and amount of phytochemicals such as caffeic acid derivatives, phenolics and helenalin esters and dihydrohelenalin esters present in the flower heads vary according to climatic conditions (i.e. temperature and rainfall) and altitudinal variations. It has been investigated by many researchers that flowers of the plant are mainly rich in active constituents.[26,29,30] The content and nature of sesquiterpene lactones vary with altitude. The flowers

collected from high-altitude healthlands contain principally helenalin esters while the flowers from lower altitude meadows contain dihydrohelenalin esters in large amount. In another study, the effect of ecological factors has been investigated on the content of sesquiterpene lactones in 10 German healthlands. Higher content of sesquiterpene lactones (0.59–1.10%) was found in the flower heads collected from the foothills of the Alps.[23]

The phytochemistry of different parts of plant is discussed below.

Whole plant (*Arnicae planta* tota)

Various analytical methods such as gas chromatography with mass selective detection (GC-MSD), spectrophotometric, reverse-phase liquid chromatography (RPLC) and proton nuclear magnetic resonance spectroscopy (1HNMR) have been used for analysing the quantity of lactones present in the plant.[28,31–33] Geographical range has significant effect on the ratios of helenalin and dihydrohelenalin esters of *A. montana*: helenalin esters are mainly present in central European collections, while dihydrohelenalin esters are present principally in Spanish collections. Pulhmann *et al.* in 1991 has reported that methylation analysis, partial acidic and enzymatic hydrolysis and 13C NMR spectroscopy have been used for the identification of two homogeneous polysaccharides from cell cultures of *A. montana*, an acidic arabino-3, 6-galactan-protein with mean molecular weight of 100 000 and a neutral fucogalactoxyloglucan with mean molecular weight of 22 500 isolated by DEAE-Sepharose CL-6B and Sephacryl S-400 column chromatography.[23]

Arnica montana flowers (Arnicae flos)

In 1992, Paßreiter *et al.* stated that '*Arnica* flower' constitutes various constituents such as flavonoids (0.4–0.6%), sesquiterpenes, acetylenes, hydroxycoumarines and phenyl acrylic acids and essential oil (0.2–0.35% in flower heads and 0.2–0.5% in leaves), phenolcarbonic acids [such as chlorogenic acid (5-o-caffeoylquinic acid), cynarin 1,3-di-O-caffeoylquinic acid, caffeic acid) (Figure 1) by TLC and HPLC, umbelliferone, scopoletin (Figure 2), 2-pyrrolidineacetic acid and C-1 epimers of the two pyrrolizidine acids and after Soxhlet extraction by methanol traces of pyrrolizidine alkaloids (tussilagin and isotussilagin) (Figure 3) have also been isolated.[21,27,34] The flowers of *Arnica* species contain especially different sesquiterpene lactones which have a pseudo-guajonolide structure, which often may occur as ester derivatives such as 2,3-dihydroaromaticin, chamissonoid, mexicanin 1 (Figure 4).[10] The total amount of sesquiterpene lactones vary with maturity of dry flowers; i.e. the amount increases from 0.5% in buds to 0.9% in withered flowers. Sesquiterpene lactones are reported as good anti-inflammatory and cytotoxic agents.[23]

Seeds

Dziki in 2009 reported that seeds contain mainly phenolic acids (chlorogenic, caffeic acid, quercetin and kaempferol) (Figure 5) and flavonoids (luteolin and apigenin) (Figure 6), respectively, as active principles.[35] Aiello in 2014 reported that the seed yield can be increased with years of cultivation if regularly fertilizers are added.[36]

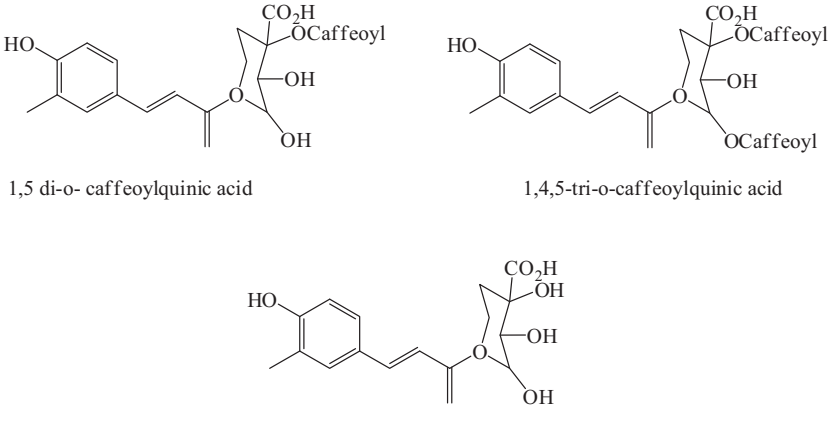

Figure 1 Dicaffeoyl quinic derivatives/ phenolic acids of *Arnica montana* plant.[23,34]

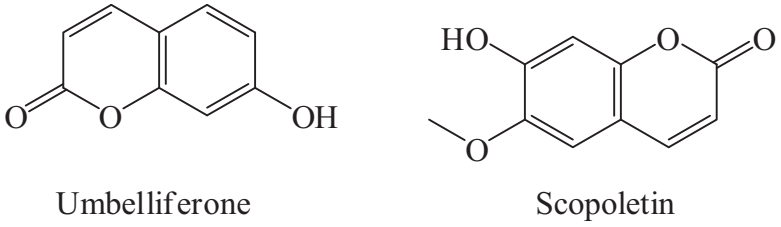

Figure 2 Coumarins of *Arnica montana* plant.[23,33]

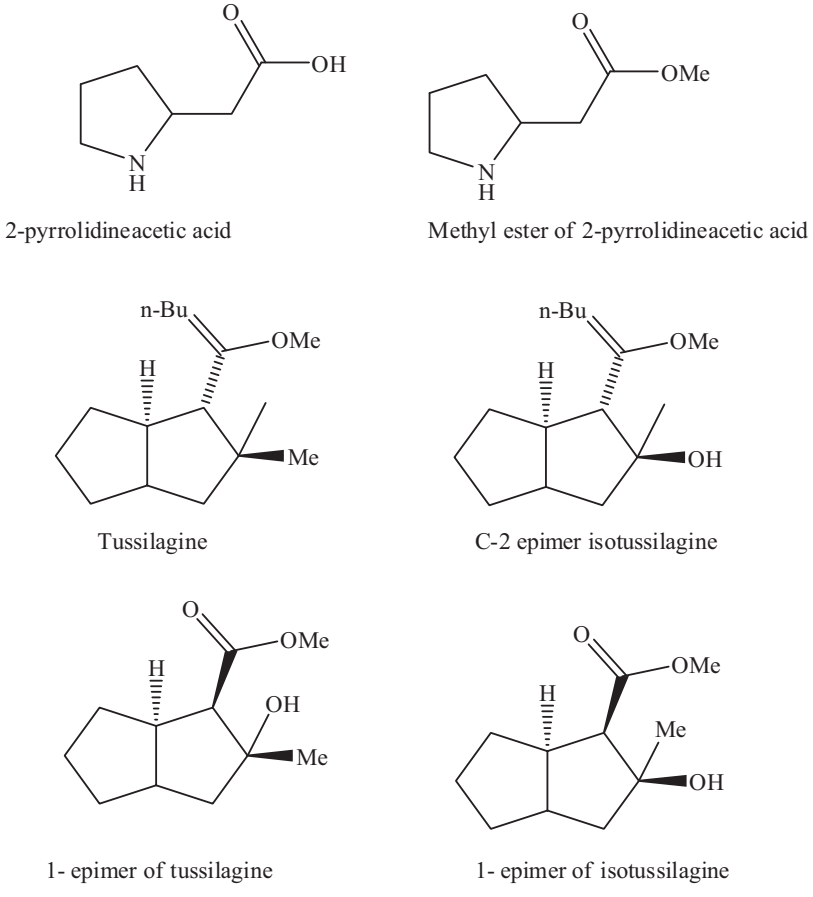

Figure 3 Pyrrolizidine Alkaloids of *Arnica montana* plant.[27]

Roots (*Arnicae radix*)

Pljevljakusic *et al.* carried out both quantitative and qualitative analyses using GC–FID and GC–MS and concluded that the main constituents of rhizome and root oils are aromatic compounds, i.e. 2,5-dimethoxyp-cymene (28.9–30.0% and 37.9–40.6%, respectively) (Figure 7), thymol methyl ether (26.1–27.1% and 9.6–10.6%, respectively) (Figure 8), pmethoxyheptanophenone (6.1–8.9% and 7.0–7.5%, respectively) and 2,6-diisopropylanisole (8.9–10.4% and 12.8–14.1%, respectively) (Figure 9) . The essential oil from roots and rhizome also contains camphene, phellandrene, limonene, 5p-mentha-2,4(8)diene, terpineol, carvacrol, methyl ether, p-diisopropyl-benzene, bornyl acetate, thymol silphiperfol-5-ene, 7-epi-silphiperfol-5-ene, silphiperfol-6-ene, modheph-2-ene, isocomene, isobornyl isobutanoate, trans-caryophyllene, 2,5-dimethoxy-para-cymene, trans-bergamotene, 2,6 diisopropylanisole, cis-farnesene, germacrene, pinchotene acetate, p-methoxy-heptanophenone, isobornyl 2-methyl butanoate, isobornyl

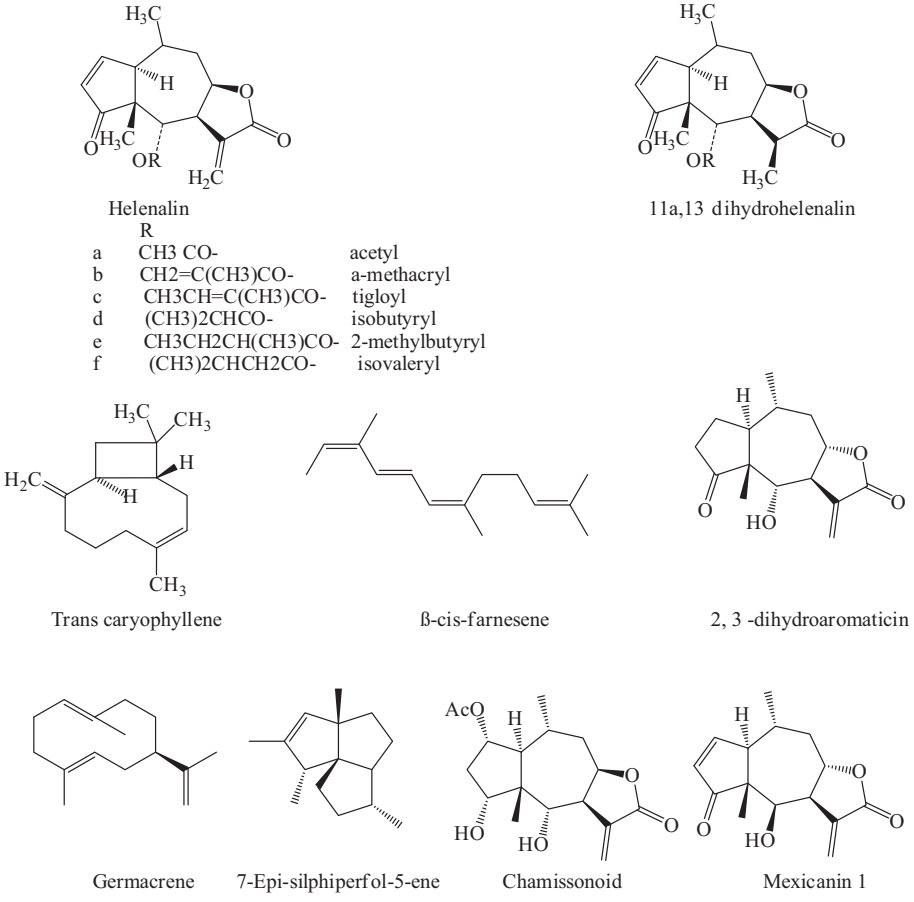

Figure 4 Sesquiterpene lactones and its derivatives of *Arnica montana* plant.[28,37]

isovalerate, sesquiphellandrene, dimethyl-ionone, lignans and zierone (Figures 4, 7 and 9). Light microscopy, scanning microscopy and transmission microscopy were used to study the secretory tissues localized as idioblastic secretory cells in the cortical region of the root and rhizome for essential oil synthesis.[37] Petrova reported that the amount of essential oils varies in different parts of *A. montana*, from 2.70 to 6.91% in rhizomes and 1.77 to 3.76% in roots. Kennedy in 1998 found that ethanolic extract of roots contains a panel of non-reducing oligofructosides in later period of growth and both non-reducing oligofructosides and reducing inulin-type oligofructosides in early growth period.[38]

In 2011, Weremczuk-Jezyna *et al.* separated 56 active principles from the essential oil of which 10-isobutyryloxy-8,9-didehydro-thymol isobutyrate and 10-isobutyryloxy-8,9-didehydro-thymol methyl ether were the main components obtained by hydrodistillation of hairy roots of the plant (Shown in Figure 3). He carried out image analysis using LEICA DCML microscope having IM1000 (Imagic Bildverarbeitung AG Software company, Opfikon, Switzerland) software and a digital camera.[39,58]

Bioactivity

Arnica montana possesses significant anti-inflammatory, antibacterial, antifungal antioxidant and immunomodulatory activity.

Anti-inflammatory activity

Arnica montana has significant anti-inflammatory potential. Huber *et al.* in 2011 disclosed that the molecular mechanism of sesquiterpene lactones differs from that of non-steroidal anti-inflammatory drugs, i.e. indomethacin and acetyl salicylic acid. These lactones significantly decrease NFkappaB-mediated inflammation as they pass through the skin easily.[40] Phosphorylation and degeneration of IkappaB, NF-kappaB's inhibitory subunit, stimulates NF-kappaB. NFkappaB activation by T cells, B cells and epithelial cells is inhibited by helenalin which in turn blocks kappaB-driven gene expression. This blockage is precise and is due to alteration of NF-kappaB/IkappaB complex, inhibiting the discharge of IkappaB by helenalin.[41] *Arnica* 6c has been

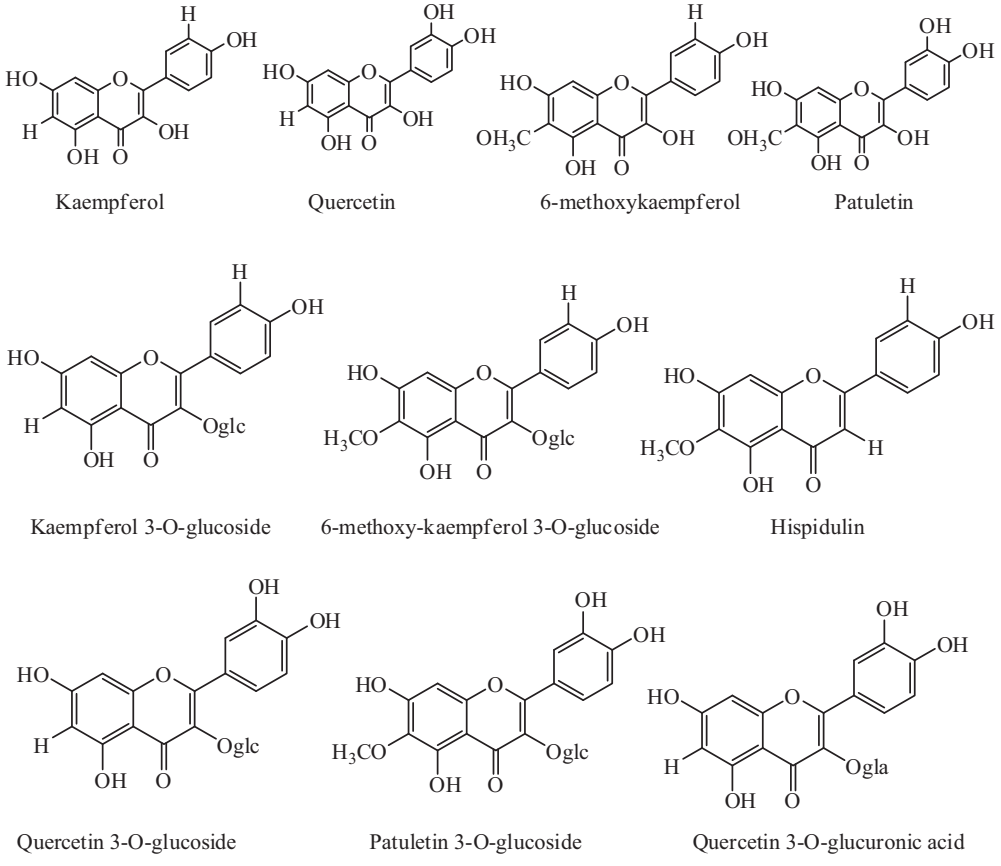

Figure 5 Flavonols of *Arnica montana* plant.[26,62]

investigated for its anti-inflammatory potential on carrageenin and rat paw oedema induced by nystatin. *Arnica* 6c significantly reduced inflammation while in case of histamine-induced oedema, the action of histamine was inhibited and the vascular permeability was increased.[42] Research also investigated that when a solution of *A. montana* 6cH, dexamethasone or 5% hydroalcoholic solution is injected into male adult Wistar rats, they show marked anti-inflammatory activity. Kawakami *et al.* in 2011 reported a series of inflammatory-positive cells, which play a major role in inflammatory process, i.e. CD54 (ICAM-1), CD18 (BETA 2 integrin), CD45RA (B lymphocytes), CD3 (T lymphocytes), CD163 (ED2 protein) and MAC 387 (monocytes and macrophages). It was concluded that rats that presented oedema after a long time exhibited minor oedema, less degranulation of mast cells and increase in diameter of lymphatic vessels.[43] In another study, it was concluded that acute non-fibrosed mastitis can be effectively treated with *Arnica* 30CH when taken orally in combination with Healwell VT-6 (comprising of *Calcarea fluorica* 200CH, *Conium* 30CH, *Silicea* 30CH, *Phytolacca* 200CH, *Belladonna* 30CH, *Ipecacuanha* 30CH and *Bryonia* 30CH).[42] It has also been reported by Sandra *et al.*,[12] that *A. montana* when administered with herbs like *Rue, Willow bark, St. John's Wort* and *Comfrey* treats by improving musculoskeletal healing in case of deep-rooted complaints like arthritis or mainly in the first 24–48 h of an accident.

Anti-osteoarthritic activity

Widrig *et al.* in 2007 prepared a topical *A. montana* gel containing helenalin, 11_,13-dihydrohelenalin and its ester that shows significant antiosteoarthritic activity by blocking the transcription factor NF-αB and NF-AT. It promotes functional capacity of hands and reduces the time period and extent of morning stiffness, intensity of pain and the number of painful joints.[44]

Immunomodulatory activity

Polysaccharide fraction of *A. montana* flowers are reported to show significant immunostimulating properties (increase of phagocytosis by granulocytes).[24]

DEAE-Sepharose CL-6B and Sephacryl S-400 column chromatographic techniques were used to isolate two

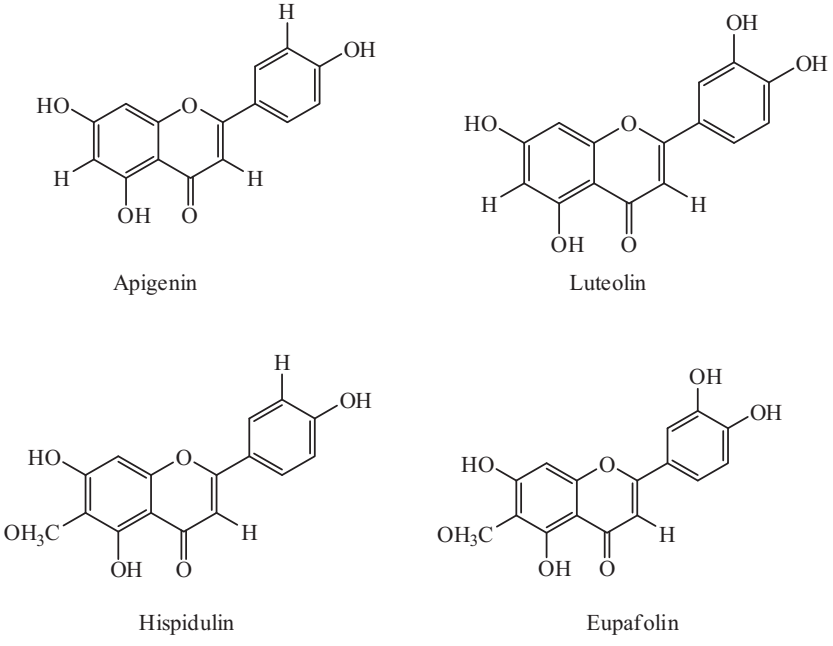

Figure 6 Flavones of *Arnica montana* plant.[62]

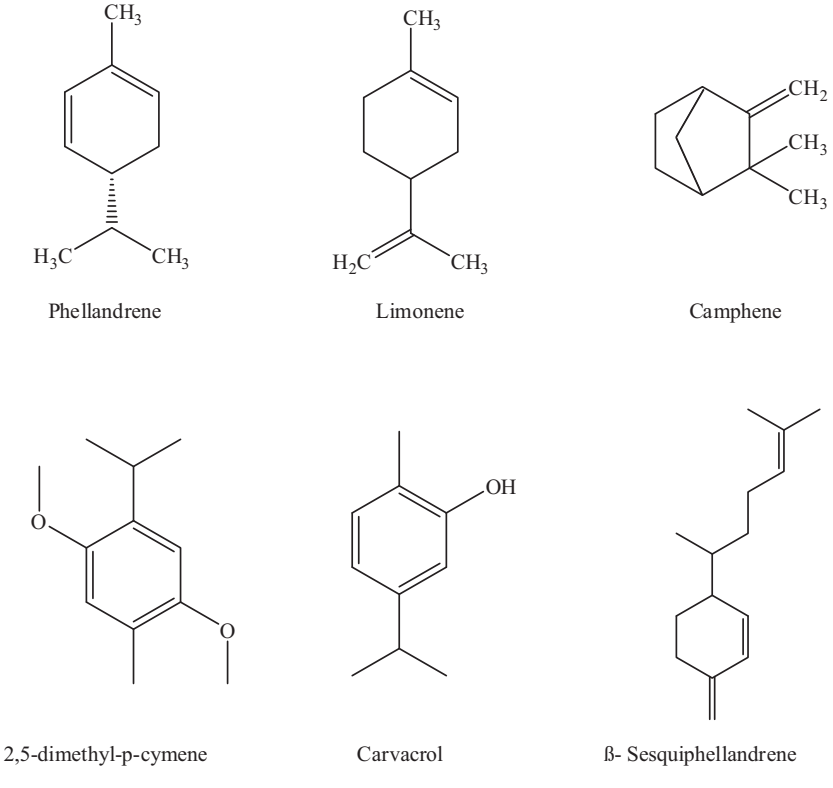

Figure 7 Terpenes of *Arnica montana* plant.[37]

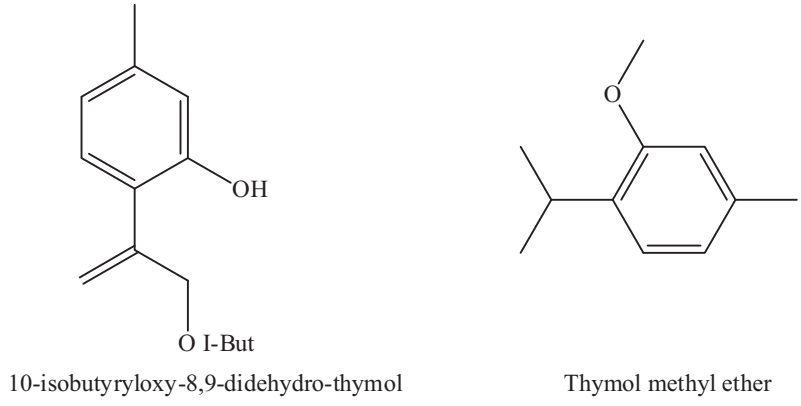

Figure 8 Thymol derivatives of *Arnica montana* plant.[37]

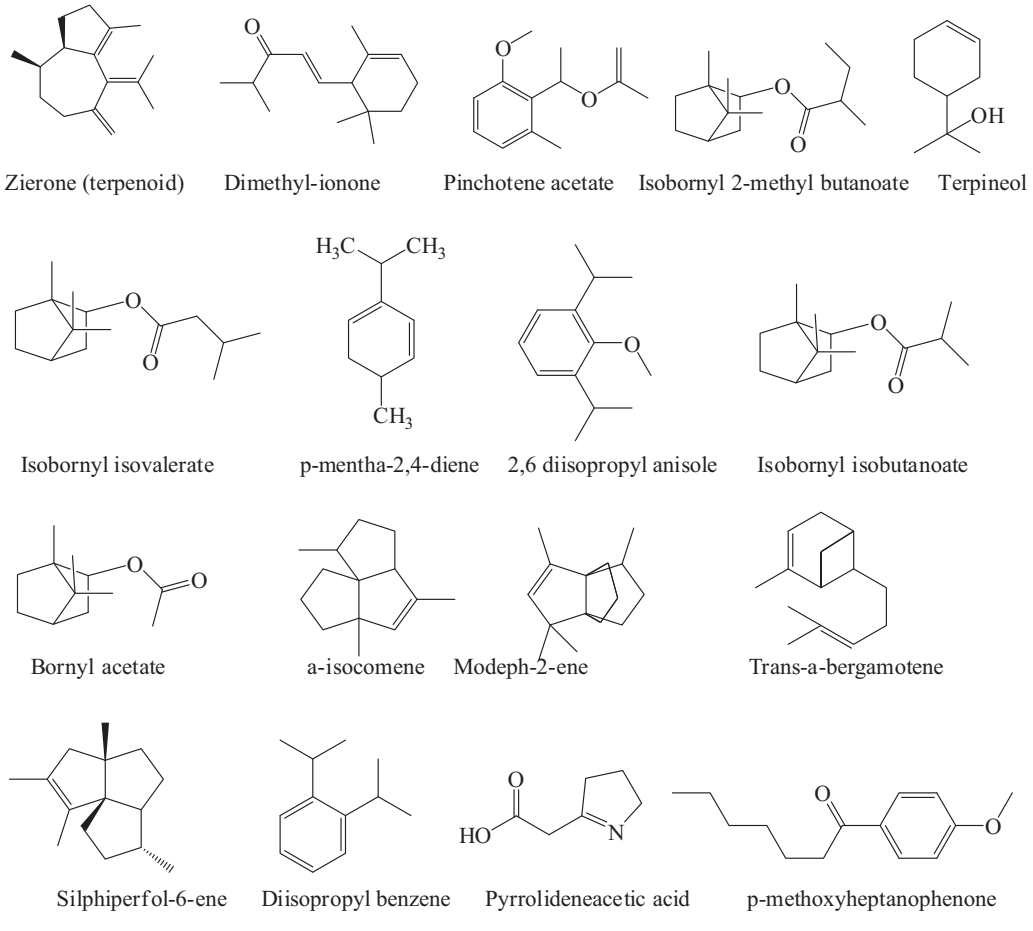

Figure 9 Other phytoconstituents of *Arnica montana* plant.[37]

polysaccharides from cell cultures of *A. montana,* i.e. an acidic arabino-3,6-galactan-protein (mean Mr 100 000), which activates macrophages to release tumour necrosis factor and possess anticomplementary activity and neutral fucogalactoxyloglucan (mean Mr 22 500), which increases phagocytosis.[45]

Antimicrobial activity

Arnica montana extracts also exhibit antimicrobial activity against *Streptococcus sobrinus* 6715 and Strep. Mutans – OMZ 175. Agar diffusion method was used, and zones of inhibition were measured. Slight inhibition was observed of the growing cells (19% for Strep. mutans – OMZ 175 and 15% for *Streptococcus sobrinus* 6715) and of water-insoluble glucan formation (29%) at these same concentrations.[46]

These thymol derivatives present in the roots of *A. montana* have been reported to have bactericidal and fungicidal property whereas the essential oil extracted from the roots of the plant shows antiphlogistic action.[21]

Anti-osteoporotic activity (ossification)

US Pat. No. 5478579 by Sawruk taught that *A. montana* is a significant source of flavonol aglycone glycoside which when combined in specific dose with calcium assists in absorption of calcium through a chelation delivery system.[47]

Improves circulation

Arnica montana is reported to relieve symptoms of diseases relating to the restricted blood flow to nerve endings and the limbs of patients, and reflex sympathetic dystrophy syndrome, which includes fibromyalgia, toxic neuropathy and diabetic neuropathy.[18]

Ureotonic activity

The alcoholic extracts of *A. montana* flower heads or sesquiterpene lactones isolated from the plant show significant uterotonic and contraction-enhancing activity in rabbits, rats and cats when injected intravenously (0.3 ml of an extract).[21,48]

Increase respiration

Sesquiterpene lactones, i.e. 6-O-acetyl-11,13-dihydrohelenalin present in *A. montana,* are also reported to increases respiration frequency and volume by 35 and 43%, respectively, in rats and rabbits when injected intravenously, 0.25 mg/kg bw.[21]

Inotropic activity

Helenalin isolated from *A. montana* show significant biphasic positive inotropic effect on the myocardium of guinea pigs at concentrations of 10^{-5}–10^{-3} mol.[49] However, concentrations above 10^{-3} mol cause an irreversible negative inotropic action leading to a block of muscle contraction.[21]

Internal use of *A. montana* at a dose of five drops, three times a day, improves the mild weakness of heart and angina pectoris.[12]

Anxiolytic activity

Ahmed *et al.* in 2013 evaluated various neuropharmacological screening tests like open field activity, stationary rod activity test and head dip activity of *A. montana*.

It was observed that the tannins and flavonoids present in *A. montana* extract decrease the exploratory activity and locomotor activity in mice and mice spent more time in light compartment and therefore had anxiolytic effect. The development of immobility during forced swimming test indicated the cessation of affective/motivational behaviour.[50]

Antioxidant and protective effect

Arnica montana extract shows significant antioxidant potential. DPPH (2,2′-diphenyl-1-picrylhydrazyl radical) free radical scavenging method and phosphomolybdate method have been utilized to determine the antioxidant potential of the plant. At concentration of 5 mg/ml, *A. montana shows* 71.52% DPPH scavenging potential and 63.68% total antioxidant activity (phosphomolybdate method) which is mainly attributed due to the presence of flavonoids and phenolic compounds.[49,51]

Camargo *et al.* in 2013, evaluated homoeopathic A. montana's effect on $Ca2^{+}$ and inorganic phosphate-induced mitochondrial oxidative stress or/and lipid peroxidation mediated by $Fe2^{+}$ citrate by alterations rates of oxygen consumed using mitochondrial suspensions prepared by the livers of Wistar strain male rats. *Arnica 30cH* showed remarkable reduction in mitochondrial O_2 consumption. *Arnica 30cH* provides protection against Ca^{2+} and inorganic phosphate-induced hepatic mitochondrial membrane permeability, lipid peroxidation mediated by Fe^{2+} citrate and reactive oxygen-mediated protein fragmentation.[52]

Hepatoprotective activity

Phenolic compounds isolated from *A. montana* are used to revive the bile forming function of liver and improve the release of chelates and bilirubin and the removal of cholesterol.[53]

Marchishin *et al.* in 1983 have reported that *Arnica* when administered to rats with carbon tetrachloride that induced liver injury increases the synthesis and excretion of bile acids, bilirubin and cholesterol; bile secretion also accelerates the activity of serum enzymes.[53]

Insecticidal activity

Arnica montana furnished insecticidal monoterpenoids which play significant role against store grain pest *Tribolium castaneum*. Alcoholic dilutions of extracts of drugs were prepared in various concentrations, increase the percentage mortality when used in concentrations, 1–100 mg/2 ml against store grain pest. In this study, methanol was used as control and permethrin as standard.[50]

Hypopigmentation activity

Skin withers with age and also by different environmental stressors such as solar ultraviolet radiation, which leads to skin damage such as thickening like plaque, deep furrowing, wrinkle formation, erythema, loss of skin tone and also hyperpigmentation as a result of increased melanin formation. AM-2 (helenalin 2-methylbutyrate) or *A. montana* extract when used to treat cultured mouse melanoma cells boosts the HSP70 gene expression with increase in dose and also activates the transcription factor for hsp genes, i.e. heat shock factor-1. It is concluded that both *A. montana* extract and AM-2 can give good results if incorporated in hypopigmenting cosmetics.[54]

Antihair loss activity

Kennedy *et al.* in 2012 concluded that *A. montana* (1.6–2.6% by weight of formulation) in combination with aqua ammonia in herbal preparations promote hair follicles, increase hair strength and growth of hair.[55] Similarly, Keeney *et al.* in 2000 introduced a solution containing aloe vera gel, *A. montana* flowers, comfrey leaves, jaborandi leaves, elkweed, chamomile flowers, colloidal silver solution, horsetail herbal extract, jojoba, collagen, napca, elastin, saponins and rosemary leaves to be applied topically for boosting growth of hair.[51]

Antiplatelet activity

Pawlaczyk *et al.* in 2009 found that hexuronic acids and phenolic glycoconjugates present in *A. montana* are responsible for the anticoagulant activity of the plant.[56] The activity was calculated tests on human plasma such as prothrombin time and activated partial thromboplastin time test.[49] In 1990, Schroder *et al.* demonstrated that the sesquiterpene lactones, i.e. helenalin and 11α-13-dihydrohelenalin, are mainly responsible for the antiplatelet activity of the plant using human venous blood for test. Helenalin contains an a-methylene-r-butyrolactone and an R-unsaturated cyclopentenone moiety which reacts with intracellular thiol groups leading to their depletion and inhibiting aggregatory activity and secretory activity in platelets. Both compounds interact with platelet sulfhydryl groups causing inhibition of formation of thromboxane, secretion of 5-hydroxytryptamine and platelet aggregation induced by collagen at 3–300 ukl concentration as a result of decreased phospholipase A2 activity.[11]

Analgesic

Arnica montana extract is also marked in literature to heal wounds. In mice, acetic acid-induced writhing test was used to measure this activity. 0.6% acetic acid per kg was injected intraperitoneal, and it was concluded that *A. montana*, reduces writhes maximally at a dose of 100 mg/kg.[49]

In another study, it is reported that *A. montana* alone or in combination with *H.perforatum* gel heals surgically induced incision on the back of Wistar rats effectively.[57]

Anticough

Arnica 6CH pills showed significant potential against oesophageal reflux which is a very productive cough, hiatus hernia. Bruises disappeared immediately, and the cough was gone too.[58]

Antihaemorrhagic activity

Stem tincture of *A. montana* was found to possess antihaemorrhagic activity in women of age group 20–35 years, which reduced postpartum blood loss, which is the significant cause of perinatal morbidity and worldwide mortality, and which occurs in 4% of vaginal deliveries.[59]

Clinical studies

Many clinical studies have been carried out on *A. montana*. Data are given in Table 1.

Toxicological studies

The oral LD50 of an extract was >5 g/kg in rats and 123 mg/kg in mice. The LD50 using intraperitoneal administration was 31 mg/kg for mice. It has been reported in literature that *Arnica* preparations does not show any signs of contact dermatitis (when used topically), or any ocular irritation, phototoxicity but shows mutagenic effects due to flavanols present in the plant. The *Arnica* extract increased the numbers of revertants 2–4 times when determined by utilizing S. Typhimurium TA98 and TA100 in the AMES test. The adverse effects may occur with a frequency of 1 : 100, and it depends on the immune system of individual.[10] Some of the laboratory findings of side effects of *Arnica* preparations are reported in Table 2.

Table 1 Clinical Studies of *Arnica montana*.

Authors (years)	Study design control type	Duration of treatment	Study and control drugs	Number of subjects by arms dose; age	Diagnosis inclusion criteria	Exclusion criteria	Efficacy results
Savage *et al.* (1978)[48]	Double-blind, placebo-controlled	3 months	**1** *Arnica* 30C, one tablet of medicated lactose after every 2 h Placebo: Lactose tablets	40 patients (20 men and 20 women) of 77.2–80.5 years	Acute stroke illness	Not reported	No statistically significant difference in both groups
Kaziro *et al.* (1984)[62]	Double-blind trial, placebo-controlled	8 days after removal of teeth	**1** Metronidazole (400 mg tablets) **2** *Arnica* 200 tablets **3** Placebo tablets	118 patients	Patients with impacted mandibular wisdom teeth	Not reported	Metronidazole reduced the pain and enhanced the healing process after surgery. *Arnica* was even less effective than the placebo
Albertini and Goldberg *et al.* (1986)[63]	Randomized placebo-controlled trial		**1** *Arnica* 7c and *Hypericum* 15c **2** Placebo	30 patients	Dental neuralgic pain after tooth extraction		76% of the patients treated with homoeopathic remedies had pain relief vs 40% of patients receiving placebo
Dorfman *et al.* (1988)[64]	Double-blind, placebo-controlled clinical study		**1** *Arnica* 5c	39 patients	Prolonged venous perfusion		*Arnica* reduced pain, hyperaemia, oedema and haematoma formation. Improvement in the blood flow and slight increase in coagulation factors and in platelet aggregation were observed after *Arnica* treatment
Brock *et al.* (1991)[10]	Double-blinded; placebo-controlled	3 weeks	**1** Combination ointment: (100 g contain: 10 g extract from *Arnica* flowers with sunflower oil (1 + 5) 4000 IU Heparin 5 mg Oil. *Chamomillae* 5 mg Guajazulen) **2** Mono-ointment: (100 g contains: 10 g extract from *Arnica* flowers with sunflower oil (1 + 5)) **3** Placebo ointment base	159 overall; not reported, how many per group; age not reported	Chronic venous insufficiency	No diuretica	Changes were in the combination treatment, but differences were not statistically significant
Lokken *et al.* (1995)[65]	Double-blind, placebo-controlled crossover trial		**1** *Arnica* 30D **2** placebo	24	Pain after surgical removal of bilaterally impacted mandibular third molars		No difference in postsurgical pain was observed between *Arnica* and placebo. Postoperative swelling and bleeding were not significantly affected by homoeopathy
Hart *et al.* (1997)[66]	Double-blind placebo-controlled	2–3 weeks after operation	**1** *Arnica* C30 **2** placebo	93 women	Patients undergoing abdominal hysterectomy	Patients with previous chronic pain or undergo operations	*Arnica* in homoeopathy has no significant effect on postoperative recovery
Tveiten *et al.* (1998)[67]	Randomized double-blind	5 days (1 day before marathon running and 3 days after the run	**1** *Arnica* D30 **2** placebo	24 in group A (27–54 years) 22 in group in group B (31–50 years)	Muscle soreness	Not reported	*Arnica* D30 has positive effect on muscle soreness than placebo but not on cell damage

Table 1 (*Continued*)

Authors (years)	Study design control type	Duration of treatment	Study and control drugs	Number of subjects by arms dose; age	Diagnosis inclusion criteria	Exclusion criteria	Efficacy results
Ernst *et al.* (1998)[58]	Computerized literature searches were performed to retrieve all placebo-controlled studies on the subject. The following databases were searched: MEDLINE, EMBASE, CISCOM, and the Cochrane Library. 89 studies were included	NA	Pure *Arnica* formulations	NA	NA	*Arnica* in combination with other herbs	Homoeopathic arnica is not efficacious beyond a placebo effect
Andrew *et al.* (1998)[68]	Double-blind placebo-controlled trial	2 days after run	**1** A homoeopathic medicine (*Arnica* 30×) **2** placebo	519 runners	Delayed-onset muscles soreness after long-distance races	Not reported	Homoeopathic *Arnica* 30× is ineffective for muscle soreness
Baillargean *et al.* (1998)[70]	Double-blind, double-period, crossover randomized	2 weeks	**1** *Arnica montana* 5CH **2** placebo	18 men of 22–46 years of age	Healthy subjects	Patients having any coagulation disorder, chronic disease, smoking or on any other medication	*Arnica montana* has no significant effect on bleeding time in minutes, and no clinical significant difference on other tests of blood coagulation was observed
Ramelet *et al.* (2000)[70]	Randomized, prospective, multicentre double-blind trial		**1** *Arnica* 5c **2** placebo	130	Saphenousstripping		No significant difference in postoperative haematomas was observed between Arnica and placebo
Brock (2001)[10]		3 weeks	**1** 100 g *Arnica* gel (contained 25 g *Arnica* tincture) **2** placebo	50 per group; 77 woman; 23 men; age in average 59.2	Chronic venous insufficiency	Not reported	Statistically significant improvement in both groups; a significant better effect in the verum group
Alonso *et al.* (2002)[71]	Double-blinded placebo-controlled	2 weeks, either in pretreatment or post-treatment	**1** *Arnica* gel (*A. montana* with 45% alcohol, purified water, with hazel, trolamine, carboner, EDTA, methyl/propyl paraben) **2** Vehicle	9 pretreatment, 10 post-treatment; dose not specified; age unknown	Facial telangiectases	Patients on anticoagulant therapy	No statistically significant difference in both groups
Rosen-zweig *et al.* (2002)[10]	Double-blinded placebo-controlled	4 weeks	**1** *Arnica* compress (prepared from the whole plant extract, 0.7%) **2** Placebo compress (contained water and food colouring)	16 Arnica 14 placebo; one compress; age unknown	Acute soft tissue pain (foot/ankle, knee, neck/shoulder)	Not reported	No statistically significant analgesic benefit compared to placebo one hour after therapy
Knuesel *et al.* (2002)[72]	This open multicentre trial	Applied twice daily for 6 weeks	**1** *Arnica montana* fresh plant gel	26 men and 53 women	Mild-to-moderate osteoarthritis (OA) of the knee	Not reported	*Arnica* gel was found to be effective in treating mild-to-moderate osteoarthritis
Jeffrey and Belcher (2002)[73]	Randomized double-blind, placebo-controlled study		**1** *Arnica* 6D tablets **2** *Arnica* Ointment **3** placebo	37	Hand surgery (endoscopic carpal tunnel release)		No difference in grip strength or wrist circumference was found between Arnica and placebo. A significant reduction in pain was observed in the Arnica-treated group vs placebo. (*P* 5 0.03)

Table 1 (*Continued*)

Authors (years)	Study design control type	Duration of treatment	Study and control drugs	Number of subjects by arms dose; age	Diagnosis inclusion criteria	Exclusion criteria	Efficacy results
Wolf *et al.* (2003)[74]	Prospective, randomized, double-blind, placebo-controlled pilot trial		**1** *Arnica* 12D **2** Placebo	60	Varicose vein surgery		Haematoma surface was reduced with *Arnica* by 75.5% and with placebo by 71.5% (not significant). Pain score decreased by 1, 6, 2.2 points with Arnica and 0.3, 6, 0.8 points with placebo. The results of the study showed a trend towards a beneficial effect of *Arnica* regarding the reduction in haematoma and pain during the postoperative course
Stevinson *et al.* (2003)[75]	Double-blind, placebo-controlled, randomized trial	21 days	**1** Three tablets daily of homoeopathic *Arnica* 30 or 6 °C or **2** Placebo for 7 days before surgery and 14 days after surgery	64 adults (18–70 years)	Adults undergoing elective surgery for carpal tunnel syndrome	Patients currently taking homoeopathic remedies, reported previous hypersensitivity to homoeopathy, were taking aspirin, or were unable to complete the study diary or attend follow-up appointments	No statistical differences were found between homoeopathic arnica over placebo in reducing postoperative pain, bruising and swelling in patients
Totonchi *et al.* (2005)[10]	Double-blinded placebo-controlled	6 days, resp. 4 days	**1** Intravenous dexamethasone intra-operatively, followed by a 6-day dose of prednisone **2** *Arnica* SinEcch **3** none (as control)	48 overall; 11 male; 37 female; age from 15 to 65	Primary rhinoplasty with osteotomy	Not reported	Statistically no significance between the groups in ecchymosis; statistically significance in reducing oedema in both groups
Oberbaum *et al.* (2005)[59]	Double-blind, placebo-controlled, randomized, clinical trial	Before delivery and 72 h after delivery	**1** *Arnica montana* C6 and *Bellis perennis* C6 **2** *Arnica montana* C30 and *Bellis perennis* C30, or **3** Double placebo	Women aged 20–35, at week 37–43 of pregnancy, after one to four previous deliveries, and scheduled for spontaneous vaginal delivery of a single fetus	Pregnant women	Women with previous Caesarean section, antepartum or postpartum haemorrhage in previous pregnancies, and coagulopathies	Homoeopathic *Arnica montana* and *Bellis perennis* may reduce postpartum blood loss, as compared with placebo
Leivers (2005)[76]	Double-blind, placebo-controlled, randomized, clinical trial	6 weeks	**1** *Arnica* gel (20% tincture) **2** placebo	89 patients	Venous insufficiency	Not reported	There was improvement in venous tone and oedema in patients on *Arnica* treatment than on placebo
Leivers (2005)[76]	Open, multicentre trail	6 weeks	**1** *Arnica* gel (20% tincture) **2** placebo	79 patients	Mild-to-moderate knee osteoarthritis	Not reported	*Arnica* decreased the pain, stiffness of knee and was effective than placebo

Table 1 (*Continued*)

Authors (years)	Study design control type	Duration of treatment	Study and control drugs	Number of subjects by arms dose; age	Diagnosis inclusion criteria	Exclusion criteria	Efficacy results
Seeley *et al.* (2006)[77]	Randomized double-blind placebo-controlled study		**1** *Arnica* (SinEcch) **2** placebo	29 patients	Rhytidectomy		Patients receiving Arnica had a smaller area of ecchymosis on postoperative days 1, 5, 7 and 10. These differences were statistically significant only on postoperative days 1 (*P*, 0.005) and 7 (*P*, 0.001)
Brinkhaus *et al.* (2006)[78]	Three randomised, placebo-controlled, double-blind, sequential clinical trials	Patients were treated and followed up for 2 (ART), 8 (CLR)or 11 days (ARJ)	Homoeopathic *Arnica* 30× (a homoeopathic dilution of 1 : 1030) administered orally with sucrose globules as the carrier substance	A total of 227 patients were enrolled patients of both genders, age 18 –75 years	Patients with knee diseases necessitating arthroscopy, artificial knee joint implantations or cruciate ligament reconstructions	Recent traumas, acute knee inflammation, autoimmune disease, tumour diseases, alcohol abuse, serious systemic mental or physical disease, severe allergic disease, pregnancy, breastfeeding, regular analgesic consumption, drug abuse or participation in another clinical trial	Patients receiving homoeopathic arnica showed a less postoperative swelling mainly in CLR trails.
Robertson *et al.* (2007)[79]	Randomised double-blind, placebo-controlled	2 tablets 6 times in the first postoperative day and then 2 tablets twice a day for the next 7 days. 14 days trail	*Arnica* 30c or identical placebo	190 patients over the age of 18	Patients under tonsillectomy	Patients who had tonsillectomy in combination with other surgery (e.g. uvulopharyngopalato-plasty	*Arnica montana* given after tonsillectomy provides a small, but statistically significant, decrease in pain scores compared to placebo
Widrig *et al.* (2007)[44]	Double-blind	Doses of gel (4 cm strip), gently rubbed over the affected joints thrice-daily for 3 weeks	Gel preparations **1** Ibuprofen (5%) **2** *Arnica* (50 g tincture/100 g, DER 1 : 20)	204 patients	Osteoarthritis of hands	Not reported	Preparation of arnica is not inferior to ibuprofen when treating osteoarthritis of hands
Totonchi and Guyuron *et al.* (2007)[80]	Randomized double-blind clinical study		**1** *Arnica* **2** Intravenous dexamethasone plus oral tapering dose of methylpred-nisone or no treatment (control group)	48 patients	Rhinoplasty		*Arnica* and dexamethasone reduced swelling oedema if compared with control (*P*, 0.0001). *Arnica* and control group exhibited more resolution of ecchymosis if compared with dexamethasone

Table 1 (*Continued*)

Authors (years)	Study design control type	Duration of treatment	Study and control drugs	Number of subjects by arms dose; age	Diagnosis inclusion criteria	Exclusion criteria	Efficacy results
Paris *et al.* (2008)[81]	A phase 3 monocentric randomized placebo-controlled study		**1** Granule composition containing *Arnica* 5c, *Bryonia alba* 5c, *Hypericum perforatum* 5c and *Ruta graveolens* 3D **2** Placebo or no treatment	158 patients	Knee ligament reconstruction		Homoeopathic treatment was not superior to placebo in reducing 24-h morphine consumption after knee ligament reconstruction. Nonsignificant difference in pain assessed by visual analog scale was observed between *Arnica* and placebo
Karow *et al.* (2008)[82]	Randomized double-blind, parallel-group study		**1** *Arnica* 4D **2** Diclofenac sodium	88 patients	Hallux valgus surgery		*Arnica* and diclofenac had equivalent efficacy on wound irritation, patient mobility and use of analgesics. Diclofenac was more effective in reducing pain if compared with Arnica
Adkison *et al.* (2010)[83]	Randomized, double-blind, placebo-controlled trial		**1** *Arnica* cream **2** placebo	53 patients	Leg pain after calf raises		*Arnica* increased pain scores if compared with placebo. No difference in muscle tenderness and ankle motion was observed
Cornu *et al.* (2010)[84]	Double-blind placebo-controlled parallel trial		**1** A combination of *Arnica montana* 5c and *Bryonia alba* 5c granules **2** Placebo	90 patients	Aortic valve surgery		No difference between homoeopathic treatment and placebo on bleeding, C-reactive protein, troponin I and cumulated morphine was observed
Leu *et al.* (2010)[85]	Randomized, double-blind placebo-controlled trial		**1** 5% vitamin K **2** 1% vitamin K and 0.3% retinol or **3** 5% vitamin K or **4** 20% *Arnica* or white petrolatum (placebo)	16 patients	595-nm pulsed-dye laser-induced bruises on the bilateral upper inner arms		The mean improvement in bruising associated with 20% *Arnica* was greater than with white petrolatum (P 5 0.003), and the mixture of 1% vitamin K and 0.3% retinol (P 5 0.01) while improvement with *Arnica* was not greater than with 5% vitamin K cream
Huber *et al.* (2011)[40]	Single-blind, randomized	30 days	Combudoron consists of an ethanolic extract of stinging nettle (*Urtica urens*) and *Arnica* (*Arnica montana*). Placebo liquid consisted of equivalent ethanol without extract from stinging nettle and *Arnica*	Two healthy male subjects (Caucasian, age 33 and 47 years, body mass index 24 and 23 kg/m^2)	Erbium YAG-Laser-induced burns	Not reported	Combudoron seems to have positive effects on healing of grade 2 laser-induced burns

Table 1 (*Continued*)

Authors (years)	Study design control type	Duration of treatment	Study and control drugs	Number of subjects by arms dose; age	Diagnosis inclusion criteria	Exclusion criteria	Efficacy results
Kucera *et al.* (2011)[86]	Double-blind placebo-controlled study	10 days	**1** Combination of *Arnica* tincture and HES (spray) **2** *Arnica* or HES or placebo	570 patients	Acute ankle joint distortion	Patients with fractures or complete tears of ligaments, sports professionals and pregnant women	On days 3–4, improvement in pain on active motion was significantly higher in the *Arnica* + HES group if compared with the other three groups
Goedemans *et al.* (2014)[87]		12 months	**1** *Arnica* cream **2** mucopolysaccharide polysulfuric acid	40 patients	Pain and bruising following postneedling infiltration		There were no statistical differences in the effects of arnica and hirudoid on pain and bruising
Clinical trials.gov (2016)[88]	Double-blind, placebo-controlled	4 days	**1** *Arnica montana* **2** Placebo	28 subjects of 18–89 years of age	Candidates for rhinoplasty surgery at UW Transformations, Ecchymosis	Patients who are prisoner, pregnant and breastfeeding women, taking anticoagulants (such as blood thinners), antiplatelet drugs (such as NSAIDS), oral corticosteroid or other homoeopathic remedies during the peri-operative period Patients with a bruising or bleeding disorder, severe liver or kidney disease, malignancy, infection, immunodeficiency, metabolic syndrome, infectious or inflammatory gastrointestinal disease, oral or contact allergies to *Arnica montana* or to any other member of the Asteraceae family	
Mariani *et al.* (2009)[89]	Not reported	Aqueous extract of *Arnica* planta tota Rh D3, administered locally subcutaneously once a day for 6 days. 15 patients (group A) received further 3 months of arnica ampoules	*Arnica* planta tota Rh D3	30 inpatients (age 50–87)	Low back pain	Patients with other pathologies	Patients improved during acute treatment with no side effect

Table 2 Laboratory findings of side effects of *Arnica montana*

Author(s), (year)	Formulation	Pathology	Side effect profile	Dose
Hausen *et al.* (1985)[10]	Body lotion containing extracts of *Arnica*	Skin lesions	Allergic contact dermatitis of the face and hands	NS
Leeuw *et al.* (1987)[10]	Jogging cream, a multicombination with 32 constituents, one of them *Arnica*		Dermatitis	
Delmonte *et al.* (1998)[10]	A cream containing 1.5% Arnica	Enlarging necrotic lesions of the face and left leg, together with malaise and high fever	Sweet's Syndrome, often correlated with leukaemia	
Knuesel *et al.* (2002)[90]	Gel (topical application)	Knee osteoarthritis	One allergic reaction (not specified)	NS
Stevinson *et al.* (2003)[90]	Tablets (oral treatment)	Hand surgery (carpal tunnel syndrome)	Dry mouth Headache Feeling 'throbby' in head/neck Drowsiness Sore tongue	*Arnica* 6c (for drowsiness and sore tongue) *Arnica* 30c (for dry mouth, headache, and feeling 'throbby')
Widrig *et al.* (2007)[90]	Gel (topical application)	Hand osteoarthritis	Skin irritations Itching Reddening Allergic eczema Increased finger pain Bronchitis Chill Cystitis Rhinitis Vertigo	NS
Karow *et al.* (2008)[90]	Pills (oral treatment)	Hallux valgus surgery	Abdominal complaints Racing heart	*Arnica* 4D
Cornu *et al.* (2010)[90]	Granules (oral treatment)	Aortic valve surgery	Cardiovascular events (observed in both homoeopathy and placebo groups)	*Arnica* 5c and *Bryonia alba* 5c

Conclusion

In this review, the morphology, distribution, pharmacological data and phytochemistry of the medicinal plant, *A. montana,* have been studied. The pharmacological and phytochemical studies of the plant have revealed that the plant possess numerous activities. Although from time immemorial, the extracts of the plant have been utilized to treat various ailments but proper investigation of its mechanism of action, pharmacotherapeutics, toxicity profile, standardization and clinical studies, modern dosage forms of various phytoconstituents present in the plant can be prepared. Till date, significant investigations have been carried out on exploring the medicinal potential of the flowers of the plant. So, now there is a need to explore the medicinal potential of other parts of the plant to produce economic and therapeutically better products.

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