Arnica montana L. – a plant of healing: review

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Arnica montana; anti-inflammatory; helenalin; sesquiterpene lactones

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 \textit{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.\textsuperscript{[1–3]} Medicinally important compounds for curing various ailments are found in some genera, e.g. species of \textit{Arnica, Centaurea granatensis Boiss., Conyza bonariensis} and \textit{Senecio doronicum}, which are reported for the treatment of variety of ailments.\textsuperscript{[3]} ‘Asteraceae’ name is give after one of the genus of this family, i.e. ‘Aster’, which is derived from the Greek word ‘\textalpha\textepsilon\tau\texti\textnu\textpi’ 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’.\textsuperscript{[4]} The plants of this family grow as annual and perennial herbs and shrubs, vines or trees in forests to high-altitude grasslands.\textsuperscript{[5]} Characteristic inflorescences (flowers in dense heads with involucrum) and the calyx forming a pappus crowning the nut are found in this family.\textsuperscript{[6]} \textit{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\textsuperscript{[7]} and had proved to be an important medicinal plant.\textsuperscript{[3]}

Occurrence, botanical description and ethnopharmacology

\textit{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 ‘\textit{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 ‘\textit{Pirmika}’ which means something that causes sneezing, and Haller and Linnaeus were the first people to use the name ‘\textit{Arnica}’ in both pharmacy and botany. In northern Spain, \textit{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 ‘\textit{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.),
Asteraceae Cass. (Conyza bonariensis (L.) Cronquist),
Cardueae Cass. (Centaurea graminatae Boiss. ex DC.),
Cichorieae Lam. & DC. (Andryala integrifolia L., A. raquisina L., Crepis paludosa (L.) Moench, C. vesicaria L. subsp. taraxacifolia (Thuill.) Thell. and Hieracium sp.),
Doronicae Panero (Doronicum carpathelianum Boiss. & Reut. Ex Willk. & Lange, D. grandiflorum Lam. and D. paralichians L.),


Madieae Jeps. (A. montana L.),

Senecioneae Cass. (Senecio dorenicum (L.) L., S. jacobaea L., and S. pyrenicus L.),[3] and the subgenera are Arctica, Andropurpurea, Austromontana, Montana and Chamissonis.[8] The flowers of the plant are traded by the following medicinal names, i.e. Arnica flors (latin), Fleur d’Arnica’ (Fr), Flor de ãarnica’ (Sp), ArnikaBluten (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 secondary bloom.

The best harvesting time for the flowers is July and August with 1 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 papus 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, eterotonic, antirheumatic and analgesic in febrile conditions.[11,12,19] 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 petrolatum 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 parodontopathy and in Mariass et al., US patent No. 4684522, a cosmetic formulation possessing antcellulitis and slandering activity comprising of required content of extracts of various plants such as Hedera haelix L., A. montana L. (containing glycols), Aesculip 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 nicotinate 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, ulmario, algae, a volatile polysiloxane and orthosophin. [17]
Paradise L. in US patent No. 5795573 A has concluded that homeopathic 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 kallkreins, it is desirable to promote healing and improve circulation to tissues nerves. US patent No. 5162037 to Whitson-Fishman discloses a homeopathic 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 semisolids 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, choleric and chologogue 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 homeopathic preparations of the plant are available in the market such as Hyland’s Arnicated hair oil, shampoo, Arnica ointment, Arnica tablets and pellets [6 x, 12 x, 30 x, 30CH, 200CH], Hyland’s Arnica spray as the plant possesses various activities. Bioactive constituents such as sesquiterpene lactones, i.e. helenanin an 11a,13-dihydrohelenalin, 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 bowel ache, cough, contusion, cuts, haematoma, headache and rheumatism. [1]

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. heñalenin,11a,13-dihydroheñalenin and their short-chain carboxylic 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, monoterpens and sesquiterpene. Other constituents of A. montana are carotenoids; diterpenes; arnidiol (a triterpene); pyrrolizidine alkaloids (tussilagine and isotussilagine) [27]; polycatelines; coumarins (umbelliferone and scopoletin); phenolic acids (chlocogenic acid, caffeic acid and cyanarin, 1.0–2.2%) [20]; lignans; dicaffeoyl quinic derivatives (1.3- 3.5 and 4.5 dicaffeoyl quinic acids); and oligosaccharides. [22] It contains sesquiterpene lactones being metacryl, isosobutyryl, tygloyl, methacryloyl, isovaleryl helenanin 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 heñalenin esters and dihydroheñalenin 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] 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]

**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]
Pljevljukis 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, germacrone, pinchotene acetate, p-methoxyheptanophenone, isobornyl 2-methyl butanoate, isobornyl
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 NF-kappaB-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...
investigated for its anti-inflammatory potential on carrageenan 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. 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. 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). It has also been reported by Sandra et al., 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.

Immunomodulatory activity

Polysaccharide fraction of A. montana flowers are reported to show significant immunostimulating properties (increase of phagocytosis by granulocytes). DEAE-Sephrose CL-6B and Sephacryl S-400 column chromatographic techniques were used to isolate two

Figure 6 Flavones of Arnica montana plant.\cite{62}

Figure 7 Terpenes of Arnica montana plant.\cite{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.\textsuperscript{[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-osteoprototic 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-dihydrohele- nalin 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

Helenaalin 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 O2 consumption. Arnica 30cH provides protection against Ca2+ and inorganic phosphate-induced hepatic mitochondrial membrane permeability, lipid peroxidation mediated by Fe2+ 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 antiagulant 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 lactates, i.e. helenalin and 11α-13-dihydro-helenalin, 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-unsatuated 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 sulphhydril 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]

Antihaeorrhagic activity

Stem tincture of A. montana was found to possess antihaeorrhagic 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.
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<th>Authors (years)</th>
<th>Study design control type</th>
<th>Duration of treatment</th>
<th>Study and control drugs</th>
<th>Number of subjects by arms dose; age</th>
<th>Diagnosis inclusion criteria</th>
<th>Exclusion criteria</th>
<th>Efficacy results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Savage et al. (1978)[48]</td>
<td>Double-blind, placebo-controlled</td>
<td>3 months</td>
<td>1 Arnica 3C, one tablet of medicated lactose after every 2 h Placebo: Lactose tablets</td>
<td>40 patients (20 men and 20 women) of 77.2–80.5 years</td>
<td>Acute stroke illness</td>
<td>Not reported</td>
<td>No statistically significant difference in both groups</td>
</tr>
<tr>
<td>Kaziro et al. (1984)[62]</td>
<td>Double-blind trial, placebo-controlled</td>
<td>8 days after removal of teeth</td>
<td>1 Metronidazole (400 mg tablets) 2 Arnica 200 tablets 3 Placebo tablets</td>
<td>118 patients</td>
<td>Patients with impacted mandibular wisdom teeth</td>
<td>Not reported</td>
<td>Metronidazole reduced the pain and enhanced the healing process after surgery. Arnica was even less effective than the placebo</td>
</tr>
<tr>
<td>Albertini and Goldberg et al. (1986)[63]</td>
<td>Randomized placebo-controlled trial</td>
<td></td>
<td>1 Arnica 7c and Hypericum 15c 2 Placebo</td>
<td>30 patients</td>
<td>Dental neuralgic pain after tooth extraction</td>
<td>76% of the patients treated with homoeopathic remedies had pain relief vs 40% of patients receiving placebo</td>
<td></td>
</tr>
<tr>
<td>Dorfman et al. (1988)[64]</td>
<td>Double-blind, placebo-controlled clinical study</td>
<td></td>
<td>1 Arnica 5c</td>
<td>39 patients</td>
<td>Prolonged venous perfusion</td>
<td>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</td>
<td></td>
</tr>
<tr>
<td>Brock et al. (1991)[10]</td>
<td>Double-blinded; placebo-controlled</td>
<td>3 weeks</td>
<td>1 Combination ointment: (100 g contain: 10 g extract from Arnica flowers with sunflower oil (1 + 5) 4000 IU Heparin 5 mg OIl Chamomille 5 mg Guajazulen) 2 Mono-ointment: (100 g contains: 10 g extract from Arnica flowers with sunflower oil (1 + 5)) 3 Placebo ointment base</td>
<td>159 overall; not reported, how many per group; age not reported</td>
<td>Chronic venous insufficiency</td>
<td>No diuretica</td>
<td>Changes were in the combination treatment, but differences were not statistically significant</td>
</tr>
<tr>
<td>Lokken et al. (1995)[65]</td>
<td>Double-blind, placebo-controlled crossover trial</td>
<td></td>
<td>1 Arnica 30D 2 placebo</td>
<td>24</td>
<td>Pain after surgical removal of bilaterally impacted mandibular third molars</td>
<td>No difference in posturgical pain was observed between Arnica and placebo. Postoperative swelling and bleeding were not significantly affected by homoeopathy</td>
<td></td>
</tr>
<tr>
<td>Hart et al. (1997)[66]</td>
<td>Double-blind placebo-controlled</td>
<td>2-3 weeks after operation</td>
<td>1 Arnica C30 2 placebo</td>
<td>93 women</td>
<td>Patients undergoing abdominal hysterectomy Patients with previous chronic pain or undergo operations</td>
<td>Arnica in homoeopathy has no significant effect on postoperative recovery</td>
<td></td>
</tr>
<tr>
<td>Tveiten et al. (1998)[67]</td>
<td>Randomized double-blind</td>
<td>5 days (1 day before marathon running and 3 days after the run)</td>
<td>1 Arnica D30 2 placebo</td>
<td>24 in group A (27–54 years) 22 in group in group B (31–50 years)</td>
<td>Muscle soreness</td>
<td>Not reported</td>
<td>Arnica D30 has positive effect on muscle soreness than placebo but not on cell damage</td>
</tr>
<tr>
<td>Authors (years)</td>
<td>Study design</td>
<td>Duration of treatment</td>
<td>Study and control drugs</td>
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<tr>
<td>Ernst et al. (1998)&lt;sup&gt;[58]&lt;/sup&gt;</td>
<td>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</td>
<td>NA</td>
<td>Pure Arnica formulations</td>
<td>NA</td>
<td>NA</td>
<td>Arnica in combination with other herbs</td>
<td>Homoeopathic Arnica is not efficacious beyond a placebo effect</td>
</tr>
<tr>
<td>Andrew et al. (1998)&lt;sup&gt;[68]&lt;/sup&gt;</td>
<td>Double-blind placebo-controlled trial</td>
<td>2 days after run</td>
<td>1 A homoeopathic medicine (Arnica 30X) 2 placebo</td>
<td>519 runners</td>
<td>Delayed-onset muscle soreness after long-distance races</td>
<td>Not reported</td>
<td>Homoeopathic Arnica 30X is ineffective for muscle soreness</td>
</tr>
<tr>
<td>Baillargean et al. (1998)&lt;sup&gt;[70]&lt;/sup&gt;</td>
<td>Double-blind, double-period, crossover randomized</td>
<td>2 weeks</td>
<td>1 Arnica montana SCH 2 placebo</td>
<td>18 men of 22 - 46 years of age</td>
<td>Healthy subjects</td>
<td>Patients having any coagulation disorder, chronic disease, smoking or on any other medication</td>
<td>Arnica montana has no significant effect on bleeding time in minutes, and no clinical significant difference on other tests of blood coagulation was observed</td>
</tr>
<tr>
<td>Ramelet et al. (2000)&lt;sup&gt;[70]&lt;/sup&gt;</td>
<td>Randomized, prospective, multicentre double-blind trial</td>
<td>1 Arnica 5c 2 placebo</td>
<td>130</td>
<td>Saphenous stripping</td>
<td>No significant difference in postoperative haematomas was observed between Arnica and placebo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brod (2001)&lt;sup&gt;[10]&lt;/sup&gt;</td>
<td>3 weeks</td>
<td>1 100 g Arnica gel (contained 25 g Arnica tincture) 2 placebo</td>
<td>50 per group; 77 women; 23 men; age in average 59.2</td>
<td>Chronic venous insufficiency</td>
<td>Not reported</td>
<td>Statistically significant improvement in both groups; a significant better effect in the verum group</td>
<td></td>
</tr>
<tr>
<td>Alonso et al. (2002)&lt;sup&gt;[71]&lt;/sup&gt;</td>
<td>Double-blinded placebo-controlled</td>
<td>2 weeks, either in pretreatment or post-treatment</td>
<td>1 Arnica gel (A. montana with 45% alcohol, purified water, with hazel, trolamine, gaultherin, EDTA, methyl/propyl paraben) 2 placebo</td>
<td>9 pretreatment, 10 post-treatment; dose not specified; age unknown</td>
<td>Facial telangiectases</td>
<td>Patients on anticoagulant therapy</td>
<td>No statistically significant difference in both groups</td>
</tr>
<tr>
<td>Rosen-zweig et al. (2002)&lt;sup&gt;[71]&lt;/sup&gt;</td>
<td>Double-blinded placebo-controlled</td>
<td>4 weeks</td>
<td>1 Arnica compress (prepared from the whole plant extract, 0.7%) 2 Placebo compress (prepared from water and food colouring)</td>
<td>16 Arnica 14 placebo; one compress; age unknown</td>
<td>Acute soft tissue pain (foot/ankle, knee, neck/shoulder)</td>
<td>Not reported</td>
<td>No statistically significant analgesic benefit compared to placebo one hour after therapy</td>
</tr>
<tr>
<td>Knuesel et al. (2002)&lt;sup&gt;[72]&lt;/sup&gt;</td>
<td>This open multicentre trial</td>
<td>Applied twice daily for 6 weeks</td>
<td>1 Arnica montana fresh plant gel</td>
<td>26 men and 53 women</td>
<td>Mild-to-moderate osteoarthritis (OA) of the knee</td>
<td>Not reported</td>
<td>Arnica gel was found to be effective in treating mild-to-moderate osteoarthritis</td>
</tr>
<tr>
<td>Jeffrey and Belcher (2002)&lt;sup&gt;[73]&lt;/sup&gt;</td>
<td>Randomized-double-blind, placebo-controlled study</td>
<td>1 Arnica 6D tablets 2 Arnica Ointment 3 placebo</td>
<td>37</td>
<td>Hand surgery (endoscopic carpal tunnel release)</td>
<td>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 0.05)</td>
<td>No statistically significant difference in both groups</td>
<td></td>
</tr>
<tr>
<td>Authors (years)</td>
<td>Study design control type</td>
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<td>Diagnosis inclusion criteria: exclusion criteria</td>
<td>Efficacy results</td>
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<tr>
<td>Wolf et al. (2003)[74]</td>
<td>Prospective, randomized, double-blind, placebo- controlled pilot trial</td>
<td>1 Arnica 12D</td>
<td>60</td>
<td>Varicose vein surgery</td>
<td>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.</td>
<td></td>
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<tr>
<td>Stevinson et al. (2003)[75]</td>
<td>Double-blind, placebo-controlled, randomized trial</td>
<td>21 days</td>
<td>64 adults (18–70 years)</td>
<td>Adults undergoing elective surgery for carpal tunnel syndrome</td>
<td>Patients currently taking homeopathic remedies, reported previous hypersensitivity to homeopathy, were taking aspirin, or were unable to complete the study diary or attend follow-up appointments</td>
<td>No statistical differences were found between homeopathic Arnica over placebo in reducing postoperative pain, bruising and swelling in patients.</td>
<td></td>
</tr>
<tr>
<td>Totonchi et al. (2005)[76]</td>
<td>Double-blind placebo-controlled</td>
<td>6 days, resp. 4 days</td>
<td>48 overall, 11 male, 37 female; age from 15 to 65</td>
<td>Primary rhinoplasty with osteotomy</td>
<td>Not reported</td>
<td>Statistically no significance between the groups in ecchymosis; statistically significance in reducing oedema in both groups.</td>
<td></td>
</tr>
<tr>
<td>Oberbaum et al. (2005)[77]</td>
<td>Double-blind, placebo-controlled, randomized, clinical trial</td>
<td>Before delivery and 72 h after delivery</td>
<td>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</td>
<td>Pregnant women</td>
<td>Women with previous Caesarean section, antepartum or postpartum haemorrhage in previous pregnancies, and coagulopathies</td>
<td>Homoeopathic Arnica montana and Bellis perennis may reduce postpartum blood loss, as compared with placebo.</td>
<td></td>
</tr>
<tr>
<td>Leivers (2005)[78]</td>
<td>Double-blind, placebo-controlled, randomized, clinical trial</td>
<td>6 weeks</td>
<td>89 patients</td>
<td>Venous insufficiency</td>
<td>Not reported</td>
<td>There was improvement in venous tone and oedema in patients on Arnica treatment than on placebo.</td>
<td></td>
</tr>
<tr>
<td>Leivers (2005)[78]</td>
<td>Open, multicentre trial</td>
<td>6 weeks</td>
<td>79 patients</td>
<td>Mild-to-moderate knee arthritis</td>
<td>Not reported</td>
<td>Arnica decreased the pain, stiffness of knee and was effective than placebo.</td>
<td></td>
</tr>
<tr>
<td>Authors (years)</td>
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<tr>
<td>Seeley et al. (2006)</td>
<td>Randomized double-blind placebo-controlled study</td>
<td>Arnica (SinEcch)</td>
<td>1</td>
<td>Arnica</td>
<td>29 patients</td>
<td>Rhytidectomy</td>
<td>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).</td>
</tr>
<tr>
<td>Brinkhaus et al. (2006)</td>
<td>Three randomised, placebo-controlled, double-blind, sequential clinical trials</td>
<td>Homoeopathic Arnica</td>
<td>2 (ART), 8 (CLR) or 11 days (ARJ)</td>
<td>Arnica</td>
<td>A total of 227 patients were treated and followed up for 2, 8, or 11 days. Patients receiving homoeopathic arnica showed a less postoperative swelling mainly in CLR trails.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Robertson et al. (2007)</td>
<td>Randomized double-blind, placebo-controlled</td>
<td>Arnica 30c or identical placebo</td>
<td>2 tablets, 6 times in the first postoperative day and then 2 tablets twice a day for the next 7 days</td>
<td>Arnica 30c or identical placebo</td>
<td>190 patients</td>
<td>over the age of 18</td>
<td>Patients under tonsillectomy</td>
</tr>
<tr>
<td>Widrig et al. (2007)</td>
<td>Double-blind</td>
<td>Gel preparations</td>
<td>3 weeks</td>
<td>Gel preparations</td>
<td>204 patients</td>
<td>Osteoarthritis of hands</td>
<td>Preparation of arnica is not inferior to ibuprofen when treating osteoarthritis of hands</td>
</tr>
<tr>
<td>Totonchi and Guyuron et al. (2007)</td>
<td>Randomized double-blind clinical study</td>
<td>Arnica</td>
<td>1</td>
<td>Arnica</td>
<td>48 patients</td>
<td>Rhinoplasty</td>
<td>Arnica and dexamethasone reduced swelling and oedema if compared with control (P, 0.0001). Arnica and control group exhibited more resolution of ecchymosis if compared with dexamethasone (P, 0.06).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Authors (years)</th>
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<th>Efficacy results</th>
</tr>
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<tr>
<td>Paris et al. (2008)</td>
<td>A phase 3 monocentric randomized placebo-controlled study</td>
<td>1 Granule composition containing Arnica 5c, Bryonia alba 5c, Hypericum perforatum 5c and Ruta graveolens 3D</td>
<td>158 patients</td>
<td>Knee ligament reconstruction</td>
<td>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</td>
<td></td>
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</tr>
<tr>
<td>Karow et al. (2008)</td>
<td>Randomized double-blind, parallel-group study</td>
<td>1 Arnica 4D</td>
<td>88 patients</td>
<td>Hallux valgus surgery</td>
<td>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</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adkison et al. (2010)</td>
<td>Randomized, double-blind, placebo-controlled trial</td>
<td>1 Arnica cream</td>
<td>53 patients</td>
<td>Leg pain after calf raises</td>
<td>Arnica increased pain scores if compared with placebo. No difference in muscle tenderness and ankle motion was observed</td>
<td></td>
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<tr>
<td>Cornu et al. (2010)</td>
<td>Double-blind placebo-controlled parallel trial</td>
<td>1 A combination of Arnica montana 5c and Bryonia alba 5c granules</td>
<td>90 patients</td>
<td>Aortic valve surgery</td>
<td>No difference between homoeopathic treatment and placebo on bleeding, C-reactive protein, troponin I and cumulated morphine was observed</td>
<td></td>
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<tr>
<td>Leu et al. (2010)</td>
<td>Randomized, double-blind placebo-controlled trial</td>
<td>1 5% vitamin K</td>
<td>16 patients</td>
<td>595-nm pulsed-dye laser-induced bruises on the bilateral upper inner arms</td>
<td>The mean improvement in bruising associated with 20% Arnica was greater than with white petrolatum (P = 0.003), and the mixture of 1% vitamin K and 0.3% retinol (P = 0.01) while improvement with Arnica was not greater than with 5% vitamin K cream</td>
<td></td>
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</tr>
<tr>
<td>Huber et al. (2011)</td>
<td>Single-blind, randomized</td>
<td>30 days</td>
<td>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</td>
<td>Two healthy male subjects (Caucasian, age 33 and 47 years, body mass index 24 and 23 kg/m²)</td>
<td>Erbium YAG-Laser-induced burns</td>
<td>Not reported</td>
<td>Combudoron seems to have positive effects on healing of grade 2 laser-induced burns</td>
</tr>
<tr>
<td>Authors (years)</td>
<td>Study design control type</td>
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<tr>
<td>Kucera et al. (2011)[86]</td>
<td>Double-blind placebo-controlled study</td>
<td>10 days</td>
<td>1 Combination of Arnica tincture and HES (spray) 2 Arnica or HES or placebo</td>
<td>570 patients</td>
<td></td>
<td>Acute ankle joint distortion</td>
<td>Patients with fractures or complete tears of ligaments, sports professionals and pregnant women</td>
</tr>
<tr>
<td>Goedemans et al. (2014)[87]</td>
<td>12 months</td>
<td>1 Arnica cream</td>
<td>2 mucopolysaccharide polysulfuric acid</td>
<td>40 patients</td>
<td></td>
<td>Pain and bruising following postneedling infiltration</td>
<td>There were no significant differences in the effects of Arnica and hirudoid on pain and bruising</td>
</tr>
<tr>
<td>Clinical trials.gov (2016)[88]</td>
<td>Double-blind, placebo-controlled</td>
<td>4 days</td>
<td>1 Arnica montana 2 Placebo</td>
<td>28 subjects of 18–89 years of age</td>
<td></td>
<td>Candidates for rhinoplasty surgery at UW Transformations, Ecchymosis</td>
<td>Patients who are prisons, pregnant and breastfeeding women, taking anticoagulants (such as blood thinners), antiplatelet drugs (such as NSAIDS), oral corticosteroid or other homeopathic remedies during the peri-operative period</td>
</tr>
<tr>
<td>Mariani et al. (2009)[89]</td>
<td>Not reported</td>
<td>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</td>
<td>Arnica planta tota Rh D3</td>
<td>30 patients (age 50–87)</td>
<td>Low back pain</td>
<td>Patients with other pathologies</td>
<td>Patients improved during acute treatment with no side effect</td>
</tr>
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Table 1 (Continued)
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.

References


6. Erbar C, Leins P. Diversity of styles and mechanisms of secondary pollen

<table>
<thead>
<tr>
<th>Author(s), (year)</th>
<th>Formulation</th>
<th>Pathology</th>
<th>Side effect profile</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hausen <em>et al.</em> (1985)</td>
<td>Body lotion containing extracts of <em>Arnica</em></td>
<td>Skin lesions</td>
<td>Allergic contact dermatitis of the face and hands</td>
<td>NS</td>
</tr>
<tr>
<td>Leeuw <em>et al.</em> (1987)</td>
<td>Jogging cream, a multicomposition with 32 constituents, one of them <em>Arnica</em></td>
<td>Dermalitis</td>
<td></td>
<td></td>
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<tr>
<td>Delmonte <em>et al.</em> (1998)</td>
<td>A cream containing 1.5% <em>Arnica</em></td>
<td>Enlarging necrotic lesions of the face and left leg, together with malaise and high fever</td>
<td>Sweet’s Syndrome, often correlated with leukaemia</td>
<td></td>
</tr>
<tr>
<td>Knuesel <em>et al.</em> (2002)</td>
<td>Gel (topical application)</td>
<td>Knee osteoarthritis</td>
<td>One allergic reaction (not specified)</td>
<td>NS</td>
</tr>
<tr>
<td>Widrig <em>et al.</em> (2007)</td>
<td>Gel (topical application)</td>
<td>Hand osteoarthritis</td>
<td>Skin irritations Itching Reddening Allergic eczema Increased finger pain Bronchitis Chill Cystitis Rhinitis Vertigo</td>
<td>NS</td>
</tr>
<tr>
<td>Cornu <em>et al.</em> (2010)</td>
<td>Granules (oral treatment)</td>
<td>Aortic valve surgery</td>
<td>Cardiovascular events (observed in both homoeopathy and placebo groups)</td>
<td><em>Arnica</em> 5c and <em>Bryonia alba</em> 5c</td>
</tr>
</tbody>
</table>


36. Kawakami AP et al. Inflammatory process modulation by homeopathic...
51. Keeney JA. Compositions for stimulating hair growth, preventing hair loss, or minimizing hair loss, and methods for preparing and using same. 2000 Patent No. US 6103272 A.
72. Seeley BM et al. Effect of homeopathic *Arnica montana* on bruising in face-lifts: results of a randomized, double-blind, placebo-controlled clinical


