

# WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Research Article
ISSN 2455-3301

SJIF Impact Factor: 4.103

WJPMR

# ETHNOBOTANICAL, PHYTOCHEMICAL, PHARMACOLOGICAL AND HOMOEOPATHIC REVIEW OF ARNICA MONTANA LINN

#### Dr. Tushita Thakur\*

B.H.M.S., MD (HOM.), Consultant Homoeopathy AYUSH Wellness Clinic, President's Estate, New Delhi, India.

\*Corresponding Author: Dr. Tushita Thakur

B.H.M.S., MD (HOM.), Consultant Homoeopathy, AYUSH Wellness Clinic, President's Estate, New Delhi, India.

Article Received on 23/04/2017

Article Revised on 14/05/2017

Article Accepted on 04/06/2017

#### **ABSTRACT**

Arnica Montana is a popular traditional remedy used in folk medicine and Homoeopathy to alleviate pain, inflammation and swelling of muscles and joints associated with rheumatoid arthritis and other inflammatory conditions. It a high-altitude perennial plant that belongs to Asteraceae (Compositae) family and is native to the mountain slopes in Europe, northern Asia, Siberia, Canada and America. This review was conducted to summarize the available scientific information obtained from literature, medical databases, laboratory studies and human clinical studies on Arnica Montana Linn. Arnica Montana Linn. contains essential oil, fatty acids, thymol, pseudoguaianolide, sesquiterpene lactones (helenalin, 11α, 13-dihydrohelenalin and their fatty acid esters) and flavonoid glycosides (spinacetin, hispidulin, patuletin and isorhamnetin). The anti arthritic efficiency of Arnica Montana is attributed to a synergism of phenolic and flavonoid compounds. The analgesic and anti-inflammatory property of Arnica Monatana has been attributed at Helenalin. Helenalin also has anti-tumour activity against a variety of chemically induced tumours. It has been pharmacologically proven for arthritis, anti-inflammatory, analgesic, anti-oxidant, wound healing and post operative healing properties. The homoeopathic preparations of Arnica Montana have been pharmacologically proven beneficial for arthritis, anti-inflammatory action, anti-haemorrhagic action, wound healing, post operative healing, cellulitis and furunculosis.

**KEYWORDS:** Arnica Montana, Ethnobotany, Homoeopathy, Pharmacology, Phytochemistry.

## INTRODUCTION

Arnica Montana is a popular traditional remedy used in folk medicine and Homoeopathy to alleviate pain, inflammation and swelling of muscles and joints associated with rheumatoid arthritis and other inflammatory conditions. [1]

Arnica Montana belongs to Asteraceae (Compositae), the largest family of flowering plants with its approximately 1,620 genera and more than 23,600 species. Asteraceae has especially diverse distribution in the tropical and subtropical regions of North America, the Andes, eastern Brazil, southern Africa, the Mediterranean region, central Asia, and southwestern China. While majority of Asteraceae species are herbaceous, an important component of the family is also constituted by shrubs and trees<sup>2</sup>. The family contains several species that are important sources of medicinal plants (Arnica, Artemisia, Achillea Millifolium, Calendula, Chamomile, Echinacea, Taraxacum, Solidago), ornamental plants (Aster, Calendula, Chrysanthemum, Dahlia, Sunflower, Zinnia) and Food (Artichokes, Chicory, Lettuce). Insecticides pyrethins are made from Chrysanthemums. [3]

Taxonomv<sup>[4]</sup>

Kingdom - Plantae

Division - Tracheophyta

Subdivision - Spermatophytina

Class - Magnoliopsida

Order - Asterales

Family - Asteraceae (Compositae)

Genus - Arnica L.

Species - Arnica montana L.
Botanical name - Arnica montana Linn.

## Vernaculur Names<sup>[5,6]</sup>

English: Celtic Nard, Leopard's Bane, European

Arnica, Mountain Arnica, Mountain Tobacco

Danish : Guldblomme Finnish : Etelänarnikki French : Arnique

German: Arnika, Berg-Wohlverleih

Swedish: Etelänarnikki, Slåttergubbe, Slåttergubbe

## **Habit and Habitat**

Arnica is a high-altitude perennial plant native to the mountain slopes in Europe, northern Asia, Siberia, Canada and America. [1,7]

#### **Botanical Discription**

Arnica Montana L. is a perennial herb, 20-50 cm high. Aerial portion consists of a basal rosette of entire oblanceolate leaves up to 17 cm long, five to seven veins, from the centre of which projects an erect, simple, glandular hairy stem up to 0.6 m high. Stem bears two to four pairs of cauline leaves, ovate, elliptic-oblong, lanceolate or oblanceolate, with rounded or roundedtoothed apex and clothed with numerous non-glandular and glandular hairs, up to 16 cm long and 5 cm wide. Peduncles are one to three, bearing alternate bracteoles, extending from the uppermost pair of cauline leaves; glandular-puberulent each terminating hemispherical or turbinate capitulum bearing orangevellow flowers, which are tubular. Tubular floret has a regular, 5 toothed, yellow, tubular corollas about 7 to 8 mm long; 5 epipetalous stamens with syngenesious anthers; pappus and ovary as in ligulate florets. Fruits, black to brown, five-ribbed, with a bristle tuft of hairs. The drug as a whole has a faint, but rather agreeable apple like odour and bitter, acrid taste. Flowers too have a pleasant sweet and aromatic odour and bitter, acrid taste.[6,8]

#### **Ethnobotany**

Arnica Montana has been extensively used as a remedy to heal wounds, reduce inflammation and soothe muscle aches by Europeans and Native North American Indians for centuries. Arnica is also used as an external application in arthritis, bruises, sprains and swellings; and as a footbath for tender feet. [9] It is one of the natural remedies most often used for rheumatologic conditions. [10] It is also used as a topical counterirritant for treatment of pain and inflammation resulting from minor injuries, bruises, ecchymoses, haematomas and petechiae. [11]

#### **Phytochemical Properties**

The major constituents of Arnica Montana Linn. include the essential oil (0.5%), fatty acids (content not specified), thymol (content not specified), pseudoguaianolide, sesquiterpene lactones (0.2–0.8%) and flavonoid glycosides (0.2–0.6%). The primary sesquiterpene lactones are helenalin,  $11\alpha$ , 13-dihydrohelenalin and their fatty acid esters. Flavonoids include glycosides and/or glucuronides of spinacetin, hispidulin, patuletin and isorhamnetin, among others. [1]

# Experimental Pharmacology Arthritis

A study conducted in Centre for Interdisciplinary Research in Basic Sciences, Jamia Millia Islamia, New Delhi and Oncology Lab, AIIMS, New Delhi that investigated Arnica Montana flower methanol extract against inflammation and oxidative stress in a collageninduced arthritis (CIA) rat model concluded that oral administration of Arnica Montana flower methanol extract reduced clinical signs and improve the histological and radiological status of the OA in hind limb joints in rats. Treated rats had lower expression

levels of nitric oxide, tumor necrosis factor- $\alpha$ , interleukins (IL-1 $\beta$ , IL-6 and IL-12) and titer of anti-type II collagen antibody compared with untreated CIA rats. Furthermore, by inhibiting these mediators Arnica Montana flower methanol extract also contributed towards the reversal of disturbed antioxidant levels and per-oxidative damage. The anti arthritic efficiency of Arnica Montana is attributed to a synergism of phenolic and flavonoid compounds, the dominant active principles, detected in a methanol extract, which was found efficient on a collagen-induced arthritis (CIA) rat model. [12]

#### Analgesic and anti-inflammatory activity

The analgesic and anti-inflammatory property of Arnica attributed Monatana has been at Helenalin. Intraperitoneal administration of 2.5-5.0 mg/kg bw of helenalin significantly (P < 0.001) inhibited carrageenaninduced hind paw oedema in rats by 77% after 72 hours. Intraperitoneal administration of 20.0 mg/kg bw of helenalin strongly inhibited acetic acid-induced writhing by 93% in mice but did not have analgesic effects in mice in the hot-plate test. Intraperitoneal administration of 2.5 mg/kg bw of helenalin to rats inhibited arthritis induced by Mycobacterium butyricum by 87%.[13] In vitro, helenalin, 5.0 µmol/l, significantly (P < 0.01) suppressed the activity of prostaglandin synthetase in and rat homogenates, and mouse human polymorphonuclear neutrophils, indicating an anti-inflamatory effect. [14]

#### **Antioxidant activity**

Arnica Montana ethanolic extracts were evaluated for their chemical composition, antioxidant activity and protective effect against hydrogen peroxide-induced oxidative stress in a mouse fibroblast-like NCTC cell line at Department of Cellular and Molecular Biology, NIRDBS, Romania. This study reported that Arnica Montana extracts are rich in flavonoids and phenolic acids, showed a good antioxidant activity and cytoprotective effect against oxidative damage in fibroblast-like cells. These results provide scientific support for the traditional use of Arnica Montana in treatment of skin wounds, bruises and contusions. [15]

### Anti-tumour activity

Helenalin (a primary sesquiterpene lactone in Arnica) is cytotoxic to a wide variety of cancer cell lines in vitro, with a median effective dose (ED50) range of 0.03–1.0  $\mu$ g/ml (24–27). Intraperitoneal administration of 1.5–33.3 mg/kg by weight of helenalin to mice and rats had anti-tumour activity against a variety of chemically induced tumours. [16,17]

#### Wound healing

The molecular aspects of wound healing properties of Arnica Montana were evaluated in a laboratory study at University of Verona and University of Bologna, Italy to elucidate This study evaluated the whole plant extract, in a wide range of dilutions, in THP-1 human cells,

differentiated into mature macrophages and into an alternative IL-4-activated phenotype involved in tissue remodelling and healing. Arnica montana affected the expression of several genes on macrophages differentiated towards the wound healing phenotype. CXC chemokine ligand 1 (CXCL1), coding for an chief chemokine, exhibited the most consistent increase of expression, while also CXC chemokine ligand 2 (CXCL2), Interleukin8 (IL8) and bone morphogenetic protein (BMP2) were slightly up-regulated, suggesting a positive influence of A. montana on neutrophil recruitment and on angiogenesis. This exploratory study concluded that Arnica montana is a promoter of healing, since some of the genes it modifies are key regulators of tissue remodelling, inflammation and chemotaxis. [18]

#### Clinical Pharmacology Arthritis

An open multicenter trial of Arnica Montana gel in OA knee was conducted in the Department of Rheumatology, Valens Clinic for Rheumatism, Switzerland to investigate the safety and efficacy of an Arnica Montana fresh plant gel, applied twice daily, in 26 men and 53 women with mild to moderate osteoarthritis (OA) of the knee. After 3 and 6 weeks, significant decreases in median total scores on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) were evident in the intention-to-treat and per-protocol populations (both P < .0001). Scores on the pain, stiffness, and function subscales also showed significant reduction. The overall local adverse-event rate of 7.6% included only one allergic reaction. The patient reported tolerability of the gel as "good" or "fairly good was 87% and and 76% of the patients said they would use it again. Topical application of Arnica montana gel for 6 weeks was a safe, well-tolerated, and effective treatment of mild to moderate OA of the knee. [19]

A double-blind study on 204 patients comparing Arnica Montana with Ibuprofen in topical applications for hand OA found no difference in terms of efficiency and side effects were less frequent for Arnica.<sup>[20]</sup>

The equipotency of Arnica with NSAID in the local treatment of hand OA was acknowledged by a Cochrane review. [21]

#### Muscle pain and muscle damage

Twenty well-trained males matched by maximal oxygen uptake (VO2 Max) completed a double-blind, randomised placebo-controlled trial to test the efficacy of topical Arnica in reducing pain, indicators of inflammation and muscle damage, and in turn improve performance in well-trained males experiencing delayed onset muscle soreness (DOMS). Topical Arnica was applied to the skin superficial to the quadriceps and gastrocnemius muscles immediately after a downhill running protocol designed to induce DOMS and reapplied every 4 waking hours for the duration of the study. Performance measures (peak torque,

countermovement and squat jump), pain assessments (visual analogue scale (VAS) and muscle tenderness) and blood analysis (interleukin-1 beta, interleukin-6, tumour necrosis factor-alpha, C-reactive protein, myoglobin and creatine kinase) were assessed at seven time points over five days (pre-, post-, 4, 24, 48, 72 and 96 hours after the downhill run). Participants in the topical Arnica group reported less pain as assessed through muscle tenderness and VAS 72 hours post-exercise. The application of topical Arnica did not affect any performance assessments or markers of muscle damage or inflammation. [22]

#### **Post-operative healing**

A review of clinical trials done to evaluate prevention and/or treatment of post-procedure ecchymosis or edema with oral arnica and topical arnica reported improvement post-procedure with arnica (4/13) in randomised control trials. It however concluded that there is insufficient data to support use of arnica for post procedure and recommend additional research to determine its efficacy and safety. [23]

A review of Effectiveness and Safety of Arnica montana in post-surgical setting, pain and inflammation concluded that it is more effective than placebo and may represent a valid alternative to non-steroidal anti-inflammatory drugs, at least when treating some specific conditions. [24]

A systematic review with meta-analysis retrieved for 11 trials with a total of 627 patients was done in the College of Medicine, Korea in the year 2017. This study concluded that the occurrence of periorbital edema and ecchymosis that usually occurs after surgical operation of Rhinoplasty was statistically decreased in the arnica administration groups versus the control group during the first 7 days postoperatively. [25]

# Homoeopathic Experimental Pharmacology Anti-inflammatory

The anti-inflammatory effect of Arnica montana 6CH was evaluated using acute and chronic inflammation models. In the acute, model, carrageenin-induced rat paw oedema, the group treated with Arnica montana 6cH showed 30% inhibition compared to control (P < 0.05). In the chronic model, Nystatin-induced oedema, the group treated 3 days previously with Arnica montana 6cH had reduced inflammation 6 h after the inflammatory agent was applied (P < 0.05). In a model based on histamine-induced increase of vascular permeability, pretreatment with Arnica montana 6cH blocked the action of histamine in increasing vascular permeability. [26]

#### Cerebral Ischemia

Homeopathic drugs were studied in the middle cerebral ischemia occlusion (MCAO) model of rat at Jamia Hamdard, New Delhi. The content of antioxidants, thiobarbituric acid reactive substances (TBARS) was elevated significantly whereas the level of reduced

glutathione (GSH) was depleted significantly in the MCAO of rats as compared to the sham group. The rats pretreated with C200 potency once daily for 5 days orally (1 drop or 21 µl) and post treated after 24 hr of MCAO with C30 potency 3 times a day for 5 days orally (1 drop or 21 µl) of Crotalus, Phosphorus, Arnica and Crocus. The pre and post treated potencies of C200 and C30 respectively has protected the activities of these enzymes significantly when compared with the animals of MCAO group. The study has shown that the Homeopathic drugs have protected most of the studied parameters significantly but further studies are required to comments on the mechanism and reproducibility of Homeopathic drugs. [27]

#### Wound healing

An animal model study concluded that Homoeopathic medicines- Arnica and Staphysagria have a significant role in wound healing and cicatrization process. [28]

#### Homoeopathic Clinical Pharmacology Arthritis

A multi-centric observational study carried out by Central Council for Research was conducted between the years 1984-2005 to identify a group of most effective homoeopathic medicines in osteoarthritis. A total of 1049 out of 1323 osteoarthritis patients enrolled were followed up regularly. Homoeopathic similimum was prescribed after detailed case taking. Arnica (n=10) was among the most effective medicines. Others included were Arsenicum album (n=10), Bryonia alba (n=86), Calcarea carbonica (n=92), Calcarea fluoricum (n=15), Causticum (n=8), Graphites (n=15), Lycopodium clavatum (n=168), Medorrhinum (n=21), Natrum mur. (n=11), Pulsatilla (n=26), Rhus toxicodendron (n=279) and Sulphur (n=83). [29]

#### **Anti-haemorrhagic activity**

The preliminary results of a randomised, double-blind, placebo-controlled study concluded that stem tincture of Arnica Montana was found to possess anti-haemorrhagic activity in women of age group 20–35 years, which reduced postpartum blood loss. [30]

#### Cellulitis

A case reported of a 55-year-old female patient with pain in the right hand and numbness in the fourth finger after cellulitis in the palmar area which was treated with antibiotics, but pain symptoms remained at 7 points on a 0-to-10-point visual analog scale (VAS) for pain despite intake of oral ibuprofen. Ten arnica patches (3X dilution according to the Homeopathic Pharmacopoeia of the United States) were dispensed to the patient and applied at night. A substantial decrease in pain symptoms (VAS = 1) and a marked decrease in numbness was reported after 3 days. This case report concluded that Arnica patch on the hand provided a marked reduction of pain and recovery of functionality of the hand and may thus represent an alternative NSAIDS. [31]

#### **Furunculosis**

A prospective, multicentre observational study was conducted on furunculosis with nine predefined trial medicines. 539 patients were enrolled of which 397 patients completed regular follow up. Predefined trial medicines were Arnica montana, Arsenicum album, Antimonium crudum, Berberis, Calcarea carbonica, Calcarea phosphoric, Echinacea, Hepar sulphuris, Sulphur and these were prescribed as individualization on holistic principles of homoeopathy. A furunculosis symptom score (FSS) was designed to assess the severity of illness. There was significant difference in the mean total FSS between baseline and end of the treatment favouring homoeopathic care. The results were found to be statistically significant (p < 0.05) with all nine predefined trial medicines. [32]

#### **Post-operative healing**

To assess whether Arnica administration affects recovery from hand surgery a double-blind, randomized comparison of oral and topical Arnica administration versus placebo was done for 37 patients undergoing bilateral endoscopic carpal-tunnel release between June 1998 and January 2000 in the Department of Plastic Surgery of Queen Victoria Hospital in West Sussex, England. Homeopathic Arnica tablets and herbal Arnica ointment compared to placebos. No difference in grip strength or wrist circumference was found between the 2 groups. However, there was a significant reduction in pain experienced after 2 weeks in the Arnica-treated group (P<.03). [33]

Twenty-nine patients undergoing face-lift surgery at a tertiary care center were treated perioperatively with either homeopathic Arnica Montana or placebo in a double-blind fashion. Postoperative photographs were analyzed using a novel computer model for color changes, and subjective assessments of postoperative ecchymosis were obtained. Patients taking perioperative homeopathic A. montana exhibited less ecchymosis, and that difference was statistically significant (P<.05) on 2 of the 4 postoperative data points evaluated. [34]

A prospective, placebo-controlled, double-blind study in which patients were randomly assigned to the administration of homeopathic Arnica Montana or placebo concurrent with unilateral upper eyelid blepharoplasty followed by contralateral treatment at least 1 month later reported no statistically significant difference in area of ecchymosis or rank order of ecchymosis severity for days 3 and 7 after treatment. [35]

A prospective randomized double-blind study was conducted to compare the effect of oral perioperative Arnica Montana homoeopathic preparation (AMHP) with placebo among patients scheduled for rhinoplasty surgery with nasal bone osteotomy by a single surgeon. Ecchymosis was measured in digital "three-quarter"-view photographs at 3 postoperative time points. Each bruise was outlined with Adobe Photoshop and change in

intensity was calculated. Compared with 13 subjects receiving placebo, 9 taking AMHP had a statistically significant difference in ecchymosis on day 7 (P = 0.097). Color change showed a statistically significant difference on day 9/10 (P = 0.074). The study concluded that Arnica montana accelerated postoperative healing, with quicker resolution of the extent and the intensity of ecchymosis.  $^{[36]}$ 

#### **Homoeopathic Uses**

In Homoeopathy, the whole plant of Arnica Montana is used for medicinal purposes. The Mother Tincture is prepared according to old method, class III of mother tincture preparation and has drug strength 1/10 (Arnica Montana in coarse powder 100 g, purified water 400 ml and strong alcohol 635 ml to make one thousand millilitres of the Mother Tincture). 2Xpotency contains one part tincture, three parts purified water and six parts strong alcohol. 3X and higher potencies are prepared with dispensing alcohol. [6]

The standard Homoeopathic Materia Medicae describe that Arnica Montana is suited to cases when any injury, however remote, seems to have caused the present trouble. It is useful after traumatic injuries with blunt objects, a muscular tonic for complaints from overuse of any organ, muscular sprains and compound fractures. It is useful in stupor from concussion with involuntary faeces and urine. Useful in conjunctival or retinal haemorrhage form injuries or cough. Venous stasis; patient complains of ecchymosed skin as from bruises. There is tendency to haemorrhage, low-grade fever, tissue degeneration, septic conditions and abscesses that do not mature. Arnica controls haemorrhage, prevents suppuration and aids absorption. Arnica is useful in traumatism of grief, remorse or sudden financial loss. The patient is nervous, cannot bear pain; whole body over-sensitive. In gout and rheumatism patient has fear of being touched or struck by persons coming near him. Cannot walk erect on account of a bruised sort of feeling in the pelvic region. Sore, lame, bruised feeling all through the body, as if beaten. Uneasiness in the painful parts; has to change position often, every place seems too hard. There is tendency to small, painful boils, one after another that are extremely sore. Constipation with loaded rectum, faeces will not come away; ribbon like stools from enlarged prostrate or retroverted uterus. Soreness of parts and/ or retention or incontinence of urine after labour; prevents post-partum haemorrhage and puerperal complications. The patient is worse from least touch; motion; rest; wine; damp cold; and better by lying down, or with head low.[37,38,39]

#### **CONCLUSION**

Arnica Montana Linn. is an important medicinal plant in used in Homoeopathy. In recent years, Arnica Montana has received much attention and its medicinal virtues have been evaluated on modern scientific lines such as phytochemical analysis, pharmacological screening and clinical trials. Its anti arthritic efficiency is attributed to a

synergism of phenolic and flavonoid compounds. The analgesic and anti-inflammatory property is attributed at Helenalin. Helenalin also has anti-tumour activity against a variety of chemically induced tumours. The important pharmacological properties of this medicinal plant include arthritis, anti-inflammatory, analgesic, anti-oxidant, wound healing and post operative healing. The homoeopathic preparations of Arnica Montana have been pharmacologically proven beneficial for arthritis, anti-inflammatory action, anti-haemorrhagic action, wound healing, post operative healing, cellulitis and furunculosis.

#### REFERENCES

- WHO Monographs of Selected Medicinal Plants, Volume 3. World Health Organisation. Geneva, 2007.
- Encyclopedia of life database. Available at http://eol.org/pages/4206/details. Accessed on, 19/05/17.
- 3. Faculty of University of Naveda. Available at https://faculty.unlv.edu/landau/asteraceae.htm Accessed on 19/05/17.
- 4. ITIS Report. Available at https://www.itis.gov/servlet/SingleRpt/SingleRpt?se arch\_topic=TSNandsearch\_value=505925#null. Accessed on 19/05/17.
- 5. Global biodiversity information database. Available at http://www.gbif.org/species/5405976/vernaculars. Accessed on 25/05/17.
- 6. Homoeopathic Pharmacopoeia of India. Combined volume I to V. Government of India, 102-103.
- 7. Obon C et al. Arnica: a multivariate analysis of the botany and ethnopharmacology of a medicinal plant complex in the Iberian Peninsula and the Balearic Islands. J Ethanopharmacol, 2012; 144: 44–56.
- 8. Physician's des reference for her al medicine. Montvale, NJ, Medical Economics Co., 1998.
- Sharma S., Arif M., Nirala R.K., Gupta R., Thakur S.C. Cumulative therapeutic effects of phytochemicals in Arnica montana flower extract alleviated collagen-induced arthritis: Inhibition of both pro-inflammatory mediators and oxidative stress. J. Sci. Food Agric, 2016; 96: 1500–1510.
- 10. Álvarez-Hernández E., César Casasola-Vargas J., Lino-Pérez L., Burgos-Vargas R., Vázquez-Mellado J. Frecuencia de uso de medicinas complementarias y alternativas en sujetos que acuden por primera vez al servicio de reumatología. Análisis de 800 casos. Reumatol. Clín, 2006; 2: 183–189.
- 11. British herbal pharmacopoeia. Exeter, British Herbal Medicine Association, 1996.
- 12. Sharma S, Arif M, Nirala RK, Gupta R, Thakur SC. Cumulative therapeutic effects of phytochemicals in Arnica montana flower extract alleviated collageninduced arthritis: inhibition of both proinflammatory mediators and oxidative stress. J Sci Food Agric, 2016 Mar 30; 96(5): 1500-10.
- 13. Hall IH et al. Anti-infl ammatory activity of sesquiterpene lactones and related compounds.

- Journal of Pharmaceutical Sciences, 1979; 68: 537–542
- 14. Lyss G et al. Helenalin, an anti-inflammatory sesquiterpene lactone from Arnica, selectively inhibits transcription factor NF-κβ. Biological Chemistry, 1997; 378: 951–961.
- 15. Craciunescu O, Constantin D, Gaspar A, Toma L, Utoiu E, Moldovan L. Evaluation of antioxidant and cytoprotective activities of Arnica montana L. and Artemisia absinthium L. ethanolic extracts. Chem Cent J., 2012 Sep 9; 6(1): 97.
- 16. Woerdenbag HJ et al. Cytotoxicity of flavonoids and sesquiterpene lactones from Arnica species. Planta Medica, 1993; 59(Suppl.): A681.
- 17. Beekman AC et al. Structure–cytotoxicity relationships of some helenanolide-type sesquiterpene lactones. Journal of Natural Products, 1997; 60: 252–257.
- 18. Olioso D, Marzotto M, Bonafini C, Brizzi M, Bellavite P. Arnica montana effects on gene expression in a human macrophage cell line. Evaluation by quantitative Real-Time PCR. Homeopathy, 2016 May; 105(2): 131-47.
- Knuesel O, Weber M, Suter A. Arnica montana gel in osteoarthritis of the knee: an open, multicenter clinical trial. Adv Ther, 2002 Sep-Oct; 19(5): 209-18.
- 20. Widrig R., Suter A., Saller R., Melzer J. Choosing between NSAID and Arnica for topical treatment of hand osteoarthritis in a randomised, double-blind study. Rheumatol. Int, 2007; 27: 585–591.
- Cameron M., Chrubasik S. Topical herbal therapies for treating osteoarthritis. CDSR, 2013; 2013: CD010538.
- 22. Pumpa KL, Fallon KE, Bensoussan A, Papalia S. The effects of topical Arnica on performance, pain and muscle damage after intense eccentric exercise. Eur J Sport Sci, 2014; 14(3): 294-300.
- 23. Ho D, Jagdeo J, Waldorf HA. Is There a Role for Arnica and Bromelain in Prevention of Post-Procedure Ecchymosis or Edema? A Systematic Review of the Literature. Dermatologic surgery, 2016 April; 42(4): 445-63.
- Iannitti T, Morales-Medina JC, Bellavite P, Rottigni V, Palmieri B. Effectiveness and Safety of Arnica montana in Post-Surgical Setting, Pain and Inflammation. Am J Ther, 2016 Jan-Feb; 23(1): e184-97.
- Lee HS, Yoon HY, Hwang SH. The effectiveness of postoperative intervention in patients after rhinoplasty: a meta-analysis. European archives of oto-rhino-laryngology, 2017 Mar 17. doi: 10.1007/s00405-017-4535-6.
- Macêdo SB, Ferreira LR, Perazzo FF, Carvalho JC. Anti-inflammatory activity of Arnica montana 6cH: preclinical study in animals. Homeopathy, 2004 Apr; 93(2): 84-7.
- 27. Khuwaja G et al. Protective role of homoeopathic medicines on cerebral ischaemia in animals. Available

- http://www.sciencedirect.com/science/article/pii/S14 75491615001289. Assessed on 20.05.17.
- 28. Alecu A, Alecu M, Mãrcus G. Effect of the homoeopathic remedies Arnica montana and Staphysagria on the time of healing of surgical wounds. Cultura Homeopática, 2007; 20: 19-21.
- CCRH completed studies. Available at http://www.ccrhindia.org/abstracts/cr/osteodisease.h tm. Assessed on, 20.05.17.
- 30. Oberbaum M et al. The effect of the homeopathic remedies Arnica mon-tana and Bellis perennis on mild post-partum bleeding a randomized, doubleblind, placebo-controlled study– preliminary results. Complement Ther Med, 2005; 13: 87–90.
- 31. Barkey E, Kaszkin-Bettag M. A Homeopathic Arnica Patch for the Relief of Cellulitis-derived Pain and Numbness in the Hand. Glob Adv Health Med, 2012 May; 1(2): 18-20.
- 32. Nayak C et al. A Prospective Multicenter Observational Study to evolve the usefulness of the nine predefined homoeopathic medicines in Furunculosis. Indian Journal of Research in Homoeopathy, January-March 2010; 4(1).
- 33. 23. Jeffrey SL, Belcher HJ. Use of Arnica to relieve pain after carpal-tunnel release surgery. Altern Ther Health Med, 2002 Mar-Apr; 8(2): 66-8.
- 34. Seeley BM, Denton AB, Ahn MS, Maas CS. Effect of homeopathic Arnica montana on bruising in facelifts: results of a randomized, double-blind, placebocontrolled clinical trial. Arch Facial Plast Surg, 2006 Jan-Feb; 8(1): 54-9.
- 35. Kotlus BS, Heringer DM, Dryden RM. Evaluation of homeopathic Arnica montana for ecchymosis after upper blepharoplasty: a placebo-controlled, randomized, double-blind study. Ophthal Plast Reconstr Surg, 2010 Nov-Dec; 26(6): 395-7.
- 36. Chaiet SR, Marcus BC. Perioperative Arnica montana for Reduction of Ecchymosis in Rhinoplasty Surgery. Ann Plast Surg, 2016 May; 76(5): 477-82.
- 37. Allen H C. Allen's Keynotes Rearranged and Classified with Leading Remedies of the Materia. B. Jain Publishers (P) Ltd, New Delhi, 2002; 42-44.
- 38. Nash E B. Leaders in Homoeopathic Therapeutics. B. Jain Publishers (P) Ltd, New Delhi, 2013; 386-390
- 39. Boericke W. Boericke's New Manual of Homeopathic Materia Medica with Repertory: third revised and augmented edition based on ninth edition. B. Jain Publishers (P) Ltd, New Delhi, 2010; 76-79.