Effectiveness and Safety of *Arnica montana* in Post-Surgical Setting, Pain and Inflammation

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*Arnica montana* has been widely used as a homeopathic remedy for the treatment of several inflammatory conditions in pain management and postoperative settings. This review gives an overview of the therapeutic use of *Arnica montana* in the above-mentioned fields also focusing on its mechanisms of action learned from animal models and *in vitro* studies. *Arnica montana* is more effective than placebo when used for the treatment of several conditions including post-traumatic and postoperative pain, edema, and ecchymosis. However, its dosages and preparations used have produced substantial differences in the clinical outcome. Cumulative evidence suggests that *Arnica montana* may represent a valid alternative to non-steroidal anti-inflammatory drugs, at least when treating some specific conditions.

**Keywords:** *Arnica montana*, homeopathy, herbal medicine, side effect profile, inflammation, pain, surgery, trauma, ecchymosis, edema

INTRODUCTION

The use of complementary therapies, including plant remedies, is widespread and rapidly expanding on a worldwide scale. Plant remedies are traditionally used in a variety of pharmacopoeias and on a large scale of doses, including extremely low-dose homeopathic formulations. Herbal medicine or botanical medicine or phytomedicine refers to the therapeutic use of herbs, herbal materials, herbal preparations, and finished herbal products containing plant materials (seeds, berries, roots, leaves, bark, or flowers) or parts as active ingredients. Homeopathy is based on the concept “similia similibus curentur”1 according to which symptoms, caused by the original substance in healthy subjects, can be reversed by the homeopathic remedy in patients having similar symptoms. Therefore, homeopathic drug administration is based on 3 principles: (1) the administration of an active element to healthy volunteers brings manifestation of a series of clinical symptoms at physical and psychological levels; (2) low doses of the same element(s) reverse pathological states in ill organisms presenting a similar symptomatologic pattern; (3) the homeopathic treatment retains its biological activity because of a peculiar method of dilution followed by vigorous shaking, that is, “suscussion”, even if, after several successive serial dilutions, the probability of the presence of any active molecule is very low.2,3 There are several models attempting to explicate how the peculiar homeopathic procedure of succussion can change solvent structure at nanoscopic level and justify the permanence of pharmacological properties throughout dilutions.4–7

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The authors have no conflicts of interest to declare.

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Arnica is one of the most popular medications in complementary medicine. This remedy can be extracted from several plant species belonging to the Asteraceae family including Arnica montana, Arnica chamissonis, Arnica fulgens, Arnica cordifolia and Arnica sororia, and it is widely sold as tincture, ointment, cream, gel, and tablet. In 2009, a study showed that Asteraceae-containing remedies were frequently used in German primary care, and their uses were not associated with serious adverse reactions.\textsuperscript{8} Arnica can be used as a homeopathic or herbal remedy. There are also Arnica-based complex formulations which can include up to 32 different plant species which share morphological characteristics and therapeutic properties to treat inflammation, wounds, hematoma, and contusion.\textsuperscript{9} Among the different varieties, Arnica montana L. is one of the most used varieties and receives different local names including leopard’s bane, wolf’s bane, mountain tobacco, and mountain snuff.\textsuperscript{10} This herb (here referred as Arnica), native of the Siberian mountains and Central Europe, has been used for the treatment of numerous pathological conditions, including pain, stiffness, and swelling associated with trauma, contusions, sprains, myocarditis, cardiac insufficiency, arteriosclerosis, angina pectoris, postoperative clinical conditions, and for symptomatic relief in osteoarthritis.\textsuperscript{10–12} In traditional medicine, patients suffering from traumatic disease often use Arnica as an “alternative” treatment, in the hope of resolving pain and reducing the use of conventional drugs which may cause adverse effects. Furthermore, according to a review concerning the use of alternative and complementary medicine for rheumatological conditions such as osteoarthritis, rheumatoid arthritis, and fibromyalgia, Arnica was used in 18% of patients attending the rheumatology department in a Mexican hospital.\textsuperscript{13} In vitro studies have shown that the most active components of Arnica, as well as of other members of the Asteraceae family, are helenalin and other sesquiterpene lactones such as 11α,13-dihydrohelenalin and chamissonolid. Early on, Lyss et al\textsuperscript{14} showed that helenalin inhibits the transcriptional factor nuclear factor kappa B (NF-κB) through the alteration and stabilization of the NF-κB/ inhibitor of kappa B (IκB) complex in T cells, B cells, and epithelial cells and abrogates kappa B-driven gene expression. This represents one of the earliest evidences of the anti-inflammatory properties of Arnica. Later work showed that helenalin can inhibit human neutrophil migration and chemotaxis\textsuperscript{15} and activities of 5-lipoxygenase and leukotriene C4 synthase.\textsuperscript{16} Helenalin dose-dependently reduced cell-proliferation in cluster of differentiation (CD)4\textsuperscript{+} T cells after the activation of the mitochondrial apoptosis pathway and p53 rapid stabilization and nuclear localization.\textsuperscript{17} Furthermore, it arrested activated CD4\textsuperscript{+} T cell cycle in the G2/M phase through an increase in p27KIP1, p21\textsuperscript{WAF1/CIP1}, and cyclin D2, and a decrease in cyclin B1 and cyclin A.\textsuperscript{17} Helenalin also decreased the expression of cell-surface receptors CD25, CD28, CD27, and CD120b which play a key role in NF-κB activation in T cells,\textsuperscript{17} supporting the mechanism proposed by Lyss et al in 1997.\textsuperscript{14} NF-κB controls the transcription of various cytokine and adhesion molecule genes in addition to genes required for antigen presentation.\textsuperscript{18} NF-κB activation is associated with the induction of pain and inflammation, as observed in animal models of inflammatory pain (rat carrageenan pleurisy and mouse carrageenan air pouch), characterized by the release of proinflammatory cytokines (tumor necrosis factor-alpha [TNF-α] and interleukin-1beta [IL-1β]) and local recruitment of leukocytes.\textsuperscript{19} The ability of Arnica to inhibit activation of transcription factors NF-κB and nuclear factor of activated T cells and proinflammatory cytokines IL-1β and TNF-α correlate with their quantitative and qualitative content of sesquiterpene lactones.\textsuperscript{20} Additionally, Arnica treatment showed a 4.5-fold inhibition of nitric oxide production, a reduction in the levels of inducible nitric oxide synthase and cyclooxygenase-2 protein, a 3-fold reduction in TNF-α level, and prevented nuclear translocation of NF-κB in J774 murine macrophage cells challenged with lipopolysaccharide.\textsuperscript{21} Furthermore, in the rat, 21-day oral treatment with Arnica 30\textsuperscript{th} centesimal dilution (30c) protected against hepatic mitochondrial membrane

\begin{figure}
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\includegraphics[width=\textwidth]{figure1.png}
\caption{Mechanisms underlying Arnica effectiveness. COX-2, cyclooxygenase-2; TNF-α, tumor necrosis factor alpha; IL-1β, interleukin-1 beta; NO, nitric oxide; iNOS, inducible nitric oxide synthase; NF-κB, nuclear factor kappa B; IκB, inhibitor of kappa B.}
\end{figure}
permeabilization induced by Ca\textsuperscript{2+} and/or Fe\textsuperscript{2+}-citrate-mediated lipid peroxidation and fragmentation of proteins due to attacks by reactive oxygen species.\textsuperscript{22} In Figure 1, we have summarized the mechanisms underlying \textit{Arnica} effectiveness. As an herbal formulation, \textit{Arnica} is generally used only topically (on the skin) because of side effects which can be observed after oral administration. Oral homeopathic remedies do contain \textit{Arnica}, but they use an extremely diluted form which is not considered dangerous. The literature concerning \textit{Arnica} in both phytotherapeutic and homeopathic formulations is rapidly increasing, together with the knowledge of its active principles and putative mechanisms of action. In this review, we grouped clinical evidence into 2 sections. The first group comprises the use of \textit{Arnica} as topical formulation, either as a phyotherapeutic extract (higher dosage not succussed) or homeopathic (diluted and succussed preparations), whereas the second group comprises the use of homeopathic preparations administered by oral or topical route. The focus was on preclinical and clinical use of \textit{Arnica} for the treatment of inflammatory conditions, in pain management and postoperative settings.

**REVIEW CRITERIA**

This review gives an overview of the literature in the aforementioned fields, from 1997 to 2013. The principal information sources are drawn from current reading of major complementary and alternative medicine journals, screening of the Hom-Inform Bibliographic Database and Information Service Databases (British Homeopathic Library, http://hominform.soutron.com/), literature search using MEDLINE, the Cochrane Database of Systematic Reviews, and cross-referencing among published articles. Our analysis includes controlled clinical trials (with and without randomization), observational studies, and case series, but it excludes single case reports. We also consulted previously published systematic reviews and meta-analyses which have covered the subject up to now. Finally, some relevant studies concerning the mechanism(s) of action and laboratory studies are reported.

**PRECLINICAL STUDIES**

\textit{Arnica} has been used as a single remedy\textsuperscript{23–25} in preclinical models of acute (carrageenan- and homologous blood-induced rat paw edema) and chronic (nystatin-induced rat paw edema) inflammation and histamine-induced increased vascular permeability.\textsuperscript{23–26} For instance, autologous blood-induced edema was reduced 1, 3, and 5 hours after subplantar but not after oral administration of \textit{Arnica} 4th decimal dilution (4D), when compared with control animals.\textsuperscript{23} Lussignoli et al\textsuperscript{26} replicated this finding and showed that administration of \textit{Arnica} alone or as a homeopathic formulation (Traumeel) an hour before or after the injection of autologous blood, decreased paw edema and enhanced the healing process. Reduction in paw edema coupled with a decrease in systemic interleukin-6 (IL-6) at 5 hours after blood edema induction.\textsuperscript{26} Subchronic oral administration of \textit{Arnica} 6c also reduced carrageenan-induced rat paw edema by 30%.\textsuperscript{25} The reduction in paw edema was evident starting from 1 hour post-carrageenan, and lasted at least 6 hours. In the same study, oral treatment with \textit{Arnica} 6c before 8.5% nystatin-induced inflammation showed a reduction in the edema at 6 hours compared with the control group. However, no effect was observed when administered after nystatin. Furthermore, \textit{Arnica} 6c blocked histamine-induced increase in vascular permeability when administered 3 days before stimulus. Oral \textit{Arnica} 6c administered every 15 minutes between 30 and 180 minutes, after 1% kappa carrageenan inoculation, was effective in reducing late but not early edema in the rat when compared with control groups.\textsuperscript{24} Edema amelioration coupled with a decrease in the mast cell degranulation and an increase in the lymphatic vessel diameter. Helenalin, a sesquiterpene lactone and one of the main active constituent of \textit{Arnica} extract,\textsuperscript{14} inhibited carrageenan-induced paw edema and complete Freund’s adjuvant-induced arthritis in the rat.\textsuperscript{27} Topical application of \textit{Arnica} 3D gel (10%), combined with microcurrent (10 μA for 2 minutes) application, significantly improved wound healing in the linear incision wound model in the rat back.\textsuperscript{28} The evidence was consistent with a significantly larger total number of cells and higher percentage of mature collagen fibers in the wound, as assessed by structural and morphometric analysis. Therefore, these results strongly support the relevance of \textit{Arnica} in the treatment of inflammatory-related processes.

**CLINICAL STUDIES**

**Topical applications of phytherapeutic preparations**

Up to now, several clinical trials involving the use of topical \textit{Arnica} have been performed aiming to reduce laser-induced bruising and osteoarthritis-related symptoms. We have summarized these studies in Table 1.

**Laser-induced bruising**

Daily application of 2 extracts based on a combination of \textit{Arnica} and stinging nettle (Combudoron liquid and Combudoron gel; 0.5 mL per lesion for 30 minutes for
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<tr>
<th>Author(s), year</th>
<th>Design</th>
<th>No. Patients</th>
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<th>Outcome</th>
<th>Homeopathy</th>
<th>Herbal medicine</th>
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<tr>
<td>Kaziro, 1984</td>
<td>Randomized double-blind placebo-controlled trial</td>
<td>118</td>
<td>Post-surgical complications after removal of impacted wisdom teeth</td>
<td>Arnica 200c versus metronidazole versus placebo</td>
<td>Metronidazole was more effective in pain control ($P &lt; 0.001$ and $P &lt; 0.01$), swelling prevention ($P &lt; 0.01$ and $P &lt; 0.05$) and healing promotion ($P &lt; 0.01$ and $P &lt; 0.01$) when compared with Arnica and placebo, respectively</td>
<td>Yes</td>
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<tr>
<td>Albertini and Goldberg, 1986</td>
<td>Randomized placebo-controlled trial</td>
<td>30</td>
<td>Dental neuralgic pain after tooth extraction</td>
<td>Arnica 7c and Hypericum 15c versus placebo</td>
<td>76% of the patients treated with homeopathic remedies had pain relief versus 40% of patients receiving placebo</td>
<td>Yes</td>
<td></td>
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<tr>
<td>Zell et al, 1988</td>
<td>Randomized double-blind placebo-controlled study</td>
<td>69</td>
<td>Acute sprains of the ankle joint</td>
<td>Traumeel ointment versus placebo</td>
<td>24 patients were pain-free on treatment day 10, whereas on the same day, only 13 patients treated with placebo had no pain</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Dorfman et al, 1988</td>
<td>Double-blind, placebo-controlled clinical study</td>
<td>39</td>
<td>Prolonged venous perfusion</td>
<td>Arnica 5c</td>
<td>Arnica reduced pain, hyperemia, edema, and hematoma formation. Improvement in the blood flow and slight increase in coagulation factors and in platelet aggregation were observed after Arnica treatment</td>
<td>Yes</td>
<td></td>
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<tr>
<td>Baillargeon et al, 1993</td>
<td>Randomized double-blind, 2-period, crossover, clinical trial</td>
<td>18</td>
<td>Blood coagulation</td>
<td>Arnica 5c versus placebo</td>
<td>An increase in bleeding time and a decrease in fibrinogen were observed 30 minutes</td>
<td>Yes</td>
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<tr>
<td>Lokken et al., 1995</td>
<td>Randomized double-blind, placebo-controlled crossover trial</td>
<td>24</td>
<td>Pain after surgical removal of bilaterally impacted mandibular third molars</td>
<td>Arnica 30D versus placebo</td>
<td>No difference in postsurgical pain was observed between Arnica and placebo. Postoperative swelling and bleeding were not significantly affected by homoeopathy</td>
<td>Yes</td>
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<tr>
<td>Hart et al., 1997</td>
<td>Randomized double-blind controlled study</td>
<td>73</td>
<td>Pain and postoperative recovery after total abdominal hysterectomy</td>
<td>Arnica 30c versus placebo</td>
<td>No significant difference was observed between Arnica and placebo</td>
<td>Yes</td>
</tr>
<tr>
<td>Vickers et al., 1998</td>
<td>Randomized, double-blind placebo-controlled trial</td>
<td>400</td>
<td>Muscle soreness after long-distance running</td>
<td>Arnica 30D versus placebo</td>
<td>No significant change in muscle soreness after long-distance running was observed when comparing Arnica to placebo.</td>
<td>Yes</td>
</tr>
<tr>
<td>Ramelet et al., 2000</td>
<td>Randomized, prospective, multicenter double-blind trial</td>
<td>130</td>
<td>Saphenous stripping</td>
<td>Arnica 5c versus placebo</td>
<td>No significant difference in postoperative hematomas was observed between Arnica and placebo</td>
<td>Yes</td>
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<tr>
<td>Alonso et al., 2002</td>
<td>Randomized double-blind, placebo-controlled trial</td>
<td>19</td>
<td>Laser-induced bruising</td>
<td>Arnica gel versus vehicle</td>
<td>No difference was observed between Arnica gel and vehicle administered prior or after injury</td>
<td>Yes</td>
</tr>
<tr>
<td>Jeffrey and Belcher, 2002</td>
<td>Randomized, double-blind placebo-controlled trial</td>
<td>37</td>
<td>Hand surgery (endoscopic carpal tunnel release)</td>
<td>Arnica tablets and gel versus Arnica placebo</td>
<td>No difference in grip strength or wrist circumference was found between Arnica and placebo</td>
<td>Yes</td>
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<tr>
<td>Knuesel et al, 2002</td>
<td>Open multicenter trial</td>
<td>79</td>
<td>Mild–moderate knee osteoarthritis</td>
<td>Arnica gel</td>
<td>Median total scores on the Western Ontario and McMaster Osteoarthritis Index were significantly decreased in the intention-to-treat and per-protocol populations (both P &lt; 0.0001). Scores on the pain, stiffness, and function subscales were also significantly decreased</td>
<td>Yes</td>
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<td>Wolf et al, 2003</td>
<td>Prospective, randomized, double-blind, placebo-controlled pilot trial</td>
<td>60</td>
<td>Varicose vein surgery</td>
<td>Arnica 12D versus placebo</td>
<td>Hematoma surface was reduced with Arnica by 75.5% and with placebo by 71.5% (not significant). Pain score decreased by 1 ± 2.2 points with Arnica and 0.3 ± 0.8 points with placebo not significant</td>
<td>Yes</td>
<td></td>
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<tr>
<td>Stevinson et al, 2003</td>
<td>Randomized double-blind placebo-controlled trial</td>
<td>62</td>
<td>Surgery for carpal tunnel syndrome</td>
<td>Arnica 6c or 30c versus placebo</td>
<td>No significant change in pain and bruising were observed after administration of Arnica or placebo</td>
<td>Yes</td>
<td></td>
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<td></td>
<td></td>
<td>82</td>
<td></td>
<td>Arnica versus placebo</td>
<td>Muscle soreness immediately after the</td>
<td>Yes</td>
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Table 1. (Continued) Clinical efficacy of Arnica montana.

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<tr>
<td>Tveiten and Bruset, 2003&lt;sup&gt;41&lt;/sup&gt;</td>
<td>Randomized double-blind placebo-controlled study</td>
<td></td>
<td>Muscle soreness and cell damage after marathon running</td>
<td></td>
<td>marathon was lower in the Arnica group versus placebo (P = 0.04)</td>
<td></td>
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<tr>
<td>Brinkhaus et al, 2006&lt;sup&gt;42&lt;/sup&gt;</td>
<td>Three randomized, placebo-controlled, double-blind, sequential clinical trials</td>
<td>227</td>
<td>Postoperative swelling and pain after arthroscopy, artificial knee joint implantation, and CLR</td>
<td>Arnica 30D versus placebo</td>
<td>Arnica was effective on swelling and pain only in the CLR trial (P = 0.019)</td>
<td></td>
<td>Yes</td>
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<tr>
<td>Seeley et al, 2006&lt;sup&gt;43&lt;/sup&gt;</td>
<td>Prospective randomized double-blind placebo-controlled study</td>
<td></td>
<td>Rhytidectomy</td>
<td>Arnica (SinEcch) versus placebo</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 &lt; 0.005) and 7 (P &lt; 0.001)</td>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>Schneider et al, 2007&lt;sup&gt;44&lt;/sup&gt;</td>
<td>Multicenter, prospective, comparative observational cohort study</td>
<td>133</td>
<td>Muscoskeletal trauma and injuries</td>
<td>Traumeel versus conventional medicines</td>
<td>Complete resolution of pain and inflammatory symptoms at the end of therapy were observed in 59.4% of patients in the Traumeel group and in 57.8% of patients in the conventional medicine group</td>
<td></td>
<td>Yes</td>
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<tr>
<td>Robertson et al, 2007&lt;sup&gt;51&lt;/sup&gt;</td>
<td>Randomized double-blind, placebo-controlled trial</td>
<td>111</td>
<td>Tonsilllectomy</td>
<td>Arnica 30c versus placebo</td>
<td>Arnica reduced pain scores (P &lt; 0.05). No difference was observed in analgesia consumption, complications, and return to normal activities when</td>
<td></td>
<td>Yes</td>
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<td>Totonchi and Guyuron, 2007</td>
<td>Randomized double-blind clinical study</td>
<td>48</td>
<td>Rhinoplasty</td>
<td>Arnica (SinEcch) versus intravenous dexamethasone plus oral tapering dose of methyl-prednisone or no treatment (control group)</td>
<td>Arnica and dexamethasone reduced swelling-edema if compared with control ($P &lt; 0.0001$). Arnica and control group exhibited more resolution of ecchymosis if compared with dexamethasone ($P &lt; 0.05$)</td>
<td>Yes</td>
<td></td>
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<tr>
<td>Widrig et al, 2007</td>
<td>Randomized, double-blind study</td>
<td>204</td>
<td>Hand osteoarthritis</td>
<td>Arnica gel versus ibuprofen gel</td>
<td>Arnica and ibuprofen were equally effective for the treatment of hand osteoarthritis as far as pain reduction, hand function, number of painful joints in both hands and intensity of morning stiffness in the worst affected hand were concerned</td>
<td>Yes</td>
<td></td>
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<tr>
<td>Paris et al, 2008</td>
<td>A phase 3 monocentric randomized placebo-controlled study</td>
<td>158</td>
<td>Knee ligament reconstruction</td>
<td>Granule composition containing Arnica 5c, Bryonia alba 5c, Hypericum perforatum 5c, and Ruta graveolens 3D versus placebo or no treatment</td>
<td>Homeopathic treatment was not superior to placebo in reducing 24 h morphine consumption after knee ligament reconstruction. No significant difference in pain assessed by visual analog scale was observed between Arnica and placebo</td>
<td>Yes</td>
<td></td>
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<tr>
<td>Karow et al, 2008</td>
<td>Randomized double-blind, parallel-group study</td>
<td>88</td>
<td>Hallux valgus surgery</td>
<td>Arnica 4D versus diclofenac sodium</td>
<td>Arnica and diclofenac had equivalent efficacy on wound irritation, patient</td>
<td>Yes</td>
<td></td>
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<tr>
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<td>Adkison et al, 2010&lt;sup&gt;46&lt;/sup&gt;</td>
<td>Randomized, double-blind, placebo-controlled trial</td>
<td>53</td>
<td>Leg pain after calf raises</td>
<td>Arnica cream versus placebo</td>
<td>Arnica increased pain scores if compared with placebo ($P &lt; 0.005$). No difference in muscle tenderness and ankle motion was observed</td>
<td>Yes</td>
<td></td>
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<tr>
<td>Cornu et al, 2010&lt;sup&gt;47&lt;/sup&gt;</td>
<td>Double-blind placebo-controlled parallel trial</td>
<td>90</td>
<td>Aortic valve surgery</td>
<td>A combination of <em>Arnica montana</em> 5c and <em>Bryonia alba</em> 5c granules versus placebo</td>
<td>No difference between homeopathic treatment and placebo on bleeding, C-reactive protein, troponin I, and cumulated morphine was observed</td>
<td>Yes</td>
<td></td>
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<tr>
<td>Leu et al, 2010&lt;sup&gt;48&lt;/sup&gt;</td>
<td>Randomized, double-blind placebo-controlled trial</td>
<td>16</td>
<td>595-nm pulsed-dye laser-induced bruises on the bilateral upper inner arms</td>
<td>5% vitamin K versus 1% vitamin K and 0.3% retinol or 5% vitamin K or 20% <em>Arnica</em> or white petrolatum (placebo)</td>
<td>The mean improvement in bruising associated with 20% <em>Arnica</em> 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 <em>Arnica</em> was not greater than with 5% vitamin K cream</td>
<td>Yes</td>
<td></td>
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<tr>
<td>Huber et al, 2011&lt;sup&gt;49&lt;/sup&gt;</td>
<td>Single-blind, randomized trial</td>
<td>2</td>
<td>Erbium YAG-laser-induced grade-2 burns</td>
<td>Combudoron gel versus Combudoron liquid or placebo gel or placebo liquid</td>
<td>Eschars treated with Combudoron fell off earlier if compared with placebo.</td>
<td>Yes</td>
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days) was tested on erbium YAG laser–induced grade 2 burns. This single-blind randomized study involved 2 healthy male subjects receiving treatment or placebo on their backs at 4 sites. After 1 week of treatment, the diameters of the lesions were only slightly different between treatments. Most notably, the eschars treated with Combudoron fell off earlier than the placebo suggesting that Combudoron has a positive effect on burn healing.49 In a randomized, double-blind 2-week study, twice a day topical application of Arnica 1 × gel on one side of the face, before or after laser treatment was compared with vehicle application on the other hemisphere in 19 patients affected by facial telangiectasias without improvement in visual analog scale (VAS) bruising.11

Contrasting results were obtained in a 2-week double-blind randomized study including 16 healthy patients who underwent creation of 7-mm standard bruises on the upper inner arms by a 595-nm pulsed-dye laser.48 Comparison of VAS-bruising scores indicated that 20% Arnica gel reduced bruising when compared with placebo and gel containing 1% vitamin K and 0.3% retinol, whereas comparison with 5% vitamin K gel did not show any significant difference.

Osteoarthritis

In a randomized, double-blind 3-week study which involved 204 patients affected by osteoarthritis of interphalangeal joints of the hands, topical application of a 4-cm gel strip of Arnica (50 g tincture/100 g) 3 times a day showed similar efficacy to ibuprofen (5%) gel in reducing pain, functional capacity of the hand, number of painful joints in both hands and intensity of morning stiffness in the worst affected hand.

Orally administered homeopathic formulations

Homeopathic formulations of Arnica have been largely used in the clinical setting for the management of knee surgery, carpal tunnel syndrome, symptoms associated with wisdom teeth removal, rhytidectomy, rhinoplasty, abdominal hysterectomy, tonsillectomy, hallux valgus surgery, venous surgery, hemorrhosis, aortic valve surgery, prolonged venous perfusion, muscular pain, dental neuralgia, and ankle sprains.

Knee surgery

Brinkhaus et al42 tested the efficacy of oral administration of Arnica 30D administered as supplement to ordinary treatment (1 × 5 globules 2 hours before surgery plus 3 × 5 globules at 3-hour intervals postoperatively the day of surgery plus 3 × 5 globules until the last follow-up) on postoperative swelling
Effectiveness and Safety of Arnica montana

and pain in patients undergoing different types of knee surgery in 3 consecutive randomized placebo-controlled clinical studies. Arnica reduced swelling and pain after cruciate ligament reconstruction (57 patients; last follow-up at day 8), but not after arthroscopy (227 patients; last follow-up at day 2), artificial knee joint implantation (35 patients; last follow-up at day 11), and cruciate ligament reconstruction (57 patients; last follow-up at day 8). Homeopathic treatment containing Arnica 5c, Bryonia Alba 5c, Hypericum perforatum 5c, and Ruta graveolens 3D (4-day treatment starting 1 day before the surgery; 5 granules per day) was not superior to placebo in reducing 24-hour morphine consumption after knee ligament reconstruction in a randomized controlled study including 158 patients.2

Carpal tunnel syndrome

In a double-blind randomized trial involving 62 patients, Arnica 30c or 6c administered daily from 7 days before to 14 days after surgery (3 tablets) was not effective in reducing bruising, swelling, and pain in patients undergoing elective surgery for carpal tunnel syndrome.3

Wisdom teeth removal

In a double-blind trial, Arnica 200c administered to 39 patients undergoing the removal of impacted wisdom teeth, was less effective for pain and swelling management compared with placebo or metronidazole.28 Arnica was also less effective in promoting healing when compared with metronidazole.29 In a randomized double-blind placebo-controlled crossover trial including 24 patients undergoing prophylactic surgical removal of identical bilaterally impacted mandibular third molars, homeopathic treatment (30D) containing Arnica, Hypericum, Staphysagria, Sedum, Phosphorus, and Plantago did not produce any improvement in VAS pain score, postoperative bleeding and swelling and side effect profile when compared with the control group.34 Furthermore, a 33% less reduction in the ability to open the mouth was observed on day 3 after homeopathic treatment with Arnica. Ernst45 criticized this study, arguing that the doses were fixed and the treatment schedule was not as flexible as homeopathic requires.

Rhytidectomy

Arnica (SinEcch, Alpine Pharmaceuticals, San Raphael, California; 1 dose every 8 hours for 4 days starting from the day of surgery) was used in patients undergoing rhytidectomy to evaluate its efficacy on brusing caused by facelift in a prospective randomized double-blind study including 29 patients.43 A reduction in ecchymosis was observed at postoperative days 1 and 7 compared with placebo, as assessed by computer-measured skin color changes.

Rhinoplasty

In a randomized double-blind clinical study involving 48 primary rhinoplasty patients, oral Arnica (SinEcch) administered 3 times a day for 4 days and 10 mg intravenous dexamethasone administered intraoperatively and followed by a 6-day oral tapering dose of methyl-prednisolone significantly reduced edema rating, but not intensity and extent of ecchymosis at day 2 post-rhinoplasty when compared with the control group. At postoperative day 8, Arnica and control group showed significantly less extent and intensity of ecchymosis when compared with dexamethasone group. Furthermore, no differences in edema rating were observed among groups at this time point.51

Abdominal hysterectomy

Negative results concerning the effect of Arnica 30c (2 doses preoperatively plus 3 doses postoperatively for 5 days) on pain, analgesia, infection, and postoperative recovery were obtained in a study including 73 women who underwent total abdominal hysterectomy.35

Tonsillectomy

Arnica was tested in patients undergoing tonsillectomy. One hundred eleven patients undergoing tonsillectomy were randomized in a double-blind fashion to receive either Arnica 30c or placebo (2 tablets for 6 times in the first postoperative day followed by 2 tablets twice a day for 7 days).32 Follow-up over 14 days after surgery showed a significant reduction in the VAS pain scores, whereas no difference was observed in analgesic consumption, complications and return to normal activities.

Hallux valgus surgery

Arnica 4D (pills; postoperatively 3 times a day for 4 days) was compared with diclofenac sodium 50 mg (postoperatively 3 times a day for 4 days) in a randomized double-blind clinical study in 88 patients undergoing hallux valgus surgery.33 Arnica 4D and diclofenac sodium had equivalent efficacy on wound irritation, patient mobility, and use of analgesics, whereas Arnica was inferior to diclofenac sodium as far as VAS pain score was concerned.

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Venous surgery

Arnica 5c, administered sublingually the night before and immediately after saphenous surgery, did not reduce postoperative hematomas, as evaluated 6 days postoperatively in a randomized, prospective, multicentric double-blind trial involving 130 patients. 37

Aortic valve surgery

Negative results were reported in a double-blind clinical study involving 90 patients undergoing aortic valve surgery assessing the efficacy of a combination of Arnica 5c and Bryonia Alba 5c. 47 Five homeopathic granules administered twice a day for 5 days, starting the evening before surgery for 5 days, did not produce any significant change in the volume of blood/liquid in the drains at their removal and postoperative blood/liquid losses at 12 and 24 hours as well as C-reactive protein, pain, temperature, and plasma troponin Ic.

Prolonged venous perfusion

In a double-blind, placebo-controlled clinical study involving patients undergoing prolonged venous perfusion, Arnica 5c reduced pain symptoms, hyperemia, edema, formation of hematomas and improved blood flow, as measured by Doppler flowmetry. Arnica treatment also slightly increased a number of coagulation factors and platelet aggregation. 32

Muscular pain

In a double-blind randomized study involving 82 marathon runners, 5 pills of Arnica 30D, given twice a day from the evening before until 3 days after the marathon, improved muscle soreness measured by VAS immediately after the competition, but it did not protect from cell damage (creatine kinase, aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, sodium, potassium, magnesium, and creatinine were analyzed) measured by muscular enzymatic reaction. 41 Contrasting results were reported in another double-blind randomized clinical study showing that Arnica 30D did not reduce muscle soreness after long-distance running in 519 runners, as assessed by VAS and Linkert scale. 30 In a randomized double-blind trial including 53 patients, Arnica cream applied immediately after performing calf raises and 24–48 hours post-exercise also failed to improve leg pain, motion, and muscle tenderness when compared with placebo. 46

Dental neuralgia

Arnica was effective for treatment of dental neuralgic pain after tooth extraction 30 in a placebo-controlled randomized clinical trial. Arnica 7c (4 granules) and Hypericum 15c (St John’s wort; 4 granules) prescribed alternately at 4-hour intervals for 2 days, starting immediately after clinical examinations, resulted in pain relief experienced by 76% of patients treated with homeopathic combination therapy versus 40% of patients treated with placebo.

Ankle sprains

Arnica tincture spray (41.5 mg) was also tested in combination with hydroxyethyl salicylate (HES; 12.5 mg) and compared with Arnica (41.5 mg), HES (12.5 mg), and placebo for treatment of ankle joint distortion-related pain in a prospective, randomized, double-blind, 4-arm parallel group phase 4 study including 570 patients. 50 Application of Arnica plus HES 4–5 times daily improved pain assessed by VAS after quickly walking a distance of approximately 10 m on day 3–4. In summary, this study suggests that Arnica can act synergistically with other medications such as HES to reduce sprained ankle joint distortion-related pain.

SAFETY OF ARNICA FORMULATIONS

Although the use of homeopathic medicines is growing, these compounds are often deemed safe and risk-free with patients not declaring their use to their general practitioner. Little evidence is available concerning the use of Arnica in pediatric patients. In this regard, herbal products are extensively used to treat children without consulting the pediatrician and without reporting their use before a surgical procedure, as showed in a study by Crowe and Lyons. 54 In this study, the parents of 601 children undergoing ambulatory surgery were asked to fill in a questionnaire about the administration of herbal medicines to their children. Sixty-six percent of children were taking herbal medicines (Arnica and Echinacea were most commonly used) or had taken them in the past, and 84.7% of parents had not told the practitioner about their use, without thinking that herbal products could lead to adverse effects and interact with anesthetic drugs and the surgical procedure itself. These observations confirm that homeopathic drugs may be used safely either in general practice or on self-prescription, although the general practitioner should be informed to avoid a delay in the choice of a classic drug treatment, if required. Further evidence shows that Arnica can be used for external and internal bruising of both mother and newborn infant. 55 Furthermore, Arnica has been extensively used for soft-tissue bruising in a cohort of patients from birth to 8.5 years of age.
the therapeutics of choice for the treatment of osteoarthritis, postoperative edema, and ecchymosis.61

Although limited evidence is available for the use of Arnica in the context of wound healing, a study suggests that it can be used instead of diclofenac after hallux valgus surgery to reduce wound irritation and at a lower cost.53 Furthermore, combined with stinging nettle, it showed promising results in 2 patients with grade 2 laser-induced burns.49 In patients undergoing the removal of impacted wisdom teeth, Arnica was less effective for the management of pain and swelling compared with placebo suggesting that it should not be used in that clinical condition.29 These findings suggest that Arnica can be used in the context of wound healing in selected clinical scenarios. However, the limited number of studies warrants further investigations. The topical use of Arnica is supported by studies evincing its efficacy in relieving acute muscle pain after excessive exercise,62 and in the symptomatic treatment of osteoarthritis.12,39 The local action is exerted: (1) at the level of the locomotor system on the muscles, calming the feeling of soreness and pain63; (2) in the joints, reducing the swelling and pain caused by rheumatic disorders; (3) in the capillaries and veins, reducing hematoma and ecchymosis and protecting blood vessels.20,62 Additionally, Arnica administered orally in homeopathic dilutions showed positive clinical effects in reducing postoperative pain, swelling, edema, and ecchymosis.15,40,42,51,52 Furthermore, topical Arnica combined with oral homeopathic dilutions significantly reduced postoperative pain.38 As to topical gels, this review points out that Arnica has clinical benefits in relieving pain and surgical complications. The topical application of Arnica thus offers an alternative to ibuprofen because of the high concentration of sesquiterpenes,12 and in particular helenalin, which is the active substance held responsible for its anti-inflammatory activity.14 The level of sesquiterpenes depends on multiple factors. For example, Douglas et al64 showed that the total amount of bioactive endogenous sesquiterpenes varies depending on which portion of the plant is being used. The concentration of sesquiterpenes was found to be higher in the disc florets than in the ray florets, lower in the receptacle, and even lower in the stalk.64 This variability in the quantity of sesquiterpenes, with a consequent variation in the biological activity, can influence the clinical efficacy of Arnica.20 To guarantee the efficacy of medicines containing Arnica, it is necessary to obtain a phytocomplex with optimal levels of active substances. This requires the use of high-quality raw material that is obtained by harvesting whole, fresh and spontaneously occurring Arnica in its natural habitat, far from any form of pollution and during the balsamic phase.

DISCUSSION

Over the past twenty years, the use of homeopathic medicines has increased worldwide in terms of both prescriptions by physicians and increased recommendation by pharmacists. In particular, Arnica is one of the homeopathic remedies used for over 100 years for the treatment of trauma-associated pain and swelling. This review summarizes the available preclinical and clinical evidence concerning the efficacy and safety of the homeopathic product Arnica in pain-related processes. Overall, Arnica (topical and/or oral formulations) has demonstrated reproducible clinical benefits, some of which are comparable with anti-inflammatory drugs such as diclofenac,53 ibuprofen12,60 and corticosteroids51 which are considered

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<table>
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<tr>
<th>Author(s), year</th>
<th>Formulation</th>
<th>Pathology</th>
<th>Side effect profile</th>
<th>Dose</th>
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<tbody>
<tr>
<td>Knuesel et al, 2002&lt;sup&gt;29&lt;/sup&gt;</td>
<td>Gel (topical application)</td>
<td>Knee osteoarthritis</td>
<td>One allergic reaction (not specified)</td>
<td>NS</td>
</tr>
<tr>
<td>Stevinson et al, 2003&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Tablets (oral treatment)</td>
<td>Hand surgery (carpal tunnel syndrome)</td>
<td>Dry mouth, Headache, Feeling “throbby” in head/neck, Drowsiness, Sore tongue</td>
<td>Arnica 6c (for drowsiness and sore tongue), Arnica 30c (for dry mouth, headache, and feeling “throbby”)</td>
</tr>
<tr>
<td>Widrig et al, 2007&lt;sup&gt;12&lt;/sup&gt;</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>Karow et al, 2008&lt;sup&gt;53&lt;/sup&gt;</td>
<td>Pills (oral treatment)</td>
<td>Hallux valgus surgery</td>
<td>Abdominal complaints, Racing heart</td>
<td>Arnica 4D</td>
</tr>
<tr>
<td>Cornu et al, 2010&lt;sup&gt;47&lt;/sup&gt;</td>
<td>Granules (oral treatment)</td>
<td>Aortic valve surgery</td>
<td>Cardiovascular events (observed in both homeopathy and placebo groups)</td>
<td>Arnica 5c and Bryonia alba 5c</td>
</tr>
<tr>
<td>Kucera et al, 2011&lt;sup&gt;50&lt;/sup&gt;</td>
<td>Spray (topical application)</td>
<td>Ankle distortion</td>
<td>Burning, reddening, itching and urticaria were observed in the group receiving Arnica and hydroxyethyl salicylate. No adverse reactions were observed in patients receiving Arnica alone.</td>
<td>Arnica tincture: 41.5 mg, Hydroxyethyl salicylate: 12.5 mg</td>
</tr>
</tbody>
</table>

NS, not specified in the article.
Reproducibility is assured by accurate botanical identification, safeguarding the freshness of the batch, and performing checks on the raw material and the finished product. The quality and safety of homeopathic medicines containing *Arnica* are guaranteed by the European Pharmacopoeia and by specific *Arnica* monographs included in the pharmacopoeias of the individual member states. Pharmaceutical companies which produce homeopathic medicines containing *Arnica* in compliance with these standards are able to guarantee its efficacy and safety. Specifically, *Arnica* use in various clinical settings is achieving a wider reputation supported by an arising number of open studies, even if comparison of this compound with traditional drugs has been rarely performed.

**CONCLUSIONS**

Cumulative evidence suggests that both *Arnica* in gel formulation and in homeopathic dilutions are more effective than placebo in treating several inflammatory conditions, in pain management and postoperative settings. Its clinical efficacy in these fields and its high tolerability make it a potential therapeutic alternative target to non-steroidal anti-inflammatory drugs, especially for patients undergoing pharmacological polytherapy as they are more exposed to the risk of drug interactions and, consequently, to their toxicity. The wide variability of formulations and therapeutic settings precludes a meta-analysis that could assess the efficacy of specific protocols. Further trials involving larger cohorts of patients are needed to support a possible effect of *Arnica* in several inflammatory conditions, in pain management and postoperative settings.

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**REFERENCES**


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