



RESEARCH ARTICLE

ANXIOLYTIC AND ANALGESIC EFFECTS OF ARNICA MONTANA EXTRACT

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ABSTRACT

Anxiety is at the rise in today's world. Anxiety neurosis is one of the commonest disorder which is found in today's youth. This particular research was aimed at studying the neuro-pharmacological (anxiolytic) & analgesic effect of arnica plant extract in students. *A. montana* crude extract exhibited potent anxiolytic & analgesic effect as compared to modern anxiolytic & analgesic drugs which include NSAID's namely diazepam derivative, paracetamol, etc. Diazepam, Paracetamol were used as reference drugs. Significant analgesic response was observed at the low dosage of arnica montana extract as compared to routine NSAID's. These results were suggestive that the extract of *A. montana* possess significant analgesic and anxiolytic effect.

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INTRODUCTION

Anxiety neurosis has become one the most prominent and commonest disorder found in today's youth. 75-80% of the youth population suffers from this disorder. Commonest drug used to treat anxiety is Benzodiazepines. (Ahmad *et al.*, 2013) They have pronounced anxiolytic effect but also have numerous unpleasant side-effects. This low safety profile of benzodiazepines drove us to undertake this research in order to explore natural world and discover new compounds with lesser adverse effects (Ahmad *et al.*, 2013). *Arnica montana* (Wolf's Bane, Leopard's bane), belongs to Compositae family. It contains volatile oil, carotenoids, flavonoids, tannins, resins and triterpenic alcohol. Arnica flowers and rhizomes contain a bitter active principle called arnicin. They also contain arnidioland faradiol which are counter irritants (Kokate 51st edition). These active principles in *A. montana*, have been reported to possess tremendous healing properties namely antiseptic, anti-inflammatory, anti-bacterial, decongestive and anti-fungal immune stimulating properties. It also stimulates the forming the granular tissues and thus accelerating the healing process (Verma, 2002; Homoeopathic Pharmacopoeia of India, 1971; Mandal and Mandal, 2012; Kokate, 51st Edition). Arnica has proved to be effective in treating variety of

ailments like pale face skin complexion, wounds, bruises and burns. The treatment of dislocations, bacterial infections, skin cancer, bronchitis, tonsillitis, pharyngitis, flu, lung cirrhosis, cystitis, nephritis, kidney infections, coronary insufficiencies, hypertension, angina, cerebral trauma, headaches, paresis, semi-paresis, insomnia, heart palpitations, nightmares, night terrors, moral depressions, neurosis, hysteria etc are the other uses of *A. montana* (Ahmad *et al.*, 2013; Kokate, 51st Edition). Inflammation plays an important role in the pathogenesis of severe diseases, such as rheumatoid arthritis, osteoarthritis, asthma, infections, skin disorders, cancer, diabetes, atherosclerosis or accelerated aging. The inflammation process occurs as a response to an infectious agent or tissue injury, recruiting immune cells (monocytes, mast cells, leucocytes) at the wounded site, which along with non-immune cells (fibroblasts, endothelial cells) regulate the production of various pro- and anti-inflammatory mediators, including cytokines (interleukin-1 (IL-1), tumor necrosis factor alpha (TNF- α), etc), chemokines (CCL2, IL-8, etc), inducible enzymes (cyclooxygenase-2 and nitric oxide synthase) or receptor molecules for cytokines. (Romanian Biotechnological letters, 2014) In terms of redox disequilibrium, the reactive oxygen species (ROS), such as superoxide anion, hydrogen peroxide, hydroxyl radical or singlet oxygen can accumulate at inflamed site and attack biological molecules (proteins, DNA) leading to cell and tissue injuries. Several natural products and plant derived formulations are used as antioxidants and inhibitors of pro-inflammatory cytokines to treat inflammatory-

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related disorders. In recent years, many plant, herb and spice extracts have been screened in cell culture models for their anti-inflammatory activities. Curcumin, the natural yellow pigment from turmeric (*Curcuma longa*), capsaicin the active component of chili peppers (*Capsicum* spp.), or the polyphenolic constituents of green tea, named catechins, have been shown to modulate the NF- κ B signaling pathway involved in the inflammation process. (Romanian Biotechnological letters, 2014) Extracts of arnica (*Arnica montana* L.) flowers were used, as tincture or ointment, in traditional and homeopathic medicine for topic treatment of skin bruises, irritations, contusions and pain, presenting antiseptic, antiphlogistic, analgesic and anti-inflammatory properties. Among the biologic active constituents of arnica extracts, the phenolic acids (e.g., caffeic, chlorogenic) and flavonoids (e.g., quercetin, patuletin) were identified and quantified by micellar capillary chromatography, while a mixture of sesquiterpene lactones (e.g., helenalin, dihydrohelenalin and their esters) was shown to have important biological activity. Arnica phenolic acids and flavonoids showed significant antioxidant and antibacterial activities. Polysaccharides from arnica had immunological properties that increased phagocytosis in cultured cells and its sesquiterpene lactones exerted anti-inflammatory effects, mainly by preventing nuclear factor NF- κ B activation, similarly to corticoid steroids. In its study, JAGER & al. (2009) noticed a better activity of total plant extracts over pure compounds isolated from arnica flowers. (Romanian Biotechnological letters, 2014) In 1984 a monograph on Arnica was established by the Commission E. The indication was covering a broad range of therapeutic conditions: for external use for injury and accidents, such as bruises, sprains, contusions, fracture-oedema, rheumatic muscle and joint pain, inflammation of the mouth and throat, furunculosis and inflammation as a result of insect bites, phlebitis. Because of possible risks the application was limited to external use, the internal use was not admitted. There is a WHO monograph on Arnica flos, which was developed with reference to the British Herbal Pharmacopoeia and the German Commission E monograph, and which is listing the following indications: as a topical counterirritant for treatment of pain and inflammation resulting from minor injuries and accidents, including bruises, ecchymoses, haematomas and petechiae and treatment of inflammation of the oral mucous membranes, insect bites and superficial phlebitis. The ESCOP monograph on Arnicae flos attributed the following indications: Treatment of bruises, sprains and inflammation caused by insect bites; gingivitis and aphthous ulcers; symptomatic treatment of rheumatic complains. (www.ema.europa.eu) The active components in arnica are sesquiterpene lactones –which are known to reduce inflammation and decrease pain-although current data does not fully explain how they exert their antiinflammatory effect. Other active principals are thymol, flavonoids, inulin, carotenoids and tannins. (www.ema.europa.eu)

Mechanism of Action

The applicable part of arnica is the flowerhead. The sesquiterpenoid lactones of arnica are the active principles and produce anti-inflammatory and analgesic effects. They also can have some antibiotic activity. Two components of arnica, helenalin and 11 α , 13-dihydrohelenalin, inhibit human

platelet function. The sesquiterpene lactones –helenalin, 11 α , 13-dihydrohelenalin and chamissonolid inhibit activation of transcription factor NF- κ B (suggests a molecular mechanism for the antiinflammatory effect of these lactones –which differs from that of other nonsteroidal anti-inflammatory drugs, like NSAIDs. Two homogeneous polysaccharides, an acidic aragino-3,6-galactan-protein and a neutral fucogalactoxyloglucan have been isolated from the arnica cell. The fucogalactoxyloglucan shows a pronounced enhancement of phagocytosis in vivo. The arabino-3,6-galactan-protein displays a strong anticomplementary effect and stimulates macrophages to excrete the tumour necrosis factor (TNF α). (www.ucdenver.edu)

Aim

This particular research was aimed at studying the neuro-pharmacological (anxiolytic) & analgesic effect of arnica plant extract in students.

Objective

The main objective behind this study was to compare the anxiolytic & analgesic effects of Arnica plant extract as compared to modern anxiolytic & analgesic drugs which include NSAID's namely paracetamol.

Purpose of selection of topic

Anxiety is becoming one of the most predominant ailment of the youth. Many youth population lands up in depression if this state is not treated on time. There are many drugs which are frequently used to treat this anxiety but they come with severe side effects. Also any kind of pain is the call of the hour for a physician. A physician must have the tools to tackle this pain effectively without any side-effects. Today's NSAID's have been proved to affect major systems of the body especially the kidneys. Keeping this into mind, the main purpose behind selecting this topic for research is to find a natural substitute to NSAID's which is equally effective in managing this anxiety and pain without any side-effects.

MATERIALS AND METHODS

Type of Study: Clinical Trial

Arnica montana plant extract was purchased from a renowned Homoeopathic Pharmacy. Arnica plant extract (Mother Tincture) is prepared by taking arnica Montana in coarse powder 100g, purified water 400 ml, and strong alcohol 635 ml to make 1 lit. Of the mother tincture. (Verma, 2002; Homoeopathic Pharmacopoeia of India, 1971) Dosage: 12-15 drops of Arnica extract in 1 cup of water, 3 times a day. The extracts obtained were stored in cool, dry place for further studies. Paracetamol tablets were purchased from the local Pharmacy and retail chemical stores. In cases of anxiety disorders, patients were already on diazepam prescription. The study was conducted in the lab of Department of Homoeopathic Pharmacy, Dr. D.Y. Patil Homoeopathic Medical College & Resarch Centre, Pimpri, Pune over a period of 1 month. Students/patients who showed signs of anxiety & pain were selected & were divided in to 5 groups (n= 3 in each group). Group I: control group, Group II: Students of anxiety

treated with diazepam derivative, Group-III: Students of anxiety treated with Arnica plant extract, Group IV: Students of pain treated with paracetamol, Group V: Students of pain treated with arnica plant extract. In each group, the positive control group was treated with the standard reference drugs. Controls were given placebo.

Inclusion Criteria: All those students/patients who show signs of anxiety and pain/inflammation may be acute or chronic.

Exclusion Criteria: All cases apart from inclusion criteria.

Informed Consent was obtained from all the participants and was voluntary.

Safety of the volunteers was the 1st priority.

Improvement scale: Mild: 1 mark
 Moderate: 3marks
 Cure: 5 marks

Observation & Analysis

Statistical analysis-I

The results were expressed as mean ± S.E.M. All statistical comparisons were made by means of Student’s *t*-test and a *P* value smaller than 0.05 was regarded as significant.

Null Hypothesis: Arnica plant extract is a potent anxiolytic therapeutic agent.

Alternative Hypothesis: Arnica plant extract has no anxiolytic therapeutic activity.

RESULTS

Student	Score of patients on diazepam derivative	x-mean	(x-mean) ²	Score of patients on arnica extract	x-mean	(x-mean) ²
1	1	-0.66	0.435	3	-0.66	0.435
2	3	1.34	1.795	5	1.34	1.795
3	1	-0.66	0.435	5	1.34	1.795
mean	1.66		Total=2.665	3.66		Total=4.025

S.D (standard deviation) =

$$s = \sqrt{\frac{\sum(x - \bar{x})^2}{n - 1}}$$

S.D 1(Diazepam derivative) = 1.154

S.D 2 (Arnica extract) = 1.418

t-test:

$$t = \frac{\bar{X}_1 - \bar{X}_2}{\sqrt{\frac{s_1^2}{N_1} + \frac{s_2^2}{N_2}}}$$

= -2.365/1.054

= -2.243

i.e. t-calc= -2.243

t- tab= 0.05

If $t_{calc} > t_{tab}$, we reject the null hypothesis and accept the alternate hypothesis. Otherwise, we accept the null hypothesis. Above we can see that t-calc (-2.243) < t-tab (0.05). Hence, we accept the null hypothesis, i.e. Arnica plant extract is a potent anxiolytic therapeutic agent. (Mahajan 6th edition)

Statistical analysis-II

The results were expressed as mean ± S.E.M. All statistical comparisons were made by means of Student’s *t*-test and a *P* value smaller than 0.05 was regarded as significant.

Null Hypothesis: Arnica plant extract is a potent analgesic therapeutic agent.

Alternative Hypothesis: Arnica plant extract has no analgesic therapeutic activity.

RESULTS

Student	Score of patients on paracetamol	x-mean	(x-mean) ²	Score of patients on arnica extract	x-mean	(x-mean) ²
1	3	0.67	0.448	5	0.67	0.448
2	3	0.67	0.448	5	0.67	0.448
3	1	-1.33	1.768	3	-1.33	1.768
mean	2.33		Total=2.664	4.33		Total=2.664

S.D (standard deviation) =

$$s = \sqrt{\frac{\sum(x - \bar{x})^2}{n - 1}}$$

S.D 1(Paracetamol) = 1.154

S.D 2 (Arnica extract) = 1.154

t-test:

$$t = \frac{\bar{X}_1 - \bar{X}_2}{\sqrt{\frac{s_1^2}{N_1} + \frac{s_2^2}{N_2}}}$$

= -2/0.941

= -2.12

i.e. t-calc= -2.12

t- tab= 0.05

If $t_{calc} > t_{tab}$, we reject the null hypothesis and accept the alternate hypothesis. Otherwise, we accept the null hypothesis. Above we can see that t-calc (-2.12) < t-tab (0.05). Hence, we accept the null hypothesis, i.e. Arnica plant extract is a potent analgesic therapeutic agent. (Mahajan 6th edition)

DISCUSSION

The main purpose behind selection of this topic for research was to test the efficacy of Arnica Montana Plant extract as an anxiolytic as well as analgesic agent compared to routine anxiolytic and analgesic drugs used like diazepam derivatives, paracetamol etc. which have adverse side effects. For this study, students who showed signs of anxiety & pain were selected & were divided in to 5 groups (n= 3 in each group). Group I: control group, Group II: Students of anxiety treated with diazepam derivative, Group-III: Students of anxiety treated with Arnica plant extract, Group IV: Students of pain treated with paracetamol, Group V: Students of pain treated with arnica plant extract. In each group, the positive control group was treated with the standard reference drugs.

Improvement scale: Mild: 1 mark
 Moderate: 3marks
 Cure: 5 marks

It was observed that in both cases of anxiety as well as pain, arnica plant extract showed potent anxiolytic as well as analgesic effect when compared to paracetamol and diazepam derivatives. Patients on arnica plant extract showed quick, gentle & complete relief of the symptoms without any adverse side effects. Statistical analysis of the marks given as per the criteria of improvement was done (mean, standard deviation, sample size etc.), t-test was applied and value of t-calc. was compared with the value of t-tab both for anxiolytic as well as analgesic effect. As calculated, t-calc (anxiolytic) was -2.243 & t-calc (analgesic) was -2.12 which were less than t-tab. which was 0.05. If $t_{calc} > t_{tab}$, we reject the null hypothesis and accept the alternate hypothesis. Otherwise, we accept the null hypothesis. Hence, we accept the null hypothesis, i.e. Arnica plant extract is a potent anxiolytic as well as analgesic therapeutic agent.

Summary & Conclusion

As we can see from the observations and statistical analysis, t-calc. < t-tab. If $t_{calc} > t_{tab}$, we reject the null hypothesis and

accept the alternate hypothesis. Otherwise, we accept the null hypothesis. Hence, from the above readings it is evident that t-calc. < t-tab. Therefore, we accept the null hypothesis, i.e. Arnica plant extract is a potent anxiolytic as well as analgesic therapeutic agent. (Mahajan 6th edition)

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