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Clinical efficacy of polyherbal formulation Eezpain spray for muscular pain relief

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Abstract: The topical herbal formulation Eezpain spray consisting of natural ingredients that have been clinically proved for its analgesic and anti-inflammatory activity. The designed formulation on application knee and wrist joints, back of neck and shoulder, forearms and lower back exhibited significant efficacy. A total of 20 subjects both male and female applied Eezpain spray consisting of Gaultheria oil, Eucalyptus oil, Turpentine oil, Clove Oil, Menthol and Camphor. All the active materials are cited that these have analgesic activity in myalgia and neuralgia. The study design was prospective and opens as pilot study followed the inclusion and exclusion criteria. All the sign and symptoms were noted at baseline and at the end of 14 days treatment performance was evaluated. The statistical analysis was done by using Microsoft Excel2007 and SPSS version 18.0. It is concluded that Eezpain spray has shown efficacy in mild to moderate cases on applying locally to the affected parts to relieve pain from different ailments.

Keywords: Analgesic, anti-inflammatory, myalgia, natural.

INTRODUCTION

In alternative medicine the essential oils are mostly used as analgesic and anti-inflammatory remedies. It is described that some compounds that confer the effects of essential oils and the molecular mechanisms are largely unknown for example, linalool, a monoterpene compound commonly found as a major component of several essential oils has seen reported to produce anti-nociception in two different pain models in mice although the mechanism of its analgesic effects is unknown (Peana AT *et al.*, 2003). Menthol, the main ingredient of *Mentha piperita* L, is used for pain relief in daily life due to anti-nociception effects to some extent (Proudfoot CJ *et al.*, 2006 and Galeotti N *et al.*, 2002). Even though high doses of menthol caused sensory irritation (Green BG, 1992) because it acts as an activator of chemical noci-sensor [TRPA1/Transient receptor potential (TRP)] in humans (Karashima Y *et al.*, 2007). *Camphor*, is also known to exert the analgesic effects due to inhibition of TRPA1 (Xu H *et al.*, 2005) and activation of thermo sensitive receptor (TRPM8) (Vogt-Eisele AK *et al.*, 2007). However, camphor is not suited for use as an analgesic compound because it causes a warm and hot sensation (Green BG, 1990), probably through TRPV1 activation (Xu H *et al.*, 2005). Herbion newly designed Eezpain spray is soothing and emollient effect that provides relief from localized muscular pain and joint pain on applying externally. It contains Gaultheria oil, Eucalyptus oil, Turpentine oil, Clove Oil, Menthol and Camphor along with excipients to formulate the dosage form as spray.

Aim of study

This study was aimed to evaluate the clinical efficacy and safety of Eezpain spray for the treatment of muscular pain and joint pain.

Methodology

Unit Composition of Eezpain Spray

The unit composition of Eezpain spray consist of the following ingredients and quantity mentioned herewith in each 100ml, as *Mentha piperata* - Menthol crystals, 1.500g; *Mentha piperata*- Menthol crystals, 0.500g; *Gaultheria procumbens* (Gaultheria oil), 3.400ml; *Eucalyptus globules* (Eucalyptus oil); Turpentine Oil, 1-135ml; *Syzygium camphora* (Clove oil), 0.470ml; whereas excipients added are Propylene Glycol, 60.385gm; Tween 20, 5.0000gm; Polyethylene Glycol PEG 400, 15.000ml; IPA, 10.000ml; Benzyl alcohol, 0-4000ml.

Stability testing on Eezpain spray

The stability testing of Eezpain spray is mentioned as mentioned as under: Reason for stability being the new product (Pet bottle with plastic cap); stability condition: Accelerated 40°C±2, RH 75%±5, long term 30°C±2, RH 65%±5, testing frequency: Accelerated: Initial, 3 & 6 long term: Initial, 3, 6, 9, 12, 18, 24, test performed: Appearance, pH, density and microbiological purity, Results: 12 months (accelerated & long term) results found satisfactory.

Study design

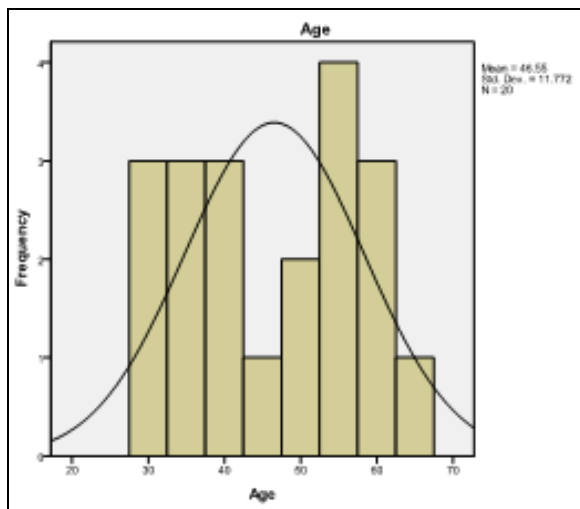
This study was prospective, open, non-comparative clinical trial. Clinical trial proforma, study protocol and product related information and informed consent forms

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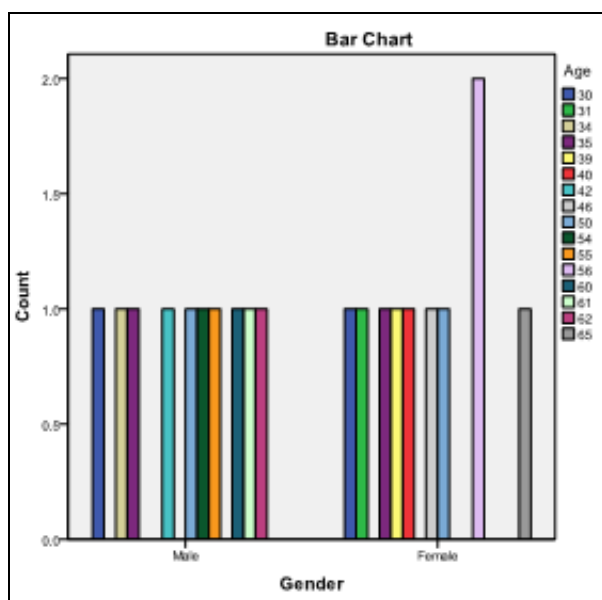
were submitted to the Research and Development Department of Herbion Pakistan (Pvt.) Limited.

Inclusion criteria

A total of 20 subjects of either sex who were diagnosed and categorized as suffering from pain into group 1 and group 2 were included in this study. Group 1 includes minor aches i.e. backache, sprains, neck pain, shoulder pain and muscular pain of limbs while group 2 includes chronic disorder i.e. rheumatoid arthritis, osteoarthritis, weight related joint disorder etc.



Graph 1(A): Age distribution of enrolled patients



Graph 1(B): Sex distribution of enrolled patients

Exclusion criteria

The patients with chronic skin problems, hypersensitivity and any other chronic ailments except group 1 and group 2 complaints.

Safety parameters

Inhaled or topical use of essential oils is much safer than oral use. However, allergic reactions to inhaled or topical plant fragrances are not uncommon. The systemic toxicity can result from ingestion or topical application at higher than recommended doses (Darben *et al.*, 1998).

Table 1: Sex and Age distribution of the respondent

S. No.	Respondents	Age	Gender
1	Respondent	65	Female
2	Respondent	56	Female
3	Respondent	61	Female
4	Respondent	50	Male
5	Respondent	40	Female
6	Respondent	54	Male
7	Respondent	30	Female
8	Respondent	34	Male
9	Respondent	39	Female
10	Respondent	42	Male
11	Respondent	35	Female
12	Respondent	30	Female
13	Respondent	50	Male
14	Respondent	46	Female
15	Respondent	35	Male
16	Respondent	31	Female
17	Respondent	56	Male
18	Respondent	55	Female
19	Respondent	60	Male
20	Respondent	62	Male

Work plan

At first the patients suffering from complaints of muscular pain or joint pain were screened out and initial history was taken on prescribed history sheet. The selected subjects were enrolled for clinical trial after taking informed consent from the patients. The patients were advised to externally apply Eezpain spray herbal formulation gently on affected part 2-3 times daily for 2-14 days with special is instruction *i. e.* avoid contact with eyes, should not apply to facial areas and do not bandage tightly or use with heated pads. The Eezpain spray has been designed only symptomatic improvement and the patients were examined at each follow up visit. Thoroughly examined the patient at every follow up visit and compare the level of improvement from baseline symptoms. The efficacy of Eezpain spray was assessed by mean of improvement in symptoms. We used generally three parameter to estimate the efficacy as excellent indicate (upto 70%), average indicate 50%) and no effect showed that there was no improvement. At the end of 14 days, the overall performance were evaluated and compared with baseline. Statistical evaluation of the collected data was done by using SPSS version 18.0 and Microsoft excels 2007. Chi-square test and cross tabulation were used for evaluation of significance of results. In this case chi square value less than 0.5 indicate

Table 2: Improvement in signs and symptoms

S. No.	Presenting Illness	Severity of Disease	Duration of Treatment	Effects			Results
				Excellent	Satisfactory	No Effect	
1.	Knee joint pain	Mild	14 Days	1	0	0	Found efficacious in mild to moderate cases of pains and inflammation
2.	Back ache	Mild	12 Days	0	1	0	
3.	Cervical pain	Severe	10 Days	0	1	0	
4.	Back ache	Moderate	12 Days	1	0	0	
5.	Ankle joint pain	Moderate	15 Days	0	0	1	
6.	Ankle Injury	Severe	10 Days	0	0	1	
7.	Knee injury inflammation	Moderate	14 Days	0	0	0	
8.	Back ache	Moderate	15 Days	0	1	0	
9.	Osteo-Arthritis	Moderate	14 Days	0	1	0	
10.	Back ache	Mild	14 Days	1	0	0	
11.	Cervical pain	Moderate	14 Days	0	1	0	
12.	Back ache	Severe	12 Days	0	0	1	
13.	Back ache	Moderate	15 Days	0	1	0	
14.	Ankle joint pain	Moderate	12 Days	0	1	0	
15.	Ankle Injury	Severe	10 Days	0	0	1	
16.	Knee injury inflammation	Moderate	14 Days	1	0	0	
17.	Back ache	Severe	12 Days	0	0	1	
18.	Osteo-Arthritis	Moderate	14 days	0	1	0	
19.	Back ache	Moderate	14 Days	0	1	0	
20.	Joint Pain	Mild	14 Days	1	0	0	

significance of the Eezpain spray. The study was conducted at Sohail Memorial Hospital, Landhi, Karachi in outpatient ward.

RESULTS

The clinical efficacy of herbal formulation Eezpain spray in the management of muscular pain (myalgia) and joint pain (Osteoarthritis and knee joint inflammation) indicated that Eezpain has statistically significant results in reducing the pain, inflammation, tenderness and provide calming effects also.

It was a pilot study conducted on 20 patients. The age limit was 30-70 years and duration was 10 day to 14 days only. The distribution of patients according to age and sex is given below in table 1 and Graph 1 and 2.

The overall efficacy of Eezpain spray is given in table 2 and 3. None of the patients complained or exhibited any adverse effects. The Eezpain spray has shown good efficacy in-group 1 and average efficacy in-group 2.

In this table the data was analyzed by using Cross tabulation in SPSS version 18.0 software and compared the efficacy of Eezpain spray by mode of application per day. It has proved that by applying Eezpain spray three times daily, its efficacy is maximum for curing the pain symptoms. No allergic reactions or side effects were noted on the use of Eezpain spray by the participants.

DISCUSSION

The application of Eezpain spray on affected part provides instant relief may be due to synergistic effects of active ingredients. The essential oil of leaves of *Gaultheria* provides quick relief from muscular pain when applied externally (Khare CP, 2004; Chopra RN *et al*, 1956; Ma XJ *et al.*, 2001). Another ingredient of Eezpain spray, camphor that is absorbed readily through skin and it provides feeling effects of cooling and good anesthetic and very effective for local anesthesia. The excellent feature of camphor is that it causes numbness of sensory nerves and affected area of application (Majid MH, 2010). When camphor applied to external skin, it numbs the nerve endings and these nerve endings then cannot transmit pain sensation (Bown D., 1995).

Turpentine has also shown a reduction in muscular pain in lumbar region and found to have an emergent effect to improve blood circulation and neuropathic pain reduction (Davydova *et al.*, 1998; Pushkareva, 1978). Menthol in *Mentha piperita* may provide instant relief from pain and provide soothing and cooling effect as it was documented that it has analgesic activity in myalgia and neuralgia (Khare CP, 2004; Haas M, 2004). As *Pinus roxburghii* sergeant has also shown the musculorelaxant and analgesic activity due to its oleoresin i.e. alpha and beta pinene constituents (Khare CP, 2004; Chopra RN *et al*, 1956).

Table 3: Level of improvement cross tabulation

Application per day * Level of Improvement Cross tabulation					
		Level of Improvement		Total	
		Mild Improvement	Moderate Improvement		
Application per day	Once daily	Count	4	4	8
		% within Application per day	50.0%	50.0%	100.0%
		% within Level of Improvement	44.4%	36.4%	40.0%
		% of Total	20.0%	20.0%	40.0%
	Twice daily	Count	5	5	10
		% within Application per day	50.0%	50.0%	100.0%
		% within Level of Improvement	55.6%	45.5%	50.0%
		% of Total	25.0%	25.0%	50.0%
	Three times in a day	Count	0	2	2
		% within Application per day	.0%	100.0%	100.0%
		% within Level of Improvement	.0%	18.2%	10.0%
		% of Total	.0%	10.0%	10.0%
Total		Count	9	11	20
		% within Application per day	45.0%	55.0%	100.0%
		% within Level of Improvement	100.0%	100.0%	100.0%
		% of Total	45.0%	55.0%	100.0%

The previous study described that the analgesic effects of the essential oil of *Syzygium aromaticum*, which was seen may be due to eugenol. It was also confirmed in another study that anti-nociceptive activity of eugenol against chemical (acetic acid tests), as well thermal stimuli. They also suggested that the eugenol predominantly inhibits the peripheral pain mechanism (Daniel AN *et al.*, 2009; Kurian R *et al.*, 2006). It is found that significant pH i.e. pH <0.5 in case of Eezapain spray calculated by using Chi square test SPSS version 18.0. Overall the results obtained of Eezpain spray on different types of pain ailments gave mild to moderate improvements in pain and these can be correlated and comparable with the earlier studies. The different constituents and mechanism are highlighted in their role to reduce pain as the overall effects.

CONCLUSION

It is concluded that Eezpain spray has shown efficacy in mild to moderate cases on applying on affected parts.

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