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EVALUATION OF CONTRAPAIN LEPA AND OIL (TOPICAL APPLICATION) FOR ANALGESIC AND ANTI-INFLAMMATORY ACTIVITIES IN MUSCULOSKELETAL DISORDERS WSR OSTEO ARTHRITIS (OA), RHEUMATOID ARTHRITIS (RA), SPONDYLITIS AND SPRAIN – A CLINICAL STUDY

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Abstract –
Background - Musculoskeletal Disorders are one of the most leading causes of disability around the world. Rheumatoid arthritis, Osteoarthritis and Back pain are the burden over the society of disability-adjusted-life years in both the developed and developing world. The prescribed formulations from contemporary science which are available in market possess certain limitations and adverse reaction. Contra pain powder and oil are proprietary Ayurveda medicines which are indicated in acute and chronic pain management.
Objective – To evaluate the Anti-inflammatory and Analgesic activities of Contra pain Lepa and Oil in Musculoskeletal Disorders.
Material and methods – A cohort of 91 human subjects were included in the study and divided into four subgroups as per disease (OA, RA, spondylitis and Sprain). Contra pain lepa and Oil application was done for a period of 7 days later follow up was done on 15th and 30th day. Primary outcomes such as Pain, Tenderness, *Shotha* (Swelling), *Stabdata* (Stiffness), Range of Motion and secondary outcomes like CBC, LFT, RFT, Physician Global Assessment were performed on baseline, 7th , 15th and 30th day.
Results - Significant improvement observed in Pain, Tenderness, Stiffness scoring in all groups on 7th, 15th and 30th day. No significant changes were observed in swelling in all groups on all assessment days. No significant changes were seen in the hematological values.
Conclusion –Contra pain Lepa and oil topical application has proved Analgesic and anti-inflammatory

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activity; it is effective and safe for application.

Key Words - Contra pain Lepa and oil, Analgesic, Anti-inflammatory, Musculoskeletal Disorders

1. Introduction -

Even though the Musculoskeletal disorders (MSD) are extensive source of morbidity in the population, yet their prominence seems to be insufficiently appreciated. Prevalence of MSD, including arthritis, rheumatism, and back/neck disorders, as a cause of chronic health problems or long-term disability [1]. MSD can be considered under *Vatavyadhi* which mainly occurs in *Vriddhavastha* due to *Dhatukshaya and Margavarodha*, which limits everyday activities. Being a *Vatavyadhi*, located in *Marmasthi sandhi* makes it *Kashtasadhya. Since Vata Dosha* has its major involvement in these disease, *Shula Pradhana Vedana* is the key feature [2].

MSD are said to be the reason for 40% of all chronic conditions, 54% of all long-term disability, 24% of restricted activity days and almost 20% of health care utilization. Osteoarthritis is the most common articular disorder begins asymptomatically in the 2ndand 3rd decades and is extremely common by age group of 60 to 70 years. Almost all persons by age 40 have some pathologic change in weight bearing joints especially in the Knee joints [3]. The incidence of Osteoarthritis in total musculoskeletal disorder is 12% and the reported prevalence from a study is 5.78%. The hip and knee are the major sites of significant disability. Knee osteoarthritis is more prevalent than hip Osteoarthritis, but taken together they affect 10-25% of those aged over 65 years [4]. Globally, low back pain affects as many as 80-90% of the people during their lifetime [5]. In contemporary science many formulations are available in market which too possess certain limitations with reference to potential efficacy and sometimes local site reactions.

In *Ayurvedic* classics[6] the treatment for above mentioned disease conditions are well defined. In the present context there is need of formulation with traditional concept so that outcome effect is ideal in management of pain and inflammation. M/s MB Life sciences has developed a formulation (Contra Pain Lepa and Oil) based on above classically mentioned ingredients and guidelines to reduce the pain and inflammation.

Table 1:- Ingredients –Contrapain Lepa (Powder):

Sl.No	Drugs	Scientific Names	Official Part	Form	Proportion
1	*Sigru*	*MoringaOleifera Lam*	Leaf	Powder	1Part
2	*Punarnava*	*Boerhaviadiffusa Linn*	(Rakta)	Powder	1Part
3	*Kunduru*	*Boswellia Serrata Roxb*	Exudate	Powder	1Part
4	*Rasna*	*Pluchea lanceolate Oliver andHiem*	Leaf	Powder	1Part
5	*Daruharidra*	*Berberisaristata DC*	Stem	Powder	1Part
6	*Shunthi*	*ZingiberofficinaleRoxb*	Rhizome	Powder	1Part

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7	*Lodhra*	*Symplocos racemose Roxb*	Stem bark	Powder	1Part
8	*Devadaru*	*Cedrusdeodara(Roxb.) Loud*	Heart wood	Powder	1Part
9	*Nausadara*	Ammonium chloride		Powder	1Part
10	*Citraka*	Plumbagozeylanical Linn	Root	Powder	1Part
11	*Sphatika*	NA	NA	Powder	1Part

Table 2:- Contrapain Oil: Herbal Pain Relieving Oil

S.No	Ingredient Name	Botanical Name	Parts used	Form	Proportion (mg)
1	*Nirgundi Patra*	*Vitex negundo Linn.*	Leaf	Powder	150 mg
2	*Eranda moola*	*Ricinus communis Linn*	Root	Powder	100 mg
3	*Rasna*	*Pluchea lanceolata Oliver andHiem.*	Leaf	Powder	150mg
4	*Mahabala*	*Sidar hombifolia Linn.*	Root	Powder	100 mg
5	*TilaTaila*	*Sesamumindicum*	Seed	Oil	5 ml
6	*Karpura*	*Camphora*			1 gm
7	Menthol -	*Mentha*			1 gm
8	Thymol (Oil)	*Traychy spermumammi*	Oil		0.25 gm
9	*Taila parnaTaila*	*Eucalyptus globulus*	Oil		0.25 ml
10	*GandhapuraTaila*	*Gaultheria fragrantissima*	Oil		1 ml
11	*Kattrina*	*Cymbopogoncitrates (Dc) Stapf.*	Panchanga	Powder	0.25 ml
12	*Katuveera*	*Capsicum annum*	Fruit	Powder	1 mg
13	Light Liquid Paraffin				q.s
14	*Twak Taila*	*Cinnamomum*	Stem bark	Oil	0.5 ml
15	*Lavanga* Taila	*Syzygium Aromaticum*	Fruit	Oil	0.5 ml

The above ingredients are formulated and tested for preclinical safety as per the ASU regulatory guidelines. The product is licensed from Dept. of AYUSH (Lno.L-155/Ayur on 28/09/2016).

2. Objective - To assess the analgesic and anti-inflammatory effect of Contrapain – Lepa and Oil topical application in Patients of Musculoskeletal Disorders

3. Material and Methods – The patients were recruited from OPD and IPD of our institution after fulfilling diagnostic criteria, inclusion criteria and signing informed consent. The Consort statement guidelines are followed for reporting the outcomes of the study

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3.1 Subjects - Among 200 screened patients 80 diagnosed case of musculoskeletal disorders were recruited from OPD and IPD department of KAHER's Shri B M Kankanawadi Ayurveda Mahavidyalaya and KLE Ayurveda Hospital and Medical Research Centre Belagavi, Karnataka.

Inclusion Criteria:
Patients with musculoskeletal pain and swelling fulfilling the diagnostic criteria of MSD, Male and female Patients with age between 20-70 years , Mild to moderate cases of MSD, Willing to consent for participation in the study, Human subjects who are currently on analgesics / NSAID were given a washout period of 7 days prior to recruitment

Exclusion Criteria:
Patients having severe MSD, K/C/O dermatitis, Pregnant and lactating women, Any other conditions whichever in the thought of Principal investigator will place the patient at risk or will influence the conduct of study or interpretation of results

Screening Methods
Human Subjects were allowed to participate in the study after screening the blood Parameters like CBC, LFT, RFT, RA, CRP, Serum Uric acid and those who are willing to give consent. The data obtained was documented systemically at proper time. Laboratory investigations were performed in our clinical laboratory, KLE Ayurveda Hospital, Belagavi.

3.2 Research Design – The study was **o**pen Labelled, non-comparative, Single group (Stratified as Four Sub Groups of Musculo- Skeletal Disease (MSD) viz. Osteo Arthritis(OA), Rheumatoid Arthritis (RA), Spondylitis and Sprain with clinical conditions of pain and inflammation). The results were assessed with Pretest and Posttest design

Intervention
All the recruited Musculo- Skeletal Disease (MSD) patients of Single group were stratified as four Sub Groups based on clinical conditions of pain and inflammation viz. OA (n=23), RA (n=21), Spondylitis (n=24) and Sprain(n=23). The Study drug Contrapain powder and oil was prepared and supplied by MB Life Sciences Pvt. Ltd., New Delhi. These patients received external application of contrapain Lepa i.e Contrapain powder (5gm) mixed with sufficient lukewarm water (15ml) made as a paste at the site of pain and left for 30 - 60 minutes later the applied Paste (Lepa) was removed by placing the part under running water and allowed to dry properly. This was followed by application of Contrapain oil at the site of pain for a period of 7 days. Previous animal studies have proven the efficacy of application of contra pain which was continued now with clinical study. The treatment procedure was explained to the subjects and written informed consent was obtained. The study was approved by Institutional ethical committee (Protocol admitted – BMK/17/PLG/01, KAHER's B M K Ayurveda Mahavidyalaya and Research Centre, Belagavi, date of Approval - 25/03/2017. CTRI Registration – CTRI/2017/09/009907). Data was collected from 1/6/17 to 28/02/18. Treatment was administered to all the recruited patients in the hospital and for outstation patients, day stay along with meals was provided in research ward of the hospital to provide treatment in the morning and evening. Subjects were educated to follow the treatment protocol and report the adverse drug events (AEs) to investigator as they come across.

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3.3 Assessment Criteria:

Primary Outcome: Pain by VAS Scale, Tenderness, *Shotha*, *Stabdata*, Range of Motion. Assessment was done on 0^{th}, 7^{th},15^{th} and 30^{th} Day using standard scientific parameters.
Secondary Outcome: CBC, LFT, RFT and Physician Global Assessment was done on 0^{th}, 7^{th},15^{th} and 30^{th} Day using standard scientific parameters.

3.4 Statistical Methods:

Statistical analysis was done using SPSS software version 20.0. Comparison of four subgroups at various time points was analyzed by Kruskal Wallis ANOVA test. Comparison between four subgroups at different time points was analyzed by Mann Whitney U test. Percentage of improvement between four subgroups from baseline to 7^{th}, 15^{th} and 30^{th} day was analyzed by Wilcoxon matched pairs test. Values are represented as mean and standard deviation. The performed test are considered as statistically significant at $p<0.05$.

4. Results:

91patients participated in the study among that 11 patients were dropped out and no severe ADRs were observed either during treatment period or during follow up period, except in two cases where mild rash with redness was seen, which was relieved on its own in few hours without medication and subjects have continued the treatment.

4.1 Primary outcomes - Significant improvement was observed within groups in Pain (VAS) scoring ($p<0.001$) on 7^{th}, 15^{th} and 30^{th} day. Pair wise comparisons between groups showed significant changes i.e OA vs Sprain ($p=0.0077$), RA vs Sprain ($p=0.0074$), Spondylosis vs Sprain ($p=0.0256$) on 30^{th} day. No significant changes were observed in swelling (within and between) on all assessment days. Significant improvement was observed within groups in tenderness scoring ($p<0.001$) on 7^{th}, 15^{th} and 30^{th} day. Pair wise comparisons between groups showed significant changes i.e OA vs Sprain ($p<0.001$), RA vs Spondylosis ($p<0.001$), Spondylosis vs Sprain ($p<0.001$) on 7^{th}, 15^{th} and 30^{th} day. Significant improvement was observed within groups in Stiffness scoring on baseline ($p= 0.026$), 7^{th} ($p= 0.05$) and 15^{th} day ($p= 0.024$). Pair wise comparisons between groups showed non-significant changes. PGAS scoring showed significant improvement ($p<0.001$) in OA, RA at 15^{th}, 30^{th} day and Sprain on 30thy day.

4.2 Secondary Outcomes – Minimal changes were seen in the haematological values like lymphocytes, monocytes, ESR, serum bilirubin, SGPT, SGOT, total protein, Creatinine, urea, uric acid, they were found to be negligible as they lie in the normal limits. Efficacy of treatment is sustainable as shown by follow up at 15^{th} and 30^{th} day observations. Trial Product has also showed its safety as observed by minimal variations in Haematological parameters like LFT and RFT.

5. Discussion

The ingredients in contrapain lepa and oil possess *Ushna guna (Punarnava, Kunduru, Rasna Daruharidra, Shunti, Devadaru, Nirgundi, Eranda Tila, Yavani, Tailaparna)* and *Kapha Vatahara propertie*[7]. Pain being one of the cardinal sign of aggravated *vata dosha* application of Lepa and taila helps in subsiding *vata dosha*. *Nirgundi* inhibits prostaglandins with the help of flavonoids present in it, which in turn decreases the pain[8]. Hence combined effect of these modalities is better in pain and tenderness. *Lepa dravya* namely *punarnava, chitraka, shigru, rasna, lodhra devadaru* are *shotha hara*, the procedure of *lepa* has *peedana* effect on part applied which has helped in the reduction of swelling[9].

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Ingredients of oil such as *Nirgundi* decreases the *vata* and *kapha dosha* hence it reduces *Shotha*. It does inhibition of Prostaglandins, COX-1 Pathways due to presence of flavonoids, which in turn decreases the inflammation[8]. *Sthamba* is a symptom produced due to *sheetaguna* of *vata* and *kapha*. The contents of contrapain lepa and oil due to their *ushna guna* and *kaphavatahara* property counteract the *sheetaguna* and counteract the stiffness in joints[7].

Transdermal route of drug administration has great potential to deliver the drugs continuously into the systemic circulation, thereby circumventing first-pass metabolism[10]. When a *Lepa* is applied over the surface of skin to the direction of hairs on it, through a proper base, the active principles of the ingredients of *Lepa* are dispersed into that base. After that, this combination enters the hair follicles and further gets absorbed through the *swedavahi srotas* and *siramukha*[11]. However, it should be kept in mind that the pila sebaceous uptake i.e. absorption of Lepa differs as per the site variation, skin condition and more important is the base through which it is applied. Thereafter it is the viable epidermis which starts off the catabolic degradation of the absorbed material with the help of essential enzymes. In due course of the above transformation, some new metabolites might be forming which pacifies the provocated *Doshas* locally and thus breaks the local pathogenesis cycle leading to the alleviation in the signs and symptoms. The physic-chemical properties of a drug in a topical dosage form affect that drug's trans-dermal delivery and topical bioavailability[10]. The molecules of the formulation after penetrating through the stratum conium and into viable epidermis and dermis produces its characteristic pharmacological response through receptors even before the blood and lymph circulations remove it, in which case it may set in a cascade of systemic effects though the horny layer is very impermeable to most chemicals, contributing the rate of absorption [10].

Most of the ingredients present in Contrapain lepa and liniment possess ushna *guna Kapha Vata hara , pachana, amadosha hara, shotha hara* properties due to which there is *stanika pachana* of *doshas* , reduction of *shotha*, *shoola* and *stamba* which are common presentations in musculoskeletal disorders[12]. The oils presents in the Contrapain liniment namely Menthol, *Karpura*, Thymol, *Tailparna*, *Gandhapura*, *Gandhatruna*, *Katuveera*, *Twak*, *Lavanga* oil possess counter irritant properties which causes irritation or mild inflammation of the skin for the purpose of relieving pain in muscles, joints and viscera distal to the site of application limiting step in trans-dermal absorption because of its high diffusion resistance, providing a small fractional area of 0.1 % only as permeable appendage shunt route[13]. Besides this route the drug molecules may penetrate through the hair follicles and sebaceous glands or through sweat ducts also and thus helps to remove or neutralize the toxins in initial stage of the drug absorption and the show its pharmacological effect.

6. Conclusion

Contra pain powder and oil are proprietary Ayurveda medicines which have proved the analgesic and anti-inflammatory properties in musculoskeletal disorders like OA, RA, Sprain and Spondylosis. The various drugs present in combine formulations possess these effects and the same are proved on multiple variables in the present study. Contra pain powder and oil application will be beneficial and solution for pain management in various musculo skeletal disorders. The formulations are safe, effective and will help in serving the society.

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Conflicts of Interest – None

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Consort Flow chart –