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A prospective, multicenter, interventional, phase IV clinical trial to evaluate the efficacy and safety of Pravek Rumakalp® tablets for the treatment of musculoskeletal pain and inflammation

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Abstract
Introduction: Musculoskeletal disorders (MSD), affecting over 1.7 billion people globally, are a leading cause of disability. These conditions, including osteoarthritis, rheumatoid arthritis, back pain, and soft tissue injuries, can severely impact quality of life, work productivity, and healthcare costs. While traditional NSAIDs provide pain relief, concerns over side effects have increased the demand for alternative treatments. Pravek Rumakalp®, an Ayurvedic non-steroidal formulation, is designed to alleviate musculoskeletal pain and inflammation, and this study evaluates its efficacy and safety.
Methods: This phase IV, multicenter, prospective, interventional trial enrolled 100 patients with musculoskeletal pain and inflammation. Participants received Pravek Rumakalp® tablets for 90 days, with a final telephonic follow-up on Day 97. The efficacy was assessed using the Pain Intensity Numeric Rating Scale (PI-NRS) and the Clinical Global Impression (CGI) scale. Safety was evaluated by monitoring adverse events (AEs), vital signs, laboratory tests and ECGs. Statistical analysis was performed using repeated measures ANOVA.
Results: Significant reductions in PI-NRS scores were observed at each follow-up visit (Day 30, Day 60, Day 90), with p-values <0.0001, indicating substantial pain relief. The safety profile was favourable, with nine mild AEs (fever, headache, nausea), all resolving during the study. No serious adverse events (SAEs) or deaths were reported. Vital signs, laboratory tests, and physical exams showed no clinically meaningful changes.
Conclusion: Pravek Rumakalp® demonstrated significant efficacy in reducing musculoskeletal pain and inflammation over 90 days of treatment, as evidenced by marked improvements in PI-NRS scores. The treatment was well-tolerated, with mild adverse events that resolved without significant safety concerns. These results suggest that Pravek Rumakalp® is a promising alternative to conventional NSAIDs for managing musculoskeletal pain and inflammation, with a favourable safety profile.

Keywords: Musculoskeletal disorders (MSD), a phase IV, pain intensity numeric rating scale (PI-NRS), pravek rumakalp®, clinical trial

Introduction
Musculoskeletal disorders (MSD) are one of the most common causes of disability worldwide, in 2020, around 1.7 billion people were reported to be affected [1]. MSD is defined as any type of the condition which cause discomfort to irreversible and disabling injury affecting the motor organs, muscles, tendons, bones, cartilage, ligaments and nerves[2]. Approximately 150 distinct conditions were included in MSD which can affect quality of life, work efficiency and health care costs of the individuals affected with [1]. They include joint diseases such as osteoarthritis[3] and rheumatoid arthritis [4], back [5] and neck pain [6, 7], osteoporosis and related fractures, soft tissue rheumatism (e.g., tendinitis, bursitis, and myofascial pain), injuries from sports or in the workplace, and trauma related to motor vehicle accidents [8]. The symptoms of musculoskeletal disorders may vary but mainly include pain, tenderness, weakness, stiffness, limited range of motion, and peripheral nerve irritation [9]. Pain may be localized, regional, or widespread. Musculoskeletal pain is typically classified as acute or chronic. Acute musculoskeletal pain is short in duration, typically less than 1 month.

Chronic pain persists for longer periods and is often more challenging to treat [10]. The pain brought on by musculoskeletal conditions can significantly impact quality of life for example, ability to work, sleep, and perform physical and social activities [11].

A variety of oral and topical analgesic medications are available for the treatment of musculoskeletal disorders and injuries [12]. These include non-steroidal anti-inflammatory drugs (NSAIDs) like acetaminophen and salicylates, which come in both over-the-counter and prescription forms [13]. It is important to note that while analgesics can provide pain relief, some carry the risk of adverse effects, including gastrointestinal, cardiovascular, and renal complications [14]. Medicinal plants contain diverse bioactive compounds, including alkaloids, flavonoids, terpenoids, phenolics, and essential oils, and have a long history of use in traditional medicine [15]. These secondary metabolites, such as flavonoids, alkaloids, and terpenoids, possess antioxidant, anti-inflammatory, and antimicrobial properties [16]. Due to their remarkable antioxidant, anticancer, cytotoxic, anti-inflammatory, cardioprotective, hepatoprotective, immunomodulatory, neuroprotective and antidiabetic properties, these compounds hold promise for treating musculoskeletal pain, swelling, and inflammation. Pravek Rumakalp® is a certified Ayurvedic, non-steroidal formulation designed as a substitute for allopathic NSAIDs, and is used to treat pain and inflammation related to rheumatoid arthritis, osteoarthritis, sciatica, spondylitis, and sprains. A phase-IV clinical trial to assess the efficacy and safety of Pravek Rumakalp® in a large Indian population will help characterize its safety profile, clinical effectiveness, and patient clinical profiles. Hence, the present study aims to generate data on the efficacy and safety of Pravek Rumakalp® tablets for treating musculoskeletal pain and inflammation in Indian patients.

Study rationale

The study is designed as a prospective, interventional trial to assess the efficacy and safety of Pravek Rumakalp® tablets in patients with musculoskeletal pain and inflammation. Enrolled subjects will receive Pravek Rumakalp® tablets for 90 days, with the first visit date serving as the index date (Day 0). Given the prospective nature of the study, the enrollment date will be the index date, making the maximum study participation period up to 97 days.

Study objectives

Primary Objective: Evaluate the efficacy of Pravek Rumakalp® tablets for the treatment of musculoskeletal pain and inflammation.

Secondary Objective: To evaluate the safety of Pravek Rumakalp® tablets for the treatment of musculoskeletal pain and inflammation.

Methods and analyses

1. Study design

A phase IV, prospective, multicenter, interventional clinical trial was conducted to assess the efficacy and safety of Pravek Rumakalp® tablets in treating musculoskeletal pain and inflammation. The study involved a 90-day treatment period, followed by a final telephonic follow-up visit on Day 97 (+2).

Study Design and Participants

Eligible participants, based on predefined inclusion/exclusion criteria, received Pravek Rumakalp® tablets for 90 days, with a maximum study duration of 97 days, including treatment and follow-up. Participants tracked their progress in a diary, which they were required to bring to each follow-up visit.

Assessments and Evaluations

- **Baseline Visit (Day -3 to Day -1):** Informed consent was obtained, Screening, demographic data, medical history, medication details and vitals & physical examination details were collected. An ECG was performed.
- **Randomization Visit-1(Day 0):** Screening for inclusion/exclusion criteria, treatment assignment and vital signs (waist circumference, pulse rate, blood pressure, respiratory rate, and body temperature) were assessed, along with physical examinations and medication details.
- **Follow-up Visits 2, 3 and 4 (Day 30, 60, and 90 ±2 days):** Medication, vital signs, physical examinations, efficacy (improvements in the Clinical Global Impression (CGI) scale, tenderness, joint mobility, muscle spasm-associated pain as measured by the Pain Intensity Numeric Rating (PI-NRS) Scale), safety (an ECG was performed and other biochemistry examinations were performed) and adverse events were monitored.
- **End-of-Study (Telephonic Follow-up) Visit (Day 97 ±2 days):** Telephonic follow-up for well-being and adverse event monitoring were conducted.

Efficacy Evaluation

Efficacy was evaluated using the Clinical Global Impression (CGI) scale to assess participant progress. Improvements in tenderness, joint mobility, and muscle spasm-related pain were measured from baseline to the final visit. Pain intensity was quantified using the Pain Intensity Numeric Rating Scale (PI-NRS) at visits on Day 0, Day 30 (+2), Day 60 (+2), and Day 90 (+2).

Safety Evaluation

Patient safety was evaluated by collecting demographic data and medical/surgical histories upon enrollment. Throughout the study, vital signs, concomitant medications, physical examinations, body weight, and BMI were regularly monitored. Furthermore, 12-lead ECGs were performed at baseline and study completion (Visit-4 (Day 90+2)), alongside haematology, biochemistry, and urine analyses. Serum pregnancy tests were conducted at scheduled visits, and any adverse events were meticulously recorded from the start of medication until the end of the study assessments.

2. Patient and public involvement

In the present study, patients with acute pain and inflammation associated with various musculoskeletal conditions, including prolapsed intervertebral disc, sprains and dislocations, spondylosis, spinal stenosis, periarthritis, frozen shoulder, prepatellar bursitis, spondylolisthesis, low-back pain, tendonitis, tenosynovitis and bursitis were enrolled based on predefined eligibility criteria. All participants who met the criteria were included in the study and received treatment with Pravek Rumakalp® tablets. The

study focused on evaluating the efficacy of Pravek Rumakalp® tablets in managing musculoskeletal pain and inflammation in these patients.

3. Participants and recruitment

The patients were selected by an investigator based on assessment against the following inclusion and exclusion criteria.

Eligibility criteria

Inclusion Criteria: Subjects were eligible for the study if they met all the following criteria: (1) Males or females aged between 18 and 60 years (inclusive); (2) Subjects capable of providing written informed consent; (3) Subjects experiencing acute pain and inflammation related to prolapsed intervertebral disc, sprains and dislocations, spondylosis (lumbar, cervical, ankylosing spondylosis), spinal stenosis, periarthritis, frozen shoulder, prepatellar bursitis, spondylolisthesis, low back pain, tendonitis, tenosynovitis, or bursitis.

Exclusion Criteria

Patients were excluded from the study if any of the following conditions were present: (1) Known hypersensitivity to the study drugs or any component; (2) Concurrent use of corticosteroids; (3) Use of medications or conditions that could pose an increased risk or interfere with the study, as determined by the study team; (4) Participation in other clinical trials within the last three months or during the study; (5) History of epilepsy, seizure risk, or current use of anti-epileptic drugs; (6) Pregnant or lactating women, or women of childbearing age not using an acceptable method of birth control; (7) Galactose or fructose intolerance; (8) Severe renal impairment, including those undergoing dialysis; (9) Active liver disease, including primary biliary cirrhosis and persistent unexplained liver function abnormalities; (10) Pre-existing gallbladder disease; (11) Subjects who have had or are planning pre- or post-surgical interventions.

Randomization method and blinding

Since this was a single-treatment study, no randomization was performed. The study was an open-label, meaning there was no blinding involved.

4. Study drug

Pravek Rumakalp® is a non-steroidal Ayurvedic formulation that effectively reduces pain and inflammation in muscles, nerves, and joints, making it a suitable alternative to allopathic NSAIDs (Non-Steroidal Anti-Inflammatory Drugs). The tablet contains powdered Shuddha Guggulu (Commiphora mukul), aqueous extracts of Nirgundi (Vitex negundo), Ashwagandha (Withania somnifera), Erandmul (Ricinus communis), Gandhaprasarini (Paederia foetida) and a decoction of Ashwagandha (Withania somnifera). The key ingredients provide various therapeutic benefits: Ashwagandha enhances muscle strength, Erandmul is effective for backaches and muscle pain, Gandhaprasarini helps relieve stiff and painful joints, Maharasnadi Kwath supports osteoarthritis management, and Shuddha Guggulu alleviates joint pain and muscle cramps.

Subject compliance monitoring

Records of treatment compliance were maintained for each subject throughout the study. Clinical Research Associates (CRAs) were responsible for monitoring treatment compliance during site visits and at study completion. The administration of the study drug was recorded in the subjects' diaries. Participants were instructed to return any unused investigational product and empty packaging to the clinic at each visit. Compliance rates were documented in the diary at each treatment visit. Subjects who were deemed non-compliant (defined as taking less than 80% of the prescribed dose) were allowed to continue in the study but were counselled on the importance of adhering to the prescribed medication regimen.

5. Study procedures

The study was conducted to evaluate the safety and efficacy of Pravek Rumakalp® tablets in patients with musculoskeletal pain and inflammation. The study enrolled adult patients who met the eligibility criteria and were willing to participate. Written informed consent was obtained, and each subject was assigned a subject identification (SID) number by the site team. The study was approved by Royal Pune Independent Ethics Committee, India.

The study drug was administered as per the treating physician's routine clinical practice, with a dosage of 1-2 tablets twice a day in lukewarm water, or as directed by the physician. The administration of study medication was recorded in the subject's diary. All prior and ongoing medications, including those for musculoskeletal pain, inflammation, and co-morbid conditions, were documented. Rescue medications were allowed at the discretion of the treating physician.

Compliance was monitored, with subjects asked to return unused or empty packs at each follow-up visit. Non-compliant subjects were counselled about the importance of adhering to the prescribed treatment regimen.

Subjects completed the study once data collection for Day 97 (telephonic follow-up visit) was finished or upon early withdrawal. The first dose of the study drug was administered on Day 0. Efficacy was evaluated through the Clinical Global Impression (CGI) scale and the Pain Intensity Numeric Rating Scale (PI-NRS) to assess improvements in tenderness, joint mobility, and muscle spasm-related pain.

Safety assessments included the monitoring of adverse events (AEs), serious adverse events (SAEs), clinical signs, vital signs, laboratory tests, and any abnormal findings during the treatment period. Early withdrawal reasons and causes were recorded, and adverse events were monitored until resolved.

At enrollment (Day 0), demographic information and medical histories were collected. The study schedule included safety tests and laboratory assessments at baseline, Day 30, Day 60, and Day 90. Additional tests were conducted as needed by the treating physician.

The follow-up visits occurred as per the treating physician's recommendation, and data collection coincided with routine clinical visits. Unscheduled visits or telephone follow-ups could be arranged if necessary. Any additional information, such as adverse events or concomitant medications, was recorded in the eCRF.

The statistical analysis plan (SAP) outlined the analysis details, including tables and figures, which were finalized before the database lock. The safety set included all patients who took at least one dose of the study drug, while the

intent-to-treat (ITT) set included all patients with a baseline value and at least one post-baseline value. The per-protocol (PP) set included patients who had baseline and follow-up data at all-time points.

Endpoints

- **Efficacy outcomes** at Day 0, 30, 60, and 90: Improvement in CGI, tenderness, joint mobility, and muscle spasm-related pain (measured by PI-NRS).
- **Safety outcomes** during the 97-day treatment period: Incidence of AEs and SAEs, severity, and relationship to study treatment.
- **Clinical profile at baseline:** Demographics, medical history, and concomitant medications.
- **Patterns of usage:** Discontinuations, dosage regimens, and compliance. The study concluded after the final data collection at Day 97.

6. Outcomes

Efficacy: The study aimed to estimate the improvement in the Clinical Global Impression scale (CGI) and the improvement in tenderness, joint mobility, and muscle spasm-associated pain from baseline to final assessment, as measured by the Pain Intensity Numeric Rating Scale (PI-NRS) at Day 0, 30, 60, and 90. The CGI scales are global measures used by clinicians to reflect a patient's overall condition [17].

Safety: Safety outcomes included the incidence of adverse events (clinical signs, symptoms, vital signs, and laboratory parameters), the incidence of adverse events of interest, and the determination of the type, frequency, severity, and relationship of reported adverse effects to the study treatment [18].

7. Sample size

The study planned to recruit 100 patients from two to four sites across India over six months. It was designed as a prospective, interventional, phase IV study in a real-world setting, enrolling all eligible patients (considered to be 100) during the recruitment period. A total of 100 patients were screened and enrolled from three sites. The intent-to-treat (ITT) and per-protocol (PP) populations both consisted of 100 patients. The safety population (N=100) included all patients who took at least one dose of the study drug. Four patients discontinued or were withdrawn from the study [19].

8. Statistical analysis

We conducted both an intention-to-treat (ITT) analysis and a per-protocol analysis [20] (for participants with perfect compliance and follow-up). Since the study was not designed as a superiority randomized controlled trial (RCT), the per-protocol analysis was included to identify potential treatment effects, as non-compliance and crossover can reduce the observed differences between visits. Descriptive statistics were used to compare baseline characteristics of participants, including means with standard deviations (SD) for continuous variables, medians with interquartile ranges (IQR) for non-normally distributed variables, ranges from minimum to maximum, and proportions for categorical variables. The same descriptive statistics were applied to demographic variables. The p-value was calculated using One-way Repeated Measurement ANOVA, with Tukey-Kramer adjustment for pairwise multiple comparisons. Visit-2, Visit-3, and Visit-4 were compared to Visit-1 (the reference visit). Lastly, the mean pain intensity with standard deviation (SD) for improvements in tenderness, joint mobility, and muscle spasm-related pain from baseline to each follow-up visit was presented in Table 2.

Results

The study assessed the efficacy and safety of a treatment for acute pain and inflammation associated with musculoskeletal conditions in 100 patients, 73% of patients were males, with a mean age of 43.69 years. The average height, weight, and BMI of the patients were 164.21 cm, 65.835 kg, and 24.39 kg/m2, respectively. Patients who met the inclusion criteria were administered the study drug orally twice daily for 90 days (Table 1).

Compliance and Monitoring

Treatment compliance was monitored by clinical research associates through patients site visits, diary entries, and by counting returned unused medication. Patients who took less than 80% of the prescribed dose were counselled on the importance of adherence. Only 4% (4) of patients were lost to follow-up after the initial visits.

Efficacy Assessment

Efficacy was measured using the Pain Intensity Numeric Rating Scale (PI-NRS), assessing improvements in tenderness, joint mobility, and muscle spasm-associated pain from baseline to the final visit-4. Significant improvements in all efficacy endpoints were observed from baseline to final visit-4 (Day 90) where the repeated measures ANOVA indicates a highly significant reduction in PI-NRS scores from baseline to each visit, with all p-values being with $p<0.0001$ (Table 2).

Safety Assessment

Safety monitoring included recording adverse events (AEs), serious adverse events (SAEs), vital signs, and laboratory investigations throughout the treatment period. Nine AEs were correlated with the treatment, the most frequent being fever, headache, and nausea, all of which were mild in nature and resolved during the study. No deaths, serious adverse events, or other significant AEs occurred (Table 3).
Table 4a, 4b, 5a, 5b &6 summarizes the data of safety from baseline (Visit-1), Visit 2, Visit-3 and Visit 4 where difference between each Visit and baseline visit-1 is performed. Some clinically significant alterations in vital signs and laboratory measurements were noted, but they did not have a clinically meaningful impact. No clinically significant alterations were found in physical examinations and echocardiograms.

Discussion

Pravek Kalp Private Limited conducted a phase IV, prospective, multicenter, interventional clinical study to assess the effectiveness of Pravek Rumakalp® tablets in 100 patients suffering from acute pain and inflammation related to conditions such as prolapsed intervertebral disc, sprains, dislocations, spondylosis, spinal stenosis, periarthritis, frozen shoulder, prepatellar bursitis, spondylolisthesis, low-back pain, tendonitis, tenosynovitis, and bursitis. Ninety-six patients completed the study, while four were lost to follow-up. Nine adverse events and nine minor protocol deviations were reported, none of which impacted patient safety during

the clinical trial. Clinical laboratory variables related to hematology, biochemistry, and urine analysis showed no clinically relevant changes.

Efficacy analysis revealed a statistically significant change from baseline to endpoint overall.

Table 1: Demographic and Other Baseline Characteristics

Parameters	Rumakalp (N=100)	Statistics		
	n	Min-Max	Median	Mean (SD)
Age (Years)	100	19-59	44.0	43.6(9.63)
Height (Cm)	100	152.00-185.00	163.700	164.206(5.9623)
Weight (kg)	100	50.00-89.02	64.100	65.835(7.7051)
Body Mass Index (kg/m^2)	100	20.0-32.7	23.90	24.39(2.022)
Gender	n (%)			
Male	73(73.0)			
Female	27(27.0)			

Note: N = Total number of subjects in treatment arm; n= Total number of non-missing subjects in specified category; SD = Standard Deviation.

Table 2: Summary of Improvement in Tenderness, Joint mobility and Muscle spasm from Baseline to Final Assessment, Measured by the Pain Intensity Numeric Rating Scale (PI-NRS)

Parameters	Rumakalp (N=100)	Statistics				
		Min-Max	Median	Mean (SD)	Estimate (95% CI)	P Value
	n				Lower-Upper	
Tenderness						
Visit-1	100	2-10	5.0	5.7(1.91)	Reference	
Visit-2	100	2-9	5.0	4.9(1.54)	0.81(0.53-1.09)	<0.0001
Visit-3	99	1-8	4.0	4.1(1.61)	1.59(1.31-1.87)	<0.0001
Visit-4	96	1-7	3.0	3.1(1.40)	2.66(2.38-2.94)	<0.0001
Joint mobility						
Visit-1	100	2-9	5.0	5.3(1.76)	Reference	
Visit-2	100	1-9	4.0	4.6(1.59)	0.64(0.35-0.93)	<0.0001
Visit-3	99	0-9	4.0	3.8(1.66)	1.45(1.15-1.74)	<0.0001
Visit-4	96	0-8	3.0	2.8(1.50)	2.48(2.19-2.78)	<0.0001
Muscle Spasm						
Visit-1	100	2-9	5.0	5.3(1.84)	Reference	
Visit-2	100	1-9	4.0	4.6(1.62)	0.75(0.38-1.12)	<0.0001
Visit-3	99	1-8	4.0	3.8(1.59)	1.47(1.10-1.84)	<0.0001
Visit-4	96	0-9	3.0	2.8(1.67)	2.55(2.18-2.92)	<0.0001

Note: N = Total number of subjects in treatment arm; n= Total number of non-missing subjects in specified category; SD = Standard Deviation; p-value is based on One-way Repeated measurement ANOVA Tukey-Kramer adjustment is performed for pairwise multiple comparisons. Visit-2, Visit-3 and Visit-4 are compared against Visit-1 (reference) respectively.

Table 3: Description of adverse events in study groups

	Rumakalp (N = 100)
Outcome	n (%)
Number of adverse events	9 (9.00)

Note: N = Total number of subjects in treatment arm. n= Total number of non-missing subjects in specified category.

Table 4a: Summary of vital signs at Visit-1, visit-2, visit3 and Visit-4 and differences of each visit compared with visit-1

Statistics	Rumakalp (N=100)						
	n						
Parameters	**Visit-1**	**Visit-2**	**Visit-1 minus Visit-2 (CFB)**	**Visit-3**	**Visit-1 minus Visit-3 (CFB)**	**Visit-4**	**Visit-1 minus Visit-4 (CFB)**
Systolic blood pressure (mm Hg)							
n	100	100	100	99	99	96	96
Mean (SD)	120.9(2.91)	122.1(4.06)	1.1(4.46)	122.7(4.54)	1.7(4.84)	122.8(4.37)	1.9(5.00)
Median	120.0	121.5	0.0	122.0	1.0	122.0	2.0
Min-Max	110-130	111-137	-9 -13	115-132	-15 -12	110-132	-10 -15
Diastolic blood pressure (mm Hg)							
n	100	100	100	99	99	96	96
Mean (SD)	81.0(2.70)	81.1(4.08)	0.1(4.07)	81.8(4.29)	0.8(4.02)	82.4(4.08)	1.4(4.50)
Median	80.0	80.5	0.0	82.0	0.0	82.0	2.0
Min-Max	72-87	62-90	-10 -10	72-96	-8 -14	70-90	-10-10
Respiratory Rate (/minute)							
n	100	100	100	99	99	96	96

Mean (SD)	53.8(32.55)	17.3(2.04)	-36.5(30.79)	17.6(1.73)	-36.5(31.09)	17.4(2.00)	-36.6(30.91)
Median	76.5	18.0	-58.0	18.0	-58.0	18.0	-58.0
Min-Max	13-90	13-20	-72-4	13-20	-71-5	13-20	-71-4
Pulse Rate (Beats/Minute)							
n	100	100	100	99	99	96	96
Mean (SD)	47.7(35.21)	84.5(6.36)	37.1(32.09)	83.8(5.90)	36.8(32.43)	84.4(5.74)	37.3(31.51)
Median	20.0	86.0	57.0	83.0	58.0	84.0	58.5
Min-Max	18-94	72-98	-19-73	72-98	-16-72	72-94	-10-72
Body Temperature (°F)							
n	100	100	100	99	99	96	96
Mean (SD)	97.91(0.710)	97.75(1.117)	-0.16(1.271)	106.66(88.062)	8.76(88.134)	97.65(0.712)	-0.31(0.839)
Median	98.10	98.00	0.00	98.00	-0.10	97.90	-0.10
Min-Max	92.4-98.6	87.8-98.6	-10.3 -5.7	96.1-974.0	-2.0-876.8	94.4-98.4	-4.0-1.1

Note: N = Total number of subjects in treatment arm; n= Total number of non-missing subjects in specified category; SD = Standard Deviation; p-value is based on One-way Repeated measurement ANOVA Tukey-Kramer adjustment is performed for pairwise multiple comparisons. Visit-2, Visit-3 and Visit-4 are compared against Visit-1 (reference) respectively.

Table 4b: Summary of vital signs at Visit-1, visit-2, visit3 and Visit-4 and differences of each visit compared with visit-1

Statistics	**Rumakalp (N=100)**						
	n						
Parameters	**Visit-1**	**Visit-2**	**Difference Between Visit-1 and visit-2 (CFB)**	**Visit-3**	**Difference Between Visit-1 and visit-3 (CFB)**	**Visit-4**	**Difference Between Visit-1 and visit-4 (CFB)**
Waist circumference (cm)							
n	100	100	100	99	99	96	96
Mean (SD)	73.1(24.63)	73.1(24.63)	0.0(0.40)	73.1(24.82)	0.1(0.55)	72.6(25.00)	0.1(0.71)
Median	80.0	80.0	0.0	80.0	0.0	80.0	0.0
Min-Max	30-109	30-109	-3-1	30-110	-3-2	30-110	-3-2
Height(cm)							
n	100	100	100	99	99	96	96
Mean (SD)	164.21(5.962)	164.21(5.927)	0.0(0.51)	164.11(5.951)	0.0(0.40)	164.21(6.004)	0.0(0.41)
Median	163.70	163.70	0.0	163.70	0.0	163.85	0.0
Min-Max	152.0-185.0	152.0-185.0	-4-3	152.0-185.0	-4-0	152.0-185.0	-4-0
Weight (kg)							
n	100	100	100	99	99	96	96
Mean (SD)	65.38(9.116)	66.11(7.624)	0.73(4.535)	66.01(7.553)	0.63(4.461)	66.16(7.705)	0.68(4.588)
Median	63.85	65.00	0.00	64.50	0.00	64.50	0.00
Min-Max	16.0-89.0	51.0-89.0	-2.2-43.1	50.0-89.0	-2.5-43.9	50.0-89.0	-3.9-44.0
Body Mass Index (kg/m2)							
n	100	100	100	99	99	96	96
Mean (SD)	24.37(2.016)	24.44(1.996)	0.07(0.387)	24.53(2.035)	0.14(0.612)	24.57(1.96)	0.17(0.597)
Median	24.00	24.25	0.00	24.20	0.00	24.40	0.00
Min-Max	20.0-32.7	20.0-32.7	-0.9-2.0	20.0-32.7	-0.9-3.9	20.0-32.7	-14-3.4

Note: N = Total number of subjects in treatment arm; n= Total number of non-missing subjects in specified category; SD = Standard Deviation; CFB= CFB = Change from baseline; Tukey-Kramer adjustment is performed for pairwise multiple comparisons. Visit-2, Visit-3 and Visit-4 are compared against Visit-1 (reference) respectively.

Table 5a: Summary of Complete blood cell count at screening, visit-2 and Visit-4 and differences of each visit compared with screening

Statistics	**Rumakalp (N=100)**				
	n				
Parameters	**Screening**	**Visit-2**	**Difference Between Screening and visit-2 (CFB)**	**Visit-4**	**Difference Between Screening and visit-4 (CFB)**
RBC Count					
n	100	98	98	96	96
Mean (SD)	4.953(0.5154)	4.814(0.5551)	-0.143(0.6161)	5.255(0.3987)	0.314(0.5474)
Median	4.800	4.650	-0.080	5.220	0.600
Min-Max	1.03-6.80	3.53-6.30	-1.77-1.30	4.30-6.30	-1.40-1.30
WBC Count					
n	100	98	98	96	96
Mean (SD)	6529.6(2146.70)	7353.7(1708.17)	836.4(2367.12)	6540.7(2190.81)	89.2(1133.76)
Median	6500.0	7705.0	580.0	6615.0	356.0
Min-Max	2387-9730	3490-10500	-4640-5433	2849-10086	-4180-3709
Platelets (lakhs)					
n	100	98	98	96	96

Mean (SD)	2.7(0.66)	2.8(0.65)	0.1(0.69)	3.4(0.93)	0.7(0.95)
Median	2.6	2.9	0.2	3.6	0.5
Min-Max	1-4	1-4	-2-1	1-5	-2-2
Haemoglobin (Hb)					
n	100	98	98	96	96
Mean (SD)	14.25(1.378)	14.81(1.248)	0.56(1.152)	14.57(1.308)	0.35(0.712)
Median	14.00	14.90	0.10	14.62	0.35
Min-Max	11.4-17.7	11.2-17.5	-1.3-4.3	11.8-17.5	-1.8-1.0
Body Neutrophils					
n	100	97	97	96	96
Mean (SD)	58.45(9.129)	55.16(8.399)	-3.24(8.897)	56.01(9.288)	-2.45(5.515)
Median	57.15	55.00	-0.40	55.00	-3.84
Min-Max	31.9-79.0	31.6-73.5	-34.3-15.0	30.8-75.6	-35.1-10.2
Eosinophils					
n	100	98	98	96	96
Mean (SD)	3.03(1.569)	3.52(1.658)	0.48(1.644)	2.95(1.501)	-0.08(1.264)
Median	3.00	3.10	0.40	3.00	-0.29
Min-Max	0.3-6.2	0.5-6.6	-4.0-5.7	0.0-6.5	-1.5-5.7
Basophils					
n	100	98	98	96	96
Mean (SD)	0.60(0.666)	0.30(0.522)	-0.31(0.674)	0.63(0.646)	0.02(0.284)
Median	0.40	0.00	0.00	0.40	0.00
Min-Max	0.0-2.0	0.0-1.9	-2.0-0.9	0.0-2.0	-0.7-0.9

Note: N = Total number of subjects in treatment arm; n= Total number of non-missing subjects in specified category; SD = Standard Deviation; p-value is based on One-way Repeated measurement ANOVA Tukey-Kramer adjustment is performed for pairwise multiple comparisons. Visit-2 and Visit-4 are compared against screening (reference) respectively.

Table 5b: Summary of Complete blood cell count at screening, visit-2 and Visit-4 and differences of each visit compared with screening

Statistics	**Rumakalp (N=100)**				
	n				
Parameters	**Screening**	**Visit-2**	**Difference Between Screening and visit-2 (CFB)**	**Visit-4**	**Difference Between Screening and visit-4 (CFB)**
Lymphocytes					
n	100	98	98	97	97
Mean (SD)	29.767(8.0393)	31.674(7.2853)	1.963(6.7789)	30.40(8.150)	0.670(3.6223)
Median	30.000	32.000	0.000	32.00	2.000
Min-Max	13.00-51.50	15.90-45.10	-25.60-19.00	9.0-45.0	-25.60-8.00
Monocytes					
n	100	98	98	97	97
Mean (SD)	6.91(2.484)	7.31(2.513)	0.31(2.298)	6.54(2.573)	-0.37(0.634)
Median	6.50	7.00	0.00	6.00	-0.30
Min-Max	2.0-13.1	2.0-12.8	-6.0-7.0	1.0-12.8	-1.0-1.7
MCH					
n	100	98	98	97	97
Mean (SD)	29.66(3.815)	30.14(2.995)	0.49(3.878)	29.38(2.701)	-0.25(2.953)
Median	29.60	30.10	0.00	29.19	-0.90
Min-Max	3.0-35.6	21.0-40.4	-6.9-27.0	22.3-34.6	-5.5-27.0
MCHC					
n	100	98	98	97	97
Mean (SD)	34.45(2.054)	35.93(2.854)	1.54(2.773)	34.47(1.961)	0.04(0.557)
Median	34.20	35.35	0.16	34.40	-0.02
Min-Max	30.2-39.6	31.2-42.8	-5.2-8.5	30.2-39.6	-1.0-2.9
MCV					
n	100	98	98	97	97
Mean (SD)	87.95(7.634)	85.34(7.159)	-2.77(5.907)	87.56(7.813)	-0.42(2.227)
Median	86.05	84.15	-0.76	85.40	-1.00
Min-Max	74.5-102.0	70.4-100.1	-22.4-12.8	73.5-101.5	-10.0-13.6
ESR					
n	60	60	60	58	58
Mean (SD)	13.3(5.06)	22.59(14.414)	9.33(12.522)	13.3(4.46)	0.0(2.06)
Median	12.5	14.00	1.50	12.0	0.0
Min-Max	4-32	5.0-44.7	-10.9-32.8	6-31	-5-5
CRP					
n	60	60	60	58	58
Mean (SD)	1.41(1.120)	67.00(79.418)	65.59(78.593)	1.44(1.122)	0.01(0.199)

Median	0.90	1.00	0.15	0.94	0.00
Min-Max	0.2-5.3	0.3-188.6	-0.6-185.5	0.3-5.0	-0.6-0.7

Note: N = Total number of subjects in treatment arm; n= Total number of non-missing subjects in specified category; SD = Standard Deviation; p-value is based on One-way Repeated measurement ANOVA Tukey-Kramer adjustment is performed for pairwise multiple comparisons. Visit-2 and Visit-4 are compared against screening (reference) respectively.

Table 6: Summary of Haematology and Biochemical parameters at screening, visit-2 and Visit-4 and differences of each visit compared with screening

Statistics	**Rumakalp (N=100)**				
	n				
Parameters	**Screening**	**Visit-2**	**Difference Between Screening and visit-2 (CFB)**	**Visit-4**	**Difference Between Screening and visit-4 (CFB)**
Haematocrit					
n	100	97	97	97	97
Mean (SD)	42.8(6.05)	54.1(21.37)	11.1(19.57)	42.8(4.70)	-0.1(3.94)
Median	42.5	43.9	0.0	42.2	-0.1
Min-Max	5-53	36-111	-4-58	36-51	-6-36
Cholesterol					
n	100	97	97	97	97
Mean (SD)	194.1(37.75)	176.2(27.71)	-17.8(53.15)	193.7(37.54)	-1.1(15.20)
Median	191.1	175.6	0.0	190.0	2.7
Min-Max	139-283	140-252	-141-73	108-279	-102-20
RBS					
n	100	97	97	98	98
Mean (SD)	102.7(21.79)	71.4(40.61)	-31.3(59.48)	102.1(18.51)	-1.0(8.67)
Median	95.0	89.4	-2.0	96.0	-2.0
Min-Max	79-177	1-132	-168-34	77-159	-37-30
Sodium Chloride					
n	100	97	97	98	98
Mean (SD)	140.4(3.07)	110.7(50.47)	-29.7(50.39)	139.5(3.14)	-0.9(1.89)
Median	140.0	140.0	-0.5	138.4	-1.7
Min-Max	134-148	20-146	-127-7	132-147	-14-6
Potassium					
n	100	96	96	98	98
Mean (SD)	4.18(0.683)	9.30(8.502)	5.12(8.790)	4.07(0.683)	-0.09(0.383)
Median	4.10	4.55	0.10	3.80	-0.20
Min-Max	2.5-5.8	3.0-31.5	-0.7-28.9	2.8-5.8	-0.7-1.1
RA factor					
n	100	60	60	57	57
Mean (SD)	11.67(11.496)	16.34(10.762)	1.16(9.905)	14.83(12.011)	-0.22(3.052)
Median	8.05	12.25	0.00	11.00	0.00
Min-Max	1.1-62.0	1.9-31.4	-31.6-23.4	1.9-59.0	-12.0-6.0

Note: N = Total number of subjects in treatment arm; n= Total number of non-missing subjects in specified category; SD = Standard Deviation; p-value is based on One-way Repeated measurement ANOVA Tukey-Kramer adjustment is performed for pairwise multiple comparisons. Visit-2 and Visit-4 are compared against screening (reference) respectively.

Conclusion

Efficacy Conclusion

The results indicate that repeated measures ANOVA demonstrated a highly significant reduction in Pain Intensity Numeric Rating Scale (PI-NRS) scores from baseline to each subsequent visit, with all p-values being less than 0.0001. This finding underscores the effectiveness of the treatment or intervention in consistently decreasing pain intensity over time. The specific reductions in mean PI-NRS scores, accompanied by decreasing standard deviations, suggest that patients experienced substantial and progressive improvements in tenderness, joint mobility, and muscle spasm with each visit. Overall, these results highlight the treatment's efficacy in alleviating pain and enhancing functional outcomes for patients over the course of the study.

Safety Conclusion: The safety assessment of the study revealed that nine subjects reported mild adverse events (AEs), with fever, headache, and nausea being the most frequently noted. All reported AEs resolved by the end of the study, and there were no deaths or serious adverse events (SAEs), indicating a favourable safety profile for the treatment. Although a few clinically significant alterations in vital signs were observed, they did not have any clinically meaningful impact on participants' health. Furthermore, physical examinations and echocardiograms showed no significant changes, with all parameters remaining within physiological limits. Laboratory investigations, including haematology, biochemistry, and urinalysis, indicated some clinically significant findings; however, these did not result in substantial alterations among the treatment arms. Overall, the findings suggest that the investigational treatment was well-tolerated by participants, with a low incidence of mild AEs and no significant safety concerns arising throughout the study duration.

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Author contributions

I confirm sole responsibility for all aspects of this study, including its conceptualization, design, data collection, analysis, interpretation, manuscript drafting, and final approval.

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