

Clinical Evaluation of an Herbal Formulation, Rhulief[®], in the Management of Knee Osteoarthritis

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Introduction

Osteoarthritis (OA) is a leading cause of physical disability and impaired quality of life. Current medical treatments to manage the condition remain symptomatic, designed to control pain and improve function and quality of life. Given the efficacy, safety and tolerability issues associated with NSAIDs, development of new agents to manage OA without adverse events remains a priority. Traditional medicines using plant-derived compounds offer a safer alternative tool for the management of many chronic diseases. One such treatment option for osteoarthritis of the knee is a combination of the active principles of *Boswellia serrata* and the common spice *Curcuma longa* (turmeric).

Curcumin, the active component of turmeric, possesses antioxidative, antiinflammatory and antiarthritic properties and can modulate an incredibly large number of signaling pathways and thus possesses an extremely wide range of biological activities. The oral bioavailability of curcumin is poor so the bioactivity has not yet been translated into clinical benefit. A proprietary formulation of curcumin with enhanced bioavailability, trade named BCM-95[®], is one of the components of the study drug.

Biological activity of *Boswellia serrata* arises from the boswellic acids (BA), of which the 3-O-acetyl-11-keto-boswellic acid (AKBA) is the most active. The AKBA content of commercial *Boswellia* extracts is low at ~2% and a preparation with enhanced AKBA content, trade named BosPure[®] with 10% AKBA was used in the present study. Glycosaminoglycan synthesis is necessary for cartilage repair. *Boswellia* prevents decrease in glycosaminoglycan levels, whereas NSAIDs can disrupt glycosaminoglycan synthesis, which can, in turn, accelerate cartilage damage.

Aim of the Study

Evaluate efficacy, safety and tolerability of Rhulief[®] compared to Celecoxib in the management of knee osteoarthritis.

Material and Methods

Randomized two arm open study with positive control. The study drug Rhulief[®] contains BCM-95[®] 350 mg and BosPure[®] 150 mg in 500 mg hard gelatin capsule. BCM-95[®] is a 100% turmeric extract with 8 times more orally bioavailable curcumin. BosPure[®] is a *Boswellia serrata* extract with acetyl boswellic acids with 10% acetyl keto BA and no beta BA.

Group I (n=15): Rhulief[®] 500 mg capsule twice daily.

Group II (n=15): Celecoxib 100 mg capsule twice daily.

Study duration: 12 weeks.

Patient Population

Inclusion criteria: Male and female patients 18 to 65 yrs, medically stable with moderate form of OA evidenced by narrowing of the medical joint space with swelling.

Exclusion criteria: Long standing OA with gross deformity, patients with severe form of OA with gross radiological findings, swelling

and restricted mobility, history of rheumatoid or reactive arthritis, significant systemic disease, malnutrition, conditions placing subject at risk or influence the conduct of the study or interpretation of results.

Study Assessment

Symptom scoring: Joint pain (measured as 'no', 'mild', 'moderate', or 'severe') and walking distance (recorded as >1000 m, 500-1000 m, 100-500 m, or <100 m).

Clinical examination of the joints: Joint tenderness (measured as 'no', 'improved', 'same', or 'worsened'); Crepitus (measured as 'no', 'mild', 'moderate', or 'severe'); Swelling (measured in cms bilaterally); Range of movements (measured in degrees using goniometer); Thigh measurements; Warmth (measured as 'yes' or 'no'); Gait (assessed as 'normal' or 'abnormal').

Safety parameters: Vital signs, Haemogram, Liver function tests and Renal function tests.

Time points: Baseline, 2, 4, 6, 8, 10, and 12 weeks.

Statistical analysis of the data was done using one-way ANOVA.

Results

54 subjects were screened, 30 got enrolled and 28 completed the study.

The demographics and baseline characteristics of the two treatment groups were comparable.

Joint pain is measured by querying the patient and scoring it as no/mild/moderate/severe during each visit. There was significant improvement in pain scores within the groups I and II over a period of 12 weeks, but there was no significant difference between the groups. At baseline 85.71% of the subjects were in moderate/severe category group I and 78.57% in group II. At the end of the study, only 21.43% subjects in group I were in moderate/severe category, whereas 50% in group II were still in the moderate/severe category.

Walking distance refers to the maximum distance a person is able to walk at a stretch without limiting pain and was recorded at each visit. Statistically significant improvement in % individuals scoring walking distance more than 1000 meters was seen within both groups over a period of 12 weeks. In group I, 92.86% of subjects could walk >1000m compared to 85.71% in group II after treatment.

Joint line tenderness was elicited by palpating along the joint line and was measured by querying the patient and recording the response as no/mild/moderate/severe. Significant improvements were seen in both groups. The % of patients in category moderate/severe decreased from 85.71 to 7.14 in group I over a period of 12 weeks, whereas in group II, it came down from 78.57 to 21.43. It showed that 92.85% of the patients in group I had improvement or has no joint line tenderness as compared to 78.57% in group II.

Significant improvement in **crepitus** and **range of movements** were seen within both groups. The other parameters studied, namely, joint swelling, warmth of joint, gait and thigh measurements were not affected by any of the drugs.

The safety of the test drug was evaluated by measuring vital signs (systolic and diastolic blood pressure, pulse rate, respiratory rate), haemogram (TC, DC, ESR), liver function tests (blood urea, serum creatinine). None of these parameters were adversely modified by Rhulief[®].

Conclusion

Rhulief[®], a natural herbal extract is effective in management of knee osteoarthritis. The drug was well tolerated and no dose-related toxicity was found. Efficacy and tolerability of Rhulief[®] used in the current study was shown to be superior to those of Celecoxib (NSAID) for treatment of knee osteoarthritis.