and placebo was also significant ($p < 0.001$) with the shortest times observed with diclofenac-N. Treatment-emergent AEs were similar across treatment groups with similar rates in subjects treated with placebo (52.9%), diclofenac-N 35 mg (60.8%) and diclofenac-N 18 mg (55.1%).
Conclusions: An investigational, proprietary, nano-formulated, lower dose, oral diclofenac demonstrated good efficacy, onset of action, and tolerability. As suggested by this phase-2 clinical trial, use of this lower dose formulation could maintain efficacy, shorten onset of action, and possibly result in an improved tolerability profile for patients with acute arthritic pain.

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THE APPLICATION OF PLATELET-RICH PLASMA IN EARLY OSTEOARTHRITIS OF KNEE

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Purpose: Platelet-rich plasma (PRP) is a natural concentrate of autologous blood growth factors experimented in different fields of medicine in order to test its potential to enhance tissue regeneration, and so emerged as a treatment option for tendinopathies and chronic wounds. In addition to release of growth factors, PRP also promotes concentrated anti-inflammatory signals including interleukin-1a, which has been a focus of emerging treatments for osteoarthritis. The primary objective is to compare a single, intra-articular injection of platelet-rich plasma (PRP) with hyruan injection in patients with early osteoarthritis of knee and to assess the clinical efficacy and safety of intra-articular platelet-rich plasma (PRP) injection in patients with low degree osteoarthritis (OA) of the knee.
Methods: Between June 2008 and October 2010, we reviewed the results of 86 consecutive primary osteoarthritic patients underwent intra-articular injection of PRP.In a group of early osteoarthritis patients, inclusion criteria was set to those who were able to be followed up for at least 6 months and showed as Kellgren-Lawrence grade I on simple radiograph or MRI, and exclusion criteria was set as severe obesity, infection, immunosuppressed patients, advanced osteoarthritis(K-L grade I, II, III), and severe deformity. PRP was injected once, in principle. Also, to compare the effects of PRP, hyruan injection was performed in 21 cases during the same period in a same target group, and the effect was compared by perfoming 3 times in an interval of 1 week. Results were evaluated at 4, 8, 12, 18, 24 weeks post-injection using radiologic study, visual analogue scale (VAS) and international knee documentation committee (IKDC) score for functional score.
Results: According to VAS, the mean preoperative scale was 8.2 (range 7–10) and the mean postoperative scale was 3.2 (range 1–4) and 2.9 (range 0–4) at 12 and 24 weeks of follow-up. In IKDC score, the mean preoperative knee score was 57.5 points (range 32–77), and the mean postoperative knee score was 77.3 points (range 60–95) and 88.9 points (range 69–98) at 12 and 24 weeks of follow-up, respectively. Patients receiving PRP experienced statistically significantly greater improvements in VAS ($p = 0.032$), and IKDC score measures, than patients receiving hyruan injection. There was no different between the safety results of the two groups. No increased risk of local adverse events was observed in the follow-up periods.
Conclusions: According to VAS, the mean preoperative scale was 8.2 (range 7–10) and the mean postoperative scale was 3.2 (range 1–4) and 2.9 (range 0–4) at 12 and 24 weeks of follow-up. In IKDC score, the mean preoperative knee score was 57.5 points (range 32–77), and the mean postoperative knee score was 77.3 points (range 60–95) and 88.9 points (range 69–98) at 12 and 24 weeks of follow-up, respectively. Patients receiving PRP experienced statistically significantly greater improvements in VAS ($p = 0.032$), and IKDC score measures, than patients receiving hyruan injection. There was no different between the safety results of the two groups. No increased risk of local adverse events was observed in the follow-up periods.

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A PHASE 2 STUDY EVALUATING THE EFFICACY AND SAFETY OF A NOVEL, PROPRIETARY, NANO-FORMULATED ORAL INDOMETHACIN

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Purpose: Nonsteroidal anti-inflammatory drugs (NSAIDs) are a common medication taken for acute pain relief. Indomethacin has a long-established efficacy and safety profile yet can have a variable and somewhat slow onset of action. Indomethacin also has the potential for gastrointestinal adverse events (AEs), suggesting the need for a new formulation which can safely provide fast onset of acute pain relief. Our objective was to evaluate the analgesic efficacy and safety of an investigational, proprietary, nano-formulated, oral indomethacin compared with placebo in subjects with acute dental pain.
Methods: This was a phase-2, multicenter, randomized, double-blind, single-dose, parallel-group, placebo-controlled study. In total, 203 subjects were enrolled who: were 18–50 years of age, had extraction of ≥2 third molars, and experienced moderate to severe pain intensity within 6 hours after surgery. Subjects received either nano-formulated indomethacin 20 mg, 40 mg, or placebo. The primary efficacy variable was the sum of total pain relief (TOTPAR) over 8 hours (TOTPAR-8). Higher scores indicated better pain relief.
Results: Nano-formulated indomethacin was significantly ($p < 0.001$) better than placebo for TOTPAR-8 (mean; 95% CI): 40 mg (12.56; 2.64); 20 mg (10.79; 2.66); placebo (3.02; 2.64). Nano-formulated indomethacin was also significantly ($p < 0.001$) better than placebo for TOTPAR-4 (mean; 95% CI): 40 mg (6.16; 4.78); 20 mg (5.47; 4.61); placebo (1.63; 2.83). The difference in time to onset of analgesia between each treatment and placebo was also significant ($p < 0.001$). Treatment-emergent AEs occurred less often in subjects treated with nano-formulated indomethacin 20 mg (38.0%) than those treated with nano-formulated indomethacin 40 mg (51.0%) or placebo (56.9%).
Conclusions: A proprietary, nano-formulated, lower dose, oral indomethacin demonstrated good efficacy, onset of action, and tolerability. The ability to utilize a lower dose and maintain efficacy could result in an improved tolerability and safety profile and is in line with the FDA directive to use the lowest effective dose for the shortest duration.

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CLINICAL EVALUATION OF A HERBAL FORMULATION, RHULIEF™, IN THE MANAGEMENT OF KNEE OSTEOARTHRITIS

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Purpose: The study was conducted to evaluate the efficacy, safety and tolerability of Rhulief™, a unique mixture of acetyl boswellic acids with acetyl 11-keto beta boswellic acid (AKBA) content of 10% w/w and BCM 95®, a composition of curcumin which is about 7 times more bioavailable than conventional curcumin, compared with non steroidal anti-inflammatory drug, Celecoxib in the management of knee Osteoarthritis.
Methods: Fifty four subjects were screened, 30 subjects were enrolled and 28 completed the study. Subjects of both sexes aged 18 to 65 years who were medically stable with moderate form of osteoarthritis evidenced by narrowing of the medial joint space with swelling were randomized into two groups and were treated for a period of 12 weeks.
Gr I: Oral administration of Rhulief™ 500 mg capsule twice daily
Gr II: Oral administration of Celecoxib 100 mg capsule twice daily
Subjects with long standing and severe form of osteoarthritis, persons with history of rheumatoid or reactive arthritis and significant systemic diseases were excluded from the study. Symptom scoring and clinical examination were done during their each visit to find out the efficacy of the drug. Safety of the drug was assessed by recording the liver function test, renal function test and haemogram.
Results: The results of the symptom scoring revealed that there was a significant ($p < 0.05$) improvement in pain scores within the groups over a period of 12 weeks and the improvement was more with Gr I. Significant ($p < 0.05$) improvement in walking distance and joint line tenderness were also observed within the groups and the effects were greater with Gr I. Statistically significant difference between range of movements were observed within both the groups ($p < 0.05$). The differences in range of movements were comparable in both groups and there was no significant change between the two groups. Vital signs, haemogram, liver function test and renal function test were not adversely modified by Rhulief™. The results of the present study concluded that the treatment was well-tolerated and did not produce any adverse effect in patients.
Conclusions: Rhulief™ at 500 mg twice a day was better than Celecoxib 100 mg twice daily in symptom scoring and clinical examination. It was equally effective as Celecoxib in alleviating crepitus and range of joint movements. The drug was well tolerated and no dose-related toxicity was found. Efficacy and tolerability of Rhulief™ used in the current