

Chondroxide Gel Manufactured by Herbion Pakistan (Pvt.) Ltd in Patients with Osteoarthritis, Rheumatoid Arthritis, Cervical Spondylosis, and Frozen Shoulder

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Abstract: *Aims and Objective:* Chondroxide gel is used topically in osteoarthritis, rheumatoid arthritis, cervical spondylosis, and frozen shoulder. This small-scale clinical survey was conducted to determine the safety and efficacy of the herbal product Chondroxide gel manufactured by Herbion Pakistan (Pvt.) Ltd. at Tulsi Medical Centre, Karachi, Pakistan. *Introduction:* Osteoarthritis is the most common disorder with joint pain and stiffness symptoms. Rheumatoid arthritis is a chronic inflammatory autoimmune disorder and another common reason for disability. At the same time, cervical spondylosis is a disease affecting the cervical spine, whereas a frozen shoulder often prolongs a disabling condition that can be managed by primary care. *Method:* This was a small-scale, open-labeled clinical survey. A total of 30 patients were enrolled in the study, out of which four patients got dropped out. 26 patients received Chondroxide gel. Statistical analysis was done by using the IBM SPSS 20. *Results:* Chondroxide gel was found safe and effective in treating osteoarthritis, rheumatoid arthritis, cervical spondylosis, and frozen shoulder and stated better response compared to the topical formulation available in the market. *Conclusion:* The results indicated improvement after applying the Chondroxide gel in patients with osteoarthritis, rheumatoid arthritis, cervical spondylosis, and frozen shoulder complaints and relieved external pain.

Keywords: Chondroxide Gel, Osteoarthritis, Rheumatoid Arthritis, Cervical Spondylosis, Frozen Shoulder

1. Introduction

Osteoarthritis (OA) is the symptoms of joint pain and stiffness. It is the most common worldwide, age-related, heterogeneous group of disorders. There is a mixture of systemic factors that lead to joint damage. Osteoarthritis joint pain is also weakly related to clinical problems [1]. Radiographic changes of osteoarthritis mainly occur in elderly age and produce significant morbidity. The joints commonly affected are the knee, hip, hand, spine, and foot with wrist, shoulders, and ankle [2]. Rheumatoid arthritis (RA) is another most common reason for disability. It is a chronic, systemic inflammatory autoimmune disorder causing symmetrical polyarthritis of large and small joints. It occurs between the age of 30-50 years. The etiology is not fully understood, but it involves genetic and environmental

factors [3]. The OA is known to show a phenotypic similarity with RA [4].

Cervical Spondylosis (CS) is a disease affecting the cervical spine at all levels. It involves a series of degenerative changes in the intervertebral discs, osteophytosis of the vertebral bodies, hypertrophy of the facets and laminal arches, and ligamentous and segmental instability. It is caused by the increase in age [5]. Frozen Shoulder (FS) is another painful, often prolonged disabling condition that the primary care setting can manage. It is associated with stiffness and sleeping difficulty on the affected side. It is uncommon in the age before 40 years. The most affected gender is female as compared to male [6].

Nonsteroidal anti-inflammatory drugs (NSAIDs) are the most commonly prescribed drugs globally. It is widely used in patients with osteoarthritis, rheumatoid arthritis, or other

musculoskeletal injuries. Regardless of the mechanism, it is also famous as Over-The-Counter (OTC) medicine among health professionals and patients [6]. The extensive use of oral NSAIDs is also responsible for adverse effects, especially serious gastrointestinal (GI) complications like peptic ulcer and GI bleeding [7]. Different approaches have been attempted to minimize the use of NSAIDs due to their adverse reaction like co-administration of gastro-protective or other agents such as selective cyclo-oxygenase-2 (COX-2) inhibitors or incorporate with nitric oxide or through a modified delivery system.

The other way to avoid the oral route is to use topical formulation [8]. Topical penetration of NSAIDs into the systemic circulation is slow and smaller in quantity. Also, its bioavailability is 5%, and plasma concentration is 15% when applied topically. Clinical studies of NSAIDs showed difficulty measuring efficacy due to highly effective other topical drugs (Heyneman, Lawless-Liday, et al., 2000).

The active ingredient of Chondroxide gel is Chondroitin sulfate. Chondroitin sulfate (CS) is a glycosaminoglycan (GAGs) with polymerized disaccharide base linked to a sulfate group. It is naturally present in the matrix of mammalian cartilages. CS acts as a cartilage protector and is responsible for most of the properties of joint cartilage due to the significant component of aggrecan. It inhibits the tissue elastase and polymorphonuclear leukocytes by increasing the synthesis of proteoglycans and interleukin 1 β (IL-1 β) inhibition in the cartilaginous matrix and by increasing the synthesis of hyaluronic acid [9-11].

The European League Against Rheumatism (EULAR) recommends "Symptomatic Slow Acting Drugs For Treating Osteoarthritis" (SYSADOA), and CS is also prescribed as SYSADOA, but it is highly suspected to have disease modifying capacities [10].

Conservative treatment as of using bioactive gels of hemp oil, quercetin and Guilu Erxian Glue have found to have healing effects on knee stiffness and mobility [12] Although Invasive techniques like Intra-articular treatment of RA are still under stud [13], however non-invasive techniques like transdermal delivery of drugs as nano-emulsion gels & micro-emulsion gels [14] have gained interests being the best from an administration point of view, but chondroitin sulfate and glucosamine have still proven to be the first line of treatment as of slow-acting drugs [15]. This study will still so far helpful for researchers to make a potential decision on prescribing natural compounds as effective treatment substitute creating the minimal risk of adverse effect.

2. Material and Method

2.1. Study Goal

The study's objective is to determine the safety and efficacy of Chondroxide gel manufactured by Herbion Pakistan (Pvt.) Ltd. in patients with osteoarthritis, rheumatoid arthritis, cervical spondylosis, and frozen shoulder and its side effects were conducted between April-July 2019.

2.2. Design

The study was conducted at Tulsi Medical Centre, Karachi, Pakistan. This was a small-scale, open-labeled questionnaire-based clinical survey to determine the safety and efficacy of Chondroxide gel manufactured by Herbion Pakistan (Pvt.) Ltd. The study duration was 14 days, starting at 1st visit with the follow-up on day 14th, using Chondroxide gel. Demographic characteristics, pain duration, and medical history were recorded during the evaluation.

2.3. Patients

A total of 30 patients were enrolled with osteoarthritis, rheumatoid arthritis, cervical spondylosis, and frozen shoulder. *Inclusion criteria:* patients above the age of 35 years of both gender, male and female, and had clinical evidence of knee pain, muscles stiffness, pain with activity (during walking, climbing stairs, sleeping at night, rest or standing). *Exclusion criteria:* inflammatory arthritis, fibromyalgia, knee surgery or knee injections, trauma, intra-articular intervention or physical therapy applied to knees within last six months, oral or topical glucosamine, paresis, or neuropathy, osteonecrosis, mental disorders.

2.4. Consent

Signed written consent was taken from all the patients according to the protocol approved by the ethical committee of Herbion Pharmaceuticals (Pvt.) Ltd, Karachi, Pakistan.

2.5. Treatment

Treatment consisted of Chondroxide gel 25 gm provided to patients after diagnosis with the complaint of muscles stiffness, pain inactivity, knee pain, or other external pain. The side effects were also observed if any.

2.6. Statistical Analysis

All the data were analyzed using a statistical package of social science, i.e., SPSS version 20. Descriptive statistics and a one-sample t-test were applied to evaluate the significance level for the result. The test results with a *p-value* below 0.05 were considered as statistically significant.

2.7. Ethical Committee Approval

The Ethical board approves this study of Herbion Pharmaceuticals (Pvt.) Ltd. Karachi, Pakistan.

2.8. Study Withdrawal

If there were violations of the study procedure or regime of the study site, the participant was pulled out from the study. Either patient refused to participate in the research or has low compliance. If there were undesirable occurrences that were dangerous for the patient's life or aggravations of accompanying diseases or unsatisfactory results were the reason for withdrawal of participants from the study.

3. Result

A total of 30 patients were enrolled in the survey, out of which 26 patients completed the entire survey, and four dropped out due to their reasons after signing the informed consent. The number of patients, according to gender, is shown in Table 1, where the frequency of the disease in males and females is presented. Figure 1 shows that the knee and joint pain complaint due to osteoarthritis among enrolled patients is more as compared to rheumatoid arthritis, cervical spondylosis, and frozen shoulder.

Table 1. Discrimination of the knee and joint complaints on the basis of gender.

Gender	Male	Female
Number of Patients	7	19
Osteoarthritis	4	8
Rheumatoid Arthritis	Nil	6
Cervical Spondylosis	1	2
Frozen shoulder	2	3

46.2% (n=12) patients including male and female, participated with complaints of osteoarthritis, 23.1% (n=6) patients with the complaint of rheumatoid arthritis, 11.5%

(n=3) patients with cervical spondylosis and 19.2% (n=5) with frozen shoulder. These results are illustrated by using statistical analysis.

Furthermore, 83% of patients felt the incidence of pain almost every day due to osteoarthritis, and few have thought it less than once a month (17%) [See Figure 2]. Patients with other complaints felt pain every day, some felt less than once a month, and few felt several times a month.

After using Chondroxide gel, Patients showed ease on the application, resulting in a mean value of 4.04 (SD±0.528) on a scale from *Poor to Excellent*, and smell/odor showed result towards pleasant with a mean value of 4.12 (SD±0.726). On applying Chondroxide gel, all patients felt pleasant with a mean value of 4.27 (SD±0.533). The primary outcome of Chondroxide gel is pain-relieving effect has shown significant results in all patients with a mean value of 4.19 (SD±0.567), shown in Figure 3. With these results value, Chondroxide gel was found safe and effective in treating osteoarthritis, rheumatoid arthritis, cervical spondylosis, and frozen shoulder and stated better response compared to the topical formulation available in the market.

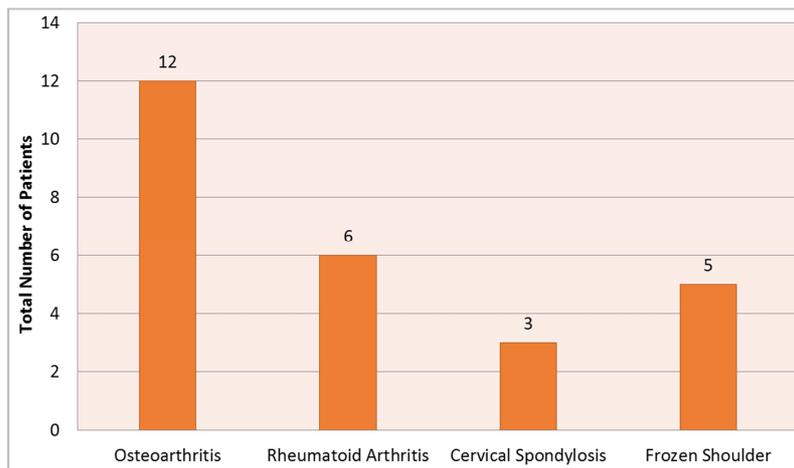
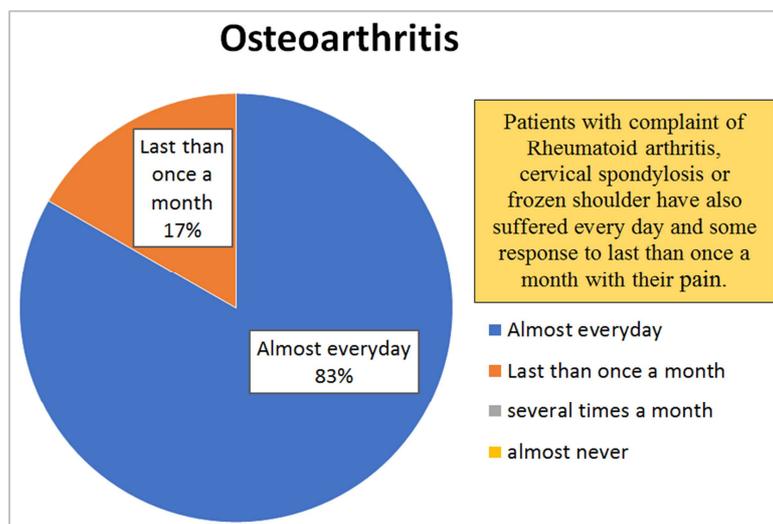
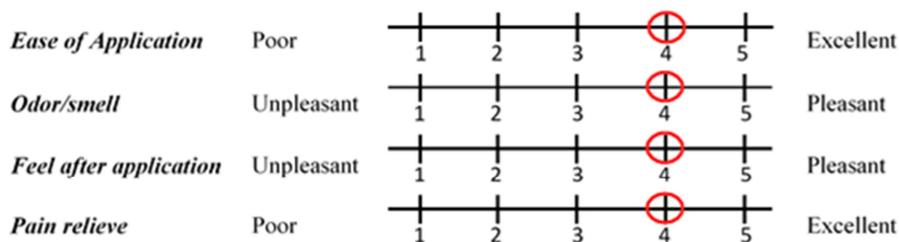


Figure 1. Total number of enrolled patients with the complaint of Osteoarthritis, Rheumatoid Arthritis, cervical spondylosis and frozen shoulder.



Patients with complaint of Rheumatoid arthritis, cervical spondylosis or frozen shoulder have also suffered every day and some response to last than once a month with their pain.

- Almost everyday
- Last than once a month
- several times a month
- almost never

Figure 2. History of patients suffering from severe pain in the condition of Osteoarthritis.**Figure 3.** Average* response of patients after use of Chondroxide gel.

*Mean response of 26 patients have ease on application is 4.04 (SD \pm 0.528), odor/smell is 4.12 (SD \pm 0.726), feel after application is 4.27 (SD \pm 0.533), and pain relieve is 4.19 (SD \pm 0.567).

4. Discussion

This study was designed to investigate the effect of Chondroxide gel in patients with joint complaints such as osteoarthritis, rheumatoid arthritis, cervical spondylosis, or frozen shoulder. These conditions are most common among the population. Our primary objective was to evaluate the efficacy and safety of the Chondroxide gel after application. It's a 14-day small-scale, open-labeled clinical survey. In this study, both genders participated with age above 35 years after signing the informed consent with clinical evidence of knee pain, muscle stiffness, and activity (during walking, climbing stairs, sleeping at night, rest or standing).

The excluded patients were those with inflammatory arthritis, fibromyalgia, knee surgery or knee injections, trauma, intra-articular intervention or physical therapy applied to knees within the last six months, oral or topical glucosamine, paresis or neuropathy, osteonecrosis, and mental disorders. Vital signs were also observed with any previous history of medical problems. Patients have been asked about their history of medication used either orally or topically and their effectiveness compared with Chondroxide gel. After evaluation, it was observed that another topical formulation for pain-relieving effects in patients had not had enough effectiveness, and they still have that pain.

Some patients have stiffness in the morning or the evening, while their pain during walking and climbing stairs is more than pain in resting, standing, or sleeping at night. However, it was also observed that pain among females is more than among males. All patients on day 14th gave a pronounced output about the Chondroxide gel application with its use, smell, application, and pain-relieving effect. The pain was relieved within 2-3 days or somewhat within a week.

Patients were also being asked about their recommendation of Chondroxide gel to others. They responded that they have better results and pain-relieving effects when compared with other topical formulations that are available in the market, such as NSAIDs like Piroxicam or Diclofenac diethylamine. Also, no one has reported any

side effects from the Chondroxide gel application.

Overall, all experiences of all enrolled patients were good, and they showed improvement in mobility, reduced swelling, improvement in climbing stairs, and said it's a well-tolerated product. Several works of literature on chondroitin sulfate are available for treating Osteoarthritis, Rheumatoid arthritis, Cervical spondylosis, or Frozen shoulder.

5. Conclusion

The results indicated improvement after applying the Chondroxide gel in patients with Osteoarthritis, Rheumatoid arthritis, Cervical spondylosis, or Frozen shoulder complaints and gave relief from external pain. Not only this, the results had given significant evidence to prescribers and researchers about how the use of organic products is safe in patients suffering from chronic diseases and could be beneficial in minimizing side effects.

This research opens an important aspect of research where findings related to reducing chronic pain by application of topical gels can not only be emphasized but also curtails the potential risk associated with oral/IV medications.

Conflict of Interest

The authors declare that they have no competing interests.

Data Availability Statement

Herbion Pakistan (Pvt.) Ltd. holds all data relevant to the study included in the article or uploaded as supplementary information and considers it confidential.

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Declaration

This study is performed in accordance with the principles

that are stated in the Declaration of Helsinki. Ethical approval was obtained from the ethical committee to confirm the study meets the research national and international guidelines.

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