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Original Research Article

Evaluation of Anti-Arthritis Activity of Topical Oxaprozin Nanogel on Animal Model

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Abstract:

Osteoarthritis (OA) is defined by the progressive and irreversible deterioration of articular cartilage accompanied by a subsequent inflammatory response. Nonetheless, most medicinal medications for osteoarthritis only mitigate symptoms without targeting the underlying disease. We engineered an inflammation-responsive carrier and encapsulated bioactive substances to address this issue. Oxaprozin is a non-steroidal anti-inflammatory agent characterised by insufficient oral bioavailability and gastrointestinal adverse effects. This project aims to develop a unique topical Oxaprozin nanogel. Arthritis was produced in Wistar rats utilising Freund's complete adjuvant (FCA), and the formulation's antiarthritic efficacy was examined. The effects were juxtaposed with those of Diclofenac. Upon the study's conclusion, blood samples were collected for biochemical as well as haematological analysis. The Oxaprozin Nanogel formulation demonstrated considerable antiarthritic efficacy, comparable to that of Diclofenac. The formulation's antiarthritic efficacy is corroborated by biochemical and haematological analyses. The oxaprozin nanogel formulation demonstrated considerable antiarthritic efficacy against FCA-induced arthritis in Wistar rats.

Keywords: Anti-arthritis, Oxaproxin, Nanogel, FCA.

Introduction

Osteoarthritis (OA) is a chronic condition characterised by significant morbidity and clinical impact, affecting almost 240 million individuals globally. [1] The principal clinical symptoms of osteoarthritis encompass joint pain, deformity, and dysfunction. The degradation of the extracellular matrix (ECM) in cartilage is regarded as the defining characteristic of osteoarthritis (OA). Under typical physiological conditions, articular cartilage can endure weights several times greater than human weight, enabling smooth and frictionless joint articulation. [2]

Oxaprocin is a non-steroidal anti-inflammatory medication utilised for management of mild to moderate pain, for alleviating symptoms linked to arthritis (osteoarthritis, rheumatoid arthritis, and juvenile rheumatoid arthritis), such as inflammation, oedema, stiffness, and joint discomfort. [3] It functions by obstructing the action of the cyclooxygenase enzyme, which catalyses the conversion of arachidonic acid into prostaglandins. [4] The negative consequences of orally administered ooxaprozin encompass dizziness, nausea, vomiting, gastrointestinal haemorrhage, and peptic ulcers. To mitigate negative effects related to oral delivery, it is formulated as a topical nanogel. [5] These are prospective polymeric nanoparticulate systems with significant biological applications, characterised by great biocompatibility, substantial drug loading capacity, excellent biodegradability, effective permeability capabilities, and tissue-mimicking features. [6,7] Nanogels exhibit a pronounced affinity for aqueous solutions, allowing them to swell or deswell upon immersion in such fluids. [8] Nanogels offer advantages such as biocompatibility, biodegradability, permeability, a high drug loading capacity, and the ability to encapsulate both hydrophilic and lipophilic medicines. [9]

Nevertheless, nanogels have several drawbacks, including residual polymers or surfactants and the costly elimination of solvents and surfactants. They can be delivered by multiple methods, including oral, pulmonary, nasal, parenteral, intraocular, and topical approaches. [10] Conventional topical dose forms, primarily in gel form, often exhibit poor therapeutic efficacy due to low bioavailability, as only a small percentage of the drug penetrates the skin barrier. [11] Currently, nanogels serve a progressively significant function as carriers for transdermal medication delivery. This study is on

the application of oxaprozin for treatment of arthritis in animal model.

Material and Methods

Four groups of Wistar rats (150-200 g) (n=6) were used to assess the in-vivo efficacy of a topical gel formulation of Oxaprozin. The experimental protocol underwent examination by the IAEC (Institutional Animal Ethical Committee) and received approval under Reference No. BMRL/IAEC/2024/07-68.

Animals have been maintained with appropriate care following the standards of CPCSEA, New Delhi (Regn. No. 2304/PO/Rc/S/2024/CPCSEA). Arthritis was produced in 2-4 groups by administering 0.1mL (0.1%w/v) suspension of inactivated Mycobacterium tuberculosis (MTB) bacteria, homogenised in liquid paraffin, into a subplantar region of rats' left hind foot. FCA was permitted to induce arthritis over a period of 21 days. Throughout the trial duration, body weight and rat paw volume of both control as well as treatment groups were assessed on the 4th, 8th, 14th, and 21st days with a digital Vernier calliper. Following confirmation of arthritis progression, diclofenac sodium (DIC-Na) gel and treatment gel formulation were given topically to left knee joint area for a duration of 22-42 days.

Table 1:

Sr. No.	Name of group	Treatment	Number of Animals Required
1	Control	Topically with gel base regarded as a normal control.	6
2	Arthritic control	Arthritic control, injecting 0.1mL (0.1%w/v) suspension of killed Mycobacterium tuberculosis bacteria	6
3	Diclofenac sodium topical gel (1%w/w)	(served as reference standard) Diclofenac sodium gel was applied topically for 22-42 days to left knee joint area	6
4	Topical gel formulation of Oxaprozin	Gel applied topically for 22-42 days to left knee joint area	6

Behavioral tests: Using a digital Vernier caliper, animals' body weight and volume of their control and treatment rat paws were measured on days 25, 29, 35, and 42 of treatment period. Animals' pain test results were visually noted at the end of 42nd day.

Haematological parameters & Biochemical tests: Following an overnight fast, the animals were given ketamine (20 mg/kg, i.p.) to induce anesthesia. Blood samples were then drawn from the retroorbital sinus, centrifuged for 10 minutes at 10,000 rpm, and examined for hematological parameters. Using standard laboratory techniques, hematological parameters such as hemoglobin (Hb), white blood cell (WBC), and red blood cell (RBC) counts were assessed.

Results and Discussion

The topical administration of DIC-Na gel and formulated Oxaprozin was examined in an arthritic model throughout 22-42 days, with alterations in rat paw volume reported on the 25th, 29th, 35th, and 42nd days (Table 1 and Figure 1). The procedure was executed according to the protocol approved by the IAEC.

Arthritic control groups (CG) exhibited indications of arthritis progression, evidenced by increased paw volume.

A significant reduction ($p<0.01$) in rat paw volume has been seen in groups treated with DIC-Na gel and topical gel version of Oxaprozin on the 21st day post-FCA induction.

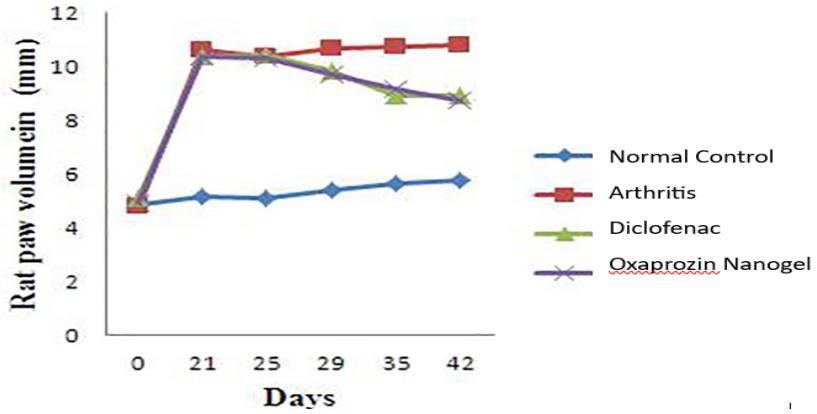

Figure 1: Topical formulation of Oxaprozin in FCA induced arthritic rats

Table 2: Effect of diclofenac sodium, F7 formulation on body weight changes in FCA Induced arthritic rats

Groups	Initial body weight (g)	Body wt after 21 days of FCA induction	Body wt after treatment 25th day	Body wt after treatment 29th day	Body wt after treatment 35 th day	Body wt after treatment 42nd day	Weight gain (g)
Normal Control	145.3 ± 0.64	171.2± 1.50	172.5 ± 1.79	175.50 ± 1.54	185.50 ± 1.12	193.70 ± 1.25	21.50±1.89
Arthritic control	144.3 ± 0.84	141.80 ± 0.79a	141.20 ± 0.94 a	138.30 ± 1.05 a	136.00 ± 1.13 a	132.70 ± 1.26 a	-11.00±1.34
Diclofenac sodium topical gel (1% w/w)	144.00± 1.15	142.20 ± 1.25 a	144.00± 1.41 ns	145.20 ± 1.35 b	147.50 ± 1.83 a	150.80 ± 1.66 c	7.66±0.66
Topical formulation of Oxaprozin	146.5 ± 1.05	142.70 ± 1.38 a	142.20 ± 1.49 ns	143.10 ± 1.34 b	143.80 ± 1.56b	148.50 ± 1.71c	5.83±0.47
Data provided as mean ± SEM (n = 6); ap<0.001 Arthritic control v/s Normal control; bp<0.05 Treated groups v/s Arthritic control; cp<0.001 Treated Groups v/s Arthritic control							

Arthritic test scores presented in Table 2 indicate that pain related to FCA-induced arthritis has been greatly reduced in the groups treated with DIC-Na gel and topical gel formulation of Oxaprozin. Marked changes in flexion pain test scores, mobility scores, as well as stance scores were reported in every treated group of rats compared to arthritic control rats. This modification of arthritic test scores corroborates the anti-arthritic efficacy of topical version of Oxaprozin. The selective decrease in arthritic score (Table 3) and the notable decrease in thymus and spleen weight across all treated groups compared to arthritic rats corroborated the anti-arthritic efficacy.

Table 3: Evaluation of anti-arthritic activity of topical formulation F7 in FCA induced arthritic rats

Groups	Rat paw volume (mm)					
	Before treatment		After treatment			
	Initial	After 21 days	25th day	29thday	35th day	42nd day
Normal control	4.85 ± 0.14	5.16± 0.23	5.09 ± 0.20	5.39±0.10	5.63 ± 0.12	5.75 ± 0.78d
Arthritic control	4.81± 0.12	10.62± 0.15a	10.65 ± 0.26a	10.68±0.17a	10.74 ± 0.23 a	10.79 ± 0.11 a
Diclofenac sodium topical gel (1%w/w)	5.10± 0.13a	10.40± 0.15a	10.47±0.22ns	9.81 ± 0.16b	8.93 ± 0.23c	8.19 ± 0.07c
Topical formulation of Oxaprozin	4.95± 0.11a	10.38± 0.14 a	10.33 ± 0.14ns	9.74 ± 0.13c	9.15 ± 0.15c	8.73 ± 0.17c
Data provided as mean ± SEM (n = 6). ap<0.001 Arthritic control V/s Normal control; bp<0.05 Treated groups V/s Arthritic control cp<0.001 Treated groups V/s Arthritic control.						

Table 4: Alterations in various pain test scores in FCA Induced arthritis in rats

Groups	Pain test		Mobility score	Stance score
	Extension	Flexion		
Arthritic control	9.5±0.34	8.33±0.33	1.33±0.21	1.50±0.22
diclofenac sodium topical gel (1%w/w)	5.16 ± 0.16d	4.66 ± 0.21 d	2.66 ± 0.21d	2.33 ± 0.21d
Topical formulation of Oxaprozin (2% w/w)	4.66 ± 0.21d	3.66 ± 0.33 d	3.16 ± 0.21d	2.83 ± 0.16d
Data provided as mean ± SEM (n = 6); dp<0.001 Treated groups V/s Arthritic control				

Hematological parameters: Rats treated with DIC-Na gel and topical formulation exhibited a reduction in WBC count and ESR, alongside growth in Hb and RBC count, compared to arthritic CGs (Table 4).

Table 5: Effect of formulation F7 on hematological parameters in FCA induced arthritic rats

Groups	Hb (mg %)		WBC (x103/mm3)		RBC (x106/mm3)	
	Before treatment (21st day)	After treatment (42nd day)	Before treatment (21st day)	After treatment (42nd day)	Before treatment (21st day)	After treatment (42nd day)
Normal control	15.92±0.18	16.38±0.15	6.53±0.15	6.85±0.12	9.64±0.06	10.22±0.20
Arthritic control	11.02 ± 0.30a	9.98±0.17a	11.97±0.22a	10.88±0.15a	7.99±0.20	6.31±0.14a
Diclofenac sodium topical gel 1% w/w	11.23±0.21a	14.97±0.26b	11.28±0.19 a	8.10±0.09b	7.36±0.25 a	8.86±0.21b
Topical gel formulation F7	12.22± 0.14a	13.48±0.18b	11.93±0.40a	9.41 ±0.04b	7.18 ±0.23a	8.16 ±0.10b

Conclusion

In-vivo investigations showed that the proposed topical gel formulation had promising anti-arthritic action for treating arthritis in rat paw oedema. It has demonstrated a comparable anti-arthritic efficacy to regular DIC-Na gel. Additional clinical investigations could reinforce application of this formulation for individuals with joint inflammatory diseases.

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