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EFFECT OF CURCUMIN ON CHEMICALLY INDUCED OSTEOARTHRITIS

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ABSTRACT: Deterioration of the joint's cartilage and the bone that supports it, together with the development of new bone, are hallmarks of osteoarthritis. A number of variables, including abnormalities in the formation of the joint, genetics, a history of joint damage, stress, and abnormalities in the limbs, may lead to osteoarthritis. Typically, pain relievers are prescribed toalleviate discomfort, edema, inflammation, and stiffness in the joints. The many adverse effects of these medications include gastrointestinal distress, nausea, vomiting, ulcers, bleeding, fluid retention, high blood pressure, kidney failure, and many more. Curcumin inhibits the enzymes glutathione S transferase, COX, and 5-LOX. Reduced histamine production is another benefit. Using nonsteroidal anti-inflammatory drugs (NSAIDs), this research tested its anti-arthritic effects. There were five groups of animals. One group served as a control.As a disease control measure, Group 2 received 40 mg/kg of nalidixic acid subcutaneously to induce arthritis. Oral administration of diclofenac sodium (13 mg/kg) was the recommended treatment for Group 3. Curcumin (200 mg/kg orally) was given to Group 4 in addition to the regular treatment. The fifth group of rats was given a curcumin pretreatment of 200 mg/kg before the osteoarthritis was induced. A number of functional and physical indicators were assessed, including hyperalgesia, motor coordination, paw volume, and arthritic index. Group 5 had no osteoarthritis symptoms or significantly reduced symptoms, whereas group 4 shown superior recoveries relative to the other groups. As an adjuvant treatment, it shows that curcumin may help cure and prevent osteoarthritis when taken with nonsteroidal anti-inflammatory drugs. Therefore, it may be included into research to create a novel adjuvant medication for the treatment of osteoarthritis, which can enhance patients' quality of life.

Keywords: Curcumin, nonsteroidal anti-inflammatory drugs (NSAIDs), osteoarthritis

INTRODUCTION:

Turmeric, scientifically known as Curcuma longa, is a member of the Zingiberaceae family of plants and contains the active ingredient curcumin, often called golden herb. Theoretically, it may have anti-inflammatory, antioxidant, anti-cancer, anti-bacterial, anti-fungal, and antiviral effects, among other pharmacological functions. Inhibiting tumor development, new blood vessel construction, cardiovascular illness, lung disease, and other similar conditions are all significantly impacted by it.

The most prevalent kind of arthritis and the most prevalent illness in contemporary culture is osteoarthritis. A degenerative condition, it causes the cartilage and bone that supports it to deteriorate over time.

Antibiotics belonging to the quinolone class work by blocking the enzymes DNAgyrase and bacterial topoisomerase. Articular cartilage may be degraded by these antibiotics because of their strong affinity for connective tissues, particularly bone. bones, and cartilage. In 24 hours, they degrade the cartilage, which manifests as a reduction in the number of chondrocytes and the creation of nodules, and causes blister-like lesions.

In this research, we will look at how curcumin helps rats with osteoarthritis that has been chemically caused. To further understand curcumin's involvement in treating osteoarthritis, we measured mean walk time, motor activity, and pain characteristics.

DATA AND PROCEDURES:

The research used 24 female Wistar rats, each weighing between 180 and 250 grams. The animals were housed in a typical environment with adequate ventilation, a temperature of 25±2º C, a humidity level of 60-70 percent, and a light/dark cycle of 12/12. They were kept in environments free of any potential diseases. The CPCSEA criteria were followed throughout the animal operations.

Hychem Laboratories of Hyderabad was consulted for the acquisition of the following chemicals: curcumin, nalidixic acid, and dimethyl sulfoxide.

The patient was given 400 mg/kg of nalidixic acid subcutaneously in a single dosage.

For 21 days, a dosage of 13 mg/kg of diclofenac sodium was given orally. For 21 days, a dosage of 200 mg/kg of curcumin was administered orally.

Methods: A week was given to the animals to acclimate or stabilize before the experiment began. The animals were then divided into five groups of six.

One group served as a control; for 21 days, the animals in this group received DMSO.

Group 2: Disease Control - Nalidixic acid was given to the animals and they were watched for 48 hours.

Third Group: Control Group—Nalidixic acid was given to the animals, and then they were given nonsteroidal anti-inflammatory drugs (NSAIDs) for 21 days.

Section 4: The Test Group After giving the animals nalidixic acid, the next step was to treat them with NSAIDs and curcumin for a total of 21 days.

The fifth group, "Pretreated," received nalidixic acid after a 21-day pretreatment with curcumin.

Motor function changes in osteoarthritis, as seen by the Rota Rod Test. In this experiment, a rat is attached to a rod that spins around. By measuring the holding capacity (in s), the revolving rod causes forced motor activity, which allows for the evaluation of specific characteristics. We timed how long it took for each group's animals to fall off the spinning rod. Five minutes was the time limit.

Pain sensitivity changes are a hallmark of osteoarthritis, which may be alleviated by analgesic action 2, 3.

Consequently, the purpose of this research was to evaluate the analgesic efficacy of different therapies. The analgesiometer or hot plate technique was used to measure the analgesic activity. The rats were moved to the analysis area half an hour before to the experiment's commencement. Analgesiometer (SISCO) is the tool that is used. Each rat was put on its own hot plate that was kept at 55 °C. All the animals had a 20-second cutoff. During the experiment, we monitored the animal's latency time for licking its paw and jumping. We also took note of how many times they jumped and licked.

Inflammation assessment: Nalidixic acid-treated animals showed signs of edema on their paws. We looked at every animal's paw. We used the Plethysmograph's mercury displacement technique to estimate the paw volumes (4, 5). Volumes of the paws were measured once the therapy was finished. We compared the drug-treated groups to the control group by calculating their percentage inhibition.

This is the formula for the percentage of inhibition: VC - VT ÷ VC × 100. In the control group, Vc is the paw volume.

Voltage at test site equals paw volume

Rats were examined daily for the presence of

nodules using a macroscopic scoring system as part of the arthritis index. Sources for the scale include 6, 7 published by Kokkola et al.

The scale used is as follows: 0= no signs of arthritis.

1= mild swelling and erythema of the paw or onedigit
2= two joints are involved
3= more than two joints are involved.
4= severe arthritis of the entire paw or digits.
Arthritis index was calculated by adding the scoresof all the four individual paws.

Spontaneous Mobility: The spontaneous activity was measured using actophotometer. An actophotometer operates on photoelectric cells which are connected in circuit with a counter. The count recorded is displayed digitally. Each individual animal was placed in actophotometer for 10 minutes. The movement of animal interrupts the beam of light falling on a photocell which was recorded as a count by the digital display. The no. of counts was recorded for all the groups.

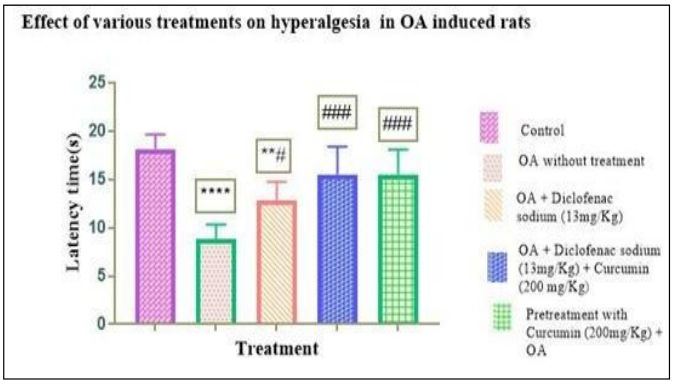
RESULTS: The present study was aimed to investigate the role of combination of curcumin and diclofenac sodium on the functional parameters or symptoms when used in the treatment ofosteoarthritis. In order to study the effect on functional parameters we divided the animals into different groups and treated them accordingly. The functional parameters considered in this study are motor function, hyperalgesia, paw volume, arthritis index and spontaneous mobility (**Table 1).**

TABLE 1: EFFECT OF VARIOUS TREATMENTS ON THE FUNCTIONAL PARAMETERS IN OA INDUCED RATS

Group	Fall off time (s)	Latency time (s)	No. of Paw lickings or jump response	Paw Volume (mm)	Arthritis Index	Spontaneous mobility
I	177.83±6.33	18.16±1.47	6.5±1.37	0.13±0.05	0	290.66±5.71
II	60±19.74	8.83±1.47	17±1.78	1.71±0.27	18.33±3.50	102.83±20.20
III	93.33±18.61	12.83±1.94	12.66±1.96	1.15±0.44	15.16±1.94	130±13.03
IV	132.5 ± 20.4	15.5±2.88	11.16±1.60	0.71±0.35	10±4.28	179.16±14.63
V	169.83±15.31	15.5±2.58	6.16±1.83	0.66±0.22	2.16±1.83	222.5±20.43

Effect of various treatments on motor function: According to the result of our experiment, the motor function has significantly increased in GroupIV (132.5±20.4) when compared with Group II (60±19.74) and Group III (93.33±18.61).

Group V (169.83±15.31) values are comparable with Group I (177.83±6.33) (**Fig. 1**).



1.94). Group V (15.5±2.58) represents value nearly equal to Group IV and Group I (18.16±1.47) indicating no symptoms of hyperalgesia. (**Fig. 2**)

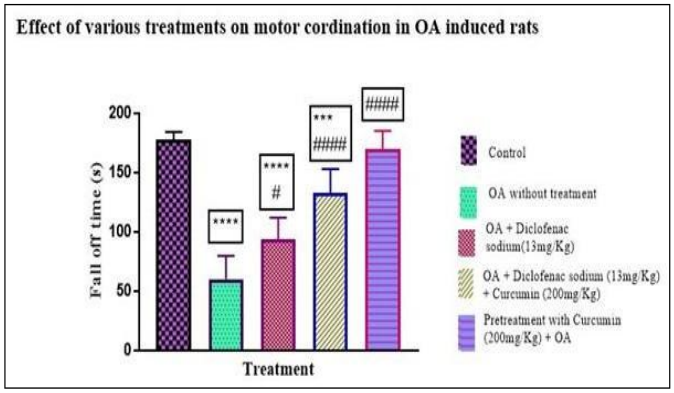


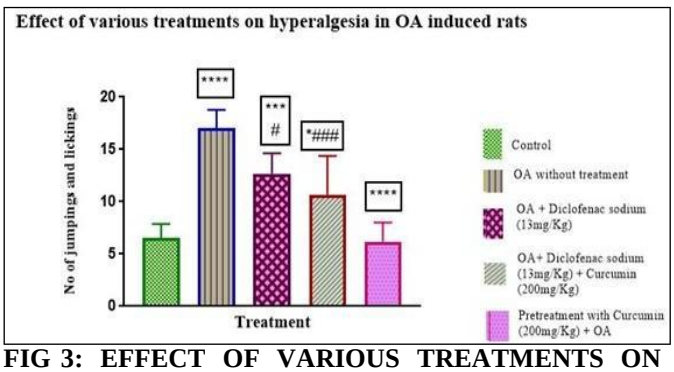
FIG. 1: EFFECT OF VARIOUS TREATMENTS ON MOTOR COORDINATION IN OA INDUCED RATS

The latency time for the licking or jumping response was recorder using Eddy's Hot plate analgesiometer for measuring hyperalgesia. It has decreased in Group IV (15.5±2.88) when compared to Group II (8.83±1.47) and Group III (12.83 ±

FIG. 2: EFFECT OF VARIOUS TREATMENTS ON HYPERALGESIA (LATENCY TIME) IN OA INDUCEDRATS

The sensitivity towards pain was also measured by measuring number of lickings and jumping using Eddy's hot plate method which decreased in the group IV (11.16±1.60) when compared to Group II (17±1.78) and III (11.16±1.60).

Group V (6.16±1.83) response is comparable toGroup I (6.5±1.37) (**Fig. 3**).



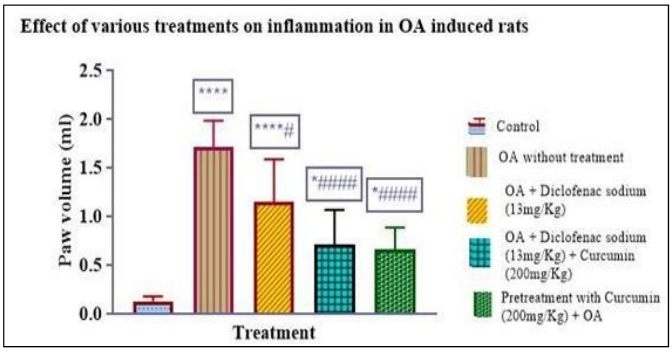


FIG 3: EFFECT OF VARIOUS TREATMENTS ON HYPERALGESIA (NO. OF JUMOING AND LICKINGS) IN OA INDUCED RATS

Effect of various treatments on paw volume: Thepaw volume of Group IV (0.71±0.35) was significantly reduced when compared to Group II (1.71±0.27) and Group III (1.15±0.44). Group V (0.66±0.22) and Group I (0.13±0.05) response values are comparable (**Fig. 4**)

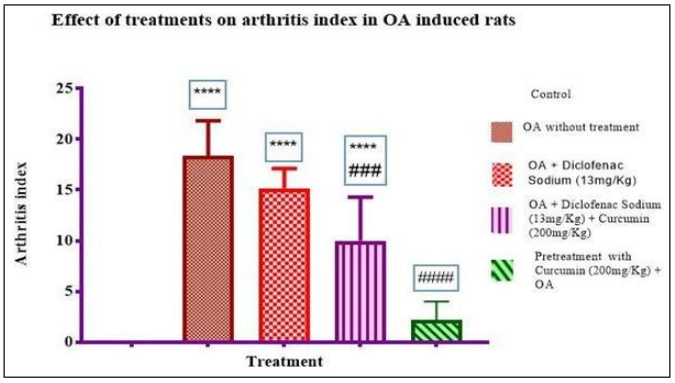
FIG. 4: EFFECT OF VARIOUS TREATMENTS ON INFLAMMATION IN OA INDUCED RATS

The percentage of inhibition was also calculated and was to be higher in Group IV (58.47%) when compared with Group II (0) and Group III (32.47%). Group V (61.4 %) represents the protective role of curcumin. **(Table 2**).

TABLE 2: EFFECT OF VARIOUS TREATMENTS ON PERCENTAGE OF INHIBITION OF INFLAMMATION IN OA INDUCED RATS

	Group	Paw volume	Percentage of inhibition
I	Control	0.13±0.05	-
II	OA without treatment	1.71±0.27	0
III	OA + Diclofenac sodium(13mg/Kg)	1.15±0.44	32.74%
IV	OA + Diclofenac sodium (13mg/Kg) + Curcumin(200mg/Kg)	0.71±0.35	58.47%
V	Pretreatment with Curcumin (200mg/Kg) + OA	0.66±0.22	61.40%

Effect of various treatments on Arthritis index:



actophotometer in Group IV (179.16±14.63) showed better activity when compared to Group II (102.83±2.20) and Group III (130±13.03). The
response of Group V animals (222.5 ± 20.43) is comparable with Group I (290.66±5.71).

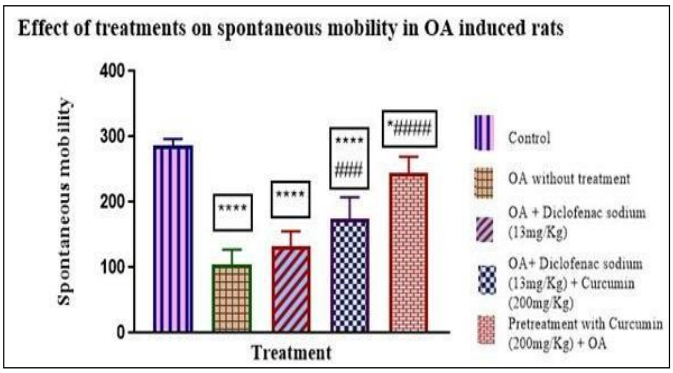


FIG. 5: EFFECT OF VARIOUS TREATMENTS ON ARTHRITIS INDEX IN OA INDUCED RATS

The arthritis index measured as number of nodules in Group IV (10.0±4.28) was found to reduce when compared to Group II (18.33±3.50) and Group III from (15.16±1.94). Group V (2.16±1.83) values arecomparable to Group I (0).

Effect of various treatments on spontaneous mobility in Osteoarthritis induced rats: The spontaneous mobility measured using

FIG. 6: EFFECT OFF VARIOUS TREATMENTS ON SPONTANEOUS MOBILITY IN OA INDUCED RATS

Statistical Analysis: All the values were expressed as mean ± standard deviation and data wasanalysed by One way Anova followed by Tukey's multiple comparison test using Graph pad prism 7

software. $P<0.05$ was considered as statistically significant.

DISCUSSION: Cartilage between joints deteriorates with age, a condition known as osteoarthritis. It is the leading cause of disability and one of the most prevalent types of arthritis in the modern world. Up to age 45, it affects more men than women. This illness is more common in women beyond the age of 45 because of hormonal changes. Obesity, a sedentary lifestyle, and joint injuries are other risk factors for OA. One of the leading causes of a decline in health-related quality of life is osteoarthritis, which manifests itself primarily as joint stiffness and discomfort. There are pharmacological treatments, non-pharmacological treatments, and psychological support options for osteoarthritis.

Pharmacologically, nonsteroidal anti-inflammatory medicines (NSAIDs) are the go-to medications for osteoarthritis pain relief because of their well-established anti-inflammatory and analgesic properties. 8. Nevertheless, adverse effects such as dyspepsia, esophagitis, sodium retention, weight gain, edema, hyperkalemia, hypertension, acute renal failure, papillary necrosis, acute interstitial nephritis, heart failure, myocardial infarction, stroke, cardiovascular death, elevated liver transaminases levels, cytopenia, dizziness, confusion, and so on are common to all nonsteroidal anti-inflammatory drugs (NSAIDs). Because of these drawbacks of current medications, there is an urgent need to develop new, more effective, and safe medications to treat osteoarthritis. Herbal remedies have long been a staple of traditional medicine, and recent advances in fundamental science have shed light on their effectiveness and action mechanism. Curcumin is the natural medicine that is the subject of this investigation because of its potential use as an additional treatment for osteoarthritis. Curcumin has a great safety record and is a pleiotropic chemical. 9.

A number of inflammatory illnesses may benefit from it, according to recent studies. Curcumin has powerful anti-inflammatory and antioxidant properties. Its capacity to selectively inhibit COX-2 is the reason for its anti-inflammatory effects. The purpose of this research was to examine the efficacy of curcumin in conjunction with the standard treatment for OA, diclofenac sodium. Functional parameters, which include, may be used to assess the pain produced by osteoarthritis.

hyperalgesia, inflammation, motor function and arthritis index. We may learn more about the disease process by connecting these functional OA changes to the underlying pathological alterations.

As far as hyperalgesia is concerned, curcumin is known to have strong antinoceptive characteristics. It inhibits the expression of the CX3CR1 receptor, which is typically expressed in microglial cells of the spinal cord, by acting on the dorsal root ganglion or spinal ganglion (10, 11, 12). This lessens neuropathic pain, blocks mechanical allodynia, and lessens reactivity to heat. thirteen, fourteen, fifteen.

Inhibiting the JAK/STAT signaling pathway is one mechanism by which curcumin enhances motor performance. 16. Many biological processes, including cell proliferation, cell differentiation, axon regeneration, apoptosis, and inflammation, rely on the JAK/STAT pathway for transmission of cytokines and other growth factors. A number of cell responses are modulated in osteoarthritis by cytokines, which activate the JAK/STAT pathway 17. Curcumin aids motor function improvement by blocking

this route.

In terms of its impact on inflammation, curcumin mediates the increase of PPAR-γ activity, making it an anti-inflammatory drug. PPAR is a member of the nuclear receptor superfamily that includes three subtypes, PPAR-α, PPAR-∐, and PPAR-γ, the latter of which has been the subject of much research. The levels of PPAR-γ protein in the liver fall during inflammatory circumstances. As an anti-inflammatory agent, curcumin upregulates PPAR-γ. There is a correlation between the anti-inflammatory effect and the inhibition of the Iκβ kinase complex, JNK activation, and the NF-κβ and AP-1 pathways, as well as 19.

As an additional anti-inflammatory effect, curcumin blocks the inflammatory enzymes COX-2, LOX, and inducible NOS 20.

The anti-inflammatory effects of curcumin may explain why it inhibited the spontaneous movement of animals given the spice. The capacity to walk improves as the swelling subsides.

Animals in Group V who get a curcumin pretreatment and then undergo osteoarthritis induction have reduced or absent symptoms across all functional metrics evaluated above. One possible explanation is that curcumin has anti-oxidant qualities, which have a protective impact on joints and may stave against osteoarthritis.

CONCLUSION: Curcumin was found to improve the motor functions of the animal when given along with NSAID which is measured by different functional parameters thereby adding benefit to the present therapy. This can improve the therapeutic strategies and quality of life in Osteoarthritic patients. As it can prevent Osteoarthrits, Curcumin is the need of the hour for osteoarthritic research studies.

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