Therapeutic Effect of Crocin in Collagen Induced Rheumatoid Arthritis Rat Model (Crocin in Rheumatoid Arthritis)

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Abstract

Introduction: Rheumatoid arthritis (RA) is an autoimmune chronic inflammatory disease where articular cartilage degeneration and inflammation are the hallmark of progressive arthritis and they represent the major causes of disability. Several medicinal plants and their isolated molecules have been used in modern medicine to fight against arthritis with the least hazardous side effects.

Aim: To evaluate the potential therapeutic antiarthritic effect of crocin, a dietary colorant carotenoid isolated from stigma of Crocus Sativus, in collagen induced arthritis in rats and to elucidate its possible underlying mechanisms.

Experimental Protocol: Rheumatoid arthritis had been established by intradermal injection of female albino rats with bovine collagen II emulsified in complete Freund’s adjuvant (day 0), then rats were given intradermal booster injection with bovine type II collagen 7 days after primary immunization. Rats were evaluated for arthritic severity by using a macroscopic scoring system.

Material and Methods: From the day following the onset of arthritic symptoms, arthritic rats, with similar arthritic scores, were randomly categorized into three groups; rheumatoid arthritis group, Ibuprofen treated rheumatoid arthritis group, crocin treated rheumatoid arthritis group. Treatment was continued for 14 days.

Evaluation of RA was performed by measuring erythrocyte sedimentation rate (ESR) and C-Reactive Protein (CRP) to assess disease activity and severity, serum level of Cartilage Oligomeric Matrix Protein (COMP), Matrix Metalloproteinase-3 (MMP-3), Acid Phosphatase were measured, inflammatory markers were estimated as Interleukin-6 (IL-6), Tumor Necrosis Factor-α (TNF-α), and Prostaglandin E2 (PGE-2), Superoxide Dismutase (SOD) and reduced Glutathione (GSH) as oxidative stress markers were also estimated.

Results: Arthritic rats showed increased arthritic score, increased ESR, CRP, cartilage and bone degradation that have been detected from increased serum levels of COMP and Acid phosphatase together with increased both inflammatory and oxidative stress markers when compared to normal control group. While, crocin administration, as well as Ibuprofen, resulted in decreased arthritic score together with significant decrease in all previous parameters when compared to arthritic group.

Conclusion: Crocin could be an effective antiarthritic agent possibly through its anti-inflammatory, antioxidant and chondroprotective effects.

Key Words: Rheumatoid arthritis – Crocin – Inflammatory markers – Oxidative stress.

Introduction

RHEUMATOID arthritis (RA) is a chronic inflammatory disease of unknown etiology and it may lead to joint damage, synovial membrane destruction, cartilage and bone damage [1]. Cartilage and bone erosion are the hallmarks of this disease and have a severe impact on human health and quality of life [2]. They occur as a result of leucocytes infiltration into the articular cavity, recurrent inflammation of synovial tissues with subsequent pannus formation [3].

Articular cartilage is a special form of connective tissue that is formed of chondrocytes surrounded by extracellular matrix (ECM) that consists of type II collagen, hyaluroran (HA), and aggrecan. During the process of rheumatoid arthritis, all ECM components are enzymatically degraded by matrix metalloproteinases (MMPs), hyaluronidases (HAases) and aggrecanases respectively [4]. Moreover, several pro-inflammatory cytokines including interleukins (IL-6, IL-1 β, IL-17) and tumor necrosis factor alpha (TNF-α), that are located in the synovium, and inflammatory mediators as PGE2 (prostaglandin E2) are important nonenzymatic mediators that have been accused in disease perpetuation [5]. In addition to inflammatory mediators, some reports showed that free radical generation worsens the disease and contribute to destruction of bone and cartilage by stimulating synovial fibroblasts...
to secrete enormous amount of inflammatory cytokines and ECM degrading enzymes [6]. All these events contribute to bone resorption and cartilage degeneration by increasing the levels of phosphatases and cathepsin-D.

Rodent models of human RA belong to two main categories, experimentally induced and spontaneously induced arthritis. Adjuvant arthritis and collagen induced arthritis were the most common experimentally induced arthritis. The rat Collagen-Induced Arthritis (CIA) is a widely used and a well-established model of arthritis that displays several immunological and pathological features of human RA [7].

A variety of anti-inflammatory agents and other potent drugs are being used for the treatment of RA. Although, these drugs are continuously updated, but their cost is high, adverse drug reactions are numerous and side effects are serious, limiting their therapeutic use and clinical efficacy [8]. For this reason, there is a growing need for newer therapeutic agents that are effective yet safe and less expensive. Several medicinal plants have been involved in modern medicine strategies to fight multifactorial human pathophysiology including arthritis. Crocin is one of these nutraceuticals isolated from the stigma of plant Crocus sativus commonly known as saffron that belongs to Iridaceae family. It is a common dietary colorant carotenoid formed by glycosyl esters of crocetin with fourteen free OH group as an active functional group and reported to possess immense therapeutic value and is the main constituent of Crocus sativus along with crocetin, safranal and picrocrocin. Saffron and its constituents are being evaluated for various pharmacological activities such as anticonvulsant, anti-tussive, anti-anxiety, hypnotic and antidepressant properties, treatment of memory impairment, aphrodisiac activity, and especially for their antitumor effect [9].

The aim of this study was to evaluate the possible therapeutic effect of crocin on rat collagen induced arthritis (CIA) and to elucidate mechanisms of its action.

Material and Methods

Experimental animals:

Female albino rats (200-250g) were housed (5 per cage) in a room with temperature ranging between 22-24°C and 12-h light/dark cycle. All animals had free access to regular standard chow diet and fresh water throughout the period of experiment. This study was conducted at Faculty of Medicine, Tanta University, on the period between May and July, 2016. Treatment and maintenance were conducted according to the guidelines established by the Research Ethical Committee of Faculty of Medicine, Tanta University, Egypt.

Induction of collagen induced arthritis (CIA):

CIA was induced as previously described [10,11]. In brief, type II collagen (CII; Sigma Chemical Co., St. Louis, MO, USA) extracted from bovine articular cartilage was dissolved overnight at 4 °C in 0.1mol/l acetic acid at 2.0mg/ml, after which the solution was emulsified in an equal volume of complete Freund’s adjuvant containing 1.0mg dry heat-killed mycobacterium tuberculosis per ml (Sigma, St Louis, MO, USA) in an ice-cold water bath. Arthritis was induced in rats by an intradermal injection of 0.1 ml of the cold emulsion at the base of tail (day 0). On the 7th day after primary immunization, all rats were given intradermal booster injection of bovine CII emulsified in complete Freund’s adjuvant [12]. The onset of arthritis in ankle joints became visually apparent between days 12 and 14 [13].

Evaluation of CIA:

Rats were clinically observed for characteristic signs and symptoms. Arthritis severity was evaluated by two independent blinded observers, to evaluate the severity of arthritis in each paw according to the degree and the extent of erythema, edema of periarticular tissue and swelling. Severity of RA was determined by calculation of arthritic index (AI) according to macroscopic scoring system ranging between 0 and 16 as described in [14] as follows: each paw was scored on a scale from 0 to 4 as follow; (grade 0= normal paw with no erythema or swelling of the joint; grade 1=erythema or swelling of one toe; grade 2=erythema or swelling of two or more toes, grade 3=erythema and swelling of the entire paw; grade 4=complete erythema and swelling of the entire paw and inability to bend the joint). All four paws were scored and the maximum possible score reached 16 (4 points for each paw). AI was evaluated every other day between day 15 and day 28 after immunization [13].

Incidence percentage:

It was calculated through dividing the number of animals with any clinical signs of arthritis over the total of the number animals in each group at specific time points [15].
Experimental design:
Experimental rats were randomly divided into four groups: Non arthritic control group (n=10): animals of this group were injected intradermally with saline in equal volume, arthritic group (n=11); Ibuprofen treated arthritic group (n=11): Received Ibuprofen (10mg/kg/day, orally), crocin treated arthritic group (n=11): Received crocin (20mg/kg/day, orally) dissolved in 5% CMC. Crocin was purchased from sigma chemicals Co. (St. Louis, MO., USA). All treatment were given from the 15th day after primary immunization (immediately after the onset of arthritis) and continued for 14 days until day 28 (the end of experimental period).

Blood samples:
At the end of experimental period (28 days after the first immunization), all animals were sacrificed by cervical decapitation after fasting for 12 hours and part of fresh blood sample was used for detection of erythrocyte sedimentation rate (ESR). The remainder of blood was collected and centrifuged for 20min at 3000rpm. Serum was then frozen at 20°C for further biochemical analysis.

ESR assay using the westergren method [16]: ESR was used as a test of choice for detecting severity of RA and as indicator of chronic inflammatory disease state [17]. Tri-sodium citrate treated blood was left to sediment for one hour in capillaries (TapvalTM tubes, Aquisel, Barcelona, Spain).

Serum C-reactive protein (CRP): As marker of acute inflammatory phase proteins, expressed as mg/mL, it was determined by using ELISA kits obtained from Sigma Chemical Co., USA. It was assayed according to method described in [18].

Assessment of cartilage and bone degradation:
Serum level of Cartilage Oligomeric Matrix Protein (sCOMP):
It is considered as a marker of cartilage breakdown in RA [19], measured by using rat COMP ELISA (AnaMar Medical, Gothenburg, Sweden), according to the manufacturer instructions as described in [20].

Serum level of matrix metallo -proteinase-3 (MMP-3):
It is used as a marker of osteocartilaginous joint destruction and also as a predictor for progression of joint damage; it is expressed as pg/ml and measured according to the method described by [21].

Serum acid phosphatase assay:
It was measured spectrophotometrically by using commercially available kits (Span Diagnostics Ltd. Surat, India) according to the manufacturer instructions described by [22]. It is expressed as Kings and Armstrong Units (KAU)/100ml serum.

Assessment of inflammation and oxidative stress:

Estimation of inflammatory cytokines:
Serum level of IL-6 was estimated according to the method described in [23], and it was expressed as pg/ml. serum level of TNF-α was determined by using an enzyme linked immunosorbent assay according to the method described in [24], and it was expressed as pg/ml.

Estimation of serum level of PGE2:
It was determined by using solid phase extraction followed by an enzyme immunoassay determination according to the manufacturer instructions described by [25], it was expressed as pg/ml.

Estimation of oxidative stress markers:
SOD was determined by using colorimetric method according to the principles described by [26]. GSH was estimated also colorimetrically as described by [27].

Statistical analysis:
All values were expressed as mean±SD. Statistical analysis was carried out using SPSS version 17 professional software (SPSS, INC., Chicago, IL, USA). The intergroup variation was measured by one way analysis of variance (ANOVA), followed by Tukey’s test for multiple comparisons as a post-hoc test. Arthritic scores were analyzed using a non-parametric Mann Whitney U-test. p-values less than 0.05 were considered to be significant.

Results

Incidence and effect of crocin on severity of arthritis in CIA rats (Fig. 1):
Fifty rats were immunized with type II collagen, only 46 animals showed arthritic manifestation with arthritic incidence (92%). Based on daily macroscopic evaluation of animals, thirty three animals only had the same arthritic index and they were chosen in our study. Animals that failed to develop arthritic lesion after immunization and those that had different arthritic scores were excluded from our study.

Signs of arthritis were detected initially in the hind limbs where the affected limb was severely swollen and red in the ankle, tarsal, metatarsal and interphalangeal joints. This was represented by increased arthritic score.
CIA rats developed arthritis on the 14th day after the 1st immunization. Our results revealed that there was significant increase in the arthritic score in RA group when compared with control non arthritic group. On the other hand, administration of crocin on the 15th day resulted in significant decrease in arthritic score (3.67 ± 2.7) when compared with RA group (8.088 ± 5.19). However, there were non-significant changes in arthritic score between crocin treated RA group (3.67 ± 2.7) and ibuprofen RA treated group (3.86 ± 2.88) throughout the treatment period.

**Effect of crocin on biomarkers of systemic disease activity in CIA rats (Fig. 2):**

There was marked increase in serum levels of CRP and ESR in RA group when compared with control non arthritic group. These biomarkers were correlated with disease activity and progression in different types of inflammatory arthritis. On the other hand crocin administration showed improvement of disease activity as crocin caused significant decrease in CRP and ESR levels when compared to RA group and the effect of crocin is quiet similar to the effect of ibuprofen.

**Effect of crocin on cartilage and bone degradation markers (Fig. 3):**

COMP was used as an indicator marker for progressive joint destruction and several studies revealed that there was elevated level of COMP either in synovial fluid or serum of patients with active rheumatoid arthritis. Our results showed that there was significant increase in sCOMP level in RA group (9.61 ± 1.644) when compared to control non arthritic group (2.89 ± 1.21). While, crocin administration resulted in significant decrease in sCOMP level (4.79 ± 1.1405) when compared to that in RA group (9.61 ± 1.644) which clearly indicates the ECM protective nature of crocin (Fig. 3A).

Moreover, MMPs are one of the best markers in understanding arthritis perpetuation where these enzymes play a very important role in enzymatic deterioration of ECM and cartilage. So serum level of MMP-3 was evaluated to assess the effect of crocin on articular cartilage degradation. Our results revealed that there was a significant increase (55.44 ± 2.169) in serum MMP-3 in RA group compared to control non-arthritic group (15.7 ± 1.823). Oral administration of crocin completely alleviated
augmented MMP-3 effectively in comparison with RA group, and this modulatory effect of crocin was more or less similar to that of ibuprofen (Fig. 3B).

Also, our results showed significant \((p<0.05)\) increase in serum acid phosphatase level in RA group \((6.47\pm0.736)\) in comparison with control non-arthritic group \((4.08\pm0.589)\). Crocin administration caused significant decrease in serum level of acid phosphatase \((4.51\pm0.79)\) when compared to that in RA group \((6.47\pm0.736)\). Bone protective effect of crocin was non statistically different from that of ibuprofen (Fig. 3C).

**Effect of crocin on inflammatory and oxidative stress markers (Table 1):**

It has been suggested that inflammatory mediators serve as non-enzymatic factors responsible for cartilage degradation along with associated immunomodulation and oxidative stress. Serum levels of TNF\(\alpha\), IL-6 and PGE2 were significantly increased \((p<0.05)\) in RA group \((90.2\pm3.51, 126.04\pm7.13\) and \(45\pm3.34\) respectively) in comparison with control non-arthritic group \((0.305\pm0.324, 31.34\pm4.22\) and \(12.5\pm3.4\) respectively). While, orally administered crocin in a dose of \((20\text{mg/kg})\) re-established the above mentioned inflammatory markers effectively \((p<0.05)\) as compared with RA group.

<table>
<thead>
<tr>
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<th>Control non-arthritic group</th>
<th>RA group</th>
<th>Ibuprofen treated RA group</th>
<th>Crocin treated RA group</th>
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<tbody>
<tr>
<td>TNF-(\alpha) (pg/ml)</td>
<td>0.305(\pm0.324)</td>
<td>90.2(\pm3.51)(^a)</td>
<td>45.33(\pm2.33)(^a,b)</td>
<td>41.836(\pm5.88)(^a)</td>
</tr>
<tr>
<td>IL-6 (pg/ml)</td>
<td>31.34(\pm4.22)</td>
<td>126.04(\pm7.13)(^a)</td>
<td>101.11(\pm5.16)(^a,b)</td>
<td>100.63(\pm5.32)(^a)</td>
</tr>
<tr>
<td>PGE2 (pg/ml)</td>
<td>12.5(\pm3.4)</td>
<td>45(\pm3.34)(^a)</td>
<td>36.85(\pm2.48)(^a,b)</td>
<td>36.39(\pm2.27)(^a)</td>
</tr>
<tr>
<td>GSH (mg/dl)</td>
<td>17.1(\pm1.293)</td>
<td>7(\pm1.218)(^a)</td>
<td>16.82(\pm0.887)(b)</td>
<td>16.5(\pm0.708)(b)</td>
</tr>
<tr>
<td>SOD (U/ml)</td>
<td>150(\pm3.446)</td>
<td>60.5(\pm5.58)(^a)</td>
<td>180(\pm4.863)(^a,b)</td>
<td>175.52(\pm2.301)(^a,b)</td>
</tr>
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\(^a\): \(p<0.05\) versus control non-arthritic group. \(^b\): \(p<0.05\) versus rheumatoid arthritis group. Data are mean\(\pm\)SD.

Our results showed that serum levels of GSH and SOD were significantly decreased \((p<0.05)\) in RA group \((7\pm1.218\) and \(60\pm5.58\) respectively) in comparison with control non-arthritic group \((17.1\pm1.293\) and \(150\pm3.446\) respectively). While, orally administered crocin in a dose of \((20\text{mg/kg})\) caused significant increase in these markers \((p<0.05)\) as compared with RA group.
Discussion

RA is an inflammatory disorder characterized by inflammatory cell infiltration of the synovial lining and fibroblast proliferation that resulted in over expression of proinflammatory cytokines and subsequent bone and cartilage destruction [28]. Despite many studies have been carried out to find the appropriate treatment for RA, there was no satisfactory treatment for this disorder. This concept made RA to be only a controllable disorder not a curable one [29]. There is no known cure for rheumatoid arthritis. To date, the goal of treatment in rheumatoid arthritis is to reduce joint inflammation and pain, maximize joint function, and prevent joint destruction and deformity. Early medical intervention has been shown to be important in improving outcomes. NSAIDS have been used for treatment of RA. However, numerous side effects associated with its use made it highly hazardous [30]. Therefore, several medicinal plants have been suggested for treatment of RA. A continuous search for highly safe and potent anti-arthritic agent that can alleviate RA and its associated complications was the target of many researchers. Current work studied the effective role of crocin in treatment of collagen induced arthritic rat model.

Arthritic score has been used as an index for clinical assessment of joint swelling [31]. Some studies showed that there was a close association between the production of pro-inflammatory cytokines and arthritic score. The alteration in plasma protein induces synthesis of pro-inflammatory cytokines, prostaglandins, leukotrienes and matrix metalloproteinases that caused fluid accumulation in the synovium. This resulted in an increase in the arthritic scores in RA group due to damage in joints and bones of the rat’s paw [32]. Our work showed that crocin administration resulted in significant decrease in arthritic score when compared with RA group. This suggests that crocin may have the ability in delaying the inflammatory response and reduces the occurrence of joints inflammatory symptoms.

Inflammatory biomarkers have been proven to be useful in evaluation of disease progression and response to therapeutic intervention in a number of systemic inflammatory disorders including rheumatoid arthritis. CRP, an acute phase protein, is one of these markers. It is produced in the liver during systemic inflammatory conditions. It has been reported to be a very useful inflammatory marker because its half-life doesn’t change in health and disease states and it directly correlates with the severity of pathological processes. CRP levels were found to be increased in clinically active human rheumatoid arthritis, and also in animal models of RA where a similar process was observed [33]. Serum CRP level was significantly decreased in crocin treated RA group when compared with RA group, and this suggests the role of crocin in amelioration of inflammatory condition in rheumatoid arthritis disease.

Inception of arthritis stimulates secretion of several enzymes at the affected joints as hyaluronidase, MMPs and aggrecanases that result in severe articular cartilage degeneration. sCOMP, that is a prominent component of articular cartilage, has been significantly increased after the onset of arthritis denoting ongoing joint destruction [19]. The elevated sCOMP levels in RA group have been attributed to uncontrolled inflammatory process. Moreover, activated synovial fibroblasts, chondrocytes and osteoclasts contribute to the underlying cartilage and bone damage [34]. Decreased serum level of sCOMP following crocin administration indicates its chondroprotective effect that may be explained by its anti-inflammatory effect.

MMP not only degrade collagens, proteoglycans and other ECM macromolecules in the cartilage but also activate other MMPs. MMP-3 is one of these MMPs and it was significantly increased in RA group. Our results regarding increased MMP-3 serum level in arthritic rats are in accordance with other results that showed increased MMP-13,-3,-1 and -9 in synovial fluids and serum of arthritic patients [35]. A possible fascinating mechanism that could explain increased MMP-3 serum level is that proteolytic fragments of ECM including fibronectin act as amplifiers in the diseased joints. Where, these proteolytic fragments have the ability to induce MMPs in cartilage [36]. Crocin administration caused significant decrease in serum level of MMP-3 may be caused by its cartilage degrading enzymes inhibition.

Bone turnover biochemical markers are two categories namely, markers of bone formation and markers of bone degradation. Several studies showed that rheumatoid arthritis were associated with decreased bone formation and increased bone resorption [37]. Acid phosphatase enzyme is one of enzymes involved in bone resorption. Our results showed that rheumatoid arthritis was associated with significant increase in serum level of ACP when compared to control group. ACP was expressed most abundantly by osteoclasts and it was exocytosed from osteoclasts together with bone matrix products into the circulation where its activity reflects the bone resorption rate [38]. Our
results were in accordance with previous results that were reported augmented levels of bone resorption enzymes \([39,40]\). On the other hand, crocin administration resulted in significant decrease in serum level of ACP enzyme when compared with rheumatoid arthritis group. These results suggest bone protective role of crocin.

Results of our study especially of arthritic non-treated group confirmed that many inflammatory cytokines and oxidative biomarkers of chronic inflammatory response as serum IL-6 and TNF-\(\alpha\) are crucial in association with the joint destruction of RA \([41]\). Our results showed that induction of arthritis in rats was associated with significant increase in serum level of inflammatory biomarkers as IL-6 and TNF-\(\alpha\) in comparison with their serum levels in control group. Results of the present study were in agreement with those of previous studies that reported that the proinflammatory cytokines such as TNF-\(\alpha\) and IL-1 \(\beta\) have been shown to mediate cartilage degradation and apoptosis in chondrocytes in degenerative joint diseases such as RA and Osteoarthritis (OA) in humans as well as in animals with experimental rheumatoid arthritis \([42]\). These proinflammatory cytokines were produced by activated synoviocytes, macrophages and chondrocytes \([43]\). These biomediators were well known to activate the ubiquitous transcription factor NF-kB that resulted in further production, expression and upregulation of proinflammatory cytokines and enzymes. These proinflammatory cytokines and enzymes were implicated in erosive bony and cartilage damage of joints in RA as Cox-2 and MMPs that in turn produce prostaglandins especially PGE2 that causes degradation of ECM macromolecules leading to cartilage degradation and further joint inflammation \([44]\). On the contrary, crocin administration caused significant decrease in serum level of TNF-\(\alpha\), IL-6 and PGE2 in comparison to rheumatoid arthritis group. These findings may suggest possible inhibitory effect of crocin on important inflammatory mediators as TNF-\(\alpha\), IL-6 and PGE2.

Moreover, arthritis perpetuation resulted in induction of oxidative stress that will bang up the severity of disease by progressive endogenous generation of ROS. Oxidative damage that has been triggered by ROS is an important mechanism underlying destructive and proliferative synovitis and articular degeneration \([45]\). ROS can act as a second messenger that stimulate NF-kB dependant expression of proinflammatory cytokines as TNF-\(\alpha\), IL-6 and oxidative stress markers. These inflammatory markers beside PGE2 have been implicated in synovial tissue proliferation, joint destruction and programmed cell death in arthritis \([46]\). GSH acts as an intracellular ROS quencher \([47]\), the excessive consumption of GSH as a defense against high level of ROS might be responsible for significant decrease in serum GSH level in arthritic group in comparison to control group. Furthermore, SOD is another enzyme that defends the cell from toxic effect of one of ROS (superoxides) \([48]\), so that our results revealed that there was significant decrease in SOD level in serum of arthritic rats in comparison to control rats. While, crocin administration resulted in significant decrease in the serum level of these antioxidant enzymes in comparison to rheumatoid arthritis group. This antioxidant effect of crocin may be attributed to direct detoxification of ROS or their intermediates or by challenging in the free radicals scavenging in serum.

**Conclusion:**

Results of this study showed that crocin may be used in suppressing collagen induced arthritis in rats, and shed the light on the possible mechanisms of action of crocin in modulating several pathways involved in the pathophysiology of RA. These results suggest that crocin could ameliorate cartilage and bone degradation possibly by abrogating the increased levels of MMPs and ACP. Moreover, crocin quenches ROS and decreased production of ROS induced inflammatory mediators. Therefore, crocin may be of choice in suppressing rheumatoid arthritis away from various side effects of NSAIDs and corticosteroids that were used in treatment of RA.

**Conflict of interest:**

We have no conflict of interest or declare.

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التأثير العلاجي للكلروسين على نموذج التهاب المفاصل الروماتويدي المستوحى بالكولاجين

الفحصية العلمية: التهاب المفاصل الروماتويدي هو مرض التهاب مزمن يسبب نقل في المناقشات الذاتية، حيث أن تحطم الفضفاض الفموي والالتهاب تحماس النمذجة لهذا المرض كما أنها يمكن أن تسبب الأسباب الرئيسية للعاجة وقد استخدمت العديد من الانتهاء الطبية في الطب الحديث لمجابة التهاب المفاصل بالآثار الجانبية.

الهدف من البحث: تقييم التأثير العلاجي المحتمل للكلروسين في التهاب المفاصل الروماتويدي المستوحى بالكولاجين في الفئران وتوضيح الآلية العلاجية الممكنة.

طرق البحث: تم إعداد نموذج التهاب المفاصل الروماتويدي من الوراثة في الفئران البيضاء وذلك عن طريق الحقن داخل الأذية لمواد مختلفة من الكولاجين (اللوكس الثاني) المستخلص من الأبقار وذلك بعد استخدام نظام للتهاب المفاصل باستخدام نظام التسجيل العصبي (بالأمين المجردة).

من اليوس التالي تظهر أعراض التهاب المفاصل تعري أعراض التهاب المفاصل على مستوى المصابات ذات التقييم الشامل للالتهاب المفاصل وتقسيمها عشوائيا إلى ثلاثة أقسام: مجموعة مصابات التهاب المفاصل الروماتويدي، مجموعة التهاب المفاصل المعالجة بالكلروسين، ومجموعة التهاب المفاصل المعالجة بالكلروسين.

النتائج: تم تقسيم المصابات بارتفاع التهاب المفاصل عن طريق قياس معدل التسبب (ESR) ميتوتين سي التفاعل (CRP) وقياسات التشخيص (COMP) جمعية الفضفاض (MMP)-3 وحلقة السائل (SOD, GSH). تم تقاسها (TUNF-α) وعامل نخر الورم ألفا (IL-6). كما أن علامات الالتهاب مثل الانتروكين (IL) قد تم قياسها وتكالع علامات الإجهاد التناكس في مراقبة وقياسها في الفئران.

النتيجة: بالمقارنة مع المجموعة الضبابية، أظهرت الفئران المصابات بالتهاب المفاصل الروماتويدي زيادة درجة التهاب المفاصل وزيادة في خاصية متابعة الفضفاض. ونذكر الفضفاض وانخفاض التهاب المفاصل والالتهاب المفاصل مع انخفاض خصائص المتابعة مع مجموعة التهاب المفاصل الروماتويدي.

الخلاصة: يمكن للكلروسين أن يكون عامل فعال ضد التهاب المفاصل الروماتويدي وذلك من خلال عمله كمضاد للالتهاب ومضاد للالتهاب حيوي مهم لمفاصل المفاصل.