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# EFFECT OF QUERCETIN ON INFLAMMATORY PATHWAYS IN ANIMAL MODEL OF OSTEOARTHRITIS

By

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## ABSTRACT

**Background:** Osteoarthritis (OA) is a a degenerative joint illness which is marked by the destruction and degeneration of the joint's cartilage. Current medications utilized to treat OA mainly target pain relive but unfortunately can't stop the disease progression. Quercetin has been approved as a potent anti-inflammatory anti-oxidant anti-apoptotic agent. It may have a protective effect on repairing OA-induced cartilage injuries.

**Objective:** To identify the possible impact of quercetin on inflammation in osteoarthritis.

**Materials and Methods:** Thirty- two adult male Sprague- Dawley rats were selected, subdivided into four equal groups: control non-osteoarthritic rats saline- treated group (negative control), control osteoarthritic rats saline- treated group (positive control), osteoarthritic rats quercetin-treated group, and osteoarthritic rats glucosamine sulfate -treated group. The experiment was completed with all rats being subjected to measurement of the following parameters: serum levels of tumor necrosis factor- alpha (TNF-α), matrix metalloproteinase 13 (MMP13), interleukin1- β (IL-1β), and nitric oxide (NO).

**Results:** OA, provoked surgically in rats, produced an incredibly crucial rise in serum MMP13 in control osteoarthritic group compared to control non-osteoarthritic rats. The group of rats that was treated by glucosamine revealed a very considerable decline in MMP-13 relative to the control OA group, while it was still much greater than the control normal group. Quercetin- treated rats produced significant decrease in MMP-13 as compared with osteoarthritic non- treated group, while it was still much greater than the control normal group. OA resulted in a highly significant rise in serum IL-1β in the osteoarthritic control rats compared to control non-arthritic rats. In glucosamine- treated group, IL-1β significantly reduced relative to the control osteoarthritis group, and this difference was highly significant. Additionally, IL-1β levels in the Compared to the osteoarthritis control group, the quercetin-treated group's levels were considerably lower. OA produced a highly significant increase in TNF-α in control osteoarthritic group as compared with control non-osteoarthritic rats. Comparing group that was treated with glucosamine to the control osteoarthritis group, the treated group showed a highly significant drop in TNF-α. Additionally, the quercetin-treated group revealed significantly decreased TNF-α contrasted with control osteoarthritis group. As regard NO; In comparison to control non-osteoarthritic rats, OA resulted in a significantly rise in NO. The NO levels measured in the glucosamine-treated group were noticeably lower than those in the osteoarthritic control group, even though they are still much higher than those of the non-arthritic control group. Additionally, the NO levels in the quercetin-treated group levels were noticeably lower as compared to the osteoarthritis control group.

**Conclusion:** Quercetin has the ability to decrease inflammation and oxidative stress in osteoarthritis, suggesting that it may be used as a disease-modifying medication used to treat osteoarthritis.

**Keywords:** Osteoarthrtis; Quercetin; Glucosamine; Inflammation; Oxidative stress.

## INTRODUCTION

Osteoarthritis (OA) is a highly prevalent disorder that affects articular cartilages and it is the most common reason of dysfunction and joint pain across the world. Several determinants influence the onset of OA *(Vina and Kwoh, 2018)*.

A gradual destruction of the joint cartilage and loss of chondrocytes is a hallmark of OA. MMP-13 is a main enzyme that cause cartilage destruction, and it is a major enzyme sharing in degenerative process of OA. So, MMP-13 is an important marker for measuring degree of severity and diagnosing of OA *(Mehana et al., 2019)*.

TNF-α and IL-1β are among the highly important pro-inflammatory cytokines that are secreted abundantly during development of OA. NO is an important indicator to oxidative stress causing inhibition of the formation of joint matrix leading to degradation of the joint *(Chow and Chin, 2020)*.

The approved drugs for treatment of OA are relatively conservative to alleviate the signs and symptoms of the disease. Drugs available to arrest or even slow down progress of OA pathological changes are not markedly effective. The anti-inflammatory drugs do not modulate cartilage degeneration or pathological changes of joint *(Michael et al., 2010)*.

Quercitin is the main nutritional flavonol present in fruits, vegetables, and beverages *(Oliveira et al., 2015)*. Several experimental studies reported the anti-proliferative, antioxidant, anti-angiogenic anti-inflammatory, and pro-apoptotic activity of that agent *(Gardi et al., 2015)*.

Glucosamine is composed from units of aminosaccharide that are considered the building block of glycosaminoglycan chains and form aggrecan and other joint proteoglycans *(Reginster et al., 2012)*. It inhibits expression of gene causing OA in vitro *(Uitterlinden et al., 2006)*. The degradation of cartilage is decreased when glucosamine sulphate is taken orally. Also, it upregulates MMP mRNA in an osteoarthritis model *(Taniguchi et al., 2011)*.

## MATERIALS AND METHODS

**Experimental animals:**

Thirty- two adult male Sprague-Dawley rats (n = 32; 200 to 250 g) were procured from the Mansoura University's Medical Experimental Research Center (MERC). The investigations were done at the Faculty of Medicine for Girls, Al-Azhar University. We kept rats in an environment with a limitless supply of food and water, normal dark/ light cycle, and a constant temperature of 25°C. Before being employed in the trials, the animals were habituated to these circumstances for at least 2 weeks, and overall conditions were tracked throughout the study. We took every reasonable step to reduce both the suffering of the animals and their utilization. Rats were kept in stainless steel cages (25 × 30 × 25 cm. for every 4 rats). We tested the possible effect of quercetin in a surgically induced OA model performed on rats as a potential OA disease modifying drug were used as potential curative drug for six weeks in daily oral dosage of 150 mg/kg b.w.d for six weeks and comparing its effect to the effect of oral Glucosamine sulfate which

was given as 250 mg /kg/ day orally for six weeks also.

**Experimental model and design:**

**Four equal groups of rats were as follows:**

**Group (1):** Control non- osteoarthritic rats saline treated.

**Group (2):** Control osteoarthritic rats saline treated.

**Group (3):** Osteoarthritic rats treated with an oral dosage of 150 mg/kg body weight each day of quercetin *(Gardi et al., 2015)*.

**Group (4):** Osteoarthritic rats treated with an oral dose of 250 mg/kg body weight each day of glucosamine sulfate *(Wen et al., 2010)*.

Rats were put through the surgically generated OA model by creating a tear in the medial meniscal. Medial collateral ligament was severed, medial meniscus was reflected medially toward the femur, and finally the medial meniscus was sliced *(Janusz et al., 2002)*.

The study lasted for three months and at its end rats had been sacrificed using an overdose of thiopental sodium (75 mg/kg body weight, i.p.) *(Damiani et al., 2003)*.

The Intuitional Research Board (IRB) authorized all animal protocols used in the execution of all experimental operations (Code number: 2022071410), Faculty of Medicine for Girls, Al-Azhar University.

**Biochemical measurements in serum:**

Cardiac blood was collected into EDTA-free tubes, allowed to clump for 30 minutes, The serum was separated after blood being centrifuged at 4000 rpm for fifteen minutes, and it was then kept frozen at -20 ℃ until the time of measurements for MMP13 (EIAab science), IL-1 (Boster biological technology co), TNF- alpha (RayBioRat), and NO *(Bio-diagnostic kit) (Montgomery and Dymock, 1961)*.

**Statistical analysis:**

The Statistical Package for the Social Sciences (SPSS) version 21 was used to examine the data. The Shapiro-Wilk test was used to determine the data's initial normality. The presentation of continuous variables was as mean SD. In order to compare the means of more than two groups, Analysis of Variance (ANOVA) was performed. To compare group means, the post- hoc Tukey test was utilized. p-values $\leq 0.05$ were deemed significant.

## RESULTS

**Consequences of oral quercetin and oral glucosamine on serum matrix metalloproteinase 13 level in osteoarthritic rats:**

OA resulted in a significant rise in serum MMP13 in control osteoarthritic group (group 2) (20.87±3.29 pg/ml) compared to control non-osteoarthritic rats (group 1) (5.95 ±2.58 pg/ml) **(Table 1)**.

Glucosamine treated group (group 3) showed significant decrease in MMP-13 (11.84 ± 2.01 pg/ml) as compared with control OA group (group 2) (20.87±3.29 pg/ml) but still significantly higher than control normal group (group 1) (5.95 ±2.58 pg/ml) **(Table 1)**.

As regard quercetin- treated rats (group 4) there was a significant decrease in MMP-13 (11.95 ± 2.65 pg/ml) as compared with osteoarthritic non- treated group (group 2) (20.87±3.29), but still significantly higher than control normal group (group 1) (5.95 ±2.58 pg/ml) **Table (1)**.

**Table (1): Effects of oral quercetin and oral glucosamine on serum matrix metalloproteinase- 13 level in osteoarthritic rats**

| Animal groups | MMP13(pg/ml) (means ± SD) | P value |
|---|---|---|
| **Group 1 (8 rats)** (Control non- osteoarthritic group) | **5.95 ±2.58** | |
| **Group 2 (8 rats)** (Control osteoarthritic group) | **20.87±3.29** | **Group 1&2 ($p \leq 0.001$)** |
| **Group 3 (8 rats)** (Oral glucosamine- treated group) | **11.84 ± 2.01** | **Group 1&3 ($p \leq 0.05$)** **Group 2&3 ($p \leq 0.001$)** |
| **Group 4 (8 rats)** (Oral quercetin- treated group) | **11.95 ± 2.65** | **Group 1&4 ($p \leq 0.05$)** **Group 2&4 ($p \leq 0.001$)** **Group 3&4 ($p > 0.05$)** |

**Effects of oral quercetin and oral glucosamine on serum interleukin 1-β level in osteoarthritic rats:**

OA resulted in a significant rise in serum IL-1β in control osteoarthritic group (group 2) (51.03±2.91 pg/ml) as compared with control non-osteoarthritic rats (group 1) (31.04±4.49 pg/ml) **(Table 2)**.

Glucosamine- treated group (group 3) produced a significant decrease in IL-1β (34.72±2.55 pg/ml) as compared with the control osteoarthritic group (group 2) (51.03±2.91 pg/ml) **(Table 2)**.

In quercetin treated group (group 4), the level of IL-1 significantly declined (44.52±2.85pg/ml) as compared with the control osteoarthritic group (group 2) (51.03±2.91 pg/ml), but still significant as compared to the control non-osteoarthritic group (group1) (31.04±4.49 pg/ml) and glucosamine- treated group (group3) (34.72±2.55 pg/ml) **(Table 2)**.

**Table (2): Effects of oral quercetin and oral glucosamine on serum interleukin 1-β level in osteoarthritic rats**

| Animal groups (8 rats in each group) | interleukin 1-β (pg/ml) (means ± SD) | P value |
|---|---|---|
| **Group 1** (Control non osteoarthritic group) | **31.04±4.49** | |
| **Group 2** (Control osteoarthritic group) | **51.03±2.91** | **Group 1&2 ($p \leq 0.001$)** |
| **Group 3** (Oral glucosamine treated group) | **34.72±2.55** | **Group 1&3 ($p > 0.05$)** **Group 2&3 ($p \leq 0.001$)** |
| **Group 4** (Oral quercetin treated group) | **44.52±2.85** | **Group 1&4 ($p \leq 0.001$)** **Group 2&4 ($p \leq 0.05$)** **Group 3&4 ($p \leq 0.001$)** |

**Effects of oral quercetin and oral glucosamine on serum tumor necrotic factor alpha level in osteoarthritic rats:**

OA resulted in a significant rise in TNF-α in control osteoarthritic group (group 2) (22.99±3.41 pg/ml) as compared with control non-osteoarthritic rats (group 1) (9.95 ±1.45pg/ml) **Table (3)**.

Glucosamine- treated group (group 3) produced a significant decrease in TNF-α (11.60±5.23 pg/ml) as compared with the control osteoarthritic group (group 2) (22.99±3.41 pg/ml) **Table (3)**.

Quercetin treated group (group 4) showed a significant decrease in TNF-α (10.25±3.37 pg/ml) as compared with the control osteoarthritic group (group 2) (22.99±3.41 pg/ml) **Table (3)**.

**Table (3): Effects of oral quercetin and oral glucosamine on serum tumor necrotic factor alpha level in osteoarthritic rats**

| Animal groups (8 rats in each group) | Serum TNF-α (pg/ml) (means ± SD) | P value |
|---|---|---|
| **Group 1** (Control non-osteoarthritic group) | **9.95 ±1.45** | |
| **Group 2** (Control osteoarthritic group) | **22.99±3.41** | **Group 1&2 ($p \leq 0.001$)** |
| **Group 3** (Oral glucosamine treated group) | **11.60±5.23** | **Group 1&3 ($p > 0.05$)** **Group 2&3 ($p \leq 0.001$)** |
| **Group 4** (Oral quercetin treated group) | **10.25±3.37** | **Group 1&4 ($p > 0.05$)** **Group 2&4 ($p \leq 0.001$)** **Group 3&4 ($p > 0.05$)** |

**Effects of oral quercetin and oral glucosamine on serum nitric oxide level in osteoarthritic rats:**

OA resulted in a significant rise in NO in control osteoarthritic group (group 2) (33.57±2.59 µmol/L) as compared with control non-osteoarthritic rats (group 1) (17.99±1.32 µmol/L) **(Table 4)**.

Glucosamine- treated group (group3) produced a significant decrease in NO (23.85±2.04 pg/ml) as compared with the control osteoarthritic group (group 2) (33.57±2.59 µmol/L), but still significally higher than control non- arthritic group (group 1) (17.99±1.32 µmol/L) **(Table 4)**.

In quercetin treated group (group 4), there was a significant decrease in NO (23.07±1.44 µmol/L) in comparison to the osteoarthritic control group (group 2) (33.57±2.59 µmol/L), but still significally higher than control non- arthritic group (group 1) (17.99±1.32 µmol/L) **Table (4)**.

**Table (4): Effects of oral quercetin and oral glucosamine on serum nitric oxide level in osteoarthritic rats**

| Animal groups (8 rats in each group) | serum nitric oxide (µmol/L) (means ± SD) | P value |
|---|---|---|
| **Group 1** (Control non-osteoarthritic group) | **17.99±1.32** | |
| **Group 2** (Control osteoarthritic group) | **33.57±2.59** | **Group 1&2 ($p \leq 0.001$)** |
| **Group 3** (Oral glucosamine treated group) | **23.85±2.04** | **Group 1&3 ($p \leq 0.05$)** **Group 2&3 ($p \leq 0.001$)** |
| **Group 4** (Oral quercetin treated group) | **23.07±1.44** | **Group 1&4 ($p \leq 0.05$)** **Group 2&4 ($p \leq 0.001$)** **Group 3&4 ($p > 0.05$)** |

## DISCUSSION

OA is a musculoskeletal degenerative disorder that destructs the cartilage and affect the function of the joint (Glyn-Jones et al., 2015). OA affect about 50% of the elderly population over the age of 60 worldwide (Collins et al., 2018). In the present experiment, surgical induction of OA caused an enormous increase in the serum level of inflammatory indicators as IL-1β, TNF-α this result is in line with the outcome of *(Zhang et al., 2019* and *Li et al., 2021)*.

Inflammation has a direct relationship to the pathogenesis of osteoarthritis *(Scanzello and Goldring, 2012)*. Numerous researches noted the existence of multiple inflammatory markers that are expressed abundantly in early OA in the articular synovial membrane *(Benito et al., 2005)* indicating that these cytokines and nuclear transcription factors are taking part in the pathways of inflammation *(Surapaneni and Venkataramana, 2007)*. Whatever the site of production of these inflammatory cytokines, increasing its concentration can activate particular aggrecanases (ADAMTS-4/-5), which specifically break the aggrecan molecule and making it inactive molecule, aggrecan is an important molecule that chare strongly in the manufacture of the cartilage tissue *(Fosang et al., 2008)*.

TNF-α especially is an important mediator in the OA pathogenesis *(Li et al., 2015)*. TNF-α may affect the pathogenesis of OA by activating different types of

cells, activating the prostaglandin E2 formation in synovial cells, stimulating excess expression of metalloproteinases and destructing bone and joint cartilage *(Zhang et al 2019)*.

In our study, quercetin significally decreased serum IL-1β and TNF-α levels compared with the osteoarthritic group. These results were the same as have been These results were the same as have been found by *(Haleagrahara et al., 2018, Feng et al., 2019, Zhang et al 2019,* and *Li et al., 2021)*.

Many previous studies reported the anti-inflammatory action of quercetin in rats on adjuvant arthritis, and quercetin could markedly decrease the levels of TNF-α and IL-1β that were released from the peritoneal macrophages *(Mamani-Matsuda et al., 2006)*. Toll-like receptor (TLR)-4/nuclear factor kappa-light-chain enhancer of activated B cells (NF-jB) signaling pathway is a crucial mechanism in the development of inflammation and quercetin may act by suppression this pathway *(Chen et al., 2016)*.

The second important mediator that share in inflammation and tissue damage in OA is IL-1β *(Wang et al., 2015)*. IL-1β can degrade the extracellular matrix and inhibit its production leading to apoptosis in the cartilage chondrocyte *(Wang and Kim, 2015)*. These cytokine increases the expression of MMP proteins *(Zeng et al., 2015),* increasing cartilage destruction, and preventing its repair accelerating the development of osteoartheritis *(Guermazi et al., 2015)*.

Within the current research, glucosamine significally decreased serum concentration of TNF-α and IL-1β as compared with the osteoarthritic group. These results were the same as have been found by *Aghazadeh-Habashi et al. (2014)* who studied how various glucosamine dosages affected rats. and discovered that oral glucosamine for six days reduced the levels of pro-inflammatory cytokines as IL-6, IL-1, and TNF-α and reduced oxidative stress as well as NO in rats with OA.

In cartilage explants, glucosamine reduces IL-1-induced expression of genes of mPGEs, iNOS, COX2, and NF-B. decreasing the formation of NO and PGE2, which are important in chondrocyte apoptosis and an elevation in inflammatory responses *(Chan et al., 2006)*. Glucosamine can decrease the process of COX-2 enzyme synthesis by different ways as prevention of the IL-1β induced NF-κB pathway *(Largo et al., 2003)*. The inhibition of COX-2 co-translational N-glycosylation and the promotion of COX-2 protein turnover are two additional mechanisms by which glucosamine hydrochloride decreases COX-2 activity *(Jang et al., 2007)*.

Inflammatory cytokines decreased the formation of cartilage material. Studies on chondrocytes of rats have reported that an essential enzyme in the formation of cartilage GAG chains is suppressed by IL-1β, which is called galactose-β-1, 3 glucuronosyltransferase I (GlcAT-I). Studies have found that glucosamine cause dose-dependent reduction in this inhibition *(Gouze et al., 2001)*.

In the current research, OA resulted in considerable elevation in serum MMP 13 which was is the same as the result of *(Haleagrahara et al., 2018,* and *Nasrabadi et al., 2022)*. MMP groups of enzymes are important in the OA

pathogenesis *(Zeng et al., 2019)*. MMPs are produced as a result of stimulatory effect of inflammatory cytokines which are produced by very large amount at early stages of OA *(Mehana et al., 2019)*. MMPs are subdivided in different types according to their domain organization and specificity *(Xie et al., 2017)*. MMP-13 in its active form is called collagenase-3 and Performs an essential role in degeneration of the cartilage by degeneration of the cartilage matrix and type II collagen. MMP is secreted by dysfunctional chondrocytes., its circulating level increase as the disease progression increase *(Li et al 2017)*.

In the current study, the serum level of MMP 13 significantly dropped after quercetin administration. This outcome was consistent with that of *Qiu & Chen (2018)* and *Nasrabadi et al. (2022)*.

Different studies have reported that in rat chondrocytes, quercetin reduces IL-1β induced inflammation and apoptosis. Another study as according to our data, demonstrated that quercetin might inhibit the IL-1β induced buildup of NO, MMP-3, and MMP-13. *(Qiu and Chen, 2018)*. Increased level of both IL-1β and TNF-α increase the production of cytokines including MMPs, stimulating inflammation, destructing the articular interstitial matrix, and disturbing bone structure *(Syggelos et al. 2013)* This may explain how quercetin can decrease serum MMP 13.

In our study, treatment of osteoarthritic rats with Glucosamine sulfate significantly inhibited MMP-13, and this result was in agreement with *Scharstuhl et al. (2001)*. Glucosamine sulfate inhibits the expression of genes responsible for MMP-13 production by affecting NF-κB pathway *(Rajapaks et al., 2007)*.

In the current research, OA resulted in a significant increase in serum NO. This result was the same as the result of *Feng et al. (2019)*. Different studies reported that, during development of OA, there is a marked increase in ROS *(Surapaneni and Venkataramana, 2007)*. Studies have found that NO induces apoptosis, and this occurs by a mitochondria-dependent mechanism leading to the destruction of the interstitial matrix, promoting chondrocytes death *(Wu et al., 2007)*. Death of the chondrocytes was caused by incubating human articular chondrocytes with the NO donor sodium nitroprusside (SNP), this happen by promoting caspase-7 and expression of caspase-3 and suppression of Bcl-2 expression *(Maneiro et al., 2005)*.

In our current study, treatment of osteoarthritic rats with oral quercetin result in significant reduction in in serum NO this result is the same as that found by *Feng et al. (2019)*.

Quercetin was shown to inhibit oxidative stress, and endoplasmic reticulum stress in chondrocytes *(Feng et al., 2019* and *Wei et al 2019)*. Quercetin displays anti oxidative role under stressful conditions in different degenerative diseases *(Roslan et al., 2017)*. In accordance with our findings, *Wei et al. (2019)* demonstrated that quercetin might take part in treatment of the degenerative conditions as OA by decreasing responses to oxidative stress and inhibiting the degradation of interstitial matrix cartilage. In addition, *Hu et al. (2019)* stated that quercetin injected intra-articular can prevent cartilage degeneration, and can

decrease death of the chondrocytes in a rat model with OA. Quercetin markedly reduces inflammation of the joint and degeneration of the cartilage in animal models of arthritis *(Mamani-Matsuda et al., 2006)*.

In that current study, treatment of osteoarthritic rats with oral glucosamine has a dramatic drop in in serum NO. This result was the same as the result of *Campo et al. (2009)*. Glucosamine has an antioxidant and anti-inflammatory action, with a significant decrease in iNOS (inducible nitric oxide synthase) expression and function. This explains why glucosamine reduce NO-induced apoptosis of chondrocytes *(Campo et al., 2009)*. Glucosamine decreases the production of NO by suppressing gene expression for NF-κB, and iNOS which is activated through IL-1β in the joints *(Chan et al., 2006)*.

## CONCLUSION

Treatment with quercetin can ameliorate the biochemical and molecular changes of osteoarthritis by attenuating inflammatory cytokines and oxidative stress. Quercetin can decrease the level pf MMP-13 with subsequent modulation of oxidative stress, and inflammation. Therefore, quercetin can be one of osteoarthritis modifying drug which can work by a mechanism affecting the pathophysiology of osteoarthritis making quercetin a possible therapeutic approach to osteoarthritis.

**Conflict of interest:**

There is no competing interest amongst the authors.

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**Authors Contributions:**

Doaa Hellal and Wafaa Abd El-Aziz Emam contributed to the study conception and design. Biochemical analyses were performed by Wafaa Abd El-Aziz Emam. Experimental procedures on animals were performed by Doaa Hellal. The published version of the manuscript has been read and approved by the two authors.

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# تأثير الكيرسيتين على مسارات الالتهاب في نموذج حيواني من خشونة المفاصل

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**خلفية البحث:** خشونة المفاصل هو اضطراب مفصلي تدريجي يتميز بتآكل الغضروف المفصلي وتدميره. العلاجات الحالية غير الجراحية لخشونة المفاصل تهدف بشكل رئيسي إلى تخفيف الألم، ولكن بالكاد يمكن أن تخفف من تطور التهاب المفاصل. وقد أظهر دواء كيرسيتين تأثيرات قوية مضادة للالتهابات.

**الهدف من البحث:** اختبرت هذه الدراسة التأثير المحتمل للكيرسيتين على تقليل الالتهاب في خشونة المفاصل عن طريق تثبيط الالتهاب والإجهاد التأكسدي وأنواع الأكسجين التفاعلية.

**مواد وطرق البحث:** تم اختيار اثنين وثلاثين من ذكور جرذان سبراغ داولي، مقسمة إلى أربع مجموعات متساوية: مجموعة الجرذان المعالجة بمحلول ملحي، المجموعة المعالجة بالمحلول الملحي للجرذان المصابة بهشاشة العظام، المجموعة المعالجة بالكيرسيتين، المجموعة المعالجة بكبريتات الجلوكوزامين. في نهاية الفترة التجريبية، خضعت جميع الجرزان للقياسات التالية: مستويات المصل من البروتين المعدني المصفوف 13(MMP13)، إنترلوكين 1(IL-1β) - β، عامل نخر الورم- ألفا (TNF-α) وأكسيد النيتريك.(NO)

**نتائج البحث:** فيما يتعلق ب MMP13؛ أدى التحريض الجراحي لخشونة المفاصل في الجرذان إلى زيادة عالية في مستوي MMP13 في المجموعة الضابطة المصابة بخشونة المفاصل مقارنة بالجرذان غير المصابة بخشونة المفاصل. أظهرت المجموعة المعالجة بالجلوكوزامين انخفاضًا ملحوظا للغاية في MMP-13 مقارنة بالمجموعة الضابطة المصابة بخشونة المفاصل. لكنها لا

تزال أعلى بكثير من المجموعة الضابطة. أنتجت الجرذان المعالجة بالكيرسيتين انخفاضًا كبيرًا في MMP-13 مقارنة بالمجموعة غير المعالجة بالتهاب المفاصل العظمي، ولكنها لا تزال أعلى بكثير من المجموعة العادية الضابطة. فيما يتعلق ب IL-1β؛ أدى التحريض الجراحي لإلتهاب المفاصل في الجرذان إلى زيادة عالية في مصل IL-1β في المجموعة الضابطة من خشونة المفاصل مقارنة بالجرذان غير المصابة بهشاشة العظام. بينما أدت المجموعة المعالجة بالجلوكوزامين إلى انخفاض كبير في IL-1β مقارنة بالمجموعة الضابطة المصابة بخشونة المفاصل. أيضا، أدت المجموعة المعالجة بالكيرسيتين إلى انخفاض كبير في IL-1β مقارنة النيتريك اوكسيد. فيما يتعلق TNF-α؛ أدى التحريض الجراحي للاصابة بخشونة المفاصل في الجرذان إلى زيادة عالية في TNF-α في المجموعة الضابطة المصابة بخشونة المفاصل مقارنة بالجرذان غير المصابة بخشونة المفاصل. بينما أنتجت المجموعة المعالجة بالجلوكوزامين انخفاضًا ملحوظا في TNF-α مقارنة بالمجموعة الضابطة المصابة بخشونة المفاصل. أيضا، أدت المجموعة المعالجة بالكيرسيتين إلى انخفاض كبير في TNF-α مقارنة بالمجموعة الضابطة المصابة بخشونة المفاصل. فيما يتعلق ب NO؛ أنتج الحث الجراحي للالتهاب المفصلي في الجرذان زيادة كبيرة في النيتريك اوكسيد في المجموعة الضابطة المصابة بخشونة المفاصل مقارنة بالجرذان غير المصابة بالفصال العظمي. بينما أنتجت المجموعة المعالجة بالجلوكوزامين انخفاضًا كبيرًا في بالمجموعة الضابطة المصابة بخشونة المفاصل. مقارنة بالمجموعة الضابطة المصابة بخشونة المفاصل. ولكن لا تزال أعلى بشكل ملحوظ من المجموعة غير المصابة بخشونة المفاصل. كما أدت المجموعة المعالجة بالكيرسيتين إلى انخفاض كبير في بالمجموعة الضابطة المصابة بخشونة المفاصل. مقارنة بالمجموعة الضابطة المصابة بخشونة المفاصل.

**الإستنتاج:** أظهرت نتائج هذه الدراسة أن الكيرسيتين لديه القدرة على تقليل الالتهاب والإجهاد التأكسدي في هشاشة العظام مما يشير إلى أنه يمكن استخدامه كعامل تعديل للمرض في علاج خشونة المفاصل.

**الكلمات الدالة:** خشونة المفاصل، كيرسيتين، الجلوكوزامين، عوامل الاكسدة.