



# Evaluation of the Anti-Rheumatic Activity of Custard Apples Fruit on Rats with Rheumatoid Arthritis Induced by Complete Freund's Adjuvant

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### ABSTRACT:

Rheumatoid arthritis (RA) affects 0.5–1% of people; it lowers a patient's quality of life. RA is an immune-mediated condition that can cause lymphocyte and fibroblast activation, which can result in joint damage. This study aimed to evaluate the impact of custard apple juice (CAJ) on reducing RA in rats. Thirty male rats were divided into two main groups and fed a standard diet. The first group, the -ve C group (n:6), and the second group (n:24) were treated with 0.1 ml of total adjuvant injected into the right tarsal joint of each animal, and this was repeated seven days later. Signs of RA appeared after 14 days. After dividing them into four equal subgroups (6 rats each), the first +ve C group and the second, third, and fourth groups were given a daily oral dose of CAJ 5, 10 and 15  $\mu\text{L/g}$  (B.W), respectively. At the end of the trial (28 days), the results indicated that supplementations of CAJ led to a decrease in the level of erythrocyte sedimentation rate, anti-citrullinated protein/peptide antibody, C-reactive protein, rheumatoid factor, malondialdehyde, and Immunoglobulin G & M compared to +ve C. In contrast, total oxidant status, catalase, and glutathione peroxidase levels were increased significantly compared to the +ve C., whereas administering rats with 15  $\mu\text{L/g}$  of CAJ achieved the best effects through improving the previous changes to near the normal levels. Conclusion: The custard apples enhance immunity, leukocyte count, and total antioxidant status while inhibiting the formation of inflammatory cells in RA.

**Keywords:** *Annona squamosa, inflammatory, rheumatoid - C-Reactive protein, immunity*

## 1. INTRODUCTION

Rheumatoid arthritis is a non-specific inflammatory disease that damages the synovium in joints, causing the joints to become distorted and sticky (1),

pathological findings associated with RA often include synovial hyperplasia, inflammatory cell infiltration, pannus development, injury to articular cartilage,

bone erosion, and extra-articular symptoms (2).

RA affects approximately 1% of people worldwide and causes inflammation, damage, and disfigurement (3), CFA is a suspension of desiccated mycobacterium in paraffin oil and mannide monooleate that induces inflammation, tissue necrosis, and ulceration. It can be used subcutaneously in the paw, or intraperitoneally in mice and rats. A period of 24 h is required for onset after injection, due to the rate of tissue necrosis, it is recommended to euthanize CFA injected animals within 1 week (4).

The tropical endemic species *Annona squamosa* L. (*Annonaceae*), commonly referred to as the "custard apple," is found in the West Indies, South and Central America, Ecuador, Peru, Brazil, India, Mexico, the Bahamas and Egypt (5), custard apple possesses potent bioactive principles in all its parts like the dietary fiber, potassium, and vitamin B1 contents are also very high, and it has a noticeable amount of vitamin C and other constituents of plant are atidine, histamine, hetisine, histidine, heterophyllisine, isoatisine, reticuline, heterophylline, oxophoebine, heterlophylline, dihydroatisine, hetisinone and benzoyl heteratisine (6), these properties, which include anticancer, anticonvulsant, anti-arthritic, antiparasitic, antimalarial, hepatoprotective, and antidiabetic properties, have been supported by numerous studies (7), research suggests

that custard apples fruit may be used to reduce rheumatoid arthritis discomfort and inflammation (8).

The methanolic extract of some plants like *Withania somnifera* L. and *Annona squamosa* L., isolated caryophyllene oxide reduced the receptor agonist by blocking inflammatory centers, cyclooxygenase, and lipoxygenase (9). The cyclooxygenases COX-1 and COX-2 were suppressed by the freeze-dried fruit extract of *Annona Muricata* L., which interacted with opioidergic receptors to reduce pain (10 and 11). *Annona squamosa* L reduces pain and has an anti-inflammatory impact in RA models (12). Natural source extracts are abundant in bioactive chemicals and exhibit a wide range of biological actions. This makes them essential for the development of novel pharmaceutical medications and high-antioxidant and Anti-inflammatories food products (13).

Therefore this study was designed to determine the efficacy of *Annona squamosa* pulp juice in treating and preventing FCA-induced rheumatoid arthritis.

## 2. MATERIALS AND METHODS

### 2.1. MATERIALS

Custard apples (*Annona squamosa*) were purchased from local market, Tanta, Gharbiya Governorate, Egypt. The chemical Complete Freund's adjuvant (infecting material) used throughout the experiment was purchased from Sigma Chemicals, Germany.

## 2.2. METHODS

### 2.2.1. Preparation of Custard apples juice

The inner core of custard apples is obtained. It was diluted with distilled water (1:1) using a mixer (14).

### 2.2.2. Experimental design:

Thirty adult male white albino rats, Albino Strain, 10 weeks age, weighing (150±10g) were used in this experiment. All rats were fed on basal diet prepared according to American Institute of Nutrition (14) for 7 consecutive days. Rats were randomly divided into two main groups and fed on standard diet, group I: negative control (6 rats), group II: rheumatoid arthritis group (24 rats). 0.1 ml of total adjuvant was injected into the right tarsal joint of each animal and this was repeated 7 days later. Signs of rheumatoid arthritis appeared after 14 days according to Taksande et al., (16). After dividing it into four equal parts Subgroups The first: the positive control group, the second, the third, and the fourth the groups received a daily oral dose 5,10 and 15 µL/g of (B.W) of custard apple juice, respectively. At the end of the experimental period (28 days), rats were anesthetized with diethyl ether after fasting for 12h and blood samples were collected and centrifuged to obtain serum and kept in frozen until analysis.

### 2.2.3. Ethical approval

The scientific Research Ethics Committee (Animals Care and Use), Faculty of Home Economics, Menoufia University, Shebin El-kom, Egypt, This work was ethically approved by the Institutional Animal Care

and Use Committee (IACUC), Menoufia University (Reg. No, MUFHE /S/NFS/23/23).

### 2.2.4. Biochemical Analysis

The methods described by Sykes (17) were utilized to measure the erythrocyte sedimentation rate (ESR1-2). According to the method defined by Tillett and Francis (18), C- Reactive Protein (CRP). Rheumatoid factors (RF) are autoantibodies against IgG. They are probably the most studied antibody since their discovery by (19). Anti-citrullinated protein antibodies (ACPAs) according to the methods described by (20). Malondialdehyde (MDA); Catalase (CAT); glutathione peroxidase (GPx) and total oxidant status (TOS) was determined according to Jentezch et al., Hu, Firestein and McInnes, Nishikimi ,Appaji and Yagi (21,22,23and24), respectively. Immunoglobulin M (IgM), and Immunoglobulin G (IgG) They were analyzed using the protocol of Burrels and Wells, (25 and 26), respectively

### 2.2.5. X-ray

The rheumatologist who examined the X-rays blindly evaluated the X-rays in relation to the clinical and laboratory data, utilizing a standardized Larsen score to gauge the advancement of joint injury at the time of the scan. Utilizing common reference films, the Larsen score was determined (27).

In rheumatoid arthritis (RA), the study of X-rays as a gauge of prognosis is acknowledged as routine procedure (28).

### 2.3. Statistical analysis:

The mean  $\pm$  SD was used to express the results. One-way analysis of variance (ANOVA) was used to analyze the data for comparisons involving multiple variables. The statistical package program called for the use of Duncan's test as a post hoc test for comparing the significance between groups (29).

## RESULTS AND DISCUSSION

Table (1) showed that exposure of rats to complete Freund's adjuvant led to significant increase ( $p \leq 0.05$ ) in the levels of erythrocyte sedimentation rate (ESR1 and ESR2) compared to the negative control. The same results were obtained by (30) who reported that onset of rheumatoid arthritis (RA) was observed  $14 \pm x$  days after injection of CFA. Also, (31) showed that ESR is elevated in acute tissue damage, rheumatic diseases such

as rheumatoid arthritis. Administration rats with custard apple juice 5-10 and 15  $\mu\text{L/g}$  of (B.W) significant ( $p \leq 0.05$ ) decrease the levels of erythrocyte sedimentation rate (ESR1 and ESR2) compared to positive control group. This may be due to custard apple, which has anti-inflammatory activity and antioxidant activities and the pulp extract of custard apple's presented potent antioxidant activities. These results agree with Gate et al., (32) who propose that an immune-suppressive mechanism is most likely responsible for the custard apple's anti-arthritis effects. Moreover, Volobuff et al., (33) reported that the pulp extract of custard apple's presented potent antioxidant activities. The highest reduction in ESR1 and ESR2 values were observed in the rats administrated with custard apple juice at dose 15  $\mu\text{L/g}$ .

**Table (1): Effect of CAJ on erythrocyte sedimentation rate of negative and rheumatoid arthritis groups**

Variables	Negative		Rheumatoid arthritis groups		
	control group	Positive control	CAJ (5 $\mu\text{L/g}$ BW)	CAJ (10 $\mu\text{L/g}$ BW)	CAJ (15 $\mu\text{L/g}$ BW)
ESR1(mm/h)	3.85e $\pm$ 0.4	80.00a $\pm$ 6.4	50.00b $\pm$ 1.4	27.50c $\pm$ 1.7	12.00d $\pm$ 0.4
ESR2(mm/h)	8.50e $\pm$ 1.1	104.00a $\pm$ 1.4	98.33b $\pm$ 3.9	67.50c $\pm$ 2.5	23.00d $\pm$ 1.4

Values are expressed as means  $\pm$  SD. Means in the same row with different letters are significantly different ( $P \leq 0.05$ ). CAJ, custard apples juice, ESR1, erythrocyte sedimentation rate, ESR2, erythrocyte sedimentation rate.

Data in table (2) indicated that effect of custard apples juice on rheumatoid factor, c-reactive Protein and anti-citrullinated peptide antibody of negative and rheumatoid arthritis groups were significant ( $p < 0.05$ ) increase in ACPA, CRP and RF in the positive group compared with the negative and

rheumatoid arthritis groups. This is due to the fact that it contains many effective compounds that have an effect on reducing inflammation rates and raising the body's immunity. These results are similar with those reported by Girbal et al., (34) who discovered that the diagnosis of RA was said to be quite specific when

using anti-citrullinated protein/peptide antibodies (ACPA). Moreover Kroot et al., Schellekens et al., (35) (36) who found that administration of complete Freund's adjuvant to rats led to significant ( $p \leq 0.05$ ) increase anti-citrullinated peptide/protein antibody compared to negative control. Anti-citrullinated peptide antibody is a highly specific autoantibody to RA, which recognizes a broad range of citrullinated peptides and appears in approximately 80% of patients with RA (37). Anti-CCP antibodies are found years in advance of joint inflammation because anti-citrullinated protein/peptide antibodies (ACPAs) have a high specificity in RA, and CRP was significantly elevated in the serum of the arthritic control group as compared to the negative control group as compared to negative control group CRP in serum was significantly ( $p \leq 0.01$ ) reduced by custard apple (38). The same results were obtained by Gate et al., (32) who found

that RF was significantly ( $p \leq 0.05$ ) elevated in the serum of arthritic positive group compared to the control group. Administration rats' custard apple juice with 5-10 and 15  $\mu\text{L/g}$  of (B.W) the significant ( $p \leq 0.05$ ) decrease the levels of anti-citrullinated protein/peptide antibody, C-reactive protein and rheumatoid factor compared with positive control group. The highest reduction in ACPA, CRP and RF values were observed in the rats administrated with custard apple juice at dose 15  $\mu\text{L/g}$ . The same results were obtained by Chinwe et al., (39) who discovered that, in comparison to the control group, the rats in the treated groups had considerably reduced CRP levels following treatment with aqueous soursop pulp extract. Therapy for arthritic rats markedly lower serum RF level and anti-arthritic efficacy, most likely due to inhibition of autoantibody formation against Fc fragments and preservation of cartilage breakdown (32).

**Table (2): Effect of CAJ anti-citrullinated protein/peptide antibody, C-reactive protein and rheumatoid factor of negative and rheumatoid arthritis groups**

Variables	Negative		Rheumatoid arthritis groups		
	control group	Positive control	CAJ (5 $\mu\text{L/g}$ BW)	CAJ (10 $\mu\text{L/g}$ BW)	CAJ (15 $\mu\text{L/g}$ BW)
ACPA (U/mL)	3.49e±0.1	80.87a±1.5	57.61b±1.8	28.39c±1.9	14.60d±0.7
CRP (mg/L)	5.96e±0.8	100.80a±1.7	69.79b±0.9	30.05c±1.6	21.95d±1.01
RF(IU/L)	28.40e±1.9	903.50a±8.8	494.50b±8.8	276.00c±24.7	143.00d±24.7

Values are expressed as means  $\pm$  SD. Means in the same row with different letters are significantly different ( $P \leq 0.05$ ). CAJ: custard apples juice, ACPA, anti-citrullinated protein/peptide antibody, CRP, C-reactive protein, RF, rheumatoid factor.

Table (3) showed that exposure of rats to complete Freund's adjuvant led to a significant increase ( $p \leq 0.05$ ) in the levels

of immunoglobulin (IGG and IGM) compared to the negative control. The same results were obtained by Chen et

al., (30) who reported that the onset of rheumatoid arthritis (RA) was observed  $14 \pm x$  days after injection of CFA malfunction occurs immunoglobulin IgG and IgM concentrations. Additionally, it was discovered by Barden et al., Jorgensen et al., (40) (41) that immunoglobulin IgG and IgM concentrations are higher in RA patients than in suitable controls. Therefore, it is clear that the elevated immunoglobulin concentrations somehow mirror the underlying immunological mechanism of RA Van der Linden et al., (42) they also mentioned that the primary pathogenic markers in arthritis caused by the progressive degeneration of joints are RF autoantibodies like IgM and IgA, which are generated against the Fc segment of

IgG and citrullinated peptides. In this study, Administration rats with custard apple juice significantly ( $p \leq 0.05$ ) decreased the levels of immunoglobulin (IGG and IGM) compared with positive control group. These results agree with Padma et al., (43) the plant's primary phytoconstituents, acetogenins, have been linked to a variety of biological activities, including anticancer, immunomodulatory, anti-spasmodic, anti-malarial, pesticidal, anti-parasitic, anti-bacterial, anti-fungal, and anti-helminthic properties. The highest reduction in IGG and IGM values were observed in the rats administrated with custard apple juice at dose 15  $\mu\text{L/g}$  by (63.16%), (59.27%) respectively. The findings justify the antioxidant activity of custard apple.

**Table (3): Effect of CAJ on immunoglobulin of negative and rheumatoid arthritis groups**

Variables	Negative		Rheumatoid arthritis groups		
	control group	Positive control	CAJ (5 $\mu\text{L/g}$ BW)	CAJ (10 $\mu\text{L/g}$ BW)	CAJ (15 $\mu\text{L/g}$ BW)
IGG (ng/ml)	153.00d $\pm$ 9.9	932.50a $\pm$ 39.9	533.00b $\pm$ 31.1	367.00c $\pm$ 24.7	343.50c $\pm$ 19.4
IGM (ng/ml)	219.00d $\pm$ 8.5	999.33a $\pm$ 6.01	499.00b $\pm$ 12.02	499.00b $\pm$ 5.7	407.00c $\pm$ 11.3

Values are expressed as means  $\pm$  SD. Means in the same row with different letters are significantly different ( $P \leq 0.05$ ). CAJ: custard apples juice, IGG, immunoglobulin G, IGM, immunoglobulin M.

Data in table (4) indicated that the levels of catalase and glutathione peroxidase (GPX) in positive control were significantly decreased after (CFA) injection for rheumatoid arthritis, while MDA and TOS had opposite trend. The decrease in the levels of catalase, GPX and the increase in MDA and TOS may be due to the cause of the oxidative stress resulting from exposure to (CFA). Catalase and GPX

were significantly increased ( $p < 0.05$ ) in the rats administered with custard apple juice with a different concentrate. The MDA levels were significantly reduced in rats administrated with custard apple juice at dose 15  $\mu\text{L/g}$ . These outcomes are consistent with (33) who demonstrated the strong antioxidant activity of custard apple pulp extract using the DPPH ( $\text{IC}_{50} = 44.08 \mu\text{g/mL}$ ) and



ABTS (IC<sub>50</sub> = 39.32 µg/mL) techniques, along with high concentrations of phenols (618.95 mg GA/g) and flavonoids (477.35 mg QE/g). Moreover (44) demonstrated the protective properties of custard apples against H<sub>2</sub>O<sub>2</sub> and free radicals (OH). Because custard apples contain acetogenin, which can be crucial in removing free radicals, they have excellent antioxidant qualities. Also, (45) showed that the pericarp of custard apple has the highest inhibitory enzyme and antioxidant properties. (46) provide data indicating that custard apples reduce oxidative damage and point to the involvement of oxygen free radicals in inflammation. Two significant antioxidant

enzymes that can be utilized to destroy free radicals and inhibited by them are CAT and GPx. the results are consistent with (47). Our results had the same trend as that of (48) that attributed this finding to custard apple ability to restore body fluids and stimulate erythropoietin. The TOS levels were significantly reduced ( $p < 0.05$ ) in rats administrated with custard apple juice at dose 15 µL/g the same trend as that of (49) who attributed this finding to custard apple extract, which decreased their TOS levels. One of the most researched phytotherapeutic compounds at the moment is custard apple, which has anti-inflammatory, antioxidant, and anti-arcinogenic properties (50).

**Table (4): Effect of custard apples juice on malondialdehyde, catalase, glutathione peroxidase, and total oxidant status of negative and rheumatoid arthritis groups**

Variables	Negative		Rheumatoid arthritis groups		
	control group	Positive control	CAJ (5 µL/g BW)	CAJ (10 µL/g BW)	CAJ (15 µL/g BW)
MDA (nmol-ml)	0.37d±0.02	12.63a±1.6	4.82b±0.2	2.64c±0.3	1.10d±0.1
CAT (ng/ml)	9.71a±0.6	0.41d±0.02	0.83d±0.04	2.933c±0.4	4.74b±0.4
GPX (U/ml)	193.05a±2.6	28.14e±2.1	44.69d±2.6	87.83c±2.4	129.15b±1.4
TOS (U/ml)	3.84e±0.6	121.26a±3.3	47.70b±1.8	22.60c±1.8	10.33d±1.8

Values are expressed as means ± SD. Means in the same row with different letters are significantly different ( $P \leq 0.05$ ). CAJ, custard apples juice, MDA, malondialdehyde, CAT, catalase, GPX, glutathione peroxidase, TOS, total oxidant status.

Data in Table (5) indicated the effect of custard apple juice on bone weight in the right leg, bone weight in the left leg, and bone weight tail of negative and rheumatoid arthritis groups was significant ( $p < 0.05$ ) decrease in bone weight in the right leg, bone weight in the left leg, bone weight tail in the positive group compared with the negative and

rheumatoid arthritis groups. This reason is due to the presence of rheumatoid arthritis. These results are similar with those reported by (51, 52 and 53) rheumatoid arthritis (RA) is known to cause bone loss, which is a complication that affects skeletal regions far from the affected joints, like the lumbar spine and proximal femur. In addition to the

presence of bone erosions in RA correlates with low bone mineral density (BMD) levels (54). The bone weight right leg, bone weight left leg, bone weight tail was significantly increase ( $p < 0.05$ ) in rats administrated with custard apple juice at dose of 15  $\mu\text{L/g}$ . The reason is that custard apples contain main nutrients. These findings are in

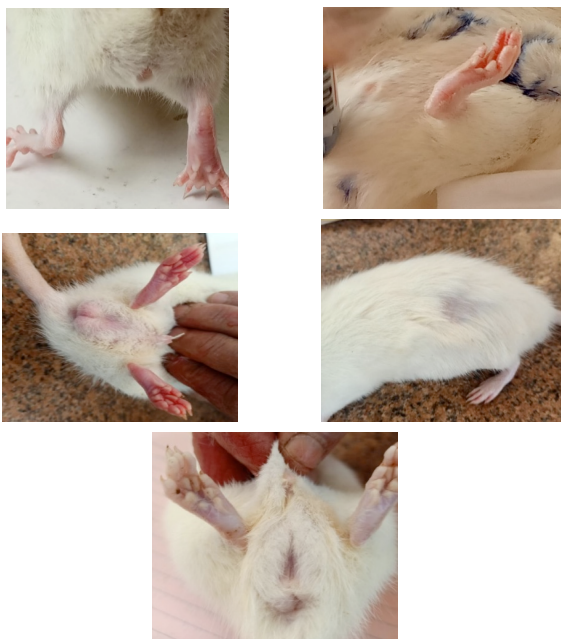
accordance with (55) custard apples are a good source of nutrients that affect the metabolism of several human activities. Their primary nutrients, vitamins and minerals, have an impact on how well these processes' function (56). The findings justify the antioxidant activity of custard apple.

**Table (5): Effect of custard apples juice on bone weight right leg, bone weight left leg, bone weight tail of negative and rheumatoid arthritis groups**

Variables	Negative	Rheumatoid arthritis groups			
	control group	Positive control	CAJ (5 $\mu\text{L/g}$ BW)	CAJ (10 $\mu\text{L/g}$ BW)	CAJ (15 $\mu\text{L/g}$ BW)
BWRL(g)	12.50a $\pm$ 0.5	8.83c $\pm$ 0.3	9.66bc $\pm$ 0.3	10.50b $\pm$ 0.5	12.25a $\pm$ 0.7
BWLL(g)	12.50a $\pm$ 0.5	8.83c $\pm$ 0.3	9.66bc $\pm$ 0.3	10.50b $\pm$ 0.5	12.25a $\pm$ 0.7
BWT(g)	16.50a $\pm$ 0.5	10.50d $\pm$ 0.5	10.58d $\pm$ 0.5	12.50c $\pm$ 0.5	14.00b $\pm$ 0.1

Values are expressed as means  $\pm$  SD. Means in the same row with different letters are significantly different ( $P \leq 0.05$ ). CAJ, custard apples juice, BWRL, bone weight right leg, BWLL, bone weight left leg, BWT, bone weight tail.

**Photo of rats describe the symptoms and signs of rheumatoid arthritis:**



The arthritis score was evaluated blindly by the same person in all rats on day 14 using photographs of the affected hind

limbs. (All photographs were taken 14 days after injection and were randomly assigned to infection groups). According to the degree of erythema and oedema of the periarticular tissue, Kinne used the images to grade each paw's arthritis severity. (57).

Effect of custard apples juice on X-ray-radiography of ankle joints of negative and rheumatoid arthritis group.

Fig. (1,2,3,4,5) show ankle radiography in rats with rheumatoid arthritis. The same person blindly assessed each animal's arthritis score on day 28 using radiographs of the afflicted hind limb. The radiographs were taken using an industrial X-ray film and a UMB Type-2 X-ray machine. Untreated rheumatoid arthritis rats exhibited a left side pelvic



fracture (between the sacral vertebrae and left ischium). Rheumatoid arthritis-treated rats exhibited Pelvis fracture between ischium and sacral vertebrae, femur dislocation, and head of femur degeneration were observed in rats treated for rheumatoid arthritis.

Custard apples have been shown to successfully stop the course of rheumatoid arthritis in rats, as evidenced by the reduction of soft tissue swelling

and bone degradation observed in ankle joint X-rays after treatment (32). According to the degree of bone loss, osteophytes, joint spaces, and joint structure as reported by Pohlers et al., (58), the radiographs from the X-rays were also utilized to assess the degree of bone and joint damage blinded by the same individual for each hind lameness.

Effect of custard apples juice on X-ray-radiography of ankle joints of negative and rheumatoid arthritis group.



Fig (1): Negative control  
Normal healthy rat

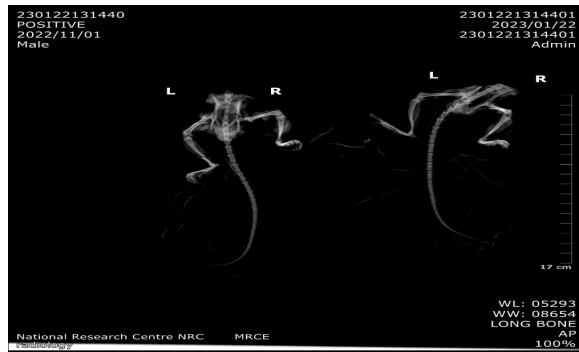


Fig (2): Positive control  
Fracture in left side of pelvis (between left ischium and sacral vertebrae).

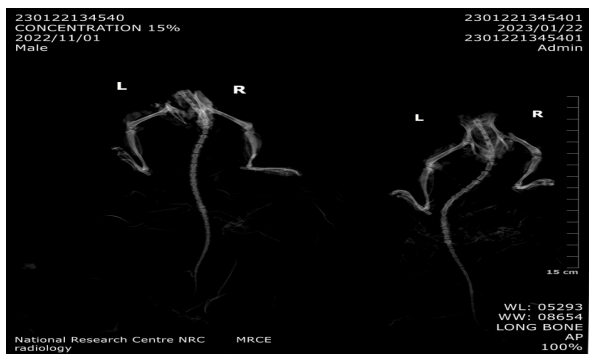
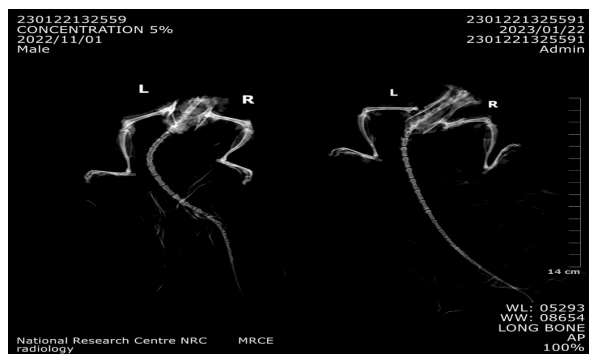


Fig (3): Rheumatoid arthritis CAJ (5 µL/g BW)  
Left leg: head of femur degeneration and dislocation of femur from the acetabulum. Right leg: femur fracture



Fig(4): Rheumatoid arthritis CAJ (10 µL/g BW)  
Deformity in right femur fracture in tibia.

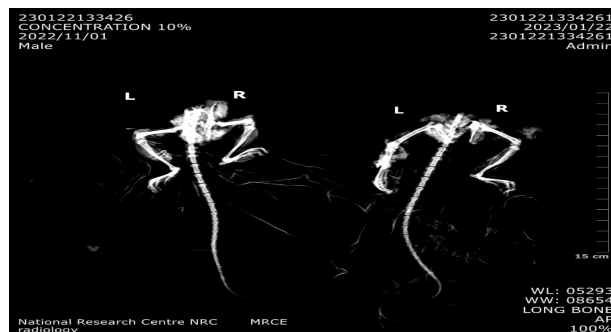


Fig (5): Rheumatoid arthritis CAJ (15 µL/g BW) Pelvis fracture between ischium and sacral vertebrae

## CONCLUSION

The study's findings obviously demonstrate that custard apples are powerful inhibitors of inflammation and improve many biological, biochemical, and Immunomodulatory activity parameters. All of these treated effects could be attributed to the high contents of many bioactive compound categories found in custard apples. Such findings provide a basis for the use of custard apples for the prevention and/or treatment of rheumatoid arthritis.

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التغذية وعلوم الاطعمة

### تقييم النشاط المضاد للروماتويد لفاكهة القشطة على الفئران المصابة بالتهاب المفاصل الروماتويدي المستحث بواسطة مساعد فرويند الكامل

أمل ناصف زكي، هبه عز الدين يوسف، ياسمين أسامه أبو المجد

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<p><b>الملخص العربي:</b> التهاب المفاصل الروماتويدي يؤثر على 0.5-1% من الأشخاص، فهو يقلل من كفاءة المريض. ويعد التهاب المفاصل الروماتويدي مرض مناعي يمكن أن يسبب تضخم الخلايا الليمفاوية والبلعامي، مما قد يؤدي إلى تلف المفاصل. هدفت هذه الدراسة إلى تقييم تأثير فاكهه القشطة في تقليل التهاب المفاصل الروماتويدي لدى الفئران. تم تقسيم 30 من الفئران الذكور إلى مجموعتين رئيسيتين وتم تغذيتهم بالغذاء القياسي. المجموعة الأولى: مجموعة ضابطه سالبه (6 فئران) والمجموعة الثانية: (24 فأراً) حققت بـ 0.1 مل من مادة مساعد فرويند الكامل وتم حقنها في المفصل الأيمن لكل فأر ويكرر ذلك بعد 7 أيام. وظهرت علامات التهاب المفاصل الروماتويدي بعد 14 يوماً. ثم تم تقسيمهم إلى أربع مجموعات فرعية (6 فئران لكل منها)، المجموعة الأولى: الضابطه الموجبه والمجموعات الثانية والثالثة والرابعة تم اعطائها جرعة يومية عن طريق الفم من عصير فاكهه القشطة بتركيز 5، 10 و 15 ميكرو لتر / جم (B.W)، على التوالي. أشارت النتائج إلى أن عصير فاكهه القشطة أدت إلى انخفاض مستوى معدل ترسيب كرات الدم الحمراء، بروتين C- التفاعلي، عامل الروماتويد، المالونداهيد، الجلوبيولين المناعي G و M مقارنة بمجموعة الضابطه الموجبه. في المقابل، زادت مستويات مضادات الاكسده الكليه و الكتاليز و جلوتاثيون اكسد بيروكسيدز مقارنة بمجموعة الضابطه الموجبه. في حين أن إعطاء الفئران 15 ميكرو لتر / جرام من عصير فاكهه القشطة حقق أفضل التأثيرات من خلال تحسين التغييرات السابقة إلى مستويات قريبة من الطبيعي. الخلاصه: فاكهه القشطة تعزز المناعه، وعدد كريات الدم البيضاء، مضادات الأكسدة الكلية بينما يمنع تكوين الخلايا الالتهابية في التهاب المفاصل الروماتويدي.</p>	<p><b>نوع المقالة</b> بحوث اصلية</p>
<p><b>المؤلف المسئول</b> أمل ناصف <a href="mailto:amal.nasif1@hec.menofia.edu.eg">amal.nasif1@hec.menofia.edu.eg</a> الجوال 2 01020608340</p>	<p><b>DOI:</b>10.21608/mkas.2024.249892.1265</p>
<p><b>الاستشهاد الي:</b> Nasef et al., 2024, Evaluation of the Anti-Rheumatic Activity of Custard Apples Fruit on Rats with Rheumatoid Arthritis Induced by Complete Freund's Adjuvant. JHE, 34 (1), 93-108</p>	<p><b>تاريخ الاستلام:</b> ١٩ نوفمبر ٢٠٢٣ <b>تاريخ القبول:</b> ٨ يناير ٢٠٢٤ <b>تاريخ النشر:</b> ١ يناير ٢٠٢٤</p>

الكلمات الكاشفة: فاكهه القشطة، الالتهابات، الروماتويد، بروتين سي التفاعلي، المناعه