العلاقة بين منتجات الرمان و مرض الفصال العظمى (خشونة المفاصل)

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Abstract:

Background: osteoarthritis diseases are a usual cause of disability and a significant public health burden. Good nutrition and a healthy lifestyle lead to improve osteoarthritis pain and symptoms. **The aim of the study:** was to determine the relationship between eating pomegranate fruits parts and osteoarthritis, and assess nutritional status, symptoms, and quality of life for axial osteoarthritis patients**. Patients& Methods:** The study sample included 114 osteoarthritis patients from 25 to 65 years, of both sexes, and free from chronic diseases, in the rheumatoid outpatient clinic at Assuit University Hospitals. They were divided into 4 groups. Group (1): taking drug therapy only (control group). Group (2): taking drug treatment +(50 mg/kg) of pomegranate seeds. Group (3): taking drug treatment +(5 mg/kg) pomegranate peels powder (ppp). Group (4): taking drug treatment+(5mg/kg) ppp +(50 mg/kg) pomegranate seeds. **Results:** The results showed that Pomegranate peels powder contains the highest amount of moisture, ash and total Carbohydrate compared to Pomegranate seeds, pomegranate peels powder contains the highest total phenol and total flavonoid compared to Pomegranate seeds, Food habits form for patients improved after nutritional awareness. there was a significant improvement in the lifestyle of osteoarthritis (OA) patients with osteoporosis at $P<0.00$. $P<0.01$, $P<0.05$) respectively, as in the following groups (3,2,1). It has been proven that patients with osteoarthritis in the cartilage of the neck and back, especially patients of the third group, after followed a healthy diet regularly for six weeks and eating pomegranate seeds and peels powder, which relieve the resulting pain in the spine. Thus, it has been proven through these results that the third group showed a better improvement in their health compared to the patients of the first and second groups; This indicates the increase in antioxidants the pomegranate seeds, and peels powder, which works as an

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improvement in arthritis. **Conclusions:** Pomegranate seeds, and peels powder consumption can improve physical function and stiffness and decrease the breakdown of cartilage enzymes in patients with axial osteoarthritis.

Keywords: osteoarthritis, pomegranate, nutritional status, lifestyle, cartilage neck, and back.

1-Introduction:

Osteoarthritis (OA) is a highly prevalent Rheumatic Musculoskeletal Disorder, that affected 303 million people globally in 2017 **(James et al., 2018).** It can affect any joint, but preferentially affects the knee, hands, hip and spine. OA has a considerable impact on the individual patient, resulting in pain and disability, so an impact on society. Also, the economic burden of OA on patients and society is considerable. In 2016 the large disease burden has led to the submission by the Osteoarthritis Research Society International of a White Paper, describing Osteoarthritis as a Serious Disease2 **(Lyn March et al., 2016).**

The commonest risk factors of OA are age, sex, race, obesity, joint trauma and genetics (**Haq et al., 2011).** There is an imbalance between anabolic synthesis or repair of the matrix components and catabolic breakdown of the matrix in OA articular cartilage**.** It is believed that the disease starts because of damage to the joint tissues. Chondrocytes respond to physical damage by stopping the production of anabolic factors and by releasing more catabolic enzymes such as matrix metalloproteinases **(Shen et al., 2012).**

The progression of the disease may be due to increased oxidative stress. The production of reactive oxygen species has been found to increase and scavenger enzymes are reduced in the cartilage of human and animal models of OA **(Shen et al., 2012)**. Pro-inflammatory cytokines are involved in the progression of OA through up-regulation of gene expression, stimulation of reactive oxygen species production, alteration of chondrocyte metabolism, and possibly increased osteoclastic bone resorption **(Miller et al., 2008)**.

Osteoarthritis commonly affects weight-bearing joints such as hips, knees, feet, neck, and spine. However, non-weight-bearing joints such as finger joints and the joint at the thumb’s base may

also be affected. It usually does not affect other joints, except when injured or put under unusual stress. Osteoarthritis also can affect any joints with a previous injury from trauma, infection, or inflammation. Some patients may develop bony knobs or "nodes" that enlarge finger joints, causing pain, stiffness, or numbness and later restricting the use of the fingers **(Glyn et al., 2015).**

At present, there is no cure for this disease. The available treatments are pharmacological and non-pharmacological therapies and reduction of symptoms (pain or inflammation), maintenance of joint mobility, and limiting the loss of function. Long-term use of available pharmacological agents such as non-steroidal anti-inflammatory drugs or cyclooxygenase inhibitor drugs is associated with serious adverse effects including cardiovascular disease or gastrointestinal disorders **(Akhtar et al., 2017).**

In recent years, experimental and in vitro studies suggested a protective role of pomegranate as a good antioxidant source for mitigating cartilage inflammation and damage. Natural products are being used either in the form of functional foods or nutraceuticals in a prophylactic manner for the treatment and management of inflammatory disorders **(Saeed et al., 2019).**

Pomegranate (*Punica granatum*)

The fruit possesses diverse phytochemical compounds having notable therapeutic significance. It is grown predominantly in the Mediterranean area. Pomegranate seeds are composed of 80% juice, 20% seed and fresh peels containing (85.4%) moisture (10.6%) total sugars, (1.4%) pectin, (0.1%) ml total acidity (as citric acid), 0.7 mg/100 ml ascorbic acid, 19.6 mg/100 ml free amino nitrogen and 0.05 /100 ml ash **(Rowayshed et al., 2013).** The chemical composition of pomegranate peels powder contains ash (4.0%), fiber (13.9%), carbohydrates (33,9 %), moisture (9.2%), protein (6,7%) and crude fat (3.5%) **(El-Beltagi et al., 2022)**.

Pomegranate is a rich source of polyphenols, tannins, and anthocyanins. Anthocyanins such as prodelphinidins and hydrolyzable tannins like ellagic acid derivatives provide antioxidant and anti-inflammatory properties of pomegranate **(Ahmed et al., 2005).**

Pomegranate seeds are widely employed as a cure for various ailments such as ulcers, diarrhea, dysentery, parasitic and microbial infections, hemorrhage (**Johanningsmeier et al., 2011),** and inflammation **(Mo et al., 2014).** Dried pomegranate rind was also used traditionally for the management of a variety of remedies such as headache, diarrhea, dysentery, colitis, and ulcers **(Bachoual et al., 2011)** pomegranate rind has been used in in vitro and in vivo studies for various infirmities. It has been shown to have significant topical anti-inflammatory **(Mo et al., 2014)** antibacterial **(Dey et al., 2012)** wound-healing **(et al., 2011),** anti-infective, anti-cancer, diuretic, and **(Karwasra et al., 2016).** In addition to this, pomegranate rind peels powder is also endowed with antioxidants, and nephroprotective **(Karwasra et al., 2016**).
In the past era, pomegranates raised the research interest of various researchers thereby assessing the nutritional and therapeutic value of pomegranates with numerous publications. On the whole, the principal benefit of pomegranate rind is due to the presence of polyphenols **(Dey et al., 2012).** Indeed, the polyphenols present in pomegranate impart significant anti-inflammatory and anti-oxidant properties for **(Ghavipour et al., 2017)** prevention of numerous ailments **(Lee et al**., **2018)**.
Wang et al., (2020) used a mouse model of osteoporosis and obtained similar results to the study by **Spilmont et al., (2014).** Indeed, treatment with punicalagin (50 mg/kg of body weight) preserved not only bone volume/surface ratio, but also the loss of bone density. The obtained data further confirm the importance of pomegranate in maintaining health status, suggesting that punicalagin may play a critical role in the prevention and treatment of skeletal tissue-related disorders (**Wang et al., 2020)**.
Therefore, study evaluated the effects of taking pomegranate on osteoarthritis patients.

2. Patients, Materials, and Methods:

2.1. Patients

The study was conducted at the Rheumatology, Rehabilitation and Physical Medicine Department Outpatient Clinics in Assuit hospital.114 Patients agreed to participate in the study. They were divided into 4 groups as follows: 1st and 3rd group (24 patients

each), 2nd group (34 patients), and the control group (32 patients); all participants were on OA medication. All groups' personal and social data (sex. age, educational level, occupation, family size, social status) was obtained. Full clinical examination evaluations were performed pre and post-pomegranate intake.

2.2. Materials

Fruit (Pomegranate seeds and peels powder).

Fresh Pomegranate was purchased from the supermarket in Assiut city.

2.3. Methods

2.3.1. Preparing pomegranate seeds and peels powder

The municipal pomegranates were washed in running tap water. The cleaned pomegranate was dried at room temperature for one hour, and then cut into vertical halves. Both peels and seeds were collected in bowls. The peels were then dried at 65C for about 16 hours in a hot air oven (Vebmlw Medizinische, Grete. 2 - Berlin, Germany), and were ground into a fine powder in a laboratory mill (LM 120 Perten Instruments USA). The ground powder pomegranate was placed into food bags at room temperature until it was utilized and analyzed.

2.3.2. Chemical composition of pomegranate seeds and peels powder. AOAC (2010) was used to determine the moisture, protein, fat, ash and crude fiber content of pomegranate seeds and peel powder. Total carbohydrate was calculated by difference.

Total carbohydrates % = 100 - (moisture% + ash % +fat % + protein% + fiber content %) **(AOAC, 2019 and El-Beltagi et al., 2022).**

2.3.3. Total phenols and Flavonoid content

The Folin-Ciocalteu reagent procedure was used to measure phenol concentration in seeds and husks with minor modifications. The reaction mixture included extract (100 µL), Folin-Ciocalteu reagent (100 µL), and 20% sodium carbonate (3 mL). After 1 hour of incubation at room temperature, the absorbance of the dark blue compound was taken at 765 nm. Gallic acid was used as a standard at concentrations ranging from 200 to 1,000 ppm. The total phenolic content was estimated as milligrams of gallic acid equivalents per 100 g dry weight of the sample.

The total flavonoid content of the extracts was estimated using the reported procedure. The reaction mixture of extracts (500 µl), distilled water (2 mL), or 5% NaNO2 (0.15 mL) was incubated at room temperature for 6 min before introducing 10% AlCl3 (0.15 mL) solution, 2 mL of 4% hydroxide Sodium. solution, and mix completely in a final volume of 10 ml with water. The absorbance of the reaction mixture was taken at 510 nm. The quercetin titration curve is used as a reference. The total flavonoid content in mg was calculated from quercetin equivalents (QE) per gram of dry sample weight. **(El-Beltagi et al., 2022)**

3. Experiment design: A total 130 subjects participated in the study and were divided into four groups equally, 16 of them was excluded from the sample to the inability to continue eating a pomegranate, so the number of participants was 114 (32 persons in the control group, and 82 patients divided into 3 groups. The 1st group was given (5 mg/kg) of pomegranate peels, the 2nd group toke (50 ml/kg) pomegranate seeds, while the 3rd group was given both pomegranate seeds and peels powder, put the peels powder in boiling water, filtered and drink them.

4. Study tools: A questionnaire was administered by the researcher and supervisors for obtaining information.

4.1. Socio-Economic and demographic data of OA patients: It was taken the patients' socio-demographic characteristics and educational level (age, gender, level of education, family size, social status, district and anthropometric measurements (weight, height and body math index BMI) of OA treatment. Weight was measured by an electronic digital scale with light clothing and no shoes to the nearest 0.1 kg. Height (H) was also measured in standing position without shoes using a wall mounted height meter. Feet were put together with heels, buttocks, shoulder and back of the head touching the wall. The Body Mass Index (BMI) of each clients was calculated by the (BMI = weight (kg) divided by the height (m2). The World Health Organization classified adults as obese (BMI >30), overweight (BMI = 25–29.99) and normal (BMI = 18.50-24.99) **(Cicekli, 2019).**

4.2. Nutritional awareness: All patients were instructed by the researcher (to eat vegetables and fruits 6 times/day and no foods between meals, drink water at least 9 cups/day, follow a low carbohydrate diet, and practice exercise **(Pem and Jeewon, 2015)**.

4.3. The SF-36 questionnaire (36-Item Short Form Survey): The nutritional habits and quality of life of all the groups (including the control) were assessed. The quality of life was evaluated twice using the SF-36 questionnaire (before the pomegranate intake and 6 weeks later). The SF-36 consists of 36 questions that cover eight health domains, including limitations in physical activities, social activities, the usual role activities (either due to physical health or emotional problems), body pain, general mental health, vitality (energy and fatigue), and general health perceptions.

5. Statistical analysis

Categorical variables were described by number and percent (N, %), while continuous variables were described by the mean and standard deviation (Mean, SD). One-way ANOVA (Analysis of variance) was used for comparison among the mean, of different groups. A two-tailed $p < 0.05$ was considered statistically significant. All analyses s were performed with the IBM SPSS 20.0 software.

Results & Discussion

The chemical composition of pomegranate seeds dry and pomegranate peel powder is represented in **Table (1).** Pomegranate peels powder contains the highest amount of moisture (11.3 ± 0.07%), ash (4.5 ± 0.1%) and total Carbohydrate (54.72 ± 1.2%) compared to Pomegranate seeds, which contains of less moisture (5.82 ± 0.01%), Ash (1.7 ± 0.01%) and total carbohydrate (38.7 ± 1.5%). On the other hand, pomegranate seeds dry include the highest quantity of Protein (13.45 ± 0.07%), fat (3.55 ± 0.06%), and total fiber (37.4 ± 0.02) compared to pomegranate peel powder, which contains less protein (7.98± 0.4%), fat (1.6 ± 0.68%), and total fiber (19.9 ± 0.2%). These findings are consistent with those of **El-Beltagi et al., (2022)** in peels powder**,** also these results are in agreement with **(Jessica, 2018).**

Table (1): Chemical Composition of Pomegranate seeds and peels powder (%on DWT)*

Components (%)	Pomegranate Seeds	Pomegranate Peels powder

Moisture	5.82 ± 0.01%	11.3 ±0.07%
Protein	13.45 ± 0.07%	7.98 ± 0.4%
Fat	3.55 ± 0.06%	1.6 ± 0.68%
Ash	1.7 ± 0.01%	4.5 ± 0.1%
Fiber	37.4 ± 0.02	19.9 ± 0.2%
Carbohydrate	38.7 ± 1.5%	54.72 ± 1.2%

*DWT basis = dry weight basis

Total phenol and flavonoid content are tabulated in **Table (2).** Pomegranate peels powder contains the highest total phenol (27 ± 1.1%) and total flavonoid (38.22± 0.1%), while the lowest in seeds total phenol (1.0 ± 0.25%) and total flavonoid (7.5± 0.22%). These results are nearest to those **(Rowayshed et al., 2013).** It is clear from these results that pomegranate peel contains many times more antioxidants than seeds **(Hakime et al., 2012).**

Table (2): Total phenol and Flavonoid content

Antioxidant content	**Pomegranate Seeds**	**Pomegranate Peels powder**
Total phenol%	1.0 ± 0.25%	27 ± 1.1%
Total flavonoid%	7.5± 0.22%	38.22± 0.1%

The data in **Table (3)** represent the average age of OA patients in the sample at 43.35 years. This agrees with **Roy, (2008)** who stated that organic farming typically begins in the late 1940s, 1950s, or 1960s and is uncommon before the age of 40. The results of this study showed that the ages of osteoporosis patients ranged between 35 and 65 years and this is in agreement with **Zhang et al., (2010)** who evaluated 2,188 patients with osteoarthritis and found that the average age of patients with osteoarthritis was 35-65 years.

The present study showed that the number of OA females was (72) patients, on another side the number of OA men was (10) patients. **Kate et al., (2005)** mentioned that OA occurs more frequently in males in people younger than 40 years, and after the age of 40, it develops more often than in females.

The educational level in **Table (3)** showed the OA patients whose education level was illiterate at 2.4% and 12.5% of the patients had a basic education, the secondary education level was 58.5%, and the patients with a higher level of education were 26.8%. That is, the rate of OA is high in patients with low educational levels. The results agree with **Kate et al., (2005)**

reported that the incidence of osteoarthritis is higher in patients with lower education levels, as 48.5% of patients with less education than high school had 0A, compared to 26.5% of college graduates.

Concerning occupation, 48.5% of patients work, and 51.5% of them are housewives. A high percentage of the OA females were unemployed but they worked in the house works which required a lot of squatting, standing, and kneeling. This result is in agreement with **(Thomas et al., 2020)** who conclude that occupational activities such as prolonged squatting and kneeling significantly increase the risk of developing knee osteoarthritis, and also agreed with **Rossignol, (2004)** who reported that in 1144 employed patients aged 25-65 years, OA disease correlates with occupational stresses.

The results showed the number of family sizes. It was 40.2% of patients have 2-5 persons in the family and 59.8% have 6-12 persons in the family. It means that a large number of OA patients were from families have 6-12 persons. The results of social status in **Table (3)** revealed that 2.0% of the sample was single, followed by 95% whose social status was married. **(Nora et al., 2018)**. Regarding districts, the result showed that 18.5% of patients live in urban communities and 81.5% in rural districts. A high percentage of patients are in rural areas. This may be due to the complicated life people have, which coincides with **Burdorf, (2006)** who reported that the highest prevalence of arthritis in the United States occurs in the central and northwestern states.

The results in **Table (3)** before eating pomegranate products showed that the average weight and body mass index were (80.33 ± 17.36) and (29.5 ± 0.7), respectively, and after eating pomegranate. Mean weight and BMI became (72.25 ± 15.33) and (26.6 ± 0.6), respectively. BMI that appeared in the results BMI >25.5 is over wight. This agreement with **Freedman et al., 2013)** who said Body mass index (BMI) = 25.0 to <30, falls within the overweight. Obesity is related to the incidence and progression of OA of both weight-bearing and non-weight-bearing joints, to the rate of joint replacement as well as surgical complications. Weight loss in OA can lead to clinically significant improvements in pain and delay the progression of structural damage to the joint **(Lauren et al., 2013).**

Table (3): Socio-demographic data and educational level of the patient

Items	Description	
Age (yrs)		
mean±S.D (min-mix)	43.35 ± 13.44 (35 - 65)	
Education level		
-Illiterate	2 (2.4%)	
-basic	10 (12.5%)	
-secondary	48 (58.5%)	
-high	22(26.8%)	
Occupation		
-work	40 (48.5%)	
-housewife	42 (51.5%)	
Family Size		
- 2-5	33 (40.2%)	
- 6-12	49 (59.8%)	
Social Status		
- Single	5 (2.0 %)	
-Married	78 (95.0%)	
District		
-Urban	15 (18.5%)	
- rural	67 (81.5%)	
Gender		
-Man	10(13.3%)	
-females	72(87.8%)	
Anthropometric measurements		
Height	165.0 ± 4.92 Pre	165.0 ± 4.92 Post
Weight	80.33 ±17.36	72.25 ±15.33
BMI	29.5± 0.7	26.6± 0.6

Table (4): Food habits form for patients after nutritional awareness

The results in **Table (4)** showed patients who don't eat a snack/day were (58.3%), (55.3%) and (16.7%) of patients in groups 1,2 and 3 respectively, also revealed patients who eat one

snack/day were (33.3%), (41.2%) and (66.7%) of patients in groups 1,2 and 3 respectively, while other patients who eat two snacks/day were (8.3%), (2.9%) and (16.7%) of patients in groups 1,2 and 3 respectively, and no one taken three snacks/day. In the present study, there are significant ($P<0.05$) differences in patient's compliance with the recommended intake of snacks. This agrees with **Jaclyn et al., (2020)** who research on Diet and nutrition risk affect mobility and general health in osteoarthritis.

The results relative to the cooking method showed that (41.7%), (87.2%), and (100%) of patients in groups 1, 2, and 3 respectively, cook by the stewing method, while (50%), (0%) and (0%) of patients cook by the fried method in groups 1, 2, and 3 respectively compared to cooked by the boiling method that (8.3%), (11.3%) and (0%) and no one in 3 groups cooking by the grilled method. It was concluded that the highest proportion of patients ate fried and stewing foods. The present study showed a significantly increased ($P<0.01$)in patient's compliance with the recommended use method of cooking. This is explained by why most patients are obese, because frying and stewing methods require the use of quantities of fat, unlike grilling and boiled methods. **Duclos, (2016)** said that these methods of cooking significantly increase the risk of developing an OA condition.

The nutritional awareness of patients has increased in the amount of daily consumption of fruits and vegetables. In **Table (4)** the results show that it is a significant ($P < 0.05$) difference of eat fruit and that there highly significant ($P<0.01$) difference of ate vegetables in patients with OA. This finding may be due to the increased awareness of information about the role of fruits and vegetables in reducing inflammation. Experts have recommended a daily intake of at least 400g of fruit and vegetables, **(Nora et al., 2018)**. This result was in agreement with **AL-Qauhiz, (2010)** in the same line, fruits and vegetables play an important role in diet owing to their protective action against autoimmune diseases, especially OA disease this agrees with (**Cassotta et al., 2021).**

The results in **Table (4)** showed that the average intake of sugar spoons/day for an individual was (3.83 ± 2.46), (3.50 ± 3.78), and (4.00 ± 4.86) in groups 1, 2, and 3, respectively. There is a significant difference ($P < 0.05$) in the intake of spoonfuls/day of sugar after nutritional awareness inpatient. A new WHO guideline

recommends adults and children reduce their daily intake of free sugars to less than 10% of their total energy intake. A further reduction to below 5% or roughly 25 grams (6 teaspoons) per day would provide additional health benefits**(WHO 2015).** Excess sugar intake causes the body to produce more cytokines, which are inflammatory proteins. People with arthritis already have high levels of cytokines, so increased inflammation can make them feel worse **(Brenda et al., 2021).** The result illustrates that the highest percentage of patients didn't eat fast food (50%), (52.9%) and (100%) in groups 1,2 and 3 compared to patients who ate fast food (50%), (47.1%) and (0%) in groups 1,2 and 3 respectively. That there highly significant (P<0.01) difference eat fast food. This result is in agreement with **Sally, (2018)** who fast food and its role in diet and nutrition in osteoarthritis.

The results shown in **Table (4)** conclude that 66.67%, 94.1%, and 83.3%, of patients in groups 1, 2, and 3 respectively. that there significant (P<0.05) difference between eating milk and dairy products in groups1, 2, and 3 respectively. Since milk is known to be good for bone development, according to a study, researchers found that there was a lower progression of osteoarthritis among women who consumed milk. It is suggested that if you do drink milk, keep it low-fat to avoid extra calories and fat as this could lead to other health issues. Depending on the type of arthritis, recommendations on drinking milk may vary according to a study by researchers of osteoarthritis among women who consumed milk **(Yvelette et al., 2021)**.

Table (4): Food habits form for patients after nutritional awareness

Item	Control **(n=32)**	Group 1 **Seeds** **(n=24)**	Group 2 **Peels powder** **(n=34)**	Group 3 **Seeds+peels powder** **(n=24)**
1- How many snacks do you have in a day?				
No-snack	12(37.5%)	14(58.3%)	19(55.9%)	4(16.7%)
1-snacks	14(43.8%)	8(33.3%)	14(41.2%)	16(66.7%)
2-snacks	4(12.5%)	2(8.3%)	1(2.9%)	4(16.7%)
3-snacks	2(6.2%)	0(0%)	0(0%)	0(0%)
P. value	0.000*			

2- Cooking methods (stewing /fried / grilled / boiled)				
1- stewing 2- fried 3- grilled 4- boiled	18(56.25%) 10(31.25%) - 4(12.5%)	10(41.7%) 12(50%) - 2(8.3%)	30(87.2%) - - 4(11.8%)	19(100%) - - -
P. value	0.000**			
3- Do you eat fruits during the day?				
YES	28(87.5%)	24(100%)	28(82.4%)	24(100%)
NO	4(12.5%)	0(0%)	6(17.6%)	0(0%)
P. value	0.000*			
4- Do you eat vegetables during the day?				
YES	22(68.8%)	20(83.3%)	26(76.5%)	20(83.3%)
NO	10(31.2%)	4(16.7%)	8(23.5%)	4(16.7%
P. value	0.000**			
5- How many spoons of sugar per day?				
	5.44±3.77	3.83 ± 2.46	3.50 ± 3.78	4.00 ± 4.86
P. value	0.000**			
6- How many times/week do you eat fast foods?				
YES	22(68.8%)	12(50.0%)	16(47.1%)	0(0%)
NO	10(31.2%)	12(50.0%)	18(52.9%)	24(100%)
P. value	0.000**			
7- How often and how many times to eat milk and dairy products (milk, cheese, and yogurt) per day?				
YES	28(87.5%)	16(66.67%)	32(94.1%)	20(83.3%)
NO	4(12.5%)	8(33.3%)	2(5.9%)	4(16.7%)
P. value	0.000*			

***P<0.05(significant difference) **P<0.01(a highly significant difference)**

Table (5): The SF-36 questionnaire

In **Table (5)** the results indicated that (36-Item Short Form Survey) All the groups' (including the control) nutritional habits and quality of life were assessed. The quality of life was evaluated twice using the SF-36 questionnaire (before the pomegranate intake and 6 weeks later). The SF-36 consists of 36 questions that cover eight health domains, including limitations in physical activities, social activities, the usual role activities (either due to physical health or emotional problems), body pain, general mental health, vitality (energy & fatigue), and general health perceptions.

It was found that there is a clear improvement significantly before and after eating the pomegranate, and this is clear in the table this agrees with researchers **Bena et al.,** (**2005)** also reported

that despite the large increase in the number of treated patients and the development of new cost medications, the rise in the cost of managing osteoarthritis seems to be well contained **(Maetzell et al., 2004)**. Reported that direct costs related to OA were up to five times higher than indirect costs incurred by patients with OA.

In this study, pomegranate supplementation was shown to reduce inflammation and improve physical function and stiffness with a significant effect on pain scores in patients with neck and back cartilage OA. To our knowledge, this study is the first clinical trial on the effect of pomegranate on OA patients at Assiut University.

This study agrees with **Yang., et al (2021)** who stated that 100 mg/kg body weight (BW) punicalin during 28 days considerably improved chondrocyte differentiation disorder in the growth plate area, promoted the formation of calcified cartilage area, and prevented cell escape in the superficial area of the tibia compared with arthritic control mice **(Shivnath et al., 2020)** who reported that 250 and 500 mg/kg of pomegranate. Peel powder for 30 days significantly reduced macroscopic lesion severity and grades of pathological cartilage tissue including lower severity in chondrocyte deformation as well as reduced superficial cartilage erosion along with lower content retention proteoglycans and collagen in collagenous induced OA rats in comparison to arthritic rats.

Significant suppression of collagen degradation and retention of proteoglycan content was also reported compared with arthritic control rats 23. In another research in collagenase-induced OA rats, **Lee et al., (2018)** indicated that administration of POMx (70% acetone from pomegranate peels powder) for 28 days considerably alleviated OA progression during the initial stages of cartilage degradation as well as OA signs and improved the weight-bearing ratio at a dose of 150 mg/kg BW in comparison with arthritic control rats. Moreover, pomegranate remarkably ameliorated thickening and hypercellularity of synovium reduced synovitis score, decreased knee swelling and cartilage matrix loss and significantly alleviated cartilage breakdown in comparison with arthritic controls **(Kong et al., 2020 and Elder et al., 2021).** Another study in surgical DMM-induced OA mice reported that 40 mg/kg BW Ellagic acid every 2 days for 56 days significantly

decreased cartilage surface destruction and proteoglycan loss, scores of Osteoarthritis Research Society International (OARSI), and synovitis compared with arthritic control mice **(Lin., 2020)**.

Furthermore **(Fu et al., 2019)** concluded that 20 mg/kg of Urolithin A for 56 days led to a significantly smoother surface of cartilage, lower OARSI scores, decreased cartilage surface calcification, and reduced joint space narrowing in surgical DMM-induced OA mice compared with arthritic control mice **(Fu et al., 2019)** Other studies in surgically-induced OA rats reported that 200 mg/kg **(Choi et al., 2018).** In addition, a significant increase in the knee, femoral, and tibial surface mineral density, focal compressive strength of meniscus and tibial cartilage, number of immune cells of the femoral and tibial meniscus, and thickness of femoral and tibial meniscus were reported compared to osteoarthritis controls **(Choi et al., 2018)**.

Another research in surgically-induced OA rabbits **(Akhtar et al., 2017)** demonstrated that 34 mg/kg BW pomegranate fruit in water for 56 and 70 days significantly decreased severity grades Of the articular macroscopic meniscus lesions, loss of mean score of Safranin-O staining, structural alterations and cluster formation, overall histology and parameter scores, number of active caspase-3 and PARP p85 cells in cartilage, and the chondrogenic caspase-mediated apoptosis pathway pathology in comparison to the arthritis control rabbits.

Another research in MIA-induced OA mice reported that 4, 10 **(Akhtar., et al 2017)** and 20 mL/kg BW pomegranate juice for 14 days significantly prevented chondrocyte damage and it resulted in a significant focal increase in the number of cells along with less damage to the epiphyseal lamina proteoglycans compared to the arthritic control mice **(Hadipour-Jahrom., et al 2010).**

In this study there is a significant statistically significant change in Table 4 (a,b,c,d): In general health , physical health, Social activities and Energy & emotions form in neck and back cartilage patients.

Table (5): The SF-36 questionnaire

Table 5 (a): General health form for neck and back cartilage patients

Symptoms	Control	Group 1:seeds		Group 2:peels powder		Group 3:seeds&peels powder		P. value
		Pre.	Post	Pre.	Post	Pre.	Post	

1- In general, would you say your health is:								
1-excellent	0(0%)	2(8.3%)	10(41.7%)	4(11.8%)	8(23.5%)	0(0%)	4(16.7%)	C VS G1 0.00**
2-very good	10(31.2%)	0(0%)	6(25.0%)	2(5.9%)	12(35.3%)	0(0%)	20(83.3%)	C VS G2 0.00**
3-good	2(6.2%)	4(16.7%)	4(16.7%)	0(0%)	8(23.5%)	0(0%)	0(0%)	C VS G3 0.00**
4-fair	2(6.2%)	8(33.3%)	4(16.7%)	20(58.8%)	6(17.6%)	16(66.7%)	0(0%)	
5-poor	18(56.2%)	10(41.7%)	0(0%)	8(23.5%)	0(0%)	8(33.3%)	0(0%)	
P. value		**		**		**		
2- Compared to one year ago, how would you rate your health in general now?								
1-Much better now than one year ago	2(6.2%)	2(8.3%)	12(50.0%)	2(5.9%)	12(35.3%)	0(0%)	20(83.3%)	C VS G1 0.00**
2- Somewhat better now than one year ago.	2(6.2%)	6(25.0%)	6(25.0%)	8(23.5%)	14(41.2%)	4(16.7%)	4(16.7%)	C VS G2 0.00**
3- About the same	10(31.2%)	4(16.7%)	6(25.0%)	2(5.9%)	2(5.9%)	4(16.7%)	0(0%)	C VS G3 0.00**
4- Somewhat worse now than one year ago	0(0%)	4(16.7%)	0(0%)	18(52.9%)	4(11.8%)	4(16.7%)	0(0%)	
5- Much worse than one year ago	18(56.2%)	8(33.3%)	0(0%)	4(11.8%)	2(5.9%)	12(50.0%)	0(0%)	
		**		**		**		

****P<0.01(a highly significant difference)**

Table 5(b): physical health form for neck and back cartilage patients

Symptoms	Control	Group 1		Group 2		Group 3		P. value
		Pre.	Post	Pre.	Post	Pre.	Post	
1- **Vigorous activities, such as running, lifting heavy objects, and participating in strenuous sports.**								
1- Yes, Limited a lot	12(37.5%)	18(75.0%)	6(25.0%)	24(70.6%)	6(17.6%)	20(83.3%)	0(0%)	C VS G1 0.00**
2- Yes, Limited a Little	4(12.5%)	4(16.7%)	10(41.7%)	10(29.4%)	16(47.1%)	4(16.7%)	0(0%)	C VS G2 0.00**
3.No, Not Limited at all	16(50%)	2(8.3%)	8(33.3%)	0(0%)	12(35.3%)	0(0%)	24(100%)	C VS G3 0.00**
P. value		**		**		**		
2- Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf								
1- Yes, Limited a Lot	4(12.5%)	18(75.0%)	6(25.0%)	24(70.6%)	2(5.9%)	20(83.3%)	0(0%)	C VS G1 0.00**
2- Yes, Limited a Little	8(25.0%)	4(16.7%)	4(16.7%)	8(23.5%)	14(41.2%)	4(16.7%)	8(33.3%)	C VS G2 0.00**
3- No, Not Limited at all	20(62.5%)	2(8.3%)	14(58.3%)	2(5.9%)	18(52.9%)	0(0%)	16(66.7%)	C VS G3 0.00**
P. value		**		**		**		
3- Lifting or carrying groceries								

1- Yes, Limited a lot	6(18.8%)	16(66.7%)	8(33.3%)	17(50.0%)	0(0%)	12(50.0%)	0(0%)	C VS G1 0.00**
2- Yes, Limited a Little	10(31.2%)	8(33.3%)	6(25.0%)	12(35.3%)	16(47.1%)	8(33.3%)	8(33.3%)	C VS G2 0.00**
3- No, Not Limited at all	16(50%)	0(0%)	10(41.7%)	5(14.7%)	18(52.9%)	4(16.7%)	16(66.7%)	C VS G3 0.00**
P. value		**		**		**		
4-Accomplished less than you would like								
1-Yes	6(18.8%)	22(91.7%)	16(66.7%)	12(35.3%)	22(64.7%)	24(100%)	8(33.3%)	C VS G1 0.03*
2- No	26(81.2%)	2(8.3%)	8(33.3%)	22(64.7%)	12(35.3%)	0(0%)	16(66.7%)	C VS G2 0.00**
P. value		*		*		**		C VS G3 0.00**

***P<0.05(significant difference) **P<0.01(a highly significant difference)**

Table 5(d): Social activities form for neck and back cartilage patients

Symptoms	Control	Group 1		Group 2		Group 3		P.value
		Pre.	Post	Pre.	Post	Pre.	Post	
1- Emotional problems interfered with your normal social activities with family, friends, neighbors, or groups								
1-Not at all	24(75.0%	6(25.0%)	12(50.0%)	8(23.5%	8(23.5%	0(0%)	8(33.3%)	C VS G1 0.00**
2- Slightly	4(12.5%)	4(16.7%)	4(16.7%)	2(5.9%)	14(41.2%)	0(0%)	4(16.7%)	C VS G2 0.00**
3- Moderately	2(6.2%)	4(16.7%)	2(8.3%)	0(0%)	4(11.8%)	4(16.7%)	4(16.7%)	C VS G3 0.00**
4- Severe	2(6.2%)	0(0%)	4(16.7%)	12(35.3%)	4(11.8%)	4(16.7%)	4(16.7%)	
5- Very Severe	0(0%)	10(41.7%)	2(8.3%)	12(35.3%)	4(11.8%)	16(66.7%)	4(16.7%)	
P. value		**		**		**		
2-How much bodily pain have you had during the past 4 weeks?								
1- None	18(56.2%)	0(0%)	6(25.0%)	4(11.8%)	4(11.8%)	0(0%)	4(16.7%)	C VS G1 0.00**
2- Very mild	4(12.5%)	0(0%)	8(33.3%)	2(5.9%)	16(47.1%)	0(0%)	12(50.0%)	C VS G2 0.00**
3- Mild	2(6.2%)	0(0%)	0(0%)	0(0%)	6(17.6%)	0(0%)	0(0%)	C VS G3 0.00**
4- Moderate	6(18.8%)	2(8.3%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	
5- Severe	2(6.2%)	4(16.7%)	6(25.0%)	18(52.9%)	6(17.6%)	4(16.7%)	0(0%)	
6- Very Severe	0(0%)	18(75.0%)	4(16.7%)	10(29.4%)	2(5.9%)	20(83.3%)	8(33.3%)	
P. value		**		**		**		
3-During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?								
1- Not at All	22(68.8%)	2(8.3%)	10(41.7%)	8(23.5%	9(26.5%)	0(0%)	8(33.3%)	C VS G1 0.00**
2- A little Bit	4(12.5%)	4(16.7%)	8(33.3%)	2(5.9%)	9(26.5%)	0(0%)	4(16.7%)	C VS G2 0.00**
3- Moderately	4(12.5%)	4(16.7%)	0(0%)	8(23.5%	6(17.6%)	0(0%)	0(0%)	C VS G3 0.00**
4- Quite	2(6.2%)	4(16.7%)	4(16.7%)	4(11.8%)	8(23.5%)	0(0%)	0(0%)	
5-a bit Extremely	0(0%)	10(41.7%)	2(8.3%)	12(35.3%)	2(5.9%)	24(100%)	12(50.0%)	
P. value		**		*		**		

***P<0.05(significant difference) **P<0.01(a highly significant difference)**

Table 5(e). Energy & emotions form in neck and back cartilage patients

Symptoms	Control	Group 1		Group 2		Group 3		P.value
		Pre.	Post	Pre.	Post	Pre.	Post	
1- Did you feel full of pep?								
1-All of the time	6(18.8%)	0(0%)	0(0%)	6(17.6%)	4(11.8%)	9(37.5%)	0(0%)	C VS G1 0.00**
2-Most of the time	4(12.5%)	2(8.3%)	6(25.0%)	2(5.9%)	2(5.9%)	7(29.2%)	1(4.2%)	C VS G2 0.00**
3-A good Bit of the Time	4(12.5%)	0(0%)	6(25.0%)	0(0%)	0(0%)	0(0%)	0(0%)	C VS G3 0.00**
4-Some of the time	10(31.2%)	12(50.0%)	8(33.3%)	24(70.6%)	26(76.5%)	0(0%)	0(0%)	
5-A little bit of the time	6(18.8%)	6(25.0%)	2(8.3%)	2(5.9%)	2(5.9%)	8(33.3%)	12(50.0%)	
6 None of the Time	2(6.2%)	4(16.7%)	2(8.3%)	0(0%)	0(0%)	0(0%)	11(45.8%)	
P. value		**		n.s		**		
5- Did you have a lot of energy?								
1-All of the time	6(18.8%)	2(8.3%)	2(8.3%)	2(5.9%)	0(0%)	8(33.3%)	0(0%)	C VS G1 0.00**
2-Most of the time	6(18.8%)	2(8.3%)	8(33.3%)	0(0%)	0(0%)	12(50.0%)	0(0%)	C VS G2 0.00**
3-A good Bit of the Time	10(31.2%)	4(16.7%)	6(25.0%)	2(5.9%)	2(5.9%)	0(0%)	0(0%)	C VS G3 0.00**
4-Some of the time	6(18.8%)	8(33.3%)	6(25.0%)	22(64.7%)	24(70.6%)	4(16.7%)	4(16.7%)	
5-A little bit of the time	4(12.5%)	4(16.7%)	0(0%)	4(11.8%)	4(11.8%)	0(0%)	4(16.7%)	
6- None of the Time	0(0%)	4(16.7%)	2(8.3%)	4(11.8%)	4(11.8%)	0(0%)	16(66.7%)	
P. value		*		n.s		**		
6- Have you felt downhearted and blue?								
1- All of the time	0(0%)	0(0%)	0(0%)	2(5.9%)	0(0%)	12(50.0%)	4(16.7%)	C VS G1 0.00**
2- Most of the time	2(6.2%)	2(8.3%)	0(0%)	2(5.9%)	2(5.9%)	12(50.0%)	4(16.7%)	C VS G2 0.00**
3- A good Bit of the Time	2(6.2%)	2(8.3%)	0(0%)	2(5.9%)	2(5.9%)	0(0%)	0(0%)	C VS G3 0.00**
4-Some of the time	4(12.5%)	4(16.7%)	6(25.0%)	26(76.5%)	28(82.4%)	0(0%)	4(16.7%)	
5- A little bit of the time	10(31.2%)	8(33.3%)	10(41.7%)	2(5.9%)	2(5.9%)	0(0%)	4(16.7%)	
6- None of the Time	14(43.8%)	8(33.3%)	8(33.3%)	0(0%)	0(0%)	0(0%)	8(33.3%)	
P. value		ns.		n.s		**		
7- Did you feel worn out?								
1- All of the time	2(6.2%)	2(8.3%)	0(0%)	2(5.9%)	0(0%)	19(79.2%)	7(29.2%)	C VS G1 0.00**
2- Most of the time	2(6.2%)	6(25.0%)	2(8.3%)	2(5.9%)	2(5.9%)	4(16.7%)	4(16.7%)	C VS G2 0.00**
3- A good Bit of the Time	2(6.2%)	6(25.0%)	4(16.7%)	0(0%)	0(0%)	0(0%)	5(20.8%)	C VS G3 0.00**
4- Some of the time	18(56.2%)	6(25.0%)	8(33.3%)	28(82.4%)	30(88.2%)	1(4.2%)	0(0%)	
5- A little bit of the time	6(18.8%)	2(8.3%)	8(33.3%)	2(5.9%)	2(5.9%)	0(0%)	0(0%)	
6- None of the Time	2(6.2%)	2(8.3%)	2(8.3%)	0(0%)	0(0%)	0(0%)	8(33.3%)	
P. value		**		n.s		**		

***P<0.05(significant difference) **P<0.01(a highly significant difference)**
n.s =non-significant.

In this study, pomegranate supplementation was shown to reduce inflammation and improve physical function and stiffness, significantly affecting pain scores in patients with neck and spine OA. To our knowledge, this study is the first clinical trial on the effect of pomegranate on OA patients at Assiut University.

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العلاقة بين منتجات الرمان ومرض الفصال العظمى (خشونة المفاصل)

الهدف: تهدف هذه الدراسة إلى تقييم تأثير منتجات الرمان على أعراض مرض الفصال العظمى (خشونة المفاصل) في المرضى الذين يعانون من الخشونة في الفقرات وتأثيرها على جودة حياتهم.

البحث: شارك عدد ١١٤ من مرضى الخشونة في الدراسة، وتم تقسيمهم إلى ٤ مجموعات على النحو التالي: المجموعة (الأولى): المرضى الذين يعانون من الخشونة ويتناولون العلاج الدوائي فقط وهي تمثل المجموعة الضابطة للبحث. المجموعة (الثانية) الذين يعانون من الخشونة ويتناولون العلاج الدوائي بالإضافة إلى (٥ ملجم/كجم) من بذور الرمان. المجموعة (الثالثة): المرضى الذين يعانون من الخشونة ويتناولون العلاج الدوائي إضافة إلى (٥٠ ملجم / كجم) قشور الرمان (في ماء مغلي). المجموعة (الرابعة): الذين يعانون من هشاشة العظام ويتناولون العلاج الدوائي مع (٥ ملجم / كجم) قشور الرمان (في ماء مغلي) + (٥٠ ملجم / كجم) بذور الرمان، وذلك لمدة ستة أسابيع لتقييم تأثير هذا منتجات الرمان على أعراض الخشونة وجودة الحياة بالنسبة لمرضى خشونة الفقرات.

النتائج: كشفت النتائج أظهرت النتائج أن مسحوق قشور الرمان يحتوي على أعلى كمية من الرطوبة والرماد والكربوهيدرات الكلية مقارنة ببذور الرمان ومسحوق قشور

الرمان يحتوي على أعلى نسبة من الفينول الكلي والفلافونويد الكلي مقارنة ببذور الرمان، وقد تحسنت العادات الغذائية للمرضى بعد الوعي الغذائي.

كان هناك تحسن ذات دلاله إحصائية في نمط حياة مرضى الزراعة العضوية الذين يعانون من هشاشة العظام عند (P <0.01 .P <0.00، P <0.05) على التوالي ، كما في المجموعات التالية (٣،٢،١). وأن جودة الحياة، في مرضى الخشونة المشاركين في الدراسة، قد تحسنت تحسن ذو دلالة إحصائية وذلك بعد اتباعهم نظاما غذائيا صحيا منتظم لمدة ٦ أسابيع وتناولوا بذور وقشور الرمان المجففة، مما أدى إلى تخفيف الآلام الناتجة عن الخشونة.

<u>الاستنتاجات:</u> نستخلص من نتائج هذه التجربة السريرية، أن استهلاك بذور الرمان وقشوره يعمل على تحسين الوظائف البدنية والنفسية في المرضى، والذي قد يرجع إلى انخفاض معدل تكسر الإنزيمات البنائية للغضروف وزيادة مضادات الأكسدة لدى المرضى الذين يعانون من خشونة الفقرات.