The effect of a barley-based food product in alleviating knee osteoarthritis discomfort symptoms in Egyptian female patients

Suzanne Fouad[a], Rasha Monir[b], Fatma A. Ibrahim[c], Ahmed M.S. Hussein[d], Heba F. Shafei[b], Aliaa El Gendy[b]

Departments of [a]Nutrition and Food Science, [b]Complementary Medicine, [c]Biochemistry, [d]Food Technology, National Research Centre, Giza, Egypt

Correspondence to Suzanne Fouad, MD, Nutrition and Food Science Department, National Research Centre, Dokki Postal Code: 12622, Giza, Egypt. Mobile: +201005286161; e-mail: suzannefouad6161@yahoo.com

Received: 5 July 2023
Revised: 4 August 2023
Accepted: 13 August 2023
Published: 26 December 2023

Journal of The Arab Society for Medical Research 2023, 18:182–190

Background/aim
Osteoarthritis is a common joint condition that causes cartilage to erode. There are numerous conventional treatments available, including nonsteroidal anti-inflammatory medicines and pharmaceuticals containing glucosamine; however, taking them can result in serious side effects. The aim of this study was to prepare barley-based food product enriched with ginger, curcumin, garlic powder, and onion powder and to evaluate the effect of consumption of the prepared macaroni for 2 months, in alleviating knee osteoarthritis discomfort symptoms in female patients complaining of grade 2–3 knee osteoarthritis.

Patients and methods
The present study enrolled 51 Egyptian middle age females patients with a mean age of 51±8.37 years, diagnosed with bilateral grade two to three knee osteoarthritis were recruited from the National Research Centre rheumatology and rehabilitation clinic. Anthropometric measurements and blood samples were collected after 8 weeks of daily barley based macaroni supplementation (75 grams raw). Serum levels of IL1β, IL4 and IL6 were measured using Elisa techniques, while Total Antioxidant Capacity, Malondialdehyde, and Glutathione S-transferase were measured by the colorimetric methods.

Results
Chemical composition analysis of the prepared barley-based macaroni demonstrated a decrease in total carbohydrate content and an increase in crude fiber, protein, and fat content compared with the control (semolina wheat-based macaroni); 100 grams of the prepared uncooked barley macaroni provided 342.46 Kcal. The reevaluation of the anthropometric parameters after 8 weeks of daily macaroni supplementation denoting improvement without statistical significance ($P>0.05$), and the clinical characteristics of knee joint osteoarthritis (Lequesne Index, WOMAC score, and Timed Up and Go test) significantly improved which meant less pain and stiffness. The serum pro-inflammatory cytokines IL1β and IL6 declined significantly and the serum anti-inflammatory cytokine IL4 raised significantly ($P\leq0.05$), besides, barley based macaroni supplementation significantly improved the antioxidant status, which was achieved through the rise of serum Total Antioxidant Capacity and the decline of Malondialdehyde and Glutathione S-transferase activity ($P\leq0.05$).

Conclusion
Barley-based prepared macaroni enriched with curcumin and ginger must be considered in alleviating the severity of knee OA symptoms to aid patients in getting their life back to near normal.

Keywords:
barley, diet therapy, knee osteoarthritis, macaroni, pasting properties

J Arab Soc Med Res 18:182–190

1687-4293

Introduction

Osteoarthritis (OA) is a degenerative disease affecting mainly the knee joints and hip joints, leading to inflammation in the cartilage of the affected joint and change in the underlying bone. The large joints are known as synovial joints, such as the knee and hip joints; this nomenclature resulting from being surrounded by a synovial membrane which lubricates the joint movement by secreting synovial fluid [1]. Inflammation is a condition in which free radicals are produced in response to toxins; inflammation causes pain, limitation of movement, and stiffness in the affected joint [2].

Foods and food products may help to alleviate the symptoms of OA as they have a potential antioxidant and/or anti-inflammatory pain reduction effect. These

products offer a safe alternative and complementary therapy to pharmacological prescriptions [3]. Patients complaining of inflammatory diseases consumed dietary supplements to treat their clinical condition. Of these food supplements that offer these health benefits are ginger, turmeric, and green tea [4]. Pasta or macaroni is known as one of the most popular dishes and is mainly prepared from milled wheat, water, and occasionally eggs [5].

Barley (Hordeum vulgare) is a cereal grain grown in Egypt and in temperate climates. It is ranked as the fourth grain in quantity production following wheat, rice, and maize. Barley is easy to incorporate into meals, such as bread and soups due to its versatility [6]. Whole grains have better heath results than refined grains; the bran, germ, and the majority of the fiber and nutrients in grains are removed during refining process. Barley and other whole grain meals have been increasingly popular in recent years as a result of the numerous health benefits they can provide. Choosing whole grains over refined grains can help to lower the risk of non-communicable diseases [7]. Some spices are known to have anti-inflammatory properties, ginger and curcumin (turmeric) being two of the most promising. Turmeric is a mustard-yellow Asian spice and has been demonstrated to relieve arthritis by suppressing the cytokines and the proinflammatory cells, according to Van Ameyde and Hodgden [8]. Ginger has antiemetic, anti-inflammatory, and antihyperglycemic actions [9]. Both spices are candidates for medical purposes [10].

The aim of this study was to evaluate the effect of consumption of barley-based macaroni enriched with spices on the management of symptomatic knee osteoarthritis with regard pain, mobility, and biochemical parameters.

Patients and methods

Food supplement formulation and evaluation

Dietary product design and preparation

All ingredients used are available in the Egyptian and worldwide markets and thus are used in the Egyptian cuisine and globally. To produce the macaroni, ingredients were mixed as follows: 90% barley enriched with 2% onion powder, 1% garlic powder, 4% turmeric powder, 2% ginger powder, and 1% Gum Arabic (acacia gum) (Fig. 1). Macaroni samples were processed using a Pasta Matic 1000 Simac Machine—Italy, under extrusion circumstances described by Hallabo *et al.* [11]. One hundred grams of semolina wheat (the control supplement) and new mixture samples barley based macaroni enriched with spices (90% barley, 4% turmeric, 2% ginger, 2% onion, 1% garlic and 1% Gum Arabic(were placed separately in the machine mixer and 33% water was added, then the mixture was mixed for 4-6 min at 30 rpm under vacuum (35 cm Hg). The macaroni samples were dried at 70°C for 10 h in a single layer on cloth-lined trays, and then dried samples were stored in polyethylene bags until analysed [12].

Chemical composition of the uncooked supplements were identified [13], carbohydrates contents were calculated by subtracting one hundred from the percentage summation of protein, fat, ash and crude fiber.

Evaluation of supplements cooking quality by measuring cooking loss, the increases in volume and weight after food cooking according to AACC [14]. Texture analysis of cooked samples was evaluated using CT3 Analyzer Manual code M08-372-C0113. The samples were cooked using tap water and boiled for the optimum cooking time. The cooked samples were evaluated for **sensory evaluation** regarding

Figure 1

Prepared raw uncooked (a) and cooked (b) barley macaroni.

appearance, flavour, taste, softness, stickiness, and overall acceptability by thirty panellists by means of nine-point hedonic scale (scale nine represented extremely like and scale one represented dislike) [11]. Firmness of cooked macaroni is a key quality attribute. It is an objective criterion for estimating the firmness of cooked macaroni. It can be applied to all macaroni and pasta shapes with a uniform and firm cross section such as spaghetti, noodles and other shapes [14]. Color measurement was assessed using Hunter Lab color Scan XE-Reston, (LX No.16379–USA). The color evaluation was based on the Hunter (L, a and b) coordinates, representing lightness, redness and yellowness respectively.

Analysis of antioxidant activity, total phenolic, and total flavonoid contents

Extracts for total phenolics, total flavonoids and antioxidant activity were prepared using methanol, using the Ultra-Turrax homogenizer. The homogenates of tested and control uncooked samples were kept at 4°C for 12 h and then centrifuged at 10,000 rpm for 20 min The supernatants were recovered and stored at −20°C until analysis. The total phenolic content was determined according to the Folin-Ciocalteu procedure by means of a calibration curve prepared with gallic acid and expressed as milligrams of gallic acid equivalent (mg GAE) per g of sample [15]. The total flavonoid content was determined according to Zhishen and others using aluminum chloride colorimetric assay, by means of a calibration curve prepared with catachine, and expressed as milligrams of catechin equivalent (mg CE) per g of sample [16]. Free radical scavenging capacity of extracts was determined using the stable DPPH according to Cheung and colleagues, and the result was expressed as mg Trolox equivalents (TE)/g sample) [17].

Practical study

Patients

Middle aged female patients suffering from symptomatic knee osteoarthritis consumed the prepared food supplements, after cooking (the equivalent of 75 grams of raw barley based macaroni), daily for eight weeks, with weekly follow up during the study period. Each patient was subjected to careful general clinical examination, detailed histories were taken and anthropometric measurements were reported with body composition analysis (BC-418MA- Japan) [18]. They discontinued all analgesic or nonsteroidal anti-inflammatory medications two weeks before starting the study.

Inclusion criteria

Middle aged female patients suffering from symptomatic grade 2 and 3 knee osteoarthritis, with clinical signs of inflammation and diagnosed by plain X-ray and MRI were included in the study.

Exclusion criteria

Patients who had a history of renal or hepatic impairment, cerebrovascular stroke, or those treated with local corticosteroid injection or any complementary therapy were excluded from the study.

Ethical consideration

The present study was conducted with the Code of Ethics of the World Medical Association, according to the principles expressed in the Declaration of Helsinki. This study has been approved by the local Ethics Committee of National Research Centre, Cairo, Egypt with approval number '16/337', a written informed consent was provided by each participant prior to their inclusion in the study, and after full explanation and clarification of the objective and plan of work.

Study design

Fifty-one female Egyptian patients completed the study, it is an experimental study by means of purposive sampling method; based on previous study, representative sample was selected.

Clinical assessment of knee osteoarthritis in the patients [19]:

(1) **Visual Analog Scale (VAS):** The patients were asked to draw a linear scale that represents the pain they feel [20].
(2) **Stiffness assessment as regards** time, duration, and inactivity stiffness.
(3) **Tenderness score** was tested by applying firm pressure to the different points in the knee (suprapatellar, infrapatellar, medial collateral ligament, lateral collateral ligament, and popliteal fossa) and the patient response was recorded from no pain (score 0) up to score 3 (sense of pain with limb withdrawal).
(4) **Range of painless flexion movement (flexion) by** universal goniometer (CARCI): The range of flexion was measured in degrees starting from the zero position of normal full extension. Flexion of 135 and over was regarded as normal [21].
(5) **X-ray and MRI** imaging were used to determine the grade of knee osteoarthritis.

Table 1 Cooking quality of prepared and control macaroni

Samples	Volume (cm^3)		Volume increase (%)	Increase in weight (%)
	Raw	Cooked		
Semolina wheat macaroni (Control)	80±0.120	215±1.121	130±1.112	152.941±2.200
New mixture (Barley-macaroni)	80±0.100	225±1.252	145±1.423	185.250±2.751

All data are represented as Mean±SD.

(6) **Western Ontario and McMaster Universities Arthritis Index (WOMAC)** to assess pain, knee joint movement, knee stiffness and function. The questionnaire consisted of twenty four questions, each question was graded qualitatively 0, 1, 2, 3, and 4 score denoting none, low, moderate, severe, and very severe respectively. Score four denoted greater impact on quality of life [22].
(7) **The distance between the hip and heel in supine position** with knee flexion was measured.
(8) **Lequesne Index** was evaluated by asking eleven questions about pain, discomfort, and knee function. A score of more than fourteen denoted severe affection of the knee joint [23,24].
(9) **Timed Up and Go**: Subjects were asked to stand up and walk three meters away on a safe, comfortable floor, then return to their initial sitting position with assistance if needed. The time measured was the time needed for termination of the task. Longer time denoted severe knee osteoarthritis affection [25].

Blood samples and biochemical analysis

Five mL of venous blood samples were collected from osteoarthritis female patients into tubes under complete aseptic conditions. The sample tubes centrifuged for 10 min at 3000 rpm and the serum was separated and stored at −80 till biochemical analysis. Malondialdehyde (MDA), Total Antioxidant Capacity (TAC), and Glutathione S-transferase (GST) were determined in serum according to the colorimetric methods of Satoh [26], Koracevic *et al.* [27], and Habig *et al.* [28], respectively.

Quantitative level of Human IL-1β, IL-4 and IL-6 were measured using the ELISA kits of Sino Gene Clon Biotech Co. (HangZhou, China), according to Schindler method [29].

Statistical analysis

All values were expressed as mean±SD. A two-tailed student t-test was used to compare between data in the same group. P values <0.05 were considered statistically significant. The SPSS Windows software version 17.0 (SPSS Inc. Chicago, IL, USA, 2008) was used and the statistical comparison of means with Confidence Interval Percentage was 95% using the SPSS program.

Results

The data represented in (Table 1) revealed that the weight of cooked barley based macaroni increased more than the control one manufactured from semolina wheat, and the volume of cooked new mixture was higher when compared with wheat macaroni.

Table 2 shows the sensory evaluation of the food supplements used in the study. Sensory aspects as color, taste, odor of the new macaroni were acceptable. Wheat-based macaroni had the highest

Table 2 Sensory evaluation of cooked macaroni

Samples	Color (9)	Taste (9)	Texture (9)	Odor (9)	Overall acceptability (9)
Semolina wheat macaroni (Control)	8.301±0.121	8.221±0.100	8.500±0.152	8.000±0.132	8.243±0.221
New mixture (Barley-macaroni)	8.506±0.160	7.110±0.091*	7.000±0.176*	7.800±0.197*	7.392±0.251*
LSD at 0.05	0.392	0.411	0.481	0.476	0.389

All data are represented as Mean±SD. *Significant difference than control group at $P<0.05$, using Student t-test.

Table 3 Color determination of the samples

Samples	Color values		
	L	a	b
Semolina wheat macaroni (Control)	75.152±1.651	1.592±0.001	4.19±0.094
New mixture (Barley-macaroni)	59.181±1.352*	5.847±0.007*	23.151±0.152*
LSD at 0.05	4.852	1.240	2.142

All data are represented as Mean±SD. *Significant difference than control group at $P<0.05$, using Student t-test.

score for different evaluated properties. The addition of turmeric influenced the macaroni color.

Data in (Table 3) indicated that macaroni from wheat had higher lightness values with decreased redness and yellowness values compared with the new mixture.

The data represented in (Table 4) demonstrates the textural profile (Hardness cycle 1&2, deformation at hardness, hardness work cycle 1&2, fracturability, and gumminess) of cooked macaroni prepared from wheat and the new mixture. From the presented results, it could be noticed that the macaroni from the mixture affected the textural properties. The values of macaroni hardness work cycle 2 and gumminess were higher compared to the wheat macaroni.

Chemical compositions of the two uncooked types of macaroni were demonstrated in (Table 5). Results showed that the macaroni manufactured from the new mixture caused an adequate increase in crude fiber, protein and fat contents, and diminish in total carbohydrate content in comparison with the macaroni manufactured from wheat. Total phenols, total flavonoids, and antioxidant activity of barley-based macaroni were 2.69 GAE/g; 1.35 mg CT/ g; 0.66 mg TE/g respectively (Table 6). Nutrient values of prepared barley macaroni are presented in (Table 7); 100 grams of the prepared uncooked barley macaroni provided 342.46 Kcal, dietary fiber (14.02 g/100 g), and fats (1.6 g/100 g) mainly from polyunsaturated fat, with no saturated fat or cholesterol content.

Fifty-one female patients with a mean age of 51±8.37 years, complaining of knee osteoarthritis were included in the study. All of them completed the study period. After 8 weeks of dietary intervention, basal metabolic rate and fat free mass increased without statistical significance ($P>0.05$), while other anthropometric measurements (BMI, BF%, waist and hip circumferences) decreased without statistical significance ($P>0.05$) (Table 8). All clinical characteristics of knee osteoarthritis evaluated during the study period showed significant improvement at $P<0.05$ level, which meant less pain and stiffness (Table 9). In addition, barley-based macaroni consumption resulted in the elevation of serum anti-inflammatory cytokine (IL-4), declination of pro-inflammatory cytokine IL-β, and a decrease in IL-6 (at $P\leq0.05$) denoting a significant enhancement in the immunological status. Moreover, prepared food supplement consumption resulted in a significant elevation in the Total Antioxidants Capacity and a decline of serum Malondialdehyde and Glutathione S-Transferase activity at $P\leq0.05$ as markers of oxidative stress (Table 10).

New mixture consists of barley, turmeric, ginger, onions, garlic, and gum Arabic.

Table 4 Texture profile analysis

Parameters	Units	Samples	
		Control	New mixture
Hardness cycle 1	N	7.780	7.461
Deformation at hardness	mm	9.332	10.012
Hardness work cycle 1	mJ	14.802	9.801
Fracturability	N	0.151	0.151
Hardness cycle 2	N	7.232	7.585
Hardness work cycle 2	mJ	6.100	7.200
Gumminess	N	3.217	5.532
Chewiness index	N	2.765	45.324

Discussion

Osteoarthritis is a common joint condition that causes cartilage to erode. There are numerous conventional treatments available, including non-steroidal anti-inflammatory medicines and pharmaceuticals containing glucosamine; however, taking them can result in serious side effects. In this study, we evaluated the effects of consuming barley-based macaroni enriched with spices among Egyptian women complaining of symptomatic knee osteoarthritison the management regarding pain, mobility, and biochemical parameters. The most

Table 5 Chemical compositions of macaroni samples

Composition (%)	Samples		LSD at 0.05
	Control	New mixture	
Moisture	13.157±0.100	14.322±0.112	1.361
Protein	11.494±0.121	12.300±0.091	1.147
Fat	1.200±0.032	2.031±0.052*	0.321
Fiber	1.851±0.071	14.024±0.131*	0.398
Ash	0.683±0.001	2.611±0.073*	0.138
Total carbohydrates	77.632±0.654	64.729±0.426*	3.870

All data are represented as Mean±SD. *Significant difference than control group at $P<0.05$, using Student t-test.

important parameter to evaluate pasta and macaroni quality is estimation of loss during cooking [30], cooking loss was much lower in the one manufactured from semolina wheat than the new mixture. This result could be explained by Zarroug and colleague [31] who attributed this to the presence of strong gluten network and the milling formula in wheat-based food preparation compared to macaroni from barley allowing during cooking process, further starch to leach out.

Pasta and macaroni are manufactured from durum wheat semolina flour, which is rich in gluten and form strong elastic dough that is easier to shape [32]. Cooking quality is determined by the macaroni's ability to keep the mechanical qualities achieved under ideal cooking circumstances even when overcooked. The rate of change in elastic

Table 6 Total phenolic content, total flavonoids content, and antioxidant activity of macaroni samples

Samples	TPC (mg GAE/g)	TFC (mg CT/ g)	Antioxidant activity (DPPH) (mg TE/g)
Semolina wheat macaroni (Control)	0.411±0.003	0.114±0.002	0.036±0.001
New mixture (Barley-macaroni)	2.691±0.09*	1.352±0.005*	0.661±0.004*
LSD at 0.05	2.211	1.053	0.411

All data are represented as Mean±SD. *Significant difference than control group at $P<0.05$, using Student t-test. CT, catechin equivalent; GAE, Gallic acid equivalent; TE, Trolox equivalent; TFC, total flavonoids contents; TPC, Total phenolic content.

Table 7 Nutrition facts of dry new barley-based macaroni per100 g

Nutrition facts of dry barley macaroni/100 g	
calories	342.430 Kcal
Carbohydrates	64.720 g
Fiber	14.022 g
Protein	12.300 g
Total fat	2.000 g
Cholesterol	0.0 mg
Vitamin A	1 μg
Vitamin E	0.811 Eq.
Vitamin B6	0.623 mg
Vitamin B3	1.226 mg
Vitamin B2	0.099 mg
Vitamin C	0 mg
Sodium	2.000 mg
Potassium	324.000 mg
Calcium	38 mg
Iron	3.214 mg
Magnesium	114 mg
Phosphorus	342 mg
Manganese	1.923 mg
Zinc	5.211 mg
Folate	50 μg

Table 8 Anthropometric parameters in female participants before and after the dietary intervention

Anthropometric parameters	Basal	After diet intervention	%change
Age (year)	51±8.37		-
Height (cm)	159.74±6.92		-
Weight (kg)	92.13±19.35	91.15±18.09	–1.06
BMI (kg/square height)	36.13±7.27	35.7±7.06	–1.19
Basal metabolic rate	1577.56±209.6	1603.8±226.3	+1.66
Body Fat %	43.4±7.5	41.47±7.7	–4.45
Fat free mass (Kg)	51.09±6.05	51.44±6.33	+0.69
Hip circumference (cm)	121.26±14.56	117.9±14.46	–2.77
Waist circumference (cm)	107±15.02	101.21±13.48	–5.41

All data are represented as Mean±SD. BMI, Body mass index.

Table 9 Osteoarthritis clinical parameters of the participants before and after the barley-based macaroni consumption

Parameters	Basal	After diet intervention	% Change
VAS	7.56±1.9	3.2±1.98*	–57.67%
NTP	4.21±2.23	1.17±1.37*	–72.21%
TS	2.82±0.39	0.65±0.65*	–76.95%
Heel to hip Distance	35.17±7.84	22±7.71*	–37.45%
WOMAC score	56.13±16.1	20.6±11.77**	–63.30%
Lequesne Index	14.13±3.8	5.9±3.4**	–58.24%
Timed Up and Go Test in second	35.78±7.1	27.26±5.4*	–23.81%
Angle of knee Flexion	73.47±18.67	117.17±15.7**	+59.48%

All data are represented as Mean±SD. *Significant difference than basal group at $P<0.05$, using Student t-test. **High-Significant difference than basal group at $P<0.01$, using Student t-test. NTP, Number of tender points; TS, tender score; VAS, Visual Analog Scale.

Table 10 Biochemical parameters of the participants before and after the barley-based macaroni consumption

Parameters	Basal	After diet intervention	% change
IL-1β (ng/l)	2.15±0.49	0.66±0.2*	–69.30
IL-4 (ng/l)	3.75±0.63	18.65±4.7**	+397.3%
IL-6 (Pg/ml)	44.23±14.2	26.05±8.75*	–41.10%
GST (U/l)	5.52±1.8	3.8±1.4*	–31.16
TAC (mM/l)	0.45±0.19	0.73±0.25*	+62.22
MDA (nmol/ml)	6.56±1.42	4.41±1.51*	–32.77

All data are represented as Mean±SD. *Significant difference than basal group at $P< 0.05$, using Student t-test. **High-Significant difference than basal group at $P< 0.01$, using Student t-test. GST, Glutathione; IL, Human Interleukin; MDA, Malondialdehyde; S, Transferase Activity; TAC, Total Antioxidants Capacity.

modulus over cooking time is a good measure of macaroni cooking quality. In other words, the lower the change occurrence, the better the product quality for cooking. The most crucial criterion for macaroni goods is that they have a high cooking quality. The consumer values aroma, flavor, and regularity of shape and color, as well as the breaking power of uncooked macaroni. The cooking quality of pasta might be regarded differently depending on the consumer's own preferences and habits.

Barley is a good source of different nutrients that can offer a range of health benefits for the cardiovascular system and bones and for maintaining a healthy weight. It is a good source of iron, phosphorus, manganese, calcium, magnesium, zinc, fibers, and choline. Electrolytes contribute to maintaining bone strength and the production of collagen, while choline helps to maintain cognitive function, muscle movement, the central nervous system, and the cell membrane. Fibers, mainly beta-glucans, help to increase satiety, reduce appetite, and promote a healthy gastrointestinal tract [33,34]. Gum Arabic or carboxy-methylcellulose could be added by the food industry to improve the quality of pasta properties [35].

Sensory evaluation of cooked barley macaroni demonstrated *acceptability* in different aspects. The yellowish color of this product was more pronounced than that made from durum semolina (control), mostly due to the presence of turmeric. The consumer accepts this color variation. Curcumin, a substance in turmeric, and the entire ginger family were approved by the Food and Drug Administration as safe food additives [36]. Studies have suspected a link between an increase in free radical unstable molecules in the human body and oxidative stress that exacerbated arthritis inflammation [37,38]. Antioxidant foods with antioxidant properties such as curcumin can neutralize these free radicals [39]. Antioxidants defend the body from free radicals [40], slow OA progression and relieve pain [41]; furthermore curcumin had anti-inflammatory properties [42]. The total phenols, total flavonoids, and antioxidant activity estimated in barley-based macaroni were higher than the conventional durum control macaroni; given the food supplement a valuable function in health defense issue [43,44]. Consumption of the prepared food supplement improved the anthropometric parameters, the clinical assessment of knee osteoarthritis (Lequesne Index, WOMAC score, and Timed Up and Go test), the inflammatory biomarkers (the serum pro-inflammatory cytokines IL1β and IL6 declined and the serum anti-inflammatory cytokine IL4 raised). Moreover, barley based macaroni supplementation significantly improved the anti-oxidant status, which was achieved through the elevation of serum Total Antioxidant Capacity and the declining of Malondialdehyde and Glutathione S-transferase activity.

Pain is a subjective sensation. There are no quantifiable readouts for any type of pain in humans. Decision-making in assessment and management of chronic pain patients involves dual criteria, subjective and objective. Subjective criteria include the patient's medical history, clinical examination, questionnaires, patient-documented response to prior treatments, and probabilities. The objective criteria are radiological investigations and reviewing the literature to describe specific laboratory biomarkers [45].

Fortunately, researchers have been searching for pain-specific objective criteria and biochemical assessments including biomarkers. They are investigated as an indicator of pathologic processes, to identify the response to therapeutic intervention, categorize individuals at risk of disease progression or improvement, and to confirm the diagnosis of medical diseases. For chronic pain, the biomarker parameters could be oxidative stress, systemic inflammation, and/or neurotransmitter destruction [46]. Moreover, the biomarker parameters can differentiate between various pathologies that chronic pain patients have or guide the management of those pathologies [47,48].

Although the definite biochemical basis of knee osteoarthritis is considered unknown, it is linked with articular cartilage inflammation, which can be the source of abnormal knee joint structures [49]. Another pathophysiological cause for the exacerbation of OA is the activation of nuclear factor-κB that is related to the presence of

proinflammatory cytokines, extracellular matrix degradation products, and repeated mechanical stress [19,38]. Conventional treatments used in this situation may lead to various serious adverse effects on the human body [50]. There is a recent shift toward assisting OA patients in order to help them self-manage their situation. Relieving pain and stiffness are the primary goals to minimize joint disability and to improve quality of life [51].

Pasta and macaroni have topped the universal review and survey of the world's preferred and favorite foods. Barley macaroni enriched with curcumin and ginger helps alleviate inflammation and reduce disability coupled with pain in the case of knee osteoarthritis. It can be considered as a complementary tool to avoid the side effects of conventional medical prescriptions.

Conclusion

Functional foods provide support to the management of chronic illness and inflammatory conditions. Accordingly, we prepared macaroni from natural ingredients for the alleviation of symptoms of knee osteoarthritis. People's perceptions of food are constantly evolving. This also applies to macaroni and pasta products. They are simple, nutritious, and easy to prepare. Alternative healthy ingredients are required to replace the expensive semolina used in the manufacturing of macaroni. Foods rich in anti-inflammatory substances and antioxidants may assist in diminishing tissue damage from inflammation.

Acknowledgements

We are grateful to all the subjects who contributed to the study and personnel who contributed to the sensory evaluation of the product. We would also like to thank the National Research Centre in Egypt.

Author's contributions: Suzanne Fouad conceived and designed the experiments, and wrote the manuscript. Aliaa El Gendy and Rasha Monir were responsible for the clinical examination and weekly follow-up of the subjects. Ahmed M. S. Hussein prepared and analyzed the food supplement. Fatma A. Ibrahim was responsible for the biochemical analysis. Heba F. Shafei revised the manuscript. The authors read and approved the final manuscript draft to be submitted.

Conflicts of interest

The authors declare that they have no competing interests.

References

1 Berenbaum F. Osteoarthritis as an inflammatory disease (osteoarthritis is not osteoarthrosis!). Osteoarthritis Cartilage 2013; 21:16–21. DOI: 10.1016/j.joca.2012.11.012

2 Martins R, Carlos AR, Braza F, Thompson JA, Bastos-Amador P, Ramos S, Soares MP. Disease tolerance as an inherent component of immunity. Annu Rev Immunol 2019; 37:405–437. DOI: 10.1146/annurev-immunol-042718-041739

3 Liu X, Machado GC, Eyles JP, Ravi V, Hunter DJ. Dietary supplements for treating osteoarthritis: a systematic review and meta-analysis. Br J Sports Med 2018; 52:167–175. DOI: 10.1136/bjsports-2016-097333

4 Koroljević ZD, Jordan K, Ivković J, Bender DV, Perić P. Curcuma as an anti-inflammatory component in treating osteoarthritis. Rheumatol Int 2022; 43:589–616. DOI: 10.1007/s00296-022-05244-8

5 Antognelli C. The manufacture and applications of pasta as a food and as a food ingredient: a review. Int J Food Sci Technol 1980; 15:125–145. DOI: 10.1111/j. 1365-2621. 1980.tb00926.x

6 Jordan HA, Sherrard ME, Manfredi KP, *et al.* The fifth leaf and spike organs of barley (Hordeum vulgare L.) display different physiological and metabolic responses to drought stress. BMC Plant Biol 2016; 16:248. DOI: 10.1186/s12870-016-0922-1

7 American Heart Association. Whole Grains and Fiber. Seconds edition, Headquarters: Dallas, Texas, United States. Paul Dudley White, Joseph Sailer, Robert H. Halse, Robert B. Preble, Hugh D. McCulloch, Lewis A. Conner. 2021. https://www.heart.org `eat-smart' nutrition-basics

8 Van Ameyde M, Hodgden J. In patients with osteoarthritis, is curcumin, compared to placebo, effective in reducing pain? J Okla State Med Assoc 2022; 115:28–30. PMID: 36304437; PMCID: PMC9605491

9 Kunnumakkara AB, Sailo BL, Banik K. Chronic diseases, inflammation, and spices: how are they linked? J Transl Med 2018; 16:14. DOI: 10.1186/s12967-018-1381-2

10 Urošević M, Nikolić L, Gajić I, Nikolić V, Dinić A, Miljković V. Curcumin: Biological Activities and Modern Pharmaceutical Forms. Antibiotics 2022; 11:135. DOI: 10.3390/antibiotics11020135

11 Hallabo SA, El-Magoli SB, Mohamed SK. Effect of processing on the chemical composition and amino acids pattern of supplemented macaroni. Bull Fac Agric Cairo Univ 1985; 36:171–186.

12 Berglund PT, Dick JW, Dreher ML. Effect of form of enrichment and iron on thiamin, riboflavin and niacinamide and cooking parameters of enriched spaghetti. J Food Sci 1987; 52:1367–1371. DOI: 10.1111/j. 1365-2621. 1987.tb14084.x

13 AOAC "OfficialMethods of Analysis of AOAC International". 2000 (17th ed.) by Horwitz, W. Suite 500, 481 North Fredric Avenue Gaithersburg, Maryland 20877-2417, USA. Methods: 925.10, 65.17, 974.24, 992.16

14 AACC International: Approved Methods of the American Association of Cereal Chemists, 2000. 10th Ed. Methods 10-10B, 26-21A, 44-19, 44-08, and 54-40A. The Association: St. Paul, MN

15 Hagerman A, Harvey-Muller I, Makkar H. Quantification of tannins in tree foliage- A laboratory manual. 2000 FAO/ IAEA, Vienna. 537. 4–7

16 Zhishen J, Mengcheng T, Jianming W. The determination of flavonoid contents in mulberry and their scavenging effects on superoxide radicals. Food Chem 1999; 64:555–559. DOI: 10.1016/S0308-8146(98)00102-2

17 Cheung LM, Cheung PCK, Ooi VEC. Antioxidant activity and total phenolics of edible mushroom extracts. Food Chem 2003; 81:249–255. DOI: 10.1016/S0308-8146(02)00419-3

18 Jelliffe DB. The assessment of the nutritional status of the community. World Health Organization, Monograph, 1966. Series No. 53, Geneva, 50-84. https://apps.who.int/iris/handle/10665/41780

19 Hsu H, Siwiec RM. Knee Osteoarthritis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls, 2022 Jan. ISBN: 9241400536. https://www.ncbi.nlm.nih.gov/books/NBK507884/

20 Delgado DAL, Boutris BS, McCulloch N, Robbins PC, Moreno AB, R M, Harris JD. Validation of digital visual analog scale pain scoring with a traditional paper-based visual analog scale in adults. J Am Acad Orthopaedic Surg Glob Res Rev 2018; 2:e088. DOI: 10.5435/JAAOSGlobal-D-17-00088

21 Marques AP. Manual de Goniometria. 2014 3rd ed. São Paulo: Manole. ISBN 9788520438978

22 Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. J Rheumatol 1988; 15:1833–1840. PMID: 3068365

23 Marx FC, Oliveira LMD, Bellini CG, Ribeiro MCC. Translation and cultural validation of the Lequesne's algofunctional questionnaire for osteoarthritis of knee and hip for Portuguese language. Revista Brasileira de Reumatologia 2006; 46:253–260. DOI: 10.1590/S0482-50042006000400004

24 Lequesne MG. The algofunctional indices for hip and knee osteoarthritis. J Rheumatol 1997; 24:779–781. PMID: 9101517

25 Piva SR, Fitzgerald GK, Irrgang JJ, Bouzubar F, Starz TW. Get up and go test in patients with knee osteoarthritis. Arch Phys Med Rehabil 2004; 85:284–289.

26 Satoh K. Serum lipid peroxide in cerebrovascular disorders determined by a new colorimetric method. Clin Chim Acta 1978; 90:37–43. DOI: 10.1016/ 0009-8981(78) 90081-5

27 Koracevic D, Koracevic G, Djordjevic V, Andrejevic S, Cosic V. Method for the measurement of antioxidant activity in human fluids. J Clin Pathol 2001; 54:356–361. DOI: 10.1136/jcp.54.5.356

28 Habig WH, Pabst MJ, Jakoby WB. Glutathione S-transferases. The first enzymatic step in mercapturic acid formation. J Biol Chem 1974; 249:7130–7139. PMID: 4436300

29 Schindler R, Mancilla J, Endres S, Ghorbani R, Clark SC, Dinarello CA. Correlations and interactions in the production of interleukin-6 (IL-6), IL-1, and tumor necrosis factor (TNF) in human blood mononuclear cells: IL-6 suppresses IL-1 and TNF. Blood 1990; 75:40–47. DOI: 10.1182/blood. V75. 1.40.40

30 Dimitrios A. Durum Wheat: Uses, Quality Characteristics, and Applied Tests. 2023; 10.5772/intechopen.110613. DOI: 10.5772/intechopen.110613

31 Zarroug Y, Djebali K, Sfayhi D, Khemakhem M, Boulares M, El Felah M *et al.* Optimization of barley flour and inulin addition for pasta formulation using mixture design approach. J Food Sci 2022; 87:68–79. DOI: 10.1111/ 1750-3841. 16009

32 Bresciani A, Pagani MA, Marti A. Pasta-making process: a narrative review on the relation between process variables and pasta quality. Foods 2022; 11:256. DOI: 10.3390/foods11030256

33 Zeng Y, Pu X, Du J, Yang X, Li X, Mandal M, Yang J. Molecular mechanism of functional ingredients in barley to combat human chronic diseases. Oxid Med Cell Longev 2020; 2020: Article ID 3836172, 26 pages, https://doi.org/ 10.1155/2020/3836172

34 Badea A, Wijekoon C. Benefits of Barley Grain in Animal and Human Diets. Cereal Grains 2021; 1:77. DOI: 10.5772/intechopen.97053

35 Mohsen SM, Yaseen A, Shouk AHA, Ammar A, Mohammad AA. quality characteristics improvement of low phenylalanine pasta. Egypt J Food Sci 2021; 49:287–296. DOI: 10.21608/ejfs.2021.76597.1105

36 Hewlings SJ, Douglas S. Curcumin: a review of its' effects on human health. Foods 2017; 6:10–92. DOI: 10.3390/foods6100092

37 Daily JW, Yang M, Park S. Efficacy of turmeric extracts and curcumin for alleviating the symptoms of joint arthritis: a systematic review and meta-analysis of randomized clinical trials. J Med Food 2016; 19:717–729. DOI: 10.1089/jmf.2016.3705

38 Nees TA, Rosshirt N, Zhang JA, Reiner T, Sorbi R, Tripel E, Moradi B. Synovial cytokines significantly correlate with osteoarthritis-related knee pain and disability: inflammatory mediators of potential clinical relevance. J Clin Med 2019; 8:1343. DOI: 10.3390/jcm8091343

39 Nakagawa Y, Mukai S, Yamada S, Matsuoka M, Tarumi E, Hashimoto T, Nakamura T. Short-term effects of highly-bioavailable curcumin for treating knee osteoarthritis: a randomized, double-blind, placebo-controlled prospective study. J Orthop Sci 2014; 19:933–939. DOI: 10.1007/s00776-014-0633-0

40 Gupta SC, Patchva S, Aggarwal BB. Therapeutic roles of curcumin: lessons learned from clinical trials. AAPS J 2013; 15:195–218. DOI: 10.1208/ s12248-012-9432-8

41 Chelsea CM, O'Brien S, Law J, Renier CM, Wendt MR. Whole-foods, plant-based diet alleviates the symptoms of osteoarthritis. Arthritis 2015; 2015: Article ID 708152, 9 pages. https://doi.org/10.1155/2015/ 708152

42 He Y, Yue Y, Zheng X, Zhang K, Chen S, Du Z. Curcumin, inflammation, and chronic diseases: how are they linked? Molecules 2015; 20:9183–9213. DOI: 10.3390/molecules20059183

43 Rahman M, Rahaman M, Islam M, Rahman F, Mithi FM, Alqahtani T, Uddin M. Role of phenolic compounds in human disease: current knowledge and future prospects. Molecules 2022; 27:233. DOI: 10.3390/molecules 27010233

44 Shahidi F, Ambigaipalan P. Phenolics and polyphenolics in foods, beverages and spices: Antioxidant activity and health effects – a review. J Funct Foods 2015; 18:XX. DOI: 10.1016/j.jff.2015.06.018

45 Davis KD, Aghaeepour N, Ahn AH, *et al.* Discovery and validation of biomarkers to aid the development of safe and effective pain therapeutics: challenges and opportunities. Nat Rev Neurol 2020; 16:381–400. DOI: 10.1038/s41582-020-0362-2

46 López-Solà M, Pujol J, Monfort J, Deus J, Blanco-Hinojo L, Harrison BJ, Wager TD. The neurologic pain signature responds to nonsteroidal anti-inflammatory treatment vs placebo in knee osteoarthritis. Pain Rep 2022; 7: e986. DOI: 10.1097/ PR9. 0000000000000986

47 El-Gendy A, Zikri EN, Shafei HF, Monir R, Elwahidy AG, Ali MA, Abdel-Wahhab KG. Evaluation of the efficacy of gallium-aluminum-arsenide laser acupuncture in the management of knee osteoarthritis. J Arab Soc Med Res 2021; 16:167–172. DOI: 10.4103/jasmr. jasmr_29_21

48 Giordano R, Petersen KK, Andersen HH, Simonsen O, Arendt-Nielsen L. Serum inflammatory markers in patients with knee osteoarthritis: a proteomic Approach. Clin J Pain 2020; 36:229–237. DOI: 10.1097/AJP. 0000000000000804

49 Kisand K, Tamm AE, Lintrop M, Tamm AO. New insights into the natural course of knee osteoarthritis: early regulation of cytokines and growth factors, with emphasis on sex-dependent angiogenesis and tissue remodeling. A Pilot Study Osteoarthritis Cartilage 2018; 26:1045–1054. DOI: 10.1016/j.joca.2018.05.009

50 Bhatia D, Bejarano T, Novo M. Current interventions in the management of knee osteoarthritis. J Pharm Bioallied Sci 2013; 5:30–38. DOI: 10.4103/ 0975-7406. 106561

51 Gohir SA, Greenhaff P, Abhishek A, Valdes AM. Evaluating the efficacy of Internet-Based Exercise programme Aimed at Treating knee Osteoarthritis (iBEAT-OA) in the community: a study protocol for a randomised controlled trial. BMJ Open 2019; 9:e030564. DOI: 10.1136/bmjopen-2019-030564