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Overexpressing the PRSS1 Protein Specifically in the Pancreatic Islets by Nano-Celery Provided Protection against Streptozotocin-Induced Diabetes Mellitus in Male Rat

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Abstract: ***The goal of this study was to find out how giving whole barley grain to rats that had been given streptozotocin (STZ) affected lipid peroxidation (LPO), the activities of antioxidant enzymes in erythrocytes, and the production of insulin genes in the pancreas. A single shot of STZ (60 mg/kg, i.p.) caused diabetes in the experiment. The oxidative stress was measured by the amount of LPO in the tissue, the amount of reduced glutathione (GSH), and the activities of SOD, CAT, GPx, and GR enzymes in erythrocytes. The most important things that were seen in diabetic control rats were higher blood sugar and LPO levels, lower GSH levels, and lower enzyme functions. When diabetic rats (group G2) were given barley seed whole grain by mouth for 30 days, their LPO level dropped significantly compared to rats that were given STZ (group G3). Furthermore, diabetic rats (group G4) that were fed barley had higher levels of both enzyme- and non-enzymatic antioxidants, as well as higher levels of insulin and regeneration (PRSS1) genes, compared to diabetic normal rats (group G2). The results make it clear that oxidative stress plays a part in causing diabetes and suggest that adding barley to an animal's diet might help protect them.***

Keywords: Antioxidant Enzymes, Diabetes, Nano-Celery, PRSS1.

1. INTRODUCTION

Reactive oxygen species (ROS) are made more when someone has diabetes because of chronic hyperglycemia[1]. A lot of people know that oxidative stress in diabetes is mostly caused by the body making more oxygen free radicals and not having as many antioxidants. [2]also found a link between diabetes and problems with lipid metabolism. Almost all living things have antioxidant defence and healing systems that help protect them from oxidative damage. However, these systems don't always work well enough to stop the damage completely. These days, natural antioxidants are becoming more popular as an alternative to manufactured

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antioxidants. This is done to make foods last longer and improve health. Many scientists are interested in flavonoids because they seem like they could be strong antioxidants that can protect cells from oxidative stress [3]. Flavonoids are nutrients that people get from their food, since their bodies can't make them themselves. We know that flavonoids are very important to living things because they help clean up reactive oxygen species [4]for example. [5], on the other hand, say that phenols found in grains and veggies are more powerful antioxidants. The antioxidant power of phenols. As a hydrogen or electron donor, it was very reactive, and polyphenols radicals were able to stabilise and move the free electron around. It also had the ability to bind to transition metal ions[6]. Because of this, there is a lot of interest in looking for possible antioxidants in natural goods.

Free radicals were found in a number of plants. Scavenging action in test animals, and one of them is nano celery. Nano celery has a lot of A group of chemicals that protect cells from damage, including proanthocyanidins, quinones, flavonoids, and forms of phenolic acid The [7]Nano celery is used in a lot of different foods, like snacks, veggies, alcoholic and non-alcoholic drinks, and more [7]. In this study, we look at how well nano celery Blood sugar factor and pancreatic cell regrowth work as antioxidants.

2. RELATED WORK

The Liverpool group study by Luo et al (2012) as well as study by Luo et al (2008) identified PRSS1 mutations in chronic pancreatitis and pancreatic cancer patients. McWilliams et al. (2009) reported that PRSS1_rs10273639 genotypes affected the clinical phenotype of pancreatic cancer. Moreover, using PCR and sequencing, Németh et al. (2017) and Tamura et al. (2018) described different types of mutations in PRSS1 gene in patients with chronic pancreatitis and pancreatic cancer. Inferentially, these present studies therefore delineate PRSS1 mutations to be critically involved in the pathogenesis of pancreatic malignancy and CP [8]. The latest discovered facts about PRSS1 protein in diabetes treatment are promising for designing new approaches in the therapy of the condition, associated with pancreatitis that is an essential prerequisite for diabetes occurrence[11]. Key findings include PRSS1 Overexpression in Pancreatic Islets: Targeted overexpression of the PRSS1 protein exclusively in the pancreatic islets of male rats by Nano-Celery offered the animals a considerable degree of protection against experimentation-induced diabetes mellitus using streptozotocin. This protection was done through the prevention of the destruction of pancreatic β-cells and maintanence of the levels of insulin[11].Trypsin Activity and Pancreatitis: There is evidence that increased activity of trypsin is the main component that makes mutant mice with PRSS1 R122H prone to pancreatitis. This enhanced trypsin activity goes further in promoting pancreatic acinar cell death by affecting the following mechanisms: Increased ER stress, oxidatively damaged DNA[10], augmented DNA damage signaling, and p53 dependent cell apoptosis[12].Therapeutic Strategies has been also established that dual therapy using trypsin inhibitor and anticoagulation treatment is an effective way of managing PRSS1 R122H mice from developing chronic pancreatitis. These antidiabetic effects might make this combination therapy a promising strategy to treat pancreatitis while preventing the development of diabetes at the same time. Animal Models: This study and others have highlighted the importance of generating animal models that develop humanlike PRSS1 R122H in the advancement of

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understanding the pathophysiology of pancreatitis and the implementation of new treatments. These models have assisted investigators to dissect the multifaceted pathology of pancreatitis, and also to find out biomarkers for treatment.ER Stress and ROS Production: Some aspects of the pathophysiology of PP include the involvement of endoplasmic reticulum (ER) stress and the generation of reactive oxygen species (ROS) in subjects with PRSS1 mutations. ER stress, oxidative stress and the generation of ROS play roles in the genesis of pancreatitis and may represent novel targets for treatment of the condition[13].The discovery, molecular characterization, and application of PRSS1 protein for diagnosing and treating pancreatitis indicate that the PRSS1 protein research has a critical and important role in the diagnosis and prevention of diabetes[9].

3. MATERIALS AND METHODS

Experimental Animals:
This study used male Sprague-Dawley rats that weighed between 150 and 200 g. Before the experiment began, they were put in animal houses at Al-Qadisiayh University in Iraq for one week to get used to their new surroundings. They lived in a lab and were fed a standard pellet diet and water along with their mother during the trial.

Drugs and Chemicals
Sigma Chemicals in the USA provided the streptozotocin. A glucose kit was bought from Randox Diagnostics in the United States. A grade of drugs was used for everything else.

Experimental Design
There were 18 rats in each of the five groups, which were then split into five groups. Group 1: Standard lab food was given to normal control rats. Pets for 30 days. Group 2: One dose of STZ (60 mg/kg) was given to diabetic control rats. Nano-Celery processors are in the third group. It was given to diabetic rats (80 mg/kg) after STZ. For 30 days, the process went on. In the group 4, insulin was used to treat .After that, insulin (4 units/ rats, subcutaneously) was given to diabetic rats. The STZ treatment went on for 30 days. The group 5 is Extract-Celery. For 30 days, treats rats were only given celery juice (100 mg/kg). With a pH of 4.5, STZ was in citrate buffer. One dose of 60 mg/kg was given ntraperitoneally (i.p.) to groups II, III, IV, and V. It has been proven that diabetes started to form three days after STZ treatment. Check the blood sugar level. Rats with blood sugar levels of 250 mg/dL or higher were thought to have diabetes. Groups Ill and V show up five days after STZ treatment. Received food with Nano-Celery in it .This went on every day until the study was over (30 days). All of the groups had blood samples taken after two and four weeks of taking Nano-Celery pills. Biochemical predictions were made from blood samples that were taken on the last day of the experiment. After that it was animals the pancreas was killed, taken out, and cleaned. Used for gene expression research after being washed in ice-cold normal saline.

Preparation of Nano –Celery
1% celery nanoemulsion, 1% soybean oil, and 40% Tween 80 dissolved in deionized water. The aqueous phase was added to the oil phase at a rate of 2 mL/min and homogenized using a

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conventional ultrasonicator in a ratio of 45:55 at room temperature (28 ± 2 °C). Homogenization was continued for 15 minutes after introduction of the aqueous phase.Based on previous research (100 mg/mouse), 400 mg/kg and 800 mg/kg of celery nanoemulsion were administered to the animals. Preparation conditions required encapsulation of 40 mg of celery nanoemulsion into the nanoemulsion. Clear nano-sized formula. It is not possible to create more than this amount because the composition becomes blurry [14].

Determination of Blood Glucose
The glucose oxidase method was used [15]with a commercial test kit from Randox diagnostic, USA, to figure out the blood glucose level.

Determination of Serum Insulin Level
A commercially available rat insulin kit from EMD Millipore USA was used to measure the serum insulin level [16].

Determination of LPO
To find out how much LPO there was, thiobarbituric acid (TBA) was mixed with malondialdehyde (MDA), which is made when membrane lipids peroxide[17] .

Determination of GSH
method was used to figure out the GSH level [18].

Determination of SOD Activity
The method of was used to measure SOD activity[19] .

Determination of CAT Activity
Method was used to measure CAT activity[20].

Determination of GPx Activity
The method of was used to measure GPx activity[21].

Determination of GR Activity
The method of was used to measure GR activity[22].

Realtime-Polymerase Chain Reaction
The RNeasy Mini RNA separation kit from Qiagen (Couraboeuf, France) was used to get total cellular RNA from the pancreas according to the manufacturer's instructions. 35 pi of RNAse-free water were used to separate the total RNA from the matrix. There was some genomic DNA left over, so the RNA solution was mixed with 15 units of RNase-free DNase I in 2 mM MgCE and left to sit for 10 minutes at 37X. The DNase was then turned off for 5 minutes at 90*C.There were 50 mM Tris-HCl (pH 8.3), 10 mM dithiothreitol, 100 ng random hexamers, 3.5 pg bovine serum albumin, 3 mM MgCb, 0.5 mM deoxynucicotide triphosphates, 30 units of RNAguard RNase inhibitor (Promega, Madison, WI), 200 units of Moloney murine leukaemia virus reverse transcriptase (M-MLV RT), and 50 pi of RNase-free

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water. It wasn't made sure that the reverse transcription processes had the same amount of total RNA.The processes were heated to 26°C for 10 minutes, then 42°C for 45 minutes, and finally 90°C for 3 minutes to break down the secondary structure of the RNA.

Extra 300 units of reverse transcriptase were added, and the processes were heated to 42°C for 45 minutes. After that, they were heated to 75°C for 10 minutes to stop the reverse transcriptase from working. By leaving out the reverse transcriptase in parallel samples, negative controls for the RT process and controls for DNA contamination were carried out. The cDNA samples were split up and kept at -80°C. Throughout the study, the same cDNA samples were used. PCR conditions included 35 cycles of initial denaturation at y'"C for 5 rain, 95°C for 45 s, 60°C for 30 s, 72°C for 1 min, and finally 72°C for 5 min. A separate PCR with primers specific for the housekeeping mRNA (GAPDH) (fw: 5'- TGAACGGATTTGGCCGTATTGGGC3'; rv: 5'-TCTTCTGGGTGGCAGTGATGGCAT-3') was used to check the viability of the RT duci. These were the rat PRSS1 primers:fw: 5*- GGTTGTTGTGCTTCCTTGAG-3'; rv: 5'-CCTTGGTGTAGACTCCAGGCTT-3'.
For 35 rounds, the PCR conditions were the same as those above. On a 1.5% agarose gel, electrophoresis was used to look at the PCR results. The QuantiTect SYBR Green PCR kit from Qiagen, the Opticon-2 PCR machine from MJ Research, white 965 PCR plates, and plain PCR caps from MJ Research were used for real-time PCR.The right annealing temperatures for all primers were confirmed by gradient PCRs.

4. RESULTS AND DISCUSSION

Blood Glucose:
Blood sugar levels were checked on day five to find the diabetic rats whose levels were higher than 200 mg/dl. The findings showed that male rats given insulin and
Compared to diabetic control rats, those that were given barley whole giain had the best hypoglycemic benefits. The amount of glucose in their blood is still higher than that of normal control rats, though. On the other hand, rats that were only given barley had significantly lower blood glucose levels ($p<0.05$) and hit the levels of normal control rats.

Antioxidants and Oxidative Markers:
In response to oxidative stress, our data showed that antioxidant enzymes also increased in streptozotocin-induced diabetic rats. These outcomes were changed.
Insulin treatment and giving them whole grains of wheat to a level similar to what was seen in control rats.

Gene Expression Analysis:
Numbers that were used to measure the expression levels of the prss1 gene are shown in Figure 2.In pancreatic tissue, their amounts were much higher than usual. Nano-Celery normal control group rats were used to compare the treatment group to the other groups in this study. When diabetic rats were given celery extract, on the other hand, prss1 gene expression levels went up significantly compared to diabetic control rats, but they still went down significantly compared to normal control rats. However, when male diabetic rats were treated with Nano-Celery, the

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Expression levels of the prss1 gene dropped significantly compared to male diabetic rats that were treated with insulin.

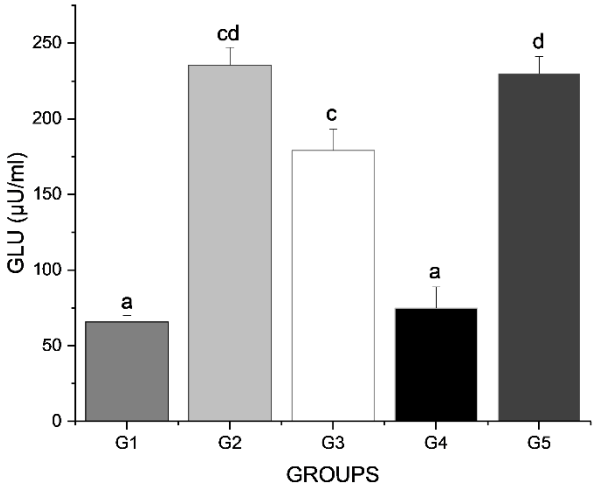


Figure 2. Nano-Celery's effect on the blood sugar level in adult male rats that were made diabetic with streptozotocin. At p < 0:05, means that begin with different letters are very different.

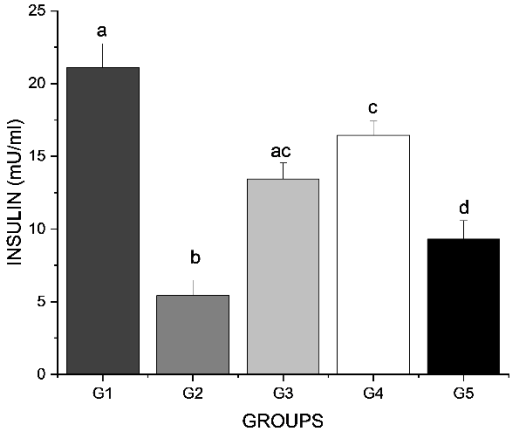


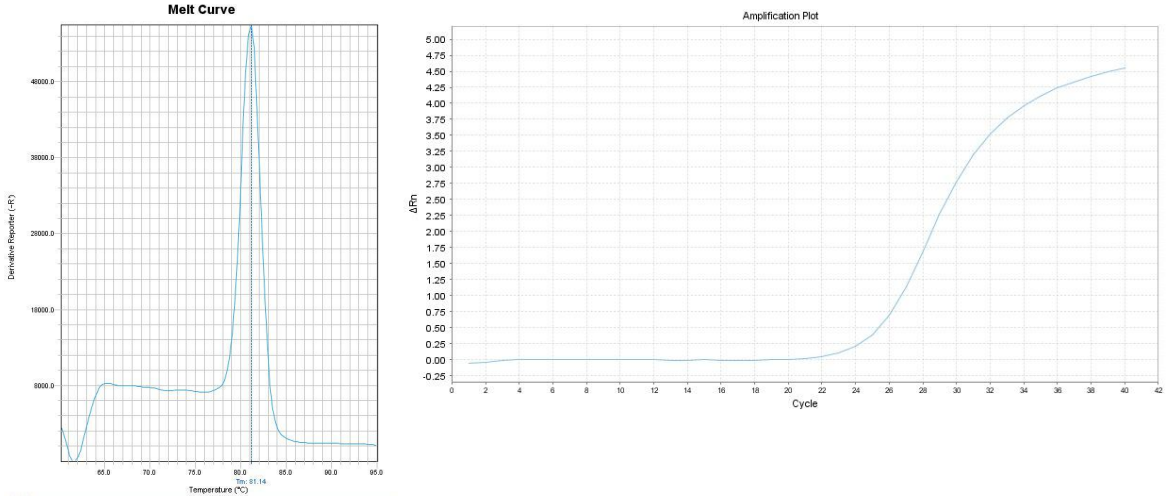
Figure 2. Nano-Celery's effect on insulin level in adult male rats that were made diabetic with streptozotocin. At p < 0:05, means that begin with different letters are very different.

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Table 1. Changes in oxidative antioxidant status markers caused by Nano-Celery.					
Groups	**G 1**	**G 2**	**G 3**	**G 4**	**G 4**
GSH (µmol/g Hb)	13.14±0.4a	6.064.6b	10.78±1.55a	12.91±1.2 a	9.18±11.09 c
MDA (nmol/g Hb)	16.11±1.65a	34.14±2.78b	18.11±2.68ac	17.21±1.5 8c	20.72±1.55 d
GST(U/g Hb)	10.12±0.34a	20.17±0.55b	12.21±0.92d	11.15±0.7 8c	16.33±1.04 e
GPx (U/g Hb)	21.23±1.02a	40.13±0.45b	25.32±0.86ac	22.09±0.9 4c	30.01±1.04 d
GR (U/g Hb)	15.11±0.77a	32.98±0.94b	19.54±0.84ac d	17.16±1.0 2c	24.5±0.14d
CAT (U/mg Hb)	67.27±0.14a	101.07±0.08 b	73.57±2.21ac	69.11±1.1 4c	88.12±0.04 d
SOD (U/g Hb)	680.43±2.78a	960.01±1.08 b	750.11±1.12 ac	701.21±2. 22c	830.14±1.1 8d
The acronyms BMI, FBG, and TC stand for Body Mass Index, Fasting Blood Sugar, and Total Cholesterol, respectively. High density lipoprotein cholesterol (HDL-C).					

Figure **2**. Dissociation curve of GapdH gene primer.



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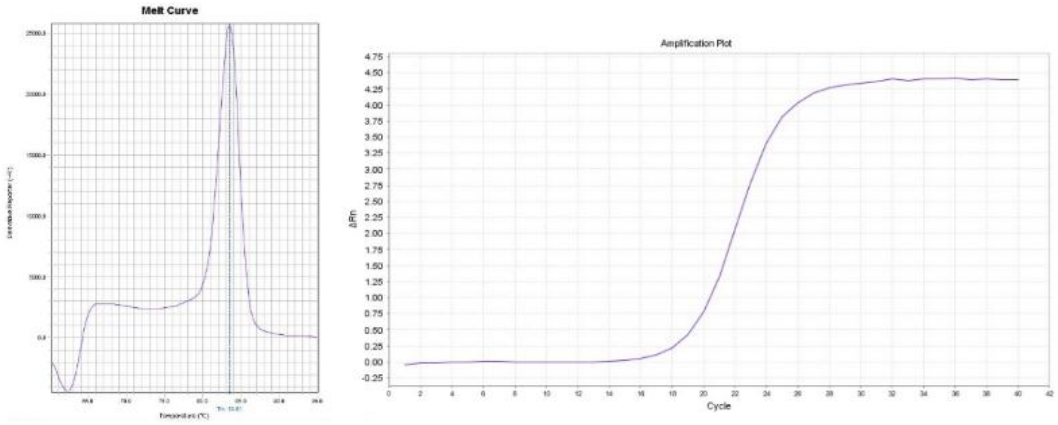


Figure 3. Effect of Nano-Celery on PRSS1 gene

Discussion

h>Poinsulinemia in people with diabetes raises the energy Fatty acyl coenzyme is an enzyme. A substance that speeds up the P-Oxidation of fatty acids, which results in lipid peroxidation. More lipid breakdown makes the membrane less strong.The way they work is by making membranes less flexible and changing Activity of enzymes and sensors that are bound to membranes most cells in the body are hurt by lipid breakdown products.

The body is linked to a lot of illnesses, like atherosclerosis and brain damage [1]. This study shows that people with diabetes have more reactive stress. higher levels of MDA and lower levels of GSH in rats in comparison to controls[23][24]. When Nano-Celery Management was used, MDA levels went down and GSH levels went up. In this case, it means he is in charge. Nano-Cells The level of reactive stress is going down[25]. This

It could be because insulin acts as a blocker to protect cells. Nano-Celery may have anti-inflammatory and antioxidant effects. Red blood cells with more catalase activity There may be a high risk of oxidative stress in the diabetic rats in this study.[26] [24][27]said that after 12 weeks of diabetes, catalase activity went up. Going Up

The higher levels of catalase activity found in diabetic rats are due to more H2O2 being made. The latest effects of adding catalase Compared to diabetes rats that were given insulin and rats that were fed Nano-Celery Based on the research by[27], the groups make sense. It can be understood in terms of possible antioxidants. The part that Nano-Celery plays. Not enough antioxidants it's possible that enzymes in red blood cells make them more likely to get sick. Stress from oxidation. [28] Say that GPx has a part to play. What it does to stop reactive damage is its main job. [29] It was found that GPx went up when H2O2 levels went up. Even with more catalase and GBX in this study. The amounts of MDA were higher in diabetic rats compared to diabetic rats that were given insulin and Nano-Celery. In this case, oxidative stress was too high for antioxidant enzymes to remove reactive oxygen species. Glutathione reductase (GR, EC 1.8.1.7) helps break down oxidised glutathione (GSSG) with the help of NADPH. To lower glutathione (GSH), which is an important part of the GSH redox cycle that makes sure there are enough low GSH levels. To protect against oxidative stress, you need a high GSH/GSSG

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ratio [30]. In this research, Nano-Celery Restoration of the activity of antioxidant enzymes (GR, GST, and GPx) in a way that is similar to how SOD and CAT work. Some researchers have found a link between Xanthine oxidase (XOD) activity and extreme oxygen production in people with diabetes [30]. Oxidation Stress in diabetes can be lowered with an XOD inhibitor that is used in medicine. So, it's likely that the active Nano-Celery (p-glucan) parts combine with different types of peroxy CfiOO. This lowers SOD operations and the goods and services tax. CAT, GR, and GPx enzymes. [31][32]Nano-Celery showed in our tests that Flavonoids [33]are likely what give antioxidants their defensive power[34][35][36][37]. Flavonoids can help in the beginning step of peroxide messes up metabolism. From an oxidising agent either by getting rid of free radicals or by messing up the microsomal enzyme system that does this job[34]. They can also get rid of fat oxides and grease. [38]Fenton's reaction was stopped when their radicals or act as chelating agents for Fe*- ions. In this study, we first looked at how well the starter worked.The outcome showed that PRSS1 was good at priming. The starters were GapdH and 2.08 and 1.6, in that order. There was less than a 4% change in how well PRSS1 and GapdH (Internal control) primer worked. This When we need a real copy number, quality control is very important. But in this case, we need to know the fold change in parsing Target genes for treatment samples compared to control samples. In this study, we used the PRSS1 primer because it worked 2.08 times as well as the other primers [39]. not making enough insulin or a problem [40]with it Producing insulin is a key part of almost all types of diabetes, including the more common type 1 (insulinemia) and type 2 (non-insulin dependence). There are some less common types of diabetes that start in adulthood in young people (Modi). Because insulin is so important in How both types of diabetes start, the PRSS1 gene It has always been thought of as a possible gene for asthma[41][42]. This study figured out when the insulin gene (PRSS1) starts to be expressed, which is a very important question in the biology of islet growth.[42][43] our The study tells us important things about the role of Nano-Celery; By showing that the expression of the PRSS1 gene in adult male rats was increased by about 4.2 times.

5. CONCLUSION

Nano-Celery does have a good effect that much is clear. Beneficial effect as an effective hypoglycemic and an antioxidant agent in diabetic people who have already reached adulthood when used for 30 days, male rats play a positive part in increasing the expression level of PRSS1 genes, which are responsible for biosynthesis of the hormone insulin. There needs to be more research. It is done so that Nano-Celery and its parts can be recommended. Different people or stressful situations cause fractures to look and feel differently.

Conflict of Interest

The authors have nothing to say about a conflict of interest.

Compliance with Ethical Standards

Disagreements about interests the writers say they don't have any goals that are at odds with each other.

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Moral approval this study was given the green light by the Al-Qadisiyah University Local Committee.

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