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EFFECT OF QUERCETIN EXTRACTED FROM ONION PEELS ON SOME PHYSIOLOGICAL PARAMETERS IN DIABETIC RATS

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Abstract:

this experiment was conducted to find out the effect of the commercial and nano-extract of quercetin on the level of glucose and some physiological parameters, which included liver functions (alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase) and kidney functions (blood urea and creatinine), malondialdehyde and antioxidant enzymes (catalase). and superoxide dismutase) and lipid profiles (cholesterol, triglycerides, high-density lipoproteins, low-density lipoproteins, and very low-density lipoproteins).

The results showed a significant decrease in the weight of diabetic animals compared with the control group and groups treated with nano- and commercial quercetin extract after 30 days of dosing with Positive (infected without treatment) On the other hand, the results showed a significant increase in the level of alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, blood urea and creatinine in the positive control group (infected without treatment) compared with groups treated with quercetin nano extract and commercial after 30 days In addition, the results showed that there was a significant increase in the level of malondialdehyde in the positive control group with the control group and the rest of the groups treated with the commercial and nano-extract quercetin, as well as a significant increase in the level of the catalase enzyme and a decrease in the level of the superoxide dismutase enzyme in the groups treated with the commercial and nano-quercetin extract compared with the positive control group

. Finally, the results showed that there was a significant increase in the level of cholesterol, triglycerides, low-density lipoproteins and very low-density lipoproteins in the positive control group compared with the negative control group (non-diabetic) and the rest of the groups treated with nano- and commercial quercetin extract, while there was a significant increase in the level of lipoproteins High density in the aggregates treated with nano-quartzite and commercial compared with the positive control.

Key words: lipoproteins, cholesterol, triglycerides.

Introduction:

The world is moving towards the use of natural medicinal materials extracted from plants with a curative and preventive ability, after the use of chemicals showed that it has negative side effects that appear in the long term. Flavonoids are considered one of the most important active substances extracted from medicinal plants and used in the treatment of many diseases because of their high ability to act as antioxidants to resist the action of free radicals produced by pathogens. Quercetin is one of the flavonoids called Flavanols, which form the pillar Backbone of many flavonoids(2009 ,.Madhavan et al) It is also the most important type of flavonoids closely related to heart diseases in particular and many other diseases that may affect the body, as the most important natural properties of quercetin are its ability to act as an antioxidant by neutralizing free radicals And rid the body of its harmful effects(Hubbard et al.,2006)

The antioxidant activity of flavonoids has attracted much attention with regard to their potential role in the prevention of chronic oxidative stress-related diseases such as heart disease and diabetes. Quercetin has been shown to have very potent antioxidant effects in preventing endothelial cell death caused by oxidants (Coskun et al.,2005 .)

It has been found that quercetin has some hypoglycemic effects, that is, it acts as an antidiabetic, by reducing oxidative stress and damage to pancreatic cells in experimental diabetes. Since quercetin has many therapeutic benefits for human health, it has the benefit of protecting the heart and blood vessels, anti-cancer, antioxidant, anti-diabetic, anti-atherosclerotic, anti-inflammatory, and it can also be used as a nutritional supplement (Verhoeyen et al.,2002 .).

With the advancement of the use of nanotechnology in medicine, some useful solutions emerge. Among the applications of nanotechnology in medicine that are currently being developed is the use of nanoparticles to deliver drugs, heat, light, or other substances to certain types of cells (such as cancer cells). A common challenge to nanotechnology today and the near future, nanoparticles cover almost all kinds of science(Hashim,2012)

A characteristic was observed that depends on the size of this small area, such as surface Plasmon resonance, high magnetism, materials used in biomedicine, and others. Nanoparticles have unexpected properties often as a result of the restriction of their electrons and the production of quantum effects, and what is worth noting is that the properties of the original materials from which the particles are made up changes completely as it approaches the nanoscale.

Recently, the system for converting molecules into nanoparticles is probably very suitable, especially for molecules that have little solubility in water, as in medicinal plants. Converting them into nanoparticles gives them high permeability and increases their resistance to metabolic.

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Silver nanoparticles have been used against reactive oxygen species that have been givenExcellent results. Antioxidants are known to have many benefits in scavenging free radicals and scavengingThe body of a lot of cardiovascular and cancerous diseases. (Taha 2019)

Nanomaterials exhibit fundamentally contradictory physical and chemical properties when compared to the basic mass. The production of different types of nanoparticles has lower end demands as a result of the rapid advances in nanotechnology.(Maki, D. S., Nemer,2019)
The tendency to deal with drugs extracted from natural sources and subject them to modern technologies such as nanotechnology gave hope to researchers in the medical sector, and currently the number of drugs based on nanotechnology available is estimated at about 200 types, in addition to 120 others in the phase of clinical trials, according to a report issued by the Nanomedicine Working Group of For the European Technology Platform, the research priorities for the development of nanomedicine during the years 2015-2020 are based On three axes: First: Developing advanced drug delivery systems in a targeted and cell-specific manner. Second: finding extended-release drug formulations that provide continuous release of the active substance in fixed amounts. Third: Developing oral vaccines for diseases: HIV, tuberculosis and malaria, by placing biomolecules such). الشربيني)2016 ،آخرون و as proteins and peptides on nanocarriers.
Experiment design:

The study included 40 albino rats, 3-4 months old, divided into 9 groups as follows: a negative control group without diabetes, a positive control group (with diabetes without treatment), the third, fourth, and fifth groups with diabetes and were dosed with quercetin nano extract and other concentrations10,20 and 40mg/kg of body weight, and the sixth, seventh, and eighth groups were dosed with commercial quercetin extract at concentrations of 15, 30, and 45 mg/kg of body weight, while the ninth group was dosed with metformin at a concentration of 45 mg/kg of body weight..
Blood was drawn from all animals after the completion of the experiment, and placed in plastic tubes free of anticoagulant at room temperature until the completion of the coagulation process, then a centrifugation process was performed at 3000 cycles / min in order to obtain serum. The serum was placed in Eppendorf tubes It was kept at a temperature of -20 degrees Celsius until chemical tests were performed, which included lipid profile , liver and kidney functions, antioxidants(catalase, superoxide dismutase)and malondialdyhide Cholesterol measurement:
Serum cholesterol concentration was measured using the diagnostic kit produced by Biolabo SA
. Measurement of triglyceride concentration:

Triglyceride concentration was measured using a diagnostic kit from Biolabo SA kit Fossati

Measurement of good high-density lipoprotein (HDL):

Measurement was carried out using the prepared diagnostic kit from Biolabo SA kit.
Malondialdehyde (MDA) level measurement:

Malondialdehyde was determined in serum using a kit from BioVision.

Results and discussion

Table 1: Study of the effect of nano- and natural quercetin on body weight in induced diabetic rats.

groups	Mean ± SE		
	Initial weight \g	The final weight \g	Gain (gm)
Negative control	179.33 ±4.09	191.67 ±2.18 ab	12.33 ±2.02 a
Positive control	179.67 ±5.04	163.33 ±4.63 c	-16.33 ±3.52 b
Diabetes + 10 mg/kg quercetin nano	156.67 ±6.69	168.33 ±9.35 bc	11.67 ±2.90 a
Diabetes + 20 mg/kg quercetin nano	184.33 ±4.09	195.00 ±6.35 a	10.67 ±2.40 a
Diabetes + 40 mg/kg quercetin nano	174.67 ±4.33	183.67 ±5.23 abc	9.00 ±1.00 a
Diabetes + 15 mg/kg quercetin commercial	179.00 ±12.42	187.00 ±12.50 ab	8.00 ±1.00 a
Diabetes + 30 mg/kg quercetin commercial	167.00 ±7.63	175.67 ±9.20 abc	8.67 ±1.76 a
Diabetes + 45 mg/kg quercetin commercial	178.00 ±3.21	186.00 ±3.78 abc	8.00 ±0.57 a
Metformin 45 mg/kg	169.67 ±10.83	177.33 ±11.02 abc	7.67 ±1.85 a
LSD	27.311 NS	23.40 *	6.237 **
P-value	0.261	0.0437	0.0001
Means having with the different letters in same column differed significantly. * (P≤0.05), ** (P≤0.01).			

The results in Table 1 showed a significant increase in the final weight (191.67 ±

2.18) g for the negative control group compared to the initial weight (179.33 ± 4.09) g for the same group, while the positive group showed a significant decrease in the final weight (163.33 ± 4.63) compared to the initial weight (179.67 ± 5.04) gm, the results showed a significant increase in the final weight of the groups treated with quercetin nano extract at concentrations of 10, 20, and 40 mg/kg. (168.33 ± 9.35, 195.00 ± 6.35, and 183.67 ± 5.23) gm, respectively, compared with the initial weight of the same concentrations (156.67 ± 6.69, 184.33 ± 4.09, and 174.67 ± 4.33) gm, respectively, as was the case for the groups treated with quercetin extract. The normal group and

the metformin group, where the results showed a significant increase in the final weight compared with the initial weight

Table 2: Study of the effect of nano- and natural quercetin on the level of glucose in the blood in rats with induced diabetes mellitus.

groups	Mean ± SE		
	Glucose/day 1 mg/dl	Glucose/day 15 mg/dl	Glucose/day 30 mg/dl
Negative control	90.33 ±5.84 c	91.33 ±2.40 c	95.67 ±6.76 d
Positive control	383.67 ±29.86 ab	500.00 ±10.02 a	480.67 ±14.31 a
Diabetes + 10 mg/kg quercetin nano	359.33 ±20.16 ab	228.33 ±12.81b	185.33 ±7.44 c
Diabetes + 20 mg/kg quercetin nano	378.00 ±16.65 ab	248.33 ±14.24 b	166.67 ±9.95 bc
Diabetes + 40 mg/kg quercetin nano	400.67 ±5.04 a	247.67 ±24.22 b	151.33 ±4.09 c
Diabetes + 15 mg/kg quercetin commercial	353.00 ±27.00 ab	250.00 ±22.03 b	201.67 ±12.03 b
Diabetes + 30 mg/kg quercetin commercial	366.33 ±14.62 ab	233.00 ±28.16 b	203.00 ±17.67 bc
Diabetes + 45 mg/kg quercetin commercial	345.00 ±33.71 ab	220.67 ±36.16 b	168.33 ±21.62 b
Metformin 45 mg/kg	332.67 ±29.22 b	197.67 ±11.34 b	141.00 ±7.37 c
LSD	66.954 **	60.850 **	37.067 **
P-value	0.0001	0.0001	0.0001
Means having with the different letters in same column differed significantly. * (P≤0.05), ** (P≤0.01).			

The results showed that there was a significant increase in the level of glucose on the first day of infection in all groups treated with alloxan, where it was in the positive control group (383.67 ± 29.86) and in the groups treated with nano-extract quercetin at concentrations of 10, 20 and 40 mg/kg (359.33 ± 20.16, 359.33 ± 20.16 and 400). 67 ±5.04) mg/dLThe groups treated with natural quercetin extract at concentrations of 15, 30, and 45 (353.00 ± 27.00, 366.33 ± 14.62, and 345.00 ± 33.71) mg/dl, while the glucose level in the negative control group (without induction of diabetes) was (90.33 ± 5.84) mg/dl. 15 days of treatment, the results showed a significant decrease

in the level of glucose in the groups treated with quercetin nano extract at concentrations 10, 20, and 40 (228.33 ±12.81, 248.33 ±14.24, and 247.67 ±24.22) mg/dl. respectively, as well as in the groups treated with quercetin extract, at concentrations of 15, 30, and 45 mg/kg (250.00 ± 22.03, 233.00 ± 28.16, 220.67 ± 36.16) mg/dl, and the level of glucose in the metformin group was (197.67 ± 11.34) mg/dl compared to the positive control group (500.00). ±10.02The results of the glucose level after 30 days of treatment with quercetin showed a significant decrease in the level of glucose in the groups treated with quercetin nano extract at concentrations 10, 20 and 40 (155.33 ± 7.44, 166.67 ± 9.95 and 151.33 ± 4.09) mg/dL, as well as in the groups treated with the extract Quercetin, at concentrations 15, 30, and 45 (201.67 ± 12.03, 168.33 ± 21.62, 203.00 ± 17.67), and the metformin group (161.00 ± 7.37mg/dL compared with the positive control group (480.67 ±14.31) and the negative control (95.67 ±6.76) mg/dL.

Table 3: Study of the effect of nano- and natural quercetin on liver function in diabetic rats

Groups	Mean ± SE IU\L		
	Alkaline phosphatase	Aspartate aminotransferase	alanine aminotransferase
Negative control	84.67 ±6.76 c	27.00 ±3.60 ef	19.67 ±1.20 e
Positive control	125.33 ±1.20 a	49.00 ±1.52 a	64.33 ±4.33 a
Diabetes + 10 mg/kg quercetin nano	94.67 ±9.52 bc	37.66 ±2.60 bc	45.00 ±1.73 bc
Diabetes + 20 mg/kg quercetin nano	108.00 ±4.51 ab	42.00 ±1.00 b	35.00 ±2.88 b
Diabetes + 40 mg/kg quercetin nano	88.67 ±6.69 bc	28.33 ±2.40 cde	31.00 ±2.88 c
Diabetes + 15 mg/kg quercetin commercial	93.00 ±2.51 bc	38.00 ±1.52 bc	43.67 ±0.88 bc
Diabetes + 30 mg/kg quercetin commercial	97.33 ±13.37 bc	33.67 ±0.88 cd	38.33 ±2.18 cd
Diabetes + 45 mg/kg quercetin commercial	92.00 ±3.60 bc	33.33 ± 3.52 def	39.00 ±2.88 cd
Metformin 45 mg/kg	87.33 ±7.53 ab	24.67 ±0.67 f	32.00 ±1.52 d
LSD	21.195 *	6.635 **	7.418 **
P-value	0.0162	0.0001	0.0001
Means having with the different letters in same column differed significantly. * (P≤0.05), ** (P≤0.01).			

The results showed that there was a significant increase in the activity level of the alkaline phosphatase enzyme in the positive control group (125.33 ± 1.20) and the group treated with quartin nano extract at a concentration of 20 mg / kg (108.00 ± 4.51) international units / liter compared with the negative control group (84.67 ± 6.76) international units / liter While the groups treated with quercetin extract at a concentration of 10 and 40 mg/kg of body weight showed (94.67 ± 9.52 and 88.67 ± 6.69) IU/L. The groups treated with natural quercetin extract at concentrations of 15, 30, and 45 (93.00 ± 2.51, 97.33 ± 13.37, and 87.00 ± 3.60) IU/L showed a significant decrease compared to the positive control group. As for the activity of the aspartate aminotransferase enzyme, the results showed a significant increase in its level in the group The positive control (49.00 ± 1.52) IU/L compared to the negative control group (27.00 ± 3.60) While the groups treated with quercetin extract at a concentration of 2010 and 40 mg/kg of body weight showed (37.66 ±
2.60, 42.00 ± 1.00, and 28.33 ± 2.40) IU/L, and the groups treated with natural quercetin extract at concentrations of 15, 30, and 45 (38.00 ± 1.52, 33.67 ± 0.88, and 33.67 ± 0.88). 33 ± 3.52) IU/L and the metformin group showed a significant decrease in enzyme concentration compared with the positive control (49.00 ± 1.52) IU/L.

On the other hand, the results showed that there was a significant increase in the activity of alanine aminotransferase in the positive control group (64.33 ± 4.33) IU/L compared to the negative control group (19.67 ± 1.20) IU/L, while the groups treated with quercetin extract showed a concentration of 2010 and 40 mg/kg. of body weight) 45.00 ±1.73, 35.00 ±2.88, and 31.00 ±2.88) IU/L The groups treated with natural quercetin extract at concentrations of 15, 30, and 45 (43.67 ± 0.88, 38.33 ± 2.18, and 39.00 ± 2.88) IU/L and the metformin group (32.00 ± 1.52) IU/L showed a significant decrease in enzyme concentration compared to the positive control (64.33 ± 4.33).)international units/liter

Table 4: Study the effect of natural and nano-quercetin on kidney function in diabetic rats

Groups	Mean ± SE	
	Creatinine mg/dl	blood urea mg/dL
Negative control	0.40 ±0.04 e	26.51 ±1.78 de
Positive control	0.93 ±0.08 a	33.32 ±0.58 a
Diabetes + 10 mg/kg quercetin nano	0.68 ±0.09 bc	29.68 ±1.74 bc
Diabetes + 20 mg/kg quercetin nano	0.74 ±0.02 b	31.00 ±0.43 ab
Diabetes + 40 mg/kg quercetin nano	0.59 ±0.04 bcd	27.12 ±0.85 cde
Diabetes + 15 mg/kg quercetin commercial	0.58 ±0.02 cd	28.47 ±0.29 bcd

Diabetes + 30 mg/kg quercetin commercial	0.48 ±0.05 de	25.84 ±0.89 de
Diabetes + 45 mg/kg quercetin commercial	0.45 ±0. 02 de	25.40 ±0.64 e
Metformin 45 mg/kg	0.46 ±0.02 de	25.32 ±0.33 e
LSD	0.15 **	2.95 **
P-value	0.0001	0.0002
Means having with the different letters in same column differed significantly. ** (P≤0.01).		

The results of Table 5 showed a significant increase in creatinine concentration in the positive control group (0.933 ± 0.08) mg/dL compared to the negative control group (0.403 ± 0.04) mg/dL, while the groups treated with quercetin extract at a concentration of 2010 and 40 mg/kg of body weight showed (0.68 ±0.09, 0.74 ±0.02, 0.59 ±0.04) mg/dL. The groups treated with natural quercetin extract at concentrations of 15, 30, and 45 (0.58 ± 0.02, 0.48 ± 0.05, 0.45 ± 2.,.) mg/dl and metformin group (0.46 ± 0.02) mg/dl showed a significant decrease in creatinine concentration compared with the positive control (0.93 ± 0.08).) mg/dl As for blood urea, the results showed a significant increase in the positive control group (33.32 ± 0.58) mg/dl Compared with the negative control group (26.51 ± 1.78) mg/dL, while the groups treated with quercetin extract at concentrations of 10 and 40 mg/kg of body weight showed (29.68 ± 1.74 and 27.12 ± 0.85) mg/dL, and the groups treated with natural quercetin extract at concentrations of 15, 30 and 45 showed (28.297 and ± 0.297). .84 ± 0.89 and 25.40 ± 0.64 (mg/dL) and metformin group (25.32 ± 0.33) mg/dL significantly decreased urea concentration compared with the positive control (33.32 ± 0.58) mg/dL.

Table No. 5 Study of the effect of nano- and natural quercetin oxidative enzymes in rats with induced diabetes mellitus

Groups	Mean ± SE		
	Malone Dialdehyde	catalase	Superoxide dismutase
Negative control	1.05 ±0.05 b	7.94 ±0.25 c	140.00 ±18.23 ab
Positive control	4.87 ±0.72 a	8.87 ±1.89 c	146.33 ±13.93 a

Diabetes + 10 mg/kg quercetin nano	2.80 ±0.45 c	11.18 ±0.38 bc	109.33 ±17.02 bc
Diabetes + 20 mg/kg quercetin nano	2.52 ±0.03 c	12.16 ±0.48 bc	105.67 ±11.76 bc
Diabetes + 40 mg/kg quercetin nano	2.29 ±0.41 c	19.74 ±3.43 a	93.67 ±20.16 cd
Diabetes + 15 mg/kg quercetin commercial	2.60 ±0.36 c	15.70 ±0.82 ab	106.67 ±7.68 bc
Diabetes + 30 mg/kg quercetin commercial	2.55 ±0.11 c	15.64 ±1.34 ab	102.66 ±9.67 c
Diabetes + 45 mg/kg quercetin commercial	2.03 ±0.31 c	17.37 ±1.67 a	63.00 ±8.02 d
Metformin 45 mg/kg	2.11 ±0.06 c	20.33 ±1.10 a	90.67 ±5.60 cd
LSD	1.064 *	4.685 **	36.841 **
P-value	0.0438	0.0001	0.0062
Means having with the different letters in same column differed significantly. * (P≤0.05), ** (P≤0.01).			

The results showed that there was a significant increase in the level of malondialdehyde in the positive control group (4.87 ± 0.72) Compared with the negative control (1.05 ± 0.05), while there was a significant decrease in the value of malondialdehyde in groups treated with quercetin extract at a concentration of 10, 40 and 20 mg/kg of body weight (2.80 ± 0.45, 2.52 ± 0.03 and 2.29 ± 0.41) and groups treated with quercetin extract. Normal concentrations of 15, 30 and 45 (2.60 ± 0.36, 2.55 ± 0.11 and 2.03 ± 0.31) and metformin group (2.11 ± 0.06) compared with the positive control (4.87 ± 0.72). In addition, the results showed that there was a significant increase in the level of activity of the enzyme catalase in the group treated with quercetin extract at a concentration of 40 mg/kg (19.74 ± 3.43) international units / liter and the groups treated with natural quercetin extract at concentrations of 15, 30 and 45 (15.70 ± 0.82 and 15.64). ±1.34 and 17.37 ±1.67) IU/L as well as the metformin group (20.33 ±1.10) IU/L compared to the positive control group (8.87 ±1.89) IU/LOn the other hand, the results showed a significant decrease in the level of superoxide dismutase activity in groups treated with quercetin extract at concentrations of 10, 30, and 40 mg/kg (109.33 ± 17.02, 105.67 ± 1.76, and 93.67 ± 20.16) IU/L and groups treated with natural quercetin extract at concentrations 15, 30, 45 (106.67 ± 7.68, 102.66 ± 9.67, and 63.00 ± 8.02) IU/L, as well as the metformin group (90.67 ± 5.60) IU/L, compared with the positive control group (146.33 ± 13.93) IU/L

Table 6: Study of the effect of nanoscale and natural Quercetin on the level of lipid profiles in rats with induced diabetes

Groups	Mean ± SE (mg/dl)				
	cholesterol	Triglyceride	High density lipoproteins	Low-density lipoproteins	Very low density lipoproteins
Negative control	95.67 ±7.22 d	84.33 ±3.48 c	35.00 ±5.19 bc	44.00 ±3.78 de	16.86 ±0.69 c
Positive control	177.00 ±10.78 a	162.67 ±3.71 a	23.00 ±2.08 e	121.67 ±10.68 a	32.53 ±0.74 a
Diabetes + 10 mg/kg quercetin nano	135.00 ±8.66 bc	116.00 ±3.78 b	29.67 ±0.33 cde	77.33 ±9.83 bc	23.20 ±0.75 b
Diabetes + 20 mg/kg quercetin nano	124.00 ±15.14 c	98.00 ±6.24 c	41.67 ±1.45 ab	63.00 ±15.14 cd	19.60 ±1.24 c
Diabetes + 40 mg/kg quercetin nano	94.67 ±6.06 d	84.00 ±3.78 c	43.00 ±2.01 a	35.33 ±8.37 de	16.80 ±0.75 c
Diabetes + 15 mg/kg quercetin	162.00 ±7.81 ab	152.00 ±5.03 a	25.67 ±1.76 de	103.33 ±10.20 ab	30.40 ±1.01 a
commercial					
Diabetes + 30 mg/kg quercetin commercial	160.33 ±10.33 ab	117.67 ±9.93 b	32.33 ±3.52 cd	104.67 ±11.20 ab	23.53 ±1.98 b
Diabetes + 45 mg/kg quercetin commercial	154.00 ±3.46 ab	128.00 ±8.32 b	33.67 ±0.88 c	95.00 ±3.51 ab	25.60 ±1.66 b
Metformin 45 mg/kg	91.67 ±9.27 d	94.00 ±5.56 c	42.33 ±1.45 ab	30.66 ±10.80 e	18.80 ±1.11 c
LSD	27.579 **	17.661 **	7.411 **	29.435 **	3.531 **
P-value	0.0001	0.0001	0.0001	0.0001	0.0001
Means having with the different letters in same column differed significantly. ** (P≤0.01).					

The results recorded in Table No. showed a significant increase in cholesterol level in the positive control group (diabetes mellitus without treatment) (177.00 ± 10.78) mg/dL compared to the negative control group (without infection) (95.67 ± 7.22) and groups treated with quercetin nano extract at concentrations of 10 And 20 mg / kg of body weight, while the results did not show

significant differences between the positive control group and the groups treated with natural quercetin at concentrations 15,30 and 45, where the results were (162.00 ±respectively On the other hand, the results showed a significant decrease in cholesterol level in the group treated with nanoquarcetin at a concentration of 40 mg/kg (94.67 ± 6.06) mg/dL and those treated with metformin at a concentration of 45 mg/kg (91.67 ±9.27) mg/dL, while the results did not show any differences. Significant difference between the two previous groups and the negative control group As for triglycerides, the results showed a significant increase in their concentration in the positive control group (162.67 ± 3.71) mg/dL compared to the control group (84.33 ± 3.48) and the groups treated with quercetin nano extract at concentrations 20, 30, and 40 (116.00 ± 3.78, 98.00 ± 6.24, and 84.00). 00 ± 3.78) mg/dl, respectively, as well as groups treated with natural quercetin extract, at concentrations of 30 and 45
(117.67 ± 9.93 and 128.00 ± 8.32) mg/dl, respectively, in addition to the metformin group (94.00 ± 5.56) mg/dl, also the results showed an increase morale In highdensity lipoproteins (good) in the groups treated with quarcetin nanoparticles at concentrations of 30 and 40 mg/kg (41.67 ± 1.45 and 43.00 ± 2.01) mg/dl, as well as the metformin group (42.33 ± 1.45) mg/dl compared with the positive control group (23.00 ± 2.08) mg/dL and the groups treated with natural quarresti extract at concentrations of 15, 30, and 45 (25.67 ±1.76, 32.33 ±3.52, and 33.67 ±0.88) mg/dL. The results showed a significant increase in the level of low-density (negative) lipoproteins. In the positive control group (121.67 ± 10.68) mg/dl and the group treated with nano-quarcetin at a concentration of 10 mg/kg (77.33 ± 9.83) mg/dl and groups treated with medical quarcetin at concentrations of 15, 30 and 45 (103.33 ± 10.20 and 104.67) ± 11.20 and 95.01 mg \dL, respectively, while the metformin-treated group (30.66 ± 10.80) mg / dL did not show any significant difference with the negative control group (44.00 ± 3.78) mg / dL. Finally, the results showed that there was a significant increase in the level of very low-density lipoproteins in the positive control group (32.53 ± 0.74) mg/dl and the groups treated with natural quercetin at concentrations of 15, 30, 45 (32.53 ± 0.74, 23.53 ± 1.98, and 25.60 ±1.66) mg/dl. Respectively, compared with the negative control group (16.86 ± 0.69) as well as the groups treated with nanoquarcetin at a concentration of 20 and 40 mg/kg (19.60 ± 1.24 and 16.80 ± 0.75) mg/dl, while the group treated with metformin (18.80 ± 1.11) mg/dl did not show any difference Significant with negative control group**.**Medicinal plants are the main source of many medicinal drugs used for various purposesEspecially in the treatment of many chronic diseases because it is a source of active substances that participate in the preparation of many pharmaceutical compounds in the form of extracts or
Almaaeny, J. 2018).

An in vitro study revealed that the ethanolic extract of A. cepa stimulates glucose uptake through GLUT4 in myotubes in a dose- and time-dependent pattern. The insulin-like activities of the extract were exerted by increased phosphorylation of insulin receptor β, its insulin receptor substrate-1, and protein kinase B (Akt) along with an elevation of GLUT4 content and translocation of this protein to the cell surface (Amin et al , 2021). Several studies have

demonstrated the healthy, hypoglycemic effect of onion and its functional components in animal models
(Kumud and K , 1995). Thirty minutes after administration of a sucrose solution (2.0 g/kg) by five-week-old male Sprague-Dawley rats, the ethanolic extract of onion skin and quercetin (both 0.5 g/kg) showed a significant decrease in blood glucose compared with acarbose (5.0 mg/kg) as an effective drug for postprandial hyperglycemia. One hour after administration, the blood sugar lowering effect of the extract disappeared but acarbose kept blood sugar near baseline value for about two hours. (Sun-Ho Kim et al ,2011). In another animal study of alloxan diabetic rats treated with daily doses of 100, 300 and 600 mg/kg of aqueous extract of A. cepa for 21 days, a decrease in blood glucose, LDL, TG, TC, AST, and ALT levels was observed. , and ALP with an increase in HDL value. The maximum dose of the extract and 2 mg/kg of glibenclamide showed approximately the same efficacy. The part of the plant containing the glycoside kaempferol improved the condition of diabetes(J. Ikechukwu etal , 2016). A meta-analysis was performed in 2008 on the antidiabetic activities of onion extract and SMCS in diabetic rats. The results showed that onion extract and SMCS significantly contributed to the control of blood sugar and body weight(Sejeong et al ,2009).Quercetin and red onion extract as a dietary supplement in C57BL/6J mice on a high-fat diet for 9 weeks decreased

PGC-1α promoter methylation and increased expression (Prasad et al, 2017).

Quercetin (0.2% w/w approximately equal to 1000 mg/day in humans according to a dose conversion factor provided by the US Food and Drug Administration)) was added to the high-fat diet of male C57BL/6J mice for 10 weeks. It reduces hyperglycemia, hyperinsulinemia, creatinine, and inflammatory markers such as Creactive protein. An increase in acyl-coenzyme A oxidase 1 (ACOX-1) gene expression was also observed in the liver while no significant changes occurred in energy expenditure, body weight, and lipid profile (Sarah et al, 2016). Because of the low bioavailability of curcumin, its beneficial antidiabetic properties were evaluated in combination with piperine and quercetin on induced diabetes in rats. After 4 weeks of daily oral feeding by this mixture (CPQ) at a dose of 100 mg/kg, improvements in fasting plasma glucose, glucose tolerance, LDL, HDL, TG, cholesterol, water, food intake, and weight loss were observed when compared to diabetic control animals receiving curcumin only. The results obtained were similar to those obtained from 10 mg/kg/day glibenclamide. It was concluded that small amounts of quercetin and piperine in CPQ may exert their effects by decreasing curcumin metabolism (Ginpreet et al, 2016). Thiosulfate (20 and 40 mg/kg) in diabetic rats through noncompetitive α-glucosidase inhibition and stimulation of pancreatic beta cells showed improvements in postprandial glycemic control, glucose tolerance, and insulin secretion with an effect similar to 10 mg/kg acarbose (Abdulrahman, 2016). S-methyl cysteine (100 mg/kg/day, orally for 60 days) along with significant decreases in blood glucose, plasma insulin concentration, TNF-α, and HOMA-IR were shown (Evaluation of a homeostatic model of insulin resistance) antioxidant properties in rats receiving
A high fructose diet. For example, a significant decrease in the serum amount of MDA and an increase in the levels of reduced glutathione (GSH), glutathione peroxidase (GPx), and catalase (Sithara et al, 2015) (CAT) were detected.

Postprandial hyperglycemia is a predisposing factor to vascular dysfunction and organ damage. α-glucosidase is a hydrolytic enzyme that increases the rate of glucose uptake and thus raises blood glucose levels. Garlic (Allium sativum L.) is a rich source of many phytonutrients, including thiosulfinate (THIO). The aim of this study was to evaluate the ability of THIO, a potent inhibitor of intestinal αglucosidase, to reduce postprandial blood glucose. Male albino rats were randomly divided into five different groups (/group). Group 1 served as the control group. Groups 2–5 were injected intraperitoneally with a single dose of streptozotocin (STZ) to induce diabetes. Group 2 consisted of untreated diabetic mice. Groups 3 and 4 contained diabetic rats that were given THIO orally (20 mg/kg bw/day and 40 mg/kg bw/day, respectively). Group 5 was the positive control group in which diabetic rats were treated orally with acarbose (10 mg/kg bw/day; positive control). Diabetic rats treated with THIO showed significantly lower blood glucose (and <0.01 by analysis of variance, respectively) and significantly higher insulin levels compared to untreated rats. THIO is a potent, non-competitive intestinal αglucosidase inhibitor that enhances hypoglycemic ( ) action in STZ-injected rats. THIO is a promising agent for the management of postprandial hyperglycemia

(Al-Malki, 2016). (2016 Ginpreet et al ,2016) combinatorial with piperine and quercetin (CPQ) in streptozotocin and nicotinamide-induced diabetic rats. Diabetes mellitus was induced with single intraperitoneal injections of streptozotocin (55 mg/kg) and nicotinamide (120 mg/kg-1). CPQ was given orally at a dose of 100 mg/kg/day for 28 days. At the end of 28 days, blood was analyzed for glucose, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and total cholesterol level. An oral glucose tolerance test (OGTT) was also performed at the end of 28 days. In hepatotoxicity induced in rats by two injections of thioacetamide (TAA, 350 mg/kg at an interval of 8 hours), the effect of quercetin was investigated. After 96 hours, TAA administration resulted in hepatic necrosis, a significant increase in serum transaminase activity, and an increase in hepatic lipid oxidation. Thioacetamide-induced hepatotoxicity also showed alterations of antioxidant enzymes in rat livers, with alterations in p-ERK 1/2 (extracellular phosphorylation signaling-related kinase 1/2) as well as an imbalance between the proapoptotic protein Bax and the anti-apoptotic protein Bcl-expression. 2. With the administration of the flavonoid quercetin (50 mg/kg i.p.) for four consecutive days after TAA, serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) activity were close to normal values in rats. Histological results indicate that quercetin had a protective effect on TAA-induced hepatic necrosis. Quercetin treatment caused a significant decrease in lipid peroxidation levels in TAA-treated mice, with some changes in the antioxidant enzymes superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx). to forbid Quercetin also altered p-ERK1/2 by TAA and significantly prevented the increase in the Bax/Bcl-2 ratio, thus preventing apoptosis. The results indicate that quercetin may have a protective effect on TAA-induced hepatotoxicity by modulating oxidative stress parameters and the apoptosis pathway (Cintia et al, 2011) .

The aim of the study (Irina et al, 2021) was to investigate the antioxidant effect of long-term consumption of an ethanolic yellow onion peel extract in long-lived laboratory rodents; Twenty male albino Wistar rats were randomly divided into two groups (n = 10): a control group and an

experimental group that received ethanolic yellow onion peel extract (2 ml/rat diluted with distilled water; activity of 4.44 µl eq. quercetin) for 188 days. Oxygen radical uptake capacity and iron reduction antioxidant capacity assays were used to determine the total antioxidant capacity of the extract, which was 941.4 ± 32.7 µmol eq. trolox/g raw material and 167.4 ± 16.4 µm eq. quercetin/g raw material, respectively. Oral administration of onion peel extract affected indices of the antioxidant system in the liver and brain but not in blood and plasma, mainly due to elevations in catalase and superoxide activity in the liver by 44.4% and 79.1%, respectively, and in the brain by threefold and 79.1%. % respectively ; The availability, cheapness, and high antioxidant potential of onion waste qualify it as a good source of functional ingredients and bioactive materials applicable in the food and pharmaceutical industries. As the presence and multiplicity of effective compounds that God Almighty placed in one plant make it a medicinal plant with the ability as an antimicrobial to resist diseases and increase immunity (Ali, 2021)

Based on the data collected by (Amin et al, 2021), it was concluded that onions can be beneficial in the prevention and treatment of dyslipidemia, hypertension, diabetes, and obesity such as metabolic syndrome disorders and thus cardiovascular diseases due to its antioxidants and anti-inflammatories. , vasodilating properties, increasing insulin secretion and response, reducing cholesterol and glucose absorption, modulating fat and carbohydrate metabolism, and inhibiting lipogenesis. These effects are mainly attributed to the ability to control associated signaling pathways, transcription factors, gene expression, and the activities of enzymes and receptors. Additional clinical investigations with sufficient population size and duration are needed to establish the efficacy and safety of A. cepa, especially in the case of potential interaction with conventional medicines.

The cholesterol-lowering effect of onion peel extract was explored in mice fed a high-cholesterol diet for 12 weeks. The results showed that the oral injection of

100 and 200 mg/kg of the extract improved TG and TC contents, liver weight, cardiac risk factor (TC/HDL-C), and arterial stiffness index ((TC-HDL-C)/HDL- C) as well as plasma TC and LDL-C. Possible mechanisms may be up-regulation of LDL receptors (LDL-R) and cholesterol 7 alpha-hydroxylase (CYP7A1) and, as a result, improved elimination of cholesterol in the stool. Red onion extract and quercetin could produce enhanced effects on paraoxonase 1 (PON1) activity, and scavenging free radicals, LDL oxidation, and lipid peroxidation against HgCl2induced oxidative stress in mice.Prolonged administration of quercetin contributes to the regulation of fatty acid utilization in the lung of mice as target tissue.Receiving 500 mg/kg/day of flavonoids for 41 weeks led to an elevation in Expression of genes related to fatty acid catabolism such as LPL (lipoprotein lipase) and ACOX1 (acyl coenzyme A oxidase 1).This effect was supported by a reduction in serum free fatty acid concentration.Addition of cycloline to the diet resulted in atherosclerosis in rats at doses 0.1% and 0.3% for 14 days decreased serum TG levels (about 40%) while there were no significant changes in TC, HDLC, weight, liver fat content, and lipogenic enzyme activities.Another study revealed that SMCS for It has hypolipidemic activities in Sprague-Dawley rats fed a cholesterol-rich diet which is comparable to 50 mg/kg/day) as a natural lipidlowering drug derived from the Commiphora mukul tree. SMCS 200 mg/kg/day, gavage for 45 days)

significantly reduced the activities of total LPL in adipose tissue and hepatic malic enzyme, serum and tissue levels of free fatty acids, TG, cholesterol, and phospholipids but significantly increased liver glycogen and fecal excretion. of bile acids and neutral sterols when compared to the control group. In a recent study, the protective ability of A. cepa against non-alcoholic fatty liver disease (NAFLD) was demonstrated in the presence of risk factors. Receiving 7% onion powder reversed the elevation in hepatic tumor necrosis factor-α (TNF-α) gene expression and plasma levels of alanine transaminase (ALT), aspartate transaminase (AST), glucose, insulin, and TG in lipid- and sugar- rich diet rats; While the increase in food consumed, body weight, gamma-glutamyl transferase, alkaline phosphatase (ALP), cholesterol and LDL-C did not change significantly after 7 weeks of intervention. Liver tissue analysis showed significant improvement in lobular inflammation and pap, hepatic steatosis, and distensible degeneration. A previous investigation showed that eating onions alone is not sufficient to treat non-alcoholic fatty liver disease, but in combination with a healthy dietary pattern has therapeutic potential (Amin, 2021)

Conclusions:

It can be concluded from this research that quercetin nanoparticles extracted from red onion peels led to a significant increase in the level of cholesterol, triglycerides, low-density lipoproteins and very low-density lipoproteins, the positive control group compared with the negative control group (non-diabetic) and the rest of the treated groups. With the commercial and nano-quarcetin extract, while there was a significant increase in the level of high-density lipoproteins in the groups treated with the commercial and nano-quarcetin compared with the positive control.

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