The Efficacy Effect of Jackfruit (*Artocarpus Heterophyllus Lam*.) on Some Biochemical Parameters in Obese Male Rats with Atherosclerosis

Hoda S. Ibrahim, Amr A. Rezq, Alaa O. Aboraya and Salwa S. Hafez
Nutrition and Food Science Dept., Faculty of Home Economics, Helwan University, Cairo, Egypt

Abstract

Cardiovascular diseases are still the leading cause of morbidity and mortality worldwide caused by fatal angina. The underlying pathological mechanism of atherosclerosis is a narrowing of the arteries caused by a buildup of plaque, leading to insufficient blood flow to vital organs, mainly the heart and the brain. The present study was conducted to find out the effectiveness the pulp, peels, seeds, and leaves of Jackfruit (*Artocarpus Heterophyllus Lam*.) on body weight changes and total visceral fat weight as well as some of biochemical parameters in obese rats with atherosclerosis. The experiment was conducted in two stages, each of 6 weeks. The objective of the first stage was to induce obesity and atherosclerosis in rats, while the second stage was to treat obese rats with atherosclerosis by feeding on the supplemented diet with 5 and 10% pulp, 5 and 7.5% peels, 5 and 7.5 % seeds and 5 and 7.5 % leaves of the jackfruits. The results, revealed that, the reduction in FBW, BWG VFW (g) and AI% as well lipid profile and increased activities of antioxidant enzymes (CAT, GPx and SOD) were significantly ameliorated with increasing levels of the jackfruit pulp, peels, seeds and leaves. The optimum results regarding to weight loss were in rats with obesity and atherosclerosis fed on the supplemented-HFCD with jackfruit peels and leaves compared to that fed on the HFCD with pulp or seeds. Generally, the ability of jackfruit pulp, peels, seeds and leaves to enhance the activity of anti-obesity and inhibit Atherogenic index as well the improvement of liver function and activities of antioxidant enzymes makes it a promising natural compound for the management of obesity and hyperlipidemia. However, more research is needed to fully understand the mechanisms of action and potential benefits of jackfruit pulp, peels, seeds and leaves in obesity and hyperlipidemia management.

Keywords: Jackfruit; Obesity; Cardiovascular diseases; hyperlipidemia

INTRODUCTION

Cardiovascular diseases (CVD) are still the leading cause of morbidity and mortality worldwide **(McNamara *et al.*, 2019).** The mortality rate of this disease is higher caused by fatal angina that occur due to not be able approach right diagnosis and its timely **(Lopshire and Zipes, 2006)**. The underlying pathological mechanism of atherosclerosis is a narrowing of the arteries caused by a buildup of plaque, leading to insufficient blood flow to vital organs, mainly the heart and the brain **(Linton *et al.*, 2019).**

Atherosclerosis already begins in childhood **(McGill *et al*., 2000)** or it may begin early in life if maternal hypercholesterolemia during pregnancy is often associated with fetus due to which deposition of fatty streaks is started in neonatal's coronary arteries **(Milei *et al*., 2008).** Additionally, studies have shown earlier occurrence of CVD in adults who had cardiovascular risk factors present as children **(Raghuveer, 2010),** so it is important to procedure a comprehensive lipid status evaluation. A well-known risk factor of atherosclerosis in humans is hypercholesterolemia, i.e., elevated total cholesterol (TC) and low-density lipoprotein cholesterol (LDLc) **(Pearson *et al*., 2002)** and other important contributors to this disease include inflammation, oxidative stress and insulin resistance **(Van Gaal *et al*., 2006).**

Moraceae family is well known as mulberry family and representing 37 genera and around 1050 species **(Sá *et al.*, 2020).** Artocarpus genus, a genus belonging to the Moraceae family, comprehends 50 species found in tropic and subtropic Asia regions (**Xu *et al.*, 2019**). Many of these types are used as a source of food and in traditional medicinal practices. Artocarpus species are known for its large edible fruit with high nutritive values **(Nayak *et al*., 2017).**

Jackfruit (*Artocarpus heterophyllus Lam*.) is part of the Moraceae family. It is native to India and also grows in other tropical and subtropical climates around the world. It is oval-shaped and spiny, but its most distinguishing feature is its mass, typically 10–30 kg **(Haque *et al*., 2015),** which is considered the world largest fruit (**Peng *et al*., 2013**). The pulp is golden-yellow and is arranged in fleshy bulbs (30–35% of the fruit's weight), each containing a single seed **(Swami *et al*., 2014).**

Jackfruit crops are economically important for most countries that cultivate them. Jackfruit can be consumed fresh as an ingredient in salads, or processed into fruit bars, cakes, jams, ice cream, chutney, jellies, juices, nectars, and

fermented beverages among others **(Fernandes *et a*l., 2011).** Various parts of the tree such as seeds, leaves, latex, and roots have been used as traditional medicines. Jackfruit bulbs are edible, and can be described as slightly acidic, creamy, smooth, fibrous, sweet, and highly fragrant, like other tropical fruits like banana or pineapple **(Prakash *et al*., 2009).** Jackfruit is a rich source of phenolics and flavonoids having good antioxidant properties. It contains many classes of phytochemicals such as carotenoids, flavonoids, volatile acids sterols, and tannins, with varying concentrations **(Jagtap *et al*., 2010).** In addition, Jackfruit pulp is rich in carbohydrates, protein, amino acid, polyphenol, fatty acid, vitamin, and minerals, which can be used as good sources for some important nutrients **(Shafiq *et al*., 2017 and Zhang *et al.*, 2017).** The seeds are also rich source of carbohydrates and proteins and good source of fiber and vitamins, also they contain β-carotene, α-carotene and jacalin is the major protein representing over 50% in seed and capable of binding to human IgA and T-Antigen **(Vazhacharickal *et al*., 2015).**

The plant flavonoids with anti-atherosclerotic activity gained much attention and were proven to reduce the risk of cardiovascular diseases such as atherosclerosis in a large number of fundamental and clinical studies **(Shen *et al*., 2014).** Therefore, the present study was conducted to investigate the possible treatment effects of the pulp, peels, seeds, and leaves of Jackfruit (*Artocarpus Heterophyllus Lam*.) on obese rats with atherosclerosis.

MATERIALS AND METHODS

Materials:

Jackfruit and its Leaves: Fresh mature Jackfruit (*Artocarpus Heterophyllus Lam*.) and its leaves were collected in August, 2021, from El Zohriya garden, Horticultural Research Institute, Agricultural Research Center, Giza, Egypt. The fruits were taxonomically at Orman Botanical Garden and National Gene Bank, Ministry of Agriculture, Doki, Egypt.

Rats: Fifty **male adult rats (Sprague Dawley Strain), weighing about 180 ± 5 g were obtained from** the experimental animal house of the Food Technology Research Institute, Agriculture Research Center, Giza, Egypt.

Constituents of Basal and High Fat-Cholesterol Diets: Basal diet constituents were purchased from the El-Gomhorya Company for Pharmaceutical and Chemical, Cairo, Egypt. Corn starch and Dextrin were obtained from Egyptian Starch and Glucose Manufacturing Co., Mostorod, Cairo, Egypt. Soybean oil and sucrose were obtained from the Egyptian local market. Cholesterol, bile acid and cholic acid were purchased from Morgan Co., for chemicals, Cairo, Egypt, while beef tallow was obtained from the local Butcher market.

Chemicals and Kits: All chemicals used in the experimental study and Kits used for the biochemical determination of the different parameters were purchased from Biodiagnostic Co. Dokki, Giza, Egypt.

Methods:

Preparation of Jackfruit Pulp, Peels, Seeds and Leaves: Whole Jackfruits and its leaves were washed under running tap water and dried with clean towels. Then, fruits were cut into two portions, and fleshy part and seeds were separated from the peel. After that, pulp, peel, seeds, and leaves were dried separately by hybrid solar drying system at the Solar Energy dept., National Research Center, Dokki, Egypt. The obtained dried portions of pulp, peel, seeds, and leaves were ground into fine powder and stored in airtight plastic bags at ambient temperature (21 to 27◦C) until used.

Preparation of The Basal and High Fat-Cholesterol Diets: The basal diet has been formulated as described by **Reeves *et al.* (1993)**. It consists of protein (casein; 20 %), carbohydrate (10 %), choline chloride (2%), fat (Soybean oil; 5%), mixed vitamins (1%), mixed salts (3.5%), and fiber (5%). The rest represents the corn starch that accounted for about 54 % of the diet.

High fat-cholesterol diet (HFCD) was used for the induction of obesity and atherosclerosis in rats, according to **Zulet *et al*. (1999)**. It was consisted of basal diet supplied with 15% beef tallow,1% cholesterol, 0.25% bile acid and 0.5% cholic acid.

Experimental Design and Grouping of Rats: All rats were housed at a room temperature of 25 ± 2 °C, relative humidity of 50–55% and light/dark cycles (12/12) in the animal house of the Faculty of Home Economics, Cairo, Egypt for one week for acclimatization. After an acclimatization period, the experiment was conducted in two stages, each of 6 weeks. In the first stage (induction of

obesity and atherosclerosis), rats were divided into two main groups; Group (1), the healthy control group (5 rats) was fed on the normal basal diet only, and the second main group (45 rats) was fed on HFCD. While, in the second stage, obese rats were divided into 9 groups (each of 5 rats) as follows:

Group (2): Untreated obese rats with atherosclerosis were fed on the HFCD during the experimental period and kept as positive control group (+ve).

Group (3): Treated obese rats with atherosclerosis were fed on the supplemented HFCD with 5% jackfruit pulp (JFP) powder during the experimental period

Group (4): Treated obese rats with atherosclerosis were fed on the supplemented HFCD with 10 % JFP powder during the experimental period

Group (5): Treated obese rats with atherosclerosis were fed on the supplemented HFCD with 5 % jackfruit peels powder (JFPs) during the experimental period

Group (6): Treated obese rats with atherosclerosis were fed on the supplemented HFCD with 7.5% JFPs during the experimental period

Group (7): Treated obese rats with atherosclerosis were fed on the supplemented HFCD with 5 % jackfruit seeds (JFS) powder during the experimental period

Group (8): Treated obese rats with atherosclerosis were fed on the supplemented HFCD with 7.5 % JFS powder during the experimental period

Group (9): Treated obese rats with atherosclerosis were fed on the supplemented HFCD with 5 % jackfruit leaves (JFLs) powder during the experimental period.

Group (10): Treated obese rats with atherosclerosis were fed on the supplemented HFCD with 7.5 % JFL powder during the experimental period.

Determination of Feed Intake, Body Weight Gain and Percent Change in Body Weight Gain: Feed intake (FI) was calculated every day during the second stage of the experimental period. The changes in body weight were determined by weighing the animals on a balance scale prior to the second stage

of the experiment (IBW) and at the end of the experimental period (FBW). The biological value of the diet was assessed by the determination of its effect on body weight gain (BWG) and the percent change of body weight gain was calculated using the following formula:

BWG = Final Body Weight - Initial Body Weight

Change of body weight gain %= BWG/IBW X 100

Determination of Visceral Fat Weight and Adiposity index: Visceral fat weight (g) and adiposity index were determined as described by **Taylor and Phillips (1996)** using the following formulas:

Visceral Fat Weight (g) = epididymis fat + retroperitoneal fat + abdominal fat

Adiposity index % = total pad fat weights/ final body weight X 100

Biochemical Assay: At the end of the experimental period, all rats were sacrificed under anesthesia after an overnight fast (12 hrs). Blood samples were collected in dry clean centrifuge tubes via heart puncture. The collected blood samples were separated by centrifugation at 3000 r.p.m for 15 min for serum separation. Then serum samples were carefully aspired using a needle and transfers into dry clean test tubes and frozen at -20°C for biochemical analysis., and kept in plastic vials well stoppered and stored at -20°C until used for biochemical analysis.

Determination of Serum Lipid Profile: Serum levels of total cholesterol (TC), triglycerides (TG), total lipids (TL), low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C) were estimated were estimated using commercial reagent kits (Biomed diagnostic, Egypt) as described by **Zöllner kirsch (1962), Vassault *et al*. (1986), Hostmark *et al.*, (1991), Friedewald *et al.* (1972) and Young (2001),** respectively. While, very low-density lipoprotein cholesterol (VLDL-C) was calculated using Friedewald's formula:

VLDL-C (mg/ dL) = TG/5

Atherogenic Index Assay: Atherogenic Index (AtI) was calculated using the following equations as described by **Dobiášová and Frohlich (2001)** formula: Log (TG/HDL-C)

Determination of LDH and Leptin Hormone Levels: The activity of lactate dehydrogenase (LDH) in serum was measured by the method of **Horecker and Kornberg (1948)**. Reaction mixture (3 ml) contained 0.2 M Tris–HCl buffer, pH 7.4, 0.1 M KCl, 50 mM sodium pyruvate, 2.4 mM NADH and suitably diluted enzyme. The enzyme activity was monitored as decrease in the absorbance at 340 nm for 3 min. The enzyme activity was expressed as M moles of NADH oxidized min−1 mg protein−1.

Serum level of leptin hormone was determined using Enzyme-linked immunosorbent assays (ELISA) as described by **Xiong *et al.* (2010)**.

Determination of Liver Functions: Serum AST, ALT activities were assayed colorimetric as described by **Bergmeyer *et al.* (1978)** using (Diamond Co, Hannover, Germany) kits. Serum alkaline phosphatase (ALP) was determined according to the method described by **Roy (1970).**

Determination of Serum Malondialdehyde (MDA): Malondialdehyde (MDA) as oxidative stress marker indicator was assayed quantitatively in serum using the MDA assay kit by a spectrophotometric method (ABCAM, UK). The MDA in the sample reacts with thiobarbituric acid (TBA) to generate an MDA-TBA adduct. The MDA-TBA adduct is quantified colorimetrically (OD = 532 nm). This assay detects MDA levels as low as 1 nmol/well colorimetrically **Draper and Hadley (1990)**.

Determination of Serum Activities of Antioxidant Enzymes:

Glutathione Peroxidase Assay: Activity glutathione peroxidase enzyme was assayed quantitatively in serum using the GPx assay kit (by a spectrophotometric method, BioAssay Systems, USA) according to the method of **Hissin and Hilf (1976).**

Superoxide Dismutase Assay: Serum activity of superoxide dismutase was assayed quantitatively in serum using the SOD assay kit (by a spectrophotometric method BioAssay Systems, USA) as described by **Kakkar *et al.* (1984).** In the assay, superoxide (O-) is 2 provided by xanthine oxidase (XO) catalyzed reaction. 2 O- reacts with a WST-1 dye to form a colored product. SOD scavenges the O2- thus less O- is available for the 2 chromogenic reaction. The color intensity (OD = 440nm) is used to determine the SOD activity in a sample. The results were expressed in U SOD/ml.

Catalase Assay: Serum activity of catalase was assayed quantitatively using the catalase assay kit (by a spectrophotometric method, Bio-Assay Systems, USA) according to method of **Sinha (1972),** measuring catalase degradation of H O was using a redox dye. The change 2 2 in color intensity at 570nm is directly proportional to the catalase activity in the sample. The procedure involves adding a Substrate to sample, incubation for 30 min, followed by a Detection Reagent and reading the optical density. The results were expressed in U Catalase/Liter. Unit definition: one unit is the amount of catalase that decomposes 1 µmole of H O per min at pH 7.0 and room 2 2 temperature.

Statistical analysis: Data was evaluated statistically using computerized SPSS package program (SPSS 22.00 software for Windows) by one-way analysis of variance (ANOVA). The obtained data was expressed as Mean ± SD and the significant difference among means was estimated at $p<0.05$ **(Snedecor and Cochran, 1980).**

RESULTS

Feed Intake, Body Weight Gain and Percent Change in Body Weight Gain: The present results in Table 1 discovers the effect of supplemented HFCD with the pulp, peels, seeds and leaves of jackfruit on FI, FBW, BWG and % change of BWG in obese rats with atherosclerosis. The results indicated that rats with obesity and atherosclerosis (positive rats) have a significant ($P<0.05$) decrease in food intake (FI) compared to that of normal rats. Whereas, the supplemented HFCD with 5 and 10% jackfruit pulp, 5% jackfruit peels or seeds caused no significant changes in FI, while the levels of 7.5% jackfruit peels or seeds, and 5 and 7.5% jackfruit leaves significantly decreased FI, compared to that of the positive rats.

Concerning the alteration in body weight, the tabulated results show that untreated rats with obesity and atherosclerosis possess a significant ($P<0.05$) increase in FBW, BWG and % change BWG, compared to that of the rats fed on the normal basal diet. While, included, the accompanied HFCD with jackfruit pulp, peels and leaves at the different levels resulted significantly decreasing ($P<0.05$) in FBW, BWG and BWG%, compared to rats with obesity and atherosclerosis feed on HFCD only. The reduction in FI, FBW, BWG and % change in BWG was significantly ameliorated with increasing levels of the jackfruit pulp, peels and leaves. As well, the optimum results at the rate of

weight loss were in rats with obesity and atherosclerosis feed on the supplemented HFCD with jackfruit peels and leaves compared to that feed HFCD with pulp or seeds.

Visceral Fat Weight and Adiposity Index: Table 2 represents the effect of jackfruit pulp, peels, seeds and leaves on visceral fat weight (VFW) and adiposity index (AI) on rats with obesity and atherosclerosis. The obtained results demonstrated that untreated rats with obesity and atherosclerosis have a significant ($P<0.05$) increase in VFW (g) and AI, compared to that of the normal rats. While, rats with obesity and atherosclerosis fed on the supplemented HFCD with the two different levels of jackfruit pulp, peels, seeds or leaves have a significant ($P<0.05$) decrease in VFW (g) and AI, compared to the rats with obesity and atherosclerosis fed on HFCD only. The reduction in VFW and AI was significantly ameliorated with increasing levels of the jackfruit pulp, peels and leaves.

Serum Lipid Profile and Atherogenic Index: In the case of the serum lipid profile, the parameters of serum TC, TG, TL, LDL-c, HDL-c, and VLDL-c levels were used to check the effect of jackfruit pulp, peels, seeds or leaves on obese rats with atherosclerosis. The results in Table 3 shows that obese rats fed on HFCD have a significant ($P<0.05$) increase in the serum concentrations of TC, TG, TL, LDL-c and VLDL-c levels, and a decrease in HDL-c levels, compared to that of the normal rats fed on normal basal diet. In contrast, the addition of the different levels of pulp, peels, seeds or leaves of jackfruit caused significant amendments in the serum levels of the above parameters, as compared to that caused by the HFCD alone in obese rats.

As shown in Figure 1, mean± SD value of Atherogenic index (AtI) of the positive control group fed on HFCD was increased significantly ($p< 0.05$) compared to that of the healthy group fed on the basal diet. On the other hand, obese rats with atherosclerosis fed on the supplemented HFCD with the different levels of the jackfruit pulp, peels, seeds, or leaves have a significant decrease in AtI values, compared with that of the positive group.

The rate of improvement in the serum levels of the above parameters and AtI were more evident with increasing the levels of the pulp, peels, seeds, or leaves of jackfruit, especially the fed on the supplemented diet with jackfruit leaves.

Table (1): The Effect of Supplemented HFCD with Jackfruit Pulp, Peels, Seeds and Leaves on FI, IBW, BWG and FER in Rats with Obesity and Atherosclerosis.

Groups \ Parameters		Parameters as Mean ± SD				
		FI (g)	IBW (g)	FBW (g)	BWG (g)	% change of BWG
Negative group		14.80±0.84^{a}	362.40±2.51^{a}	313.40±3.21^{f}	51.80±3.81^{b}	19.44±1.56^{b}
Positive group		12.50±0.50^{c}	323.80±2.77^{b}	404.60±2.70^{a}	80.80±1.30^{a}	24.96±0.51^{a}
Obese rats with atherosclerosis fed on the supplemented HFCD with Jackfruit…	**Pulp at level of**					
	- 5%	12.50±0.50^{c}	322.80±2.17^{b}	365.40±1.51^{b}	42.60±1.67^{c}	13.20±0.60^{c}
	- 10%	12.00±0.71^{c}	323.40±1.82^{b}	358.20±1.92^{c}	34.80±2.05^{d}	10.78±0.67^{d}
	Peels at level of					
	- 5%	11.0±0.71^{cd}	324.20±1.30^{b}	357.00±2.12^{c}	32.80±1.48^{de}	10.12±0.45^{de}
	- 7.5%	10.80±0.57^{d}	323.00±2.12^{b}	335.00±1.71^{e}	11.00±1.41^{f}	3.58±0.28^{f}
	Seeds at level of					
	- 5%	11.7±0.67^{bc}	323.2±2.11^{b}	359.20±2.59^{c}	36.00±2.85^{d}	11.15±1.60^{d}
	- 7.5%	10.80±0.27^{d}	322.6±2.51^{b}	352.40±2.51^{d}	29.80±3.96^{e}	9.24±1.29^{e}
	Leaves at level of					
	- 5%	10.30±0.45^{d}	322.6±1.82^{b}	356.80±2.05^{c}	34.20±2.59^{d}	10.61±0.84^{d}
	- 7.5%	10.40±0.42^{d}	324.6±2.70^{b}	334.20±2.59^{e}	9.60±2.89^{f}	2.96±0.29^{f}

Values expressed as means ± SD; Means with different letters in each column are significantly differs at $p< 0.05$. Values expressed as means ± SD; **HFCD:** High Fat-cholesterol Diet; **FI**: Food Intake; **IBW**: Initial Body Weight; **FBW**: Final Body Weight; **BWG**: Body Weight Gain.

Table (2): The Effect of Supplemented HFCD with Jackfruit Pulp, Peels, Seeds and Leaves on VFW and AI in Rats with Obesity and Atherosclerosis.

Parameters / Groups		VFW (g)	AI (%)
Normal rats		8.90±0.42^{e}	2.75±0.13^{d}
Positive rats		15.80±0.27^{a}	3.85±0.15^{a}
Obese rats with atherosclerosis fed on the HFCD with supplemented Jackfruit…	**Pulp at level of**		
	- 5%	11.80±0.57^{b}	3.23±0.16^{b}
	- 10%	9.90±0.42^{d}	2.76±0.12^{d}
	Peels at level of		
	- 5%	10.70±0.27^{c}	2.92±0.06^{c}
	- 7.5%	8.80±0.27^{e}	2.59±0.09^{e}
	Seeds at level of		
	- 5%	9.60±0.42^{d}	2.68±0.13^{de}
	- 7.5%	9.60±0.22^{d}	2.73±0.07^{de}
	Leaves at level of		
	- 5%	9.80±0.27^{d}	2.75±0.08^{de}
	- 7.5%	8.70±0.27^{e}	2.82±0.091^{de}

Values expressed as means ± SD; Means with different letters in each column are significantly differs at p< 0.05. Values expressed as means ± SD; **VFW:** Visceral fat Weight**; AI=** Adiposity Index; **HFCD:** High Fat-cholesterol Diet**.**

Table (3): The Effect of Supplemented HFC-Diet with Jackfruit Pulp, Peels, Seeds and Leaves on TC, TG, TL, LDL-c, HDL-c and VLDL-c in Rats with Obesity and Atherosclerosis.

Parameters / Groups		Parameters as Mean ± SD					
		TC (mg/dl)	TG (mg/dl)	TL (mg/dl)	LDL-c (mg/dl)	HDL-c (mg/dl)	VLDL-c (mg/dl)
Negative group		113.8±2.77^{e}	71.8±2.49^{e}	323.4±2.3^{f}	63.4±1.52^{f}	47.0±2.12^{bc}	14.36±0.50^{e}
Positive group		243.4±2.07^{a}	105.8±1.1^{a}	583.2±3.11^{a}	183.0±2.12^{a}	32.4±2.51^{f}	21.16±0.22^{a}
Obese rats with atherosclerosis fed on the supplemented HFCD with Jackfruit.	**Pulp at level of - 5%**	183.2±2.05^{b}	96.6±1.52^{b}	451.0±1.41^{b}	147.2±1.92^{b}	36.8±2.05^{e}	19.32±0.30^{b}
	- 10%	136.8±1.79^{cd}	88.2±2.95^{c}	418.4±2.30^{c}	113.8±1.64^{d}	41.8±1.64^{d}	17.64±0.59^{c}
	Peels at level of - 5%	135.0±2.00^{cd}	87.6±2.51^{c}	332.0±2.74^{e}	65.8±3.59 ^{f}	47.2±1.48^{bc}	17.52±0.50^{c}
	- 7.5%	134.4±0.89^{cd}	81.4±2.19^{d}	325.6±2.61^{f}	65.6±2.61^{f}	50.2±1.79^{a}	16.28±0.44^{d}
	Seeds at level of - 5%	137.4±2.51^{c}	88.2±2.95^{c}	419.0±3.08^{c}	122.2±2.17^{c}	40.2±1.79^{d}	17.64±0.59^{c}
	- 7.5%	134.0±2.24^{d}	86.4±4.72^{c}	403.2±2.05^{d}	113.8±2.77^{d}	45.2±1.10^{c}	17.28±0.94^{c}
	Leaves at level of - 5%	134.0±2.65^{d}	88.2±2.95^{c}	333.6±2.19^{e}	101.8±2.05^{e}	42.2±2.17^{d}	17.64±0.59^{c}
	- 7.5%	115.8±2.95^{e}	72.4±2.51^{e}	325.8±1.10^{f}	63.0±2.74^{f}	49.0±1.00^{ab}	14.48±0.50^{e}

Values expressed as means ± SD; Means with different letters in each column are significantly differs at $p< 0.05$. Values expressed as means ± SD; **HFCD:** High Fat-cholesterol Diet; **TC:** Total cholesterol; **TG:** Triglyceride; **TL:** Total Lipid; **HDL-c:** High Density Lipoproteins Cholesterol; **LDL-c:** Low Density Lipoproteins Cholesterol; **VLDL-c:** Very Low Density Lipoproteins Cholesterol

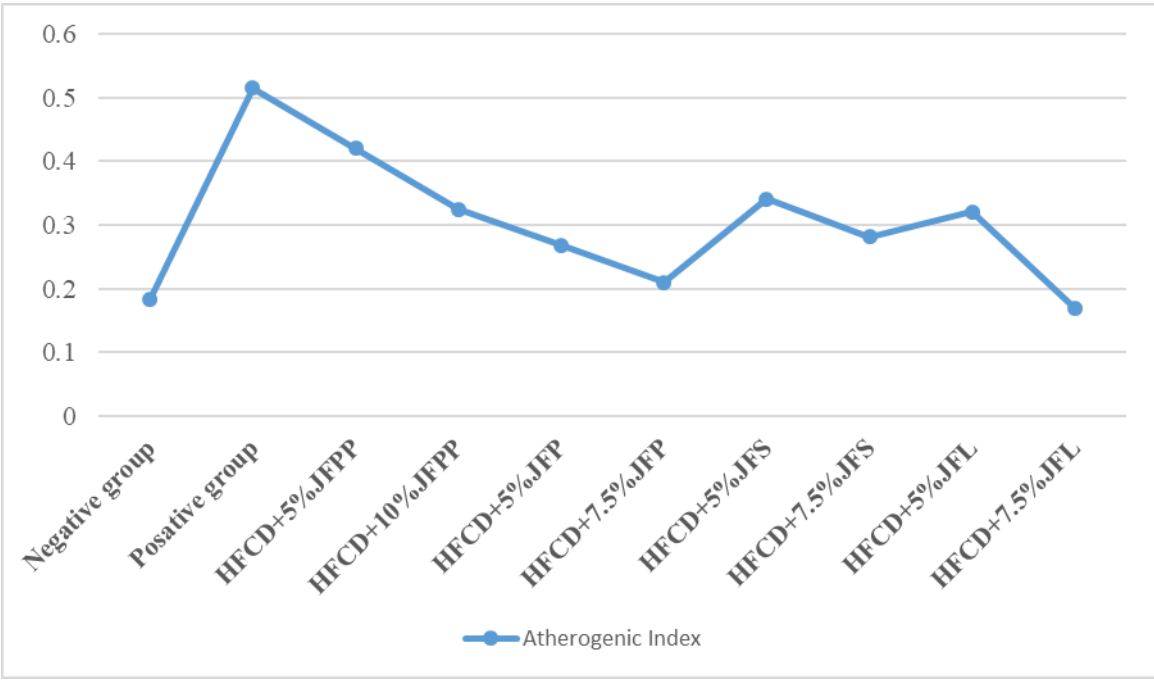

Figure 1: The Effect of Supplemented HFCD with Jackfruit Pulp, Peels, Seeds and Leaves on Atherogenic index (AtI) in Rats with Obesity and Atherosclerosis.

Serum Levels of LDH and Leptin Hormones: The present results in Table 4 demonstrate the effect of a supplemented HFCD with jackfruit pulp, peels, seeds, and leaves on lactate dehydrogenase (LDH) and leptin hormone levels in rats with obesity and atherosclerosis. The data proved that HFCD caused significant ($P<0.05$) increased serum levels of LDH and leptin hormones in untreated rats with obesity and atherosclerosis, compared to that resulting from the normal basal diet in normal rats.

In contrast, the supplemented HFCD with the two different levels of Jackfruit pulp, peels, seeds, or leaves caused a significant ($P<005$) decrease in serum levels of LDH and leptin hormones, compared to that induced by the HFCD only in rats with obesity and atherosclerosis.

The lowering in serum levels of LDH and leptin hormones of rats with obesity and atherosclerosis was significantly enhanced by increasing the levels of the jackfruit pulp, peels, seeds, or leaves. While, the superior results were in

rats fed on the supplemented HFCD with jackfruit leaves compared to that feed HFCD with pulp, peels, or seeds.

Table (4): The Effect of Supplemented HFCD with Jackfruit Pulp, Peels, Seeds or Leaves on LDH and Leptin Hormones Levels in Rats with Obesity and Atherosclerosis.

Parameters / Groups		Parameters as Mean ± SD	
		LDH (mmol/L)	Leptin (mmol/L)
Normal rats		36.00±1.00^{d}	3.90±0.42^{d}
Positive rats		77.60±1.67^{a}	7.60±0.65^{a}
Obese rats with atherosclerosis fed on the supplemented HFCD with Jackfruit.	**Pulp at level of**		
	- 5%	60.80±0.84^{b}	6.70±0.27^{b}
	- 10%	45.00±0.71^{c}	4.70±0.57^{c}
	Peels at level of		
	- 5%	60.40±0.89^{b}	6.40±0.22^{b}
	- 7.5%	44.60±0.55^{c}	4.40±0.42^{cd}
	Seeds at level of		
	- 5%	60.20±1.09^{b}	6.50±0.35^{b}
	- 7.5%	44.80±0.84^{c}	4.70±0.57^{c}
	Leaves at level of		
	- 5%	43.60±1.14^{c}	6.40±0.22^{b}
	- 7.5%	36.40±1.34^{d}	4.40±0.42^{cd}

Values expressed as means ± SD; Means with different letters in each column are significantly differs at p< 0.05. Values expressed as means ± SD; **HFCD:** High Fat-cholesterol Diet**; LDH:** Lactate Dehydrogenase.

Liver Functions: The current results in Table 5 illustrate the effect of supplemented HFCD with jackfruit pulp, peels, seeds or leaves on the serum activities of AST, ALT and ALP enzymes in rats with obesity and atherosclerosis. It demonstrated that HFCD caused a significant raise in the serum activities of AST, ALT, and ALP enzymes in rats with obesity and atherosclerosis, compared to that resulting by normal basal diet in normal rats.

In comparison, rats with obesity and atherosclerosis fed on the supplemented HFCD with the different levels of jackfruit pulp, peels, seeds or leaves have significant decreases (P<0.05) in the serum activities of AST, ALT, and ALP enzymes, compared to that of untreated rats with obesity and atherosclerosis (positive rats). In addition, the higher level of the jackfruit pulp, peels, seeds, or

leaves (10, 7.5, 7.5, and 7.5%, respectively) significantly lowered serum activities of AST, ALT, and ALP as compared to that of the other levels (5%). The most favorable results were in rats fed on the supplemented HFCD with jackfruit peels and leaves compared to that fed HFCD with pulp or seeds.

Table (5): The Effect of Supplemented HFCD with Jackfruit Pulp, Peels, Seeds and Leaves on The Serum Activities of AST, ALT and ALP Enzymes in Rats with Obesity and Atherosclerosis.

Parameters / Groups		Parameters as Mean ± SD		
		AST (U/ml)	**ALT (U/ml)**	**ALP (U/ml)**
Normal rats		20.20±0.84^{e}	24.80±0.84^{e}	59.60±1.67^{e}
Positive rats		35.20±1.30^{a}	40.60±1.14^{a}	103.80±1.30^{a}
Obese rats with atherosclerosis fed on the supplemented HFCD with Jackfruit.	**Pulp at level of**			
	- 5%	29.90±1.48^{b}	34.20±0.84^{b}	90.40±1.67^{b}
	- 10%	25.00±1.22^{cd}	29.40±0.89^{c}	76.40±0.89^{c}
	Peels at level of			
	- 5%	25.40±1.14^{c}	28.40±1.34^{c}	71.00±1.41^{d}
	- 7.5%	21.40±1.34^{e}	24.60±1.14^{e}	60.20±1.10^{e}
	Seeds at level of			
	- 5%	24.80±0.84^{cd}	28.40±1.14^{c}	76.60±0.55^{c}
	- 7.5%	24.60±1.14^{cd}	27.00±1.00^{d}	75.60±0.89^{c}
	Leaves at level of			
	- 5%	23.40±1.52^{d}	27.00±0.71^{d}	69.80±0.45^{d}
	- 7.5%	20.80±1.30^{e}	26.60±1.22^{e}	59.80±1.48^{e}

Values expressed as means ± SD; Means with different letters in each column are significantly differs at p< 0.05. Values expressed as means ± SD; **HFCD:** High Fat-cholesterol Diet**; AST**: Aspartate transaminase; **ALT:** Alanine transaminase; **ALP**: Alkaline phosphatase.

Serum Level of MDA and Activities of Antioxidant Enzymes: The results of the effect of supplemented HFCD with jackfruit pulp, peels, seeds or leaves on serum levels of MDA, and the activities of CAT, GPx and SOD Enzymes in rats with obesity and atherosclerosis are recorded in Table 6. Results exhibit that untreated rats with obesity and atherosclerosis have a significant increase ($p<0.05$) in serum levels of MDA, compared with those of the normal rats.

Feeding rats with obesity and atherosclerosis on accompaniment HFCD with the two different levels of jackfruit pulp, peels, seeds, or leaves has a significant decrease of $p<0.05$ in serum levels of MDA, compared with that of the untreated rats (positive group) fed on HFCD only. About serum activities of antioxidant

enzymes (CAT, GPx, and SOD), results showed a significant (P<0.05) decrease in serum activities of antioxidant enzymes in positive rats fed on HFCD alone, compared to the normal rats fed on the basal diet. In contrast, the supplemented HFCD with jackfruit pulp, peels, seeds, or leaves significantly increased activities of CAT, GPx, and SOD, compared to HFCD alone.

Results noted that the rate of amelioration in the levels of antioxidant enzymes was better with increasing the proportion of jackfruit pulp, peels, seeds, or leaves. The most favorable results were in rats feed on the supplemented HFCD with jackfruit peels and leaves comparison to that feed HFCD with pulp or seeds.

Table (6): The Effect of Supplemented HFC-Diet with Jackfruit Pulp, Peels, Seeds or Leaves on Serum Levels of MDA, and Activities of CAT, GPx and SOD Enzymes in Rats with Obesity and Atherosclerosis.

Parameters / Groups		Parameters as Mean ± SD			
		MDA (mmol/L)	CAT (mmol/L)	GPx (mmol/L)	SOD (mmol/L)
Normal rats		1.20±0.10^{d}	18.60±1.34^{a}	15.00±0.71^{a}	31.60±1.52^{a}
Positive rats		2.64±0.21^{a}	9.00±0.71^{d}	9.00±0.70^{d}	11.40±1.34^{e}
Obese rats with atherosclerosis fed on the supplemented HFCD with Jackfruit.	**Pulp at level of - 5%**	1.48±0.05^{c}	14.40±0.55^{c}	10.80±0.84^{c}	26.60±0.55^{c}
	- 10%	1.26±0.05^{d}	16.80±0.84^{b}	14.00±1.00^{ab}	28.60±0.54^{b}
	Peels at level of - 5%	1.62±0.13^{b}	14.60±0.55^{c}	13.40±0.55^{b}	27.00±0.71^{c}
	- 7.5%	1.28±0.08^{d}	16.20±0.84^{b}	14.20±0.45^{ab}	28.40±0.55^{b}
	Seeds at level of - 5%	1.72±0.04^{b}	14.20±0.84^{c}	11.80±0.84^{c}	24.40±0.89^{d}
	- 7.5%	1.46±0.05^{c}	16.80±0.84^{b}	13.20±0.83^{b}	25.20±0.84^{d}
	Leaves at level of - 5%	1.44±0.05^{c}	16.00±1.00^{b}	14.00±1.00^{ab}	27.60±0.55^{bc}
	- 7.5%	1.28±0.08^{d}	16.60±0.55^{b}	14.00±1.00^{ab}	28.80±0.84^{b}

Values expressed as means ± SD; Means with different letters in each column are significantly differs at p< 0.05. Values expressed as means ± SD; **HFCD:** High Fat-cholesterol Diet**; MDA:** Malondialdehyde; **CAT:** Catalase; **GPx:** Glutathione Peroxidase; **SOD**: Superoxide Dismutase.

DISCUSSION

The present study was conducted to find out the effectiveness of the pulp, peel, seeds, and leaves of Jackfruit (*Artocarpus Heterophyllus Lam.*) on body weight changes, total visceral fat weight and Atherogenic index as well as some of biochemical parameters in obese rats with atherosclerosis.

High fat and cholesterol-diet (HFCD) has been deemed the most folk pattern among researchers to induce obesity with atherosclerosis in rats. Therefore, the present study used HFCD to causes obesity with atherosclerosis in normal animals before starting the study. The obtained data revealed that obese rats with atherosclerosis fed on the HFCD alone have a significant increase ($P<0.05$) in final body weight (FBW), body weight gain (BWG) and % change of BWG, and decrease in feed intakes (FI), compared to that of the normal rats feed on the basal diet alone. The increases in body weight was independent of the amount of food consumed by the rats. The present results were in accordance with **Rezq (2017)** who recorded that rats fed on HFCD have a significant increase in the body weight and no significant difference in the food intake, compared to the normal rats fed on the normal basal diet. Additionally, **Kunle *et al.* (2017)** reported that a high-fat diet caused a significant increase in FBW and significant decrease in FI, compared to the rats fed on normal regular diets. Also, **Mohamed *et al*. (2021)** and **Hoda *et al*. (2022)** showed significantly higher BW of rats fed on an HFD compared to that fed on a normal basal diet.

Obesity is characterized by increased adipose tissue mass that results from both increased fat cell number and increased fat cell size **(Lafontan and Langin, 2009).** A biogenesis is a part of the adipocyte differentiation process from preadipocyte precursors into mature adipocytes with the formation and enlargement of intracellular lipid droplets **(Ali *et al*., 2013).** This process is associated with the development of obesity. Excess energy intake and reduced energy expenditure results in abnormal excessive growth of white adipose tissue (WAT), which can lead to the development of obesity in rats **(Jo *et al*., 2009).** The obtained results were confirmed by the significant ($P<0.05$) increase in visceral fat weight (VFW), relative weight of visceral fat % and adiposity index (AI), compared to that of the rats fed on a normal basal diet (normal rats). Also, the present results were agreed with **Hoda *et al*. (2022)** who mentioned that rats fed on HFCD only (positive rats) had a significant ($P<0.05$) increase in VFW (g) and AI, compared to that of the rats fed on a normal basal diet. In the other

context, the reduction in food intake is associated with complex hormonal and neuronal pathways involving appetite and satiety regulation. Reduced food intake simply reduces energy intake that eventually lowers blood glucose and fat mass **(Benton and Young, 2017).** The possible mechanism of a substance to prevent the development of obesity could be simply due to the reduction of food intake. In support of the above statement, our finding showed that the quantity of food intake was altered by jackfruit pulp, peels, seeds and leaves supplementation. Thus, the prevention of obesity symptoms as BWG, VFW (g) and AI%, by jackfruit pulp, peels, seeds and leaves supplementation was likely to correspond with reduction of food intake. The reduction in FBW, BWG VFW (g) and AI% were significantly ameliorated with increasing levels of the jackfruit pulp, peels, seeds and leaves. The optimum results at the rate of weight loss were in rats with obesity and atherosclerosis feed on the supplemented HFCD with jackfruit peels and leaves compared to that feed HFCD with pulp or seeds. The obtained results agreed with **Zeng *et al*. (2023)** who found that jackfruit pulp restrained body weight gain in obese rats and improved serum lipid profile. In addition, **Koh *et al.* (2023)** revealed that high-fat diet-fed obese mice treated with jackfruit beverages showed great improvement in the weight management control and significant body weight loss compared to a commercial anti-obesity drug. In addition, jackfruit pulp is a rich source of polysaccharides that exert immunomodulatory, antioxidant and other pharmacological effects **(Zhu *et al*., 2019).** As mentioned by **Sang *et al*. (2021)** these polysaccharides from the Jackfruit inhibited obesity in mice, mainly by suppressing elevated blood lipids and inflammation, increasing the production of short-chain fatty acids, improving intestinal microbiota dysbiosis, and maintaining intestinal barrier function, which were at least partially responsible for the suppression of obesity. Recently, **Zeng *et al*., (2023)** suggested that increasing the intake of dietary polysaccharides is a promising means of achieving weight loss.

On the other hand, the outer peel of jackfruit is rich in fibrous compounds **(Begum *et al*., 2014).** Pectin is a unique fiber found in fruits and vegetables. It's a soluble fiber known as a polysaccharide, which is a long chain of indigestible sugars (**Wikiera *et al*., 2014**). In human studies, increased fiber intake has been linked to a decreased risk of overweight and obesity. It's believed that this is because fiber is filling, and most high fiber foods are lower in calories than low fiber foods (**Solah *et al*., 2017**). Additionally, animal studies have demonstrated

that pectin supplements promoted for weight loss and fat burn in rats with obesity (**Zhan *et al*., 2019**).

As well, **Goswami *et al.* (2021)** mentioned that mice fed on supplemented diet with Jackfruit seeds have significant reduction in food intake and body weigh with improving lipid profile in comparison to the high-sugar diet. Because of their high fiber content, the seeds can lessen the risk of heart disease, prevent constipation, and encourage weight loss **(Khan *et al*., 2021).** Also, **Agiang *et al*. (2017)** found that there is a decrease ($p<0.05$) in body weight with increase in the percentage of supplementation of jackfruit seed in the diet leading to a negative decrease at 50%. This is reflected in the significantly ($p<0.05$) lower daily food intake by the experimental rats compared to the control though rats Jackfruit seeds contain lignans, isoflavones, saponins, and other phytonutrients, which have a wide range of health benefits **(Kareem *et al.*, 2022).**

The jackfruit leaves are broad, elliptic, dark green in color and alternate (**Prakash *et al*., 2009**). The effect of jackfruit leaves on lowering body weight of obese rats indicated that jackfruit leaves may possess anti-obesity effects due to its fiber content. The obtained results agreed with **Sabidi *et al*. (2020)** who reported that there were significant differences ($p < .05$) in the lower body weight gained of treated rats groups with jackfruit leaves as opposed to control group, indicating the potential anti-obesity effect of fermented jackfruit extracts. Also, epidemiological studies support that dietary fiber (plant leaves) intake strongly prevents obesity and is inversely associated with body fat and body mass index at all levels of fat intake **(Cruz-Bravo *et al.*, 2011).** High-fiber foods have much less energy density compared with high-fat diets and can displace energy. Eating an equal weight of high-fiber food increases satiety. The bulking and viscosity properties of dietary fiber are mainly responsible for the influencing satiety **(Slavin, 2005).**

Dyslipidemia is another important lineament in the manner of development of obesity which characterized by hyperlipidemia, hypertriglyceridemia with increased level of LDL-c and VLDL-c. Hypercholesterolemia is one of the risk factors for the emergence of atherosclerosis, which is an inflammatory disorder in artery walls characterized by the formation of atheroma **(Newby *et al.*, 2014).** In the present study, obese rats fed on HFCD have a significant ($P<0.05$) increase in the serum concentrations of TC, TG, TL, LDL-c and VLDL-c levels,

and AtI, and a decrease in HDL-c levels, compared to that of the normal rats fed on the basal diet. The present results were in accordance with **Rezq and El-Khamisy (2011)** who showed that high-fat diet results in dyslipidaemic changes by increasing serum TG, VLDL, TC and LDL-c and decrease serum HDL-c levels. In agreement with the present study, **Sa'adah *et al.* (2017**) concluded that a lipid-rich diet for 30 days caused an increase in the total cholesterol, LDL-C levels, and atherogenic index significantly ($p<0.01$) compared with control rats. This may be due to cholesterol leading to the down regulation of LDL-receptors which are involved in cholesterol incorporation in the liver thus LDL cannot influx into cells and its serum levels are raised **(Heibashy, 2000).** Also, the obtained results were agreed with **Puskás *et al.* (2004) and Rezq (2017)** who mentioned that intracellular lipid accumulation in cardiomyocytes is in response to cholesterol diet. Excess cholesterol in the bloodstream can form plaque in artery walls. The cholesterol or plaque build-up causes the arteries to become thicker, harder and less flexible, slowing down and sometimes blocking blood flow to the heart and results in a heart attack. When there is too much LDL-c in the blood, it is deposited inside the blood vessels, where it can build up to hard deposits and cause atherosclerosis. In addition, **Hoda *et al.* (2022)** showed high blood total cholesterol and LDL-C levels have been linked to an increased risk of cardiovascular disease and have been linked to atherosclerosis. A number of inflammatory and oxidative changes inside the artery wall contribute to atherosclerosis, a serious degenerative disease of the arteries **(Fan and Watanabe, 2003)** Nitric oxide levels drop as a result of oxidative excess in the vasculature, which also damages tissue and DNA and causes protein oxidation, while also triggering pro-inflammatory reactions **(Xu and Touyz, 2006).** Elevation of blood LDL: HDL ratio is one of the major risk factors for the development of coronary heart diseases **(Esmaillzadeh and Azadbakht, 2008).** Oxidation of LDL contributes to atherosclerosis which involves a series of inflammatory and oxidative modifications within the arterial wall **(Heinecke, 2006)**.

With regard to the effect of jackfruit pulp, peels, seeds and leaves, the present study revealed the addition of the different levels of pulp, peels, seeds or leaves of jackfruit caused significant amendments in the serum levels of the above parameters, as compared to that caused by the HFCD alone in obese rats. The rate of improvement in the serum levels of the above parameters and AtI

were more evident with increasing the levels of the pulp, peels, seeds, or leaves of jackfruit, especially the fed on the supplemented diet with jackfruit leaves. The obtained results agreed with **(Zeng *et al*., 2023)** who showed that jackfruit pulp restrained BW gain and improved serum lipid profile caused by high-fat diet in mice. In addition, **Sang *et al.* (2021)** revealed that polysaccharides from the jackfruit pulp inhibited obesity in mice, mainly by suppressing elevated blood lipids and inflammation, increasing the production of short-chain fatty acids, improving intestinal microbiota dysbiosis, and maintaining intestinal barrier function. In addition, antioxidants are the compounds that are able to delay, retard or prevent oxidation process. They protect the body and biomolecules from the damage caused by generation of excess free radicals. Jackfruit contains a wide range of phytonutrients such as carotenoids that can act as antioxidants (**Mushumbusi, 2015**). **Jagtap *et al.* (2010)** state that the antioxidant activities of jackfruit flesh extracts are correlated with the total phenolic and flavonoids content. Also, a phytochemical found in jackfruit is called resveratrol (trans-3,5,4-trihydroxystilbene), which is well-identified for its anti-inflammatory and cardioprotective properties **(Shen *et al*., 2009).** All the trans-carotene in jackfruit pulb is crucial for human health as an antioxidant **(Haq, 2006).** Carotenoids found in jackfruit have a key role in the prevention of a number of chronic degenerative illnesses, including cataracts and age-related macular degeneration as well as cancer, inflammation and cardiovascular disease, and cancer **(Stahl and Sies, 2005).** All-trans-lutein, all-trans-carotene, all-trans-neoxanthin, 9-cis-neoxanthin, and 9-cis-violaxanthin are the major carotenoids in jackfruit **(Chandrika *et al*., 2006). Kaczmarczyk *et al*. (2012)** suggested that dietary fiber may also reduce a person's risk of heart diseases. The outer peel of jackfruit is rich in fibrous compounds, calcium, and pectin **(Moorthy *et al*., 2017).** The main mechanisms of the lipid-lowering properties of dietary fiber suggest a range of potential mechanisms including the capacity of soluble dietary fiber to form viscous solutions that delay gastric emptying, increase bile acid excretion, modulate the gut microbiome, and may decrease lipid uptake from the intestinal tract **(Jenkins *et al*., 2000). Aulia *et al.* (2019)** revealed that the administration of 500mg/200gBW /day jackfruit peel extract and 750mg/200gBW/ day decreased lipid profile in rat fed a high fat diet.

On the other hand, jackfruit seeds is a good source of both soluble and insoluble fiber. Soluble fiber can help lower LDL cholesterol levels. Both

carbohydrates and dietary fiber are abundant in jackfruit seeds. Phytonutrients present in jackfruit seeds, such as lignans, isoflavones, and saponins, have a variety of health advantages **(Haq, 2006).** Animal studies suggest that jackfruit seeds may help reduce levels of low-density lipoprotein (LDL) cholesterol and raise levels of high-density lipoprotein (HDL) cholesterol. Rats who ate a diet rich in jackfruit seeds had increased levels of HDL cholesterol and reduced levels of LDL cholesterol, compared with the rats who ate fewer seeds **(Okafor *et al.*, 2015).** According to **Soong and Barlow (2004)**, fresh seed and flesh possess substantial ascorbic acid antioxidant effects and gallic acid contents, which are believed to have contributed to about 70% of the total antioxidant activity. As well, **Swami *et al.* (2012)** reported that jackfruit contains functional compounds that have capability to reduce various diseases such as high blood pressure, heart diseases, and strokes. It is also capable of reducing homocysteine levels in the blood. Jackfruit is also rich in potassium which aids in lowering blood pressure and reversing the effects of sodium that causes a rise in blood pressure that affects the heart and blood vessels. This in turn prevents heart disease, strokes, and bone loss and improves muscle and nerve function. Also, **Ranasinghe *et al.* (2019)** mentioned that jackfruit seeds possess a good amount of ascorbic acid and gallic acid which may protect the body from the negative effects of excess free radical production thus promoting antioxidant activity. Therefore, it can be concluded that jackfruit seeds may help in contributing to the antioxidant activity.

In the other context, jackfruit leaves are frequently used due to the presence of chemicals that are hypoglycemic and hypolipidemic **(Baliga *et al.*, 2011).** Extracts of the fruit's leaves also exhibit attenuation of hyperglycemia and hyperlipidemia that gives rise to outstanding antioxidant activity **(Omar *et al.*, 2011).** Fresh jackfruit leaves and fruits have been shown to contain a variety of chemicals, including sterols, phenolic acids, carotenoids, stilbenes, phenolic acids, and flavonoids, particularly prenylflavonoids **(Baliga *et al.*, 2011).** Beta-carotene, the main precursor of vitamin A and retinoic acid, is able to promote fatty acid oxidation in adipocytes and other tissues **(Coronel *et al.*, 2019).** Besides its relationship with vitamin A, the intake of carotenoids in the diet plays an important role in reducing oxidative stress and modulating the immune response, LDL levels, atherogenic processes, and many physiological processes,

thus reducing the risk of developing chronic diseases, especially some types of cancer, cardiovascular and metabolic diseases **(Chaudhary *et al.*, 2018).**

Adipocytes secrete a variety of peptide hormones called adipocytokines such as leptin, adiponectin, visfatin, resistin, tumour necrosis factor-α and interleukin-6, which play a role in energy regulation **(Garg, 2006).** Leptin is a common protein produced by the adipose tissue and highly correlates with body fat, suggesting that obese persons are insensitive to endogenous leptin production. It is a key fat-derived regulator of food intake and energy expenditure and its secretion levels are usually positively correlated with the extent of the triglyceride stores in adipocytes **(Staiger and Häring, 2005).** The hormone leptin critically regulates body weight and metabolism at central level in the brain **(Elena *et al.*, 2017),** and disruption of leptin/leptin receptor (LEPR) signaling results in morbid obesity and severe metabolic disease **(Zhang and Chua, 2018 and Zhou and Rui, 2013).** One of the peripheral functions of leptin is a regulatory role in the interplay between energy metabolism and the immune system, which is, in part, responsible for the inflammatory state associated to obesity **(Pérez-Pérez *et al.*, 2017).**

In the present study, result showed that serum activity of lactate dehydrogenase (LDH) enzyme and level of leptin hormone were increased significantly in the HFCD control group compared with the normal control group. The present experimental diet consisted of more fat and this might have accounted for the elevated levels of leptin, consistent with literature reports **(Handjieva-Darlenska and Boyadjieva, 2009). Saravanan *et al.* (2014)** showed that rats fed on high fat-diet had high serum leptin hormone level when compared with those fed on normal basal diet.

In contrast, the supplemented HFCD with the two different levels of Jackfruit pulp, peels, seeds, or leaves caused a significant ($P<005$) decrease in serum levels of LDH and leptin hormones, compared to that induced by the HFCD only in rats with obesity and atherosclerosis. The lowering in serum levels of LDH and leptin hormones of rats with obesity and atherosclerosis was significantly enhanced by increasing the levels of the jackfruit pulp, peels, seeds, or leaves. While, the superior results were in rats fed on the supplemented HFCD with jackfruit leaves compared to that feed HFCD with pulp, peels, or seeds. The reduction of leptein hormone may be attributed to the reduction of

adipose tissue and total body fat and the reduction in the level of triglyceride stores in adipocytesas indicated above.

The liver, a vital digestive gland, plays a crucial role in regulating metabolism, deoxidation, detoxification, excretion and secretion of bile. Many investigations have reported the correlation between high-fat diet with NAFLD and other metabolic diseases, such as obesity and diabetes, and cardiovascular diseases. In addition, a high-fat diet also generates inflammation and liver injury **(Im *et al.,* 2021).** Since the high effectiveness of liver enzymes (ALT, AST) in the blood is the best indicator of liver damage, their high levels in the blood can be used to predict inflammatory changes in the liver **(Singh *et al.,* 2011).** Hepatic enzymes AST and ALT are the most specific intracellular enzymes that are associated with cell leakage and serve as a marker of hepatocellular injury with greater grades of hepatic steatosis and fibrosis in several studies. The elevation in the hepatic enzymes may be attributed to an increase in the production of free radicals that initiate lipid peroxidation of membrane leading to loss of integrity of cell membranes and damage of hepatic cells. The metabolic processes resulting from a high-fat diet (HFD) can cause oxidative stress in mitochondria and the endoplasmic reticulum, as well as induce de novo lipogenesis and inflammation in liver cells **(Yang *et al.,* 2019).** The present study showed significant elevation in serum activities of AST, ALT and ALP enzymes in untreated obese rats with atherosclerosis. The obtained results were in agreement with **Al Shammari (2020)** who founded that HFD caused significant increase in serum ALT, AST and ALP enzymes as compared to negative control group. Recently, **Huang *et al.,* (2022)** reported the high fat diet significantly elevated the levels of TG, TC, LDL-c, AST, ALT and lowered HDL-c in male mice **(Huang *et al.,* 2022).** However, rats with obesity and atherosclerosis fed on the supplemented HFCD with the different levels of jackfruit pulp, peels, seeds or leaves have significant decreases ($P<0.05$) in the serum activities of AST, ALT, and ALP enzymes, compared to that of untreated rats with obesity and atherosclerosis (positive rats). In addition, the higher level of the jackfruit pulp, peels, seeds, or leaves significantly lowered serum activities of AST, ALT, and ALP. The most favorable results were in rats fed on the supplemented HFCD with jackfruit peels and leaves compared to that fed HFCD with pulp or seeds. The obtained result, were somewhat consistent with **Zeng *et al.* (2022**) who mentioned jackfuit pulp reduced liver weight, liver index

and improve liver function in high-fat diets (HFD) -induced mice. These results may be attributed to its a polysaccharide by modulating the expression of genes involved in lipid metabolism, such as peroxisome proliferator activated receptor alpha (PPARα), hormonesensitive lipase (HSL), carnitine palmitoyltransferase 1A (CPT1), lipoprotein lipase (LPL), acetyl-CoA carboxylase alpha (ACC), fatty acid synthase (FAS) and sterol regulatory element binding transcription factor (SREBP-1c) Also, **Phukan *et al.*, (2018)** mentioned that the aqueous extract of Jackfruit seed, leaf and fruit have beneficial effects on liver function. It is assumed that this hepataprotective effect may be due to the presence of secondary metabolites that respond to stimuli in natural environment and the influence of abundant calcium, potassium, magnesium content. In the study of **Sabidi *et al.* (2020**) on safety assessment of fermented jackfruit (Artocarpus heterophyllus) pulp and leaves in Sprague-Dawley rats, results showed that the oral administrations of high dose fermented jackfruit and its leaves extracts did not change the physiology function of liver and kidneys rats. As well, **El Hilaly *et al.* (2004)** that indicated that the normal levels of ALT, ALP, AST, total bilirubin, total protein, creatinine, urea and cholesterol are good indicators of liver and kidney functions.

The present study provides a perfect correlation between serum lipid peroxidation products as indicator by MDA and the activity of antioxidant enzymes, which play an important role in the antioxidant system. It showed that fed rats on HFCD induced significant increase of serum MDA level, and decrease serum GSH level and activities of GPx and SOD enzymes, compared to that fed on normal basal diet. The decrease in serum activity of antioxidant enzymes, as seen in serum of obese rats, can lead to the excessive availability of superoxide and peroxyl radicals, which in turn generate hydroxyl radicals, resulting in the initiation and propagation of more lipid peroxidation products. High-fat diets result in the release of free fatty acids by the action of lipoprotein lipase with increase serum triglycerides and cause lipotoxicity, which results in insulin receptor dysfunction. The release of excessive free fatty acids provokes lipotoxicity, as lipids and their metabolites create oxidative stress **(Zhang *et al.*, 2007).** The present result was agreed with **Amirkhizi *et al.* (2007)** who showed that increase the production of reactive oxygen species as well as reduced antioxidant defense mechanisms have been suggested to play a role in both humans and animal models of obesity. Further, lipid alterations have been

considered as contributory factors to oxidative stress in obesity **(Leopold and Loscalzo, 2008).** Hypertriglyceridemia results in obese rats participate in the alteration of oxidant-antioxidant balance, suggesting increase the bioavailability of free fatty acids and lipid peroxidation **Amirkhizi *et al.* (2007)**. Hyperlipidemia induces oxidative stress and increase lipid peroxidation **(Moussa, 2008).** Recently, **Denisenko and Novgorodtseva (2013)** showed that fed animals on high fat diet inhibits activity of blood antioxidant enzymes and elevate lipid peroxidation (MDA).

The prooxidative effects have been documented as it decreases the activity of antioxidant enzymes such as SOD, CAT, and GPX and increased the concentration of malondialdehyde (MDA), which is the main marker of lipids peroxidation **(Capatina *et al.*, 2020).** MDA is the product of oxidative degradation, and it reflects the level of lipid peroxidation. CAT; GSH and GPx act as free radical scavengers to decompose H2O2 **(Qin *et al*., 2019).**

The present study provides a perfect correlation between serum lipid peroxidation products as indicator by MDA and activities of some antioxidant enzymes which play an important role in the antioxidant system. It showed that fed rats on HFCD have a significant increase in serum level of MDA and decrease in serum activities of CAT and GPx and SOD enzymes, compared to that fed rats on normal basal diet. High-fat diets result in the release of free fatty acids by the action of lipoprotein lipase with increase serum triglycerides and cause lipotoxicity, which results in insulin receptor dysfunction. The release of excessive free fatty acids provokes lipotoxicity, as lipids and their metabolites create oxidative stress **(Zhang *et al.*, 2007)**. The present result was agreed with **Amirkhizi *et al*. (2007)** who showed increased in the production of reactive oxygen species with reduced in antioxidant defense mechanisms in obese animal models. Further, lipid alterations have been considered as contributory factors to oxidative stress in obesity **(Leopold and Loscalzo, 2008).** Additionally, **Denisenko and Novgorodtseva (2013)** showed that fed animals on high fat diet inhibits activity of blood antioxidant enzymes and elevate lipid peroxidation (MDA). Also, **Rezq (2017)** reported that fed rats for 4 weeks on high-fat diet decreased significantly serum activities of GSH, GPx, SOD and CAT enzymes, and increased serum MDA level, compared to that fed on basal diet.

In contrast, the present study documented feeding rats with obesity and atherosclerosis on accompaniment HFCD with the two different levels of

jackfruit pulp, peels, seeds, or leaves has a significant decrease of $p<0.05$ in serum levels of MDA, compared with that of the untreated rats (positive group) fed on HFCD only. About serum activities of antioxidant enzymes (CAT, GPx, and SOD), results showed a significant ($P<0.05$) decrease in serum activities of antioxidant enzymes in positive rats fed on HFCD alone, compared to the normal rats fed on the basal diet. In contrast, the supplemented HFCD with jackfruit pulp, peels, seeds, or leaves significantly increased activities of CAT, GPx, and SOD, compared to HFCD alone.

Jackfruit is a tropical fruit known for its rich nutritional profile and bioactive constituents, including phytochemicals, antioxidants, and dietary fiber **(Maradesha *et al*., 2022).** Fresh jackfruit leaves and fruits have been shown to contain a variety of chemicals, including sterols, phenolic acids, carotenoids, stilbenes, phenolic acids, and flavonoids, particularly prenylflavonoids **(Baliga *et al*., 2011).** With a rich composition of phytochemicals such as flavonoids, phenolic compounds, and saponins, A. heterophyllus exhibits a wide range of biological activities, including antioxidant, anti-inflammatory, antimicrobial, and anticancer properties **(Ajiboye *et al*., 2020).** Also, the fruits and leaves extract exhibit attenuation of hyperglycemia and hyperlipidemia that gives rise to outstanding antioxidant activity **(Omar *et al*., 2011).** Jackfruit contains many functional components including polysaccharides, flavonoids, sterols, prenylated chromones and so on. Moreover, it possesses numerous functional properties, such as antibacterial, anti-inflammatory, antioxidant, anti-tumor, hypoglycemic, hypolipidemic and immunomodulatory **(Zhang *et al*., 2021).** As well, jackfruit pulp displayed a potent antioxidant activity after gastrointestinal digestion in vitro and regulated the composition of the intestinal flora in vivo **(Zhu *et al*., 2021).** Recently, studies have shown that the bioactive compounds present in fruits have potential health benefits by reducing inflammation and oxidative stress **(Farag *et al*., 2020).** Among several actions that these substances can exert from the biological point of view are the regulation of the production of reactive oxygen species, the expression of phase I and phase II detoxification enzymes, the immune system, the gene expression, the activation of nuclear factor kB (NF-kB) and apoptosis; reduction of platelet aggregation; inhibition of angiogenesis; anti-inflammatory, antiviral and antibacterial effects. Due to these effects, these compounds have been described as capable of reducing the incidence of several chronic diseases **(Pratheeshkumar *et al*., 2012).** Bioactive

compounds are divided into three main chemically distinct groups: terpenes, phenolic compounds and nitrogen compounds. The first two is the most found in fruits, mainly in the form of carotenoids and flavonoids. Meanwhile, phenolic compounds are divided into flavonoids and non-flavonoids **(Farag *et al*., 2020).**

Flavonoids are a huge class of substances that constitute natural pigments, wich are classified into flavonols, flavones, flavonones, catechins, anthocyanins and isoflavonoids. The main sources of flavonoids are fruits. Among the flavones, quercetin and myricetin are the most commonly found in fruits **(Verruck *et al*., 2018).** Flavonoids are natural antioxidant polyphenol compounds can reduce cholesterol and triglyceride levels in the blood, protect from arterial damage, and reduce the amount of cholesterol deposited on the surface of the arterial endothelium. Research in rat showed that flavonoids can reduce lipid peroxidation **(Ratty and Das, 1998).** Also, it is known that flavonoids and proanthocyanidins can decrease the inflammatory processes by increasing the activity of enzymes that control the oxidation of the cell membrane **(Rauf *et al*., 2019).**

Carotenoids belong to the terpene group, they are fat-soluble pigments, hydrophobic and exhibit a range of colors from yellow to red in plants **(Zia-Ul-Haq *et al*., 2012).** Besides its relationship with vitamin A, the intake of carotenoids in the diet plays an important role in reducing oxidative stress and modulating the immune response, LDL levels, atherogenic processes, and many physiological processes, thus reducing the risk of developing chronic diseases, especially some types of cancer, cardiovascular and metabolic diseases **(Chaudhary *et al*., 2018).** Studies have also explored the anti-inflammatory role of jackfruit, which can be important for the prevention of the progression of obesity-associated low grade inflammation and its complications. Phytochemical investigations of ethyl acetate extracts of jackfruit led to the isolation of the phenolic compound artocarpesin [5,7,2′,4′-tetrahydroxy-6-(3-methylbut-3-enyl) flavone], which was further shown to possess potent anti-inflammatory effects in RAW264.7 murine macrophage cells by suppressing lipopolysaccha-ride (LPS) induced production of nitric oxide (NO) and prostaglandin E 2 (PGE2). NO and PGE2 are potential inflammatory molecules and play important roles in the pathogenesis of the low-grade state of inflammation associated with obesity and its complications **(Vuolteenaho *et al*., 2009).** Further, artocarpesin significantly suppressed LPS-induced inflammation by reducing NO

synthesizing enzyme [inducible nitric oxide synthase (iNOS)] and PGE2 producing enzyme [cyclooxygenase 2 (COX2)] protein expressions **(Fang *et al*., 2008).** Moreover, the antioxidant capacity of jackfruit is fairly well established **(Jagtap and Bapat, 2010).** The ethanolic extracts of jackfruit were shown to have DPPH scavenging activity (IC50 410 μg/ml). The antioxidant characteristics of prenylflavones from jackfruit inhibited ferric-induced lipid peroxidation in rat brain homogenate. Cycloheterophyllin scavenged 1,1-diphenyl-2-picrylhydrazyl (DPPH), and artonins A and B scavenged hydroxyl and peroxyl radicals that were generated by 2,2′-azobis (2- amidinopropane) dihydrochloride and the Fe3+–ascorbate–EDTA–H2O system **(Ko *et al*., 1998).** Interestingly, the seeds of jackfruit demonstrate much higher antioxidant capacities than the edible portion **(Jagtap and Bapat, 2010).**

CONCLUSION:

Generally, the ability of jackfruit pulp, peels, seeds and leaves to enhance the activity of anti-obesity and inhibit atherogenic index as well the improve ment of liver function and activities of antioxidant enzymes makes it a promising natural compound for the management of obesity and hyperlipidemia. However, more research is needed to fully understand the mechanisms of action and potential benefits of jackfruit pulp, peels, seeds and leaves in obesity and hyperlipidemia management.

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تأثير فعالية فاكهة الجاك فروت على بعض القياسات البيوكيميائية في ذكور الفئران المصابة بالسمنة وتصلب الشرايين

هدى سلامة إبراهيم، عمرو عبد المرضي رزق، الاء اسامة أبو رية، سلوى سلامة حافظ

قسم التغذية وعلوم الاطعمة، كلية الاقتصاد المنزلي، جامعة حلوان، القاهرة، مصر

الملخص العربي

لا تزال أمراض القلب والأوعية الدموية السبب الرئيسي للامراض والوفيات في جميع أنحاء العالم بسبب الذبحة الصدرية المميته. تعد الآلية المرضية الكامنة وراء تصلب الشرايين هي ضيق الشرايين بسبب تراكم الدهون مما يؤدي إلى عدم كفاية تدفق الدم إلى الأعضاء الحيوية، خاصة القلب والدماغ. أجريت الدراسة الحالية لمعرفة فعّالية لب وقشور وبذور وأوراق الجاك فروت على تغيرات وزن الجسم وإجمالي وزن الدهون الحشوية بالإضافة إلى بعض التحاليل البيوكيميائية في الفئران البدينة المصابة بتصلب الشرايين. أُجريت التجربة على مرحلتين، كل منهما مدتها ستة أسابيع. كان الهدف من المرحلة الأولى هو إحداث السمنة وتصلب الشرايين، بينما كانت المرحلة الثانية لعلاج الفئران البدينة المصابة بتصلب الشرايين من خلال التغذية على النظام الغذائي المكمل ب ٥ و ١٠٪ لب، ٥ و ٧,٥٪ قشور، ٥ و ٧,٥٪ بذور، ٥ و ٧,٥٪ أوراق من الجاك فروت. أظهرت النتائج أن الانخفاض في وزن الجسم النهائي ووزن الدهون الحشوية ومؤشر السمنة بالإضافة إلى صورة الدهون الكاملة وزيادة نشاط الإنزيمات المضادة للأكسدة (الكتاليز، بيروكسيداز الجلوتاثيون، فوق اكسيد الدسموتاز) قد تحسنت بشكل كبير مع زيادة مستويات لب وقشور وبذور وأوراق الجاك فروت. كانت النتائج المثلى لمعدل فقدان الوزن في الفئران البدينة المصابة بتصلب الشرايين والتي تتغذى على النظام الغذائي عالي الدهون والكوليسترول المكمل بـقشور وأوراق الجاك فروت مقارنةً بتلك التي تتغذى على النظام الغذائي عالي الدهون والكوليسترول المكمل باللب أو البذور. بشكل عام، فإن قدرة لب الجاك فروت وقشوره وبذوره وأوراقه على تعزيز نشاط مكافحة السمنة وتثبيط مؤشر تصلب الشرايين وكذلك تحسين وظائف الكبد ونشاط إنزيمات مضادات الأكسدة تجعله مركبًا طبيعيًا واعدًا لإدارة السمنة وفرط شحميات الدم. ومع ذلك، هناك حاجة إلى مزيد من البحث لفهم آليات العمل والفوائد المحتملة للب وقشور وبذور وأوراق الجاك فروت في إدارة السمنة وفرط شحميات الدم.

الكلمات المفتاحية: الجاك فروت؛ السمنة؛ أمراض القلب والأوعية الدموية؛ فرط شحميات الدم