The Effectiveness of Jackfruit (*Artocarpus Heterophyllus Lam.*) on Histopathological Changes of Heart and Aorta in Obese Male Rats with Atherosclerosis

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Abstract

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 histopathological changes of heart and aorta in obese rats with atherosclerosis. The experiment was conducted in two stages (each of 6 weeks), the objective of the first stage was the induction of obesity and atherosclerosis, 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, seeds and leaves) of the jackfruits. The results revealed that 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 on the HFCD-supplemented diet with the pulp or seeds. With regard to the effect of jackfruit pulp, peels, seeds and leaves on the histopathological changes of heart and aorta, the present study revealed that photomicrograph of heart and aorta sections of obese rats with atherosclerosis fed on the supplemented HFCD with jackfruit pulp, peels, seeds or leaves at the different levels showing gradual improvement with increasing the levels, especially with jackfruit leaves, compared with the positive group. Generally, the ability of jackfruit pulp, peels, seeds and leaves to enhance the activity of anti-obesity and inhibit heart and aorta degeneration 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 (LDL-c) (**Pearson *et al.,* 2002**) and other important contributors to this disease include inflammation, oxidative stress and insulin resistance (**Van Gaal *et al.,* 2006**).

Atherosclerosis is a chronic inflammatory process that leads to arterial lumen narrowing **(Bentzon *et al.,* 2014).** Its pathophysiology is complex, involving endothelial dysfunction, intimal thickening, and atheromatous plaque formation **(Sakakura *et al.,* 2013)**. Plaque rupture forming a thrombus, or continued plaque growth leading to stenosis, can both occlude arteries leading to ischemia and infarction **(Li *et al.,* 2017).**

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 al.*, 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 find out the effectiveness of the pulp, peels, seeds, and leaves of Jackfruit (*Artocarpus Heterophyllus Lam*.) on body weight changes and total visceral fat weight as well as histopathological changes of heart and aorta in 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.

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 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 fa t+ retroperitoneal fat+ abdominal fat

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

Histopathological Study: Heart and aorta of all rats was immersed in neutral buffered formalin (10%) for 24 hr. The fixed tissues were processed routinely, embedded in paraffin, sectioned, deparaffinized and rehydrated using the standard techniques according to the method of **Bancroft and Gamble (2002)**. The extent of high-fat diet induced obesity and hyperlipidemia was evaluated by assessing the morphological changes in the heart and aorta sections stained with hematoxylin and eosin (H and E).

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** discover the effect of supplemented HFC-diet with jackfruit pulp, peels, seeds and leaves on FI, IBW, BWG and FER in rats with obesity and atherosclerosis. The results indicated that untreated rats with obesity and atherosclerosis (positive rats) have a significant ($P<0.05$) decrease in food intake (FI) compared to that of normal rats. The supplemented HFCD with 5 and 10% jackfruit pulp, 5% jackfruit peels and 5% jackfruit 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 fed rats on the normal basal diet. Included, the accompanied HFCD with jackfruit pulp, peels, seeds 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, 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.

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 results demonstrated that untreated rats with obesity and atherosclerosis had a significant ($P<0.05$) increase in VFW (g) and AI, compared to that of normal rats. While, feeding the rats with obesity and atherosclerosis on the supplemented HFCD with the two different levels of jackfruit pulp, peels, seeds and leaves has a significant ($P<0.05$) decrease in VFW (g) and AI, compared to the rats with obesity and atherosclerosis feeding on HFCD only.

The reduction in VFW and AI was significantly improved with increasing levels of the jackfruit pulp, peels and leaves.

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

Groups \ Parameters		FI (g)	IBW (g)	FBW (g)	BWG (g)	% change of BWG
		Parameters as Mean ± SD				
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.

Groups \ Parameters		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 supplemented HFCD with 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**.**

Histopathological Examination of Heart:

Photomicrograph of heart sections from the healthy control rats showed normal heart muscle and blood vessel as shown in **Photo 1**. In untreated obese rats with atherosclerosis fed on HFCD (positive control rats), examine sections of heart revealed dilated blood vessel with thick muscle wall (**Photo 2)** and intermuscular hemorrhages (**Photo 3)**. Photomicrograph of heart sections from treated obese rats with atherosclerosis fed on the supplemented HFCD with 5 % of jackfruit pulp, peels or seeds showing edema with atrophied myocardial muscles (**Photo 4**). Heart sections from treated obese rats with atherosclerosis fed on the supplemented HFCD with jackfruit pulp, peels or seeds at levels of 10 or 7.5%, respectively revealed few leucocytic cells infiltration as shown in **Photo 5**. Heart sections from treated obese rats with atherosclerosis fed on the supplemented HFCD with 5 and 7.5% of jackfruit leaves noticed severely dilated and congested blood vessel (**Photo 6**) and congested blood vessel (**Photo 7**), respectively.

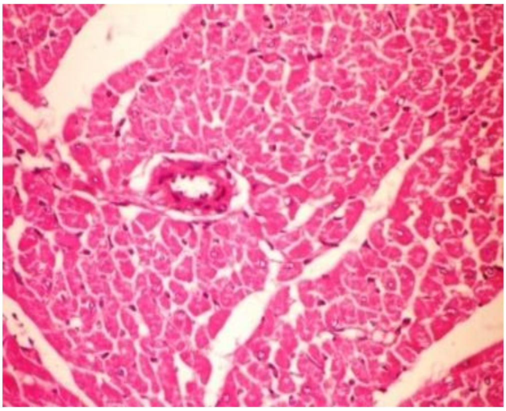


Photo 1: Photomicrograph of heart sections from the healthy control group showing apparently normal heart muscle and blood vessel (H & E x 400).

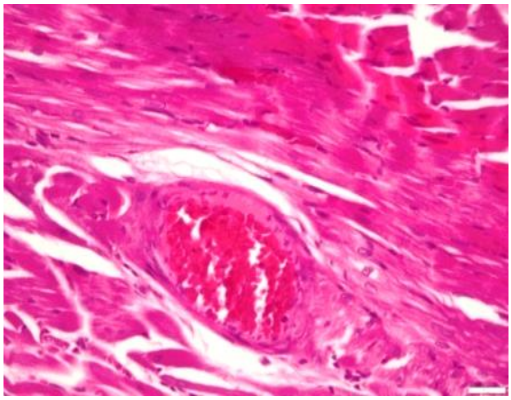


Photo 2: Photomicrograph of heart sections from the positive control group showing dilated blood vessel with thick muscle wall (H & E x 400).

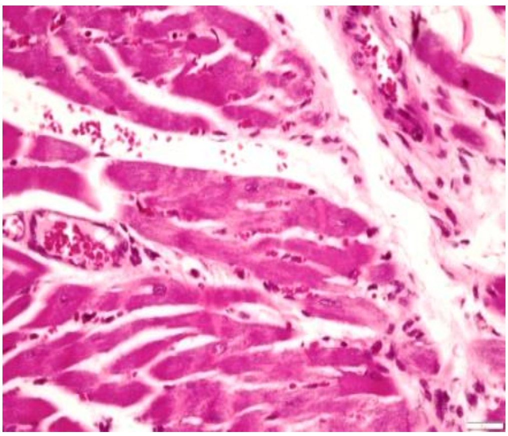


Photo 3: Photomicrograph of heart sections from the positive control group showing intermuscular hemorrhages (H & E x 400).

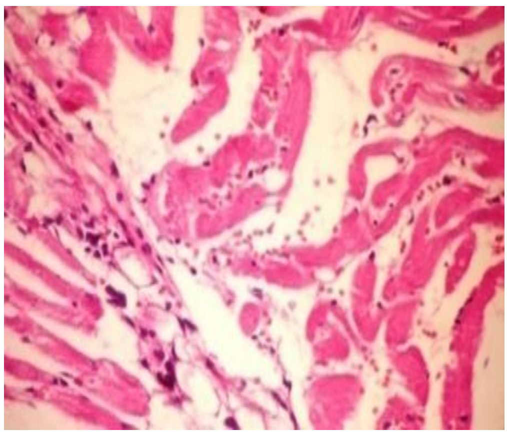


Photo 4: Photomicrograph of heart sections from treated obese rats with atherosclerosis fed on the supplemented HFCD with jackfruit pulp, peels or seeds at levels of 5%, showing edema with atrophied myocardial muscles (H & E x 400).

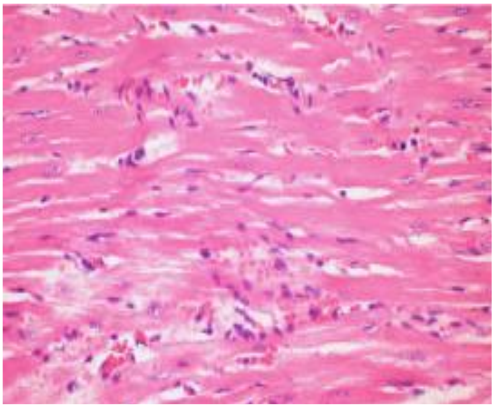


Photo 5: Photomicrograph of heart sections from treated obese rats with atherosclerosis fed on the supplemented HFCD with jackfruit pulp, peels or seeds at levels of 10 or 7.5%, respectively showing few leucocytic cells infiltration (H & E x 400).

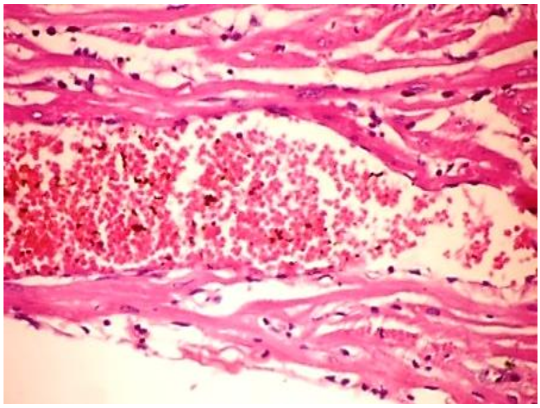


Photo 6: Photomicrograph of heart sections from treated obese rats with atherosclerosis fed on the supplemented HFCD with 5 and 7.5% of jackfruit leaves showing severely dilated and congested in blood vessel (H&E x 400).

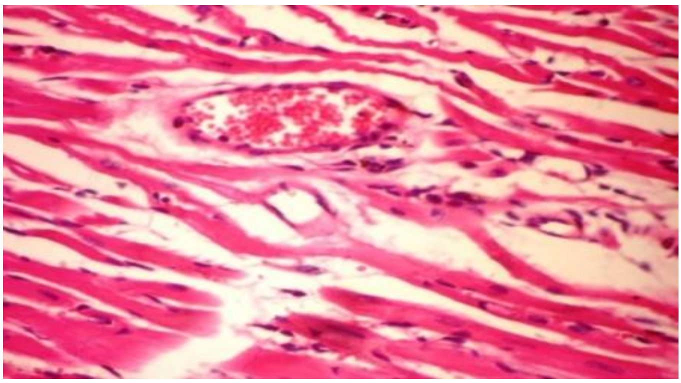


Photo 7: Photomicrograph of heart sections from treated obese rats with atherosclerosis fed on the supplemented HFCD with 5 and 7.5% of jackfruit leaves showing congested blood vessel (H&E x 400).

Histopathological Examination of Aorta:

Photomicrograph of aorta sections under usual conditions in the healthy control group showed that the endothelial cells in the tunica intima (TI) had a flattened shape and were linked to the basement membrane in a regular pattern. Elastin fibers and smooth muscle cells make up the tunica media (TM) as shown in **Photo 8**. While, aorta sections of untreated obese rats with atherosclerosis fed on HFCD (positive control rats) revealed irregular elastin fibers structure describes the injury, multifocal deterioration, smooth muscle cell displacement, and vacuolation in tunica medium cells. As well, the tunica adventitia (TA) was edematous with congestion features with proliferation of tunica media. Pyknotic/ necrotic smooth muscle cell nuclei. In addition, mononuclear cells invasion was seen, distributed arrangement of both tunica adventitia and media. Also, some regions showed severe increased of tunica media (TM) thickness and there was congested area appeared within TM as shown in **Photo 9 and 10**.

With regard to aorta sections from treated obese rats with atherosclerosis fed on the supplemented HFCD with jackfruit pulp (5 and 10 %), peels or seeds (5 and 7.5%) or leaves (5%), respectively showing signs of improvement features. Where showed normal aorta structure with standard layers' thickness. The endothelial cells lining the tunica intima (TI) remain consistent, and the majority of the smooth muscle cells in the tunica media (TM) are orientated horizontally to the aortic canal. In their tunica media, well-formed elastic fibers are organized in a lamellar manner. However, other areas still displayed pathological alternations such as, the tunica medium diameter is moderate in some areas and increased in others. Tunica media has small vacuoles, as well as, Lymphatic infiltration and congestion were detected (**Photos 11 to 17**). As shown in **Photos 18 and 19**, treated obese rats with atherosclerosis fed on the supplemented HFCD with 7.5 % of jackfruit leaves was the better group. The intimae of aorta sections were thin and lacking edema, the endothelial cells were mostly intact and did not desquamate, and the smooth muscle cells were allocated in an ordered arrangement. In addition, the tunica medium and adventitia diameters are normal.

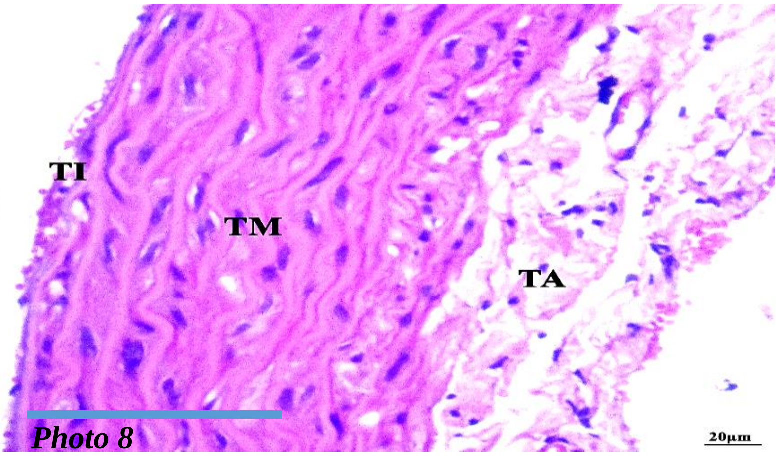
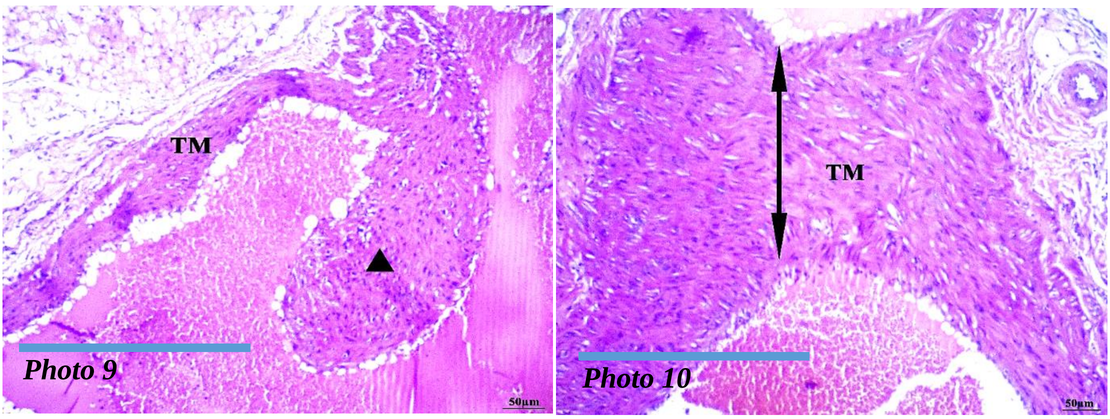


Photo 8: Photomicrographs of aorta sections from the healthy control group showed that the endothelial cells in TI had a flattened shape and were linked to the basement membrane in a regular pattern, as well as elastin fibers and smooth muscle cells were made up TM (H & E x 200).



Photos 9 and 10: Photomicrographs of aorta sections from the positive control rats revealed irregular elastin fibers structure, multifocal deterioration, smooth muscle cell displacement, vacuolation in tunica medium cells, edematous in TA, congestion with proliferation of TM and Pyknotic/ necrotic smooth muscle cell nuclei. In addition, mononuclear cells invasion was seen, distributed arrangement of both tunica adventitia and media. Also, some regions showed severe increased of TM thickness and there was congested area appeared within TM (H & E x 400).

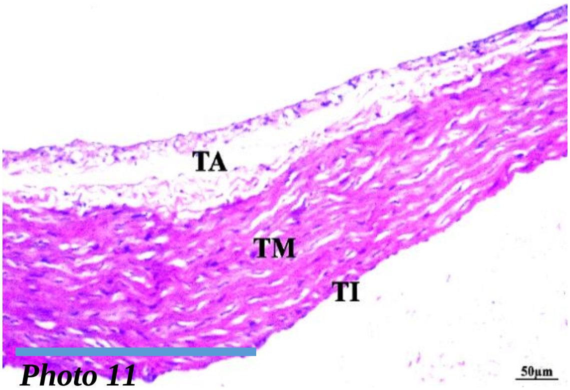


Photo 11

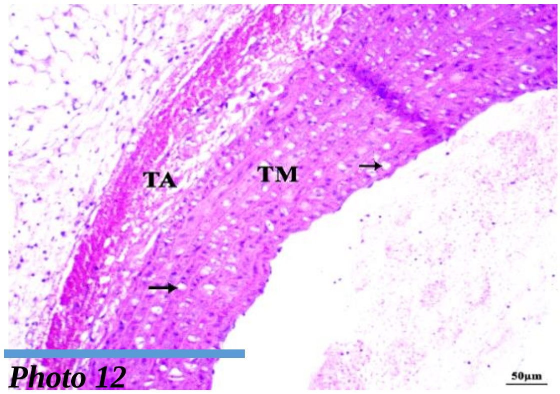


Photo 12

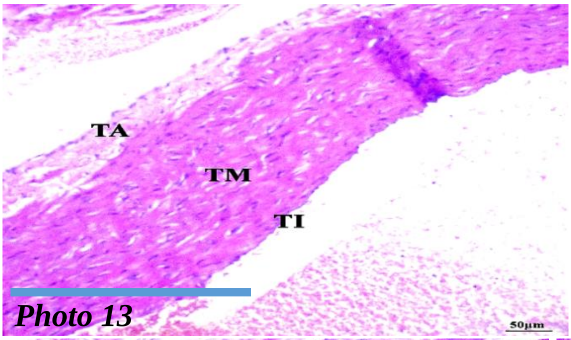


Photo 13

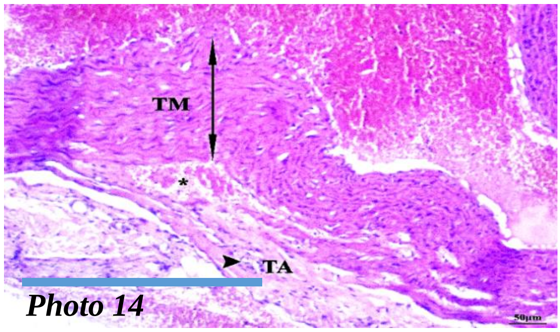


Photo 14

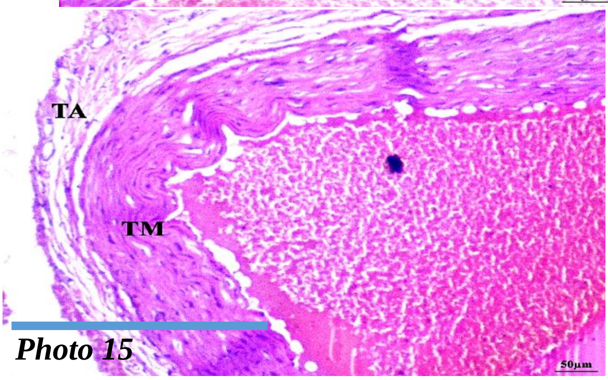


Photo 15

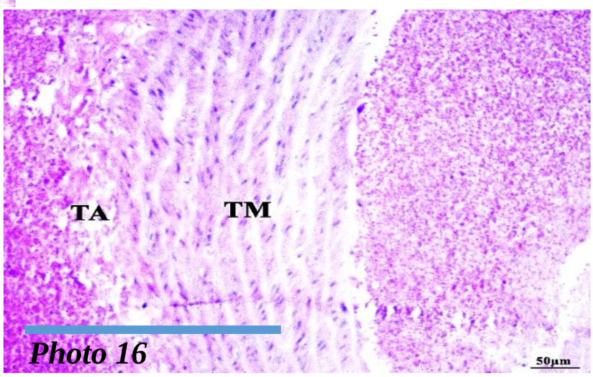


Photo 16

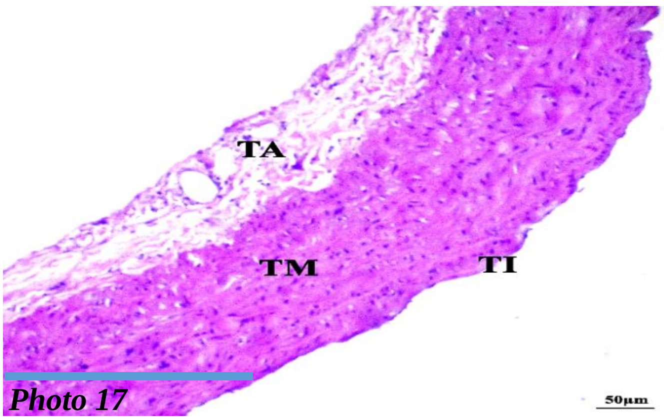
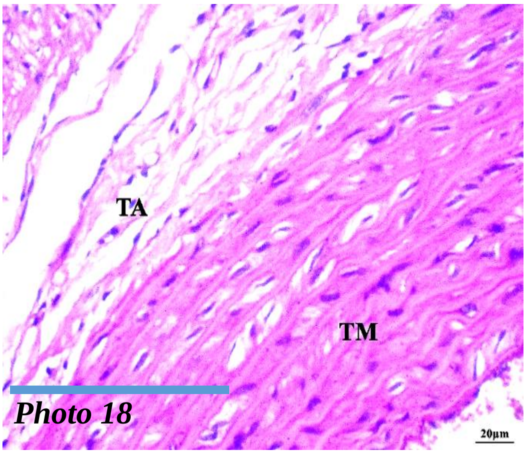
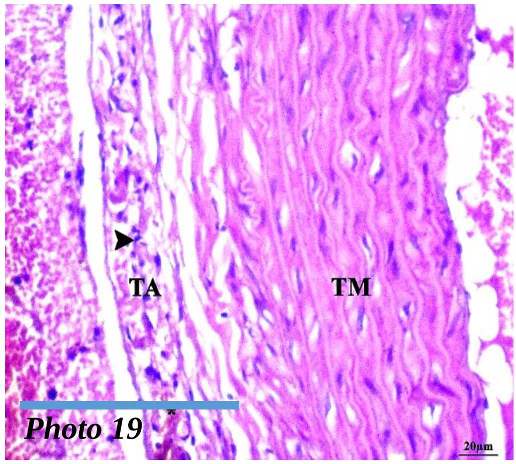


Photo 17

Photos from 11 to 17: Photomicrographs of aorta sections from treated obese rats with atherosclerosis fed on the supplemented HFCD with jackfruit pulp (5 and 10 %), peels or seeds (5 and 7.5%) or leaves (5%), respectively showing signs of improvement features. Where showed normal aorta structure with standard layers' thickness. The endothelial cells lining the TI were consistent, and the majority of the smooth muscle cells in the TM are orientated horizontally to the aortic canal. However, other areas still displayed pathological alternations such as, the tunica medium diameter is moderate in some areas and increased in others with small vacuoles, as well as, Lymphatic infiltration and congestion were detected (H & E x 400).





Photos 18 and 19: Photomicrographs of aorta sections from treated obese rats with atherosclerosis fed on the supplemented HFCD with 7.5 % of jackfruit leaves showed that the intimae of aorta sections were thin and lacking edema, the endothelial cells were mostly intact and did not desquamate, and the smooth muscle cells were allocated in an ordered arrangement. In addition, the tunica medium and adventitia diameters are normal (H & E x 200).

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 and total visceral fat weight as well as histopathological changes of heart and aorta 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 cause obesity with atherosclerosis in normal animals before starting the study. The obtained data revealed that obese rats with atherosclerosis fed on HFCD alone have a significant increase ($P<0.05$) in final body weight (FBW), body weight gain (BWG) and % change of BWG, and decreased ($P<0.05$) in feed intakes (FI), compared to that of the normal rats feed on the basal diet alone. This result shows that the increases in body weight are 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 had a significant increase in body weight and there was no significant difference in the food intake, as compared to 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.

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. 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**). 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 fed rats on a normal basal diet (normal rats) in the current study. 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 fed rats on a normal basal diet (normal rats).

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 (18.5–20.2%) 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 being 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 weight loss and fat burn in rats with obesity (**Zhan *et al.,* 2019**).

As well as **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 colour 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, HFCD exposure resulted several histopathological changes, photomicrograph of untreated obese rats with atherosclerosis revealed dilated blood vessel with thick muscle wall and intermuscular hemorrhages in the heart sections. In addition, there were irregular elastin fibers structure describes the injury, multifocal deterioration, smooth muscle cell displacement, and vacuolation in tunica medium cells. As well, the tunica adventitia (TA) was edematous with congestion features with proliferation of tunica media. Pyknotic/ necrotic smooth muscle cell nuclei. In addition, mononuclear cells invasion was seen, distributed arrangement of both tunica adventitia and media. Also, some regions showed severe increased of tunica media (TM) thickness and there was congested area appeared within TM in aorta sections of untreated obese rats with atherosclerosis. 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 that there were focal areas of dysfunction and myocyte cytolysis and some sections of cytoplasm that hyper acidophilic and Pyknotic nuclei in heart muscle. As well as, endothelial desquamation and irregular elastin fibers structure that describe the injury, multifocal deterioration, smooth muscle cell displacement, vacuolation in tunica medium cells, edematous of the tunica adventitia, and enlarged in both the tunica media and adventitia were showed in aorta sections of untreated obese rats. Also, 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 that photomicrograph of heart and aorta sections from treated obese rats with atherosclerosis fed on the supplemented HFCD with jackfruit pulp, peels, seeds or leaves at the different levels showing gradual improvement with increasing the levels, especially with jackfruit leaves, compared with the positive group. 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).**

Conclusion:

Generally, the ability of jackfruit pulp, peels, seeds and leaves to enhance the activity of anti-obesity and inhibit heart and aorta degeneration 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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فعالية فاكهة الجاك فروت على التغيرات النسيجية المرضية للقلب والشريان الأورطي في ذكور الفئران المصابة بالسمنة و بتصلب الشرايين

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الملخص العربي

لقد أجريت هذه الدراسة لمعرفة فعّالية لب وقشور وبذور وأوراق الجاك فروت على تغيرات وزن الجسم وإجمالي وزن الدهون الحشوية وكذلك التغيرات النسيجية المرضيه للقلب والشريان الأورطي في الفئران المصابة بالسمنة و بتصلب الشرايين. لقد تم إجراءُ التجربةِ على مرحلتين (كلاً منهما مدتها ستة أسابيع)، كان الهدف من المرحلة الأولى هو إحداث السمنة وتصلب الشرايين، بينما كانت المرحلة الثانية لعلاج الفئران البدينة و المصابة بتصلب الشرايين من خلال التغذية على نظام غذائي مكمل بـ ٥ و ١٠٪ لب، ٥ و ٧,٥٪ (قشور، بذور، أوراق الجاك فروت). أظهرت النتائج أنخفاض في وزن الجسم النهائي وزيادة وزن الجسم ووزن الدهون الحشوية ومؤشر السمنة قد تحسن بشكل كبير مع زيادة مستويات لب وقشور وبذور وأوراق الجاك فروت. لقد كانت النتائج المُثلى في معدل فقدان الوزن في الفئران البدينة المصابة بتصلب الشرايين التي تتغذى على النظام الغذائي عالي الدهون والكوليسترول المكمل بقشور وأوراق الجاك فروت عن تلك التي تتغذى على النظام الغذائي عالي الدهون والكوليسترول المكمل باللب والبذور. وفيما يتعلق بتأثير لب وقشور وبذور وأوراق الجاك فروت على التغيرات النسيجية المرضيه للقلب والشريان الأورطي، فقد كشفت التصوير المجهري لمقاطع القلب والشريان الأورطي في الفئران البدينة والمصابه بتصلب الشرايين التي تم تغذيتها على النظام الغذائي عالي الدهون والكوليسترول المكمل بلب وقشور وبذور وأوراق الجاك فروت على مستويات مختلفة يظهر تحسناً تدريجياً مع زيادة المستويات، وخاصةً مع أوراق الجاك فروت، مقارنة بالمجموعة الإيجابية. بشكل عام ، فإن قدرة لب وقشور وبذور وأوراق الجاك فروت على تعزيز نشاط مكافحة السمنة وتثبيط تنكس القلب والشريان الأورطي تجعل فاكهة الجاك فروت مصدراً طبيعيا واعداً للتحكم في السمنة وزيادة دهون الدم. ومع ذلك، فإن هناك حاجة إلى مزيد من البحث لفهم آليات العمل والفوائد المحتملة للب وقشور وبذور وأوراق الجاك فروت في التحكم السمنة وزيادة دهون الدم.

الكلمات المفتاحية: الجاك فروت؛ السمنة؛ أمراض القلب والأوعية الدموية؛ دهون الدم.