DOI: https://doi.org/10.31351/vol35iss2pp201-208

Possible Hepatoprotective Effect of Two Different Doses of Acai Berry Extract Alone and in Combination with Orlistat on High-Carbohydrate, High-Fat Diet-Induced Obesity in Male Rats

Shihab Hattab Mutlag[1], Ali Faris Hassan [*,1] and Hiba Zaki Hammoodi[1]
[1]Department of Pharmacology and Toxicology, College of Pharmacy, University of Baghdad, Baghdad, Iraq.
[*]**Corresponding author**
Received 22/6/2024, Accepted 24/12/2025, Published 24/6/2026

Abstract

Obesity is a complex and chronic disease. It has a negative impact on general health, quality of life, and elevation in mortality rate. The liver is the most affected organ by obesity. The use of plants' different active constituents, which had different pharmacological effects. One of these constituents is the polyphenols, which have antioxidant and anti-inflammatory effects. Accordingly, polyphenols nowadays have become one of the most important therapeutic protocols. Acai berry extract has had different pharmacological benefits due to its anti-inflammatory and antioxidant activity. The aim of the present study is to assess the hepatoprotective impact of acai berry extract in rats fed a diet rich in fat and carbohydrates. To achieve this aim, 48 albino rats were divided into Group I: rats receive normal diets; group II: rats on high-fat and carbohydrate diets; Groups III and IV: rats on high-carbohydrate and fat diets with acai berry extract (250 and 500 mg/kg per day, respectively); and Groups V and VI: rats fed with high-carbohydrate and fat diets with 10 mg/kg/day of orlistat and 250 and 500 mg/kg per day of acai berry extract. All the groups received their treatments for 12 weeks. At the end of the study, serum was collected, and liver tissue was obtained to determine anti-oxidative, inflammatory, and liver function. In the present study, it has been found that there was a significant elevation in the level of superoxide dismutase and glutathione peroxidase in tissue homogenate ($p < 0.05$) and a significant reduction in the levels of liver function enzymes and malondialdehyde, tumor necrosis factor alpha, tumour growth factors, and interleukin-B1 ($p < 0.05$) when compared between groups III and IV and the induction group. The present study showed that the extract of acai berries had hepatoprotective effects.
Keywords: Acai berry, Anti-inflammatory, Antioxidant, Hepatoprotective, Orlistat

Introduction

Obesity is a complex and chronic disease with a bad prognosis for quality of life, health, and life span. WHO describes obesity as a global epidemic, a heterogeneous disease that quickly rises and links to a serious issue. obesity, which is manifested by abnormal or excessive fat accumulation with a body mass index (BMI) more than 30 kg/m ^{2}. Major causes of obesity are overeating, a sedentary lifestyle, and other factors that may eventually lead to metabolic illnesses. Adults living with obesity will increase by more than 115% between 2010 and 2030, from 524 million to 1.13 billion [(1)]. There is a strong association between obesity and inflammatory conditions, in which they found that obese people had high levels of proinflammatory mediators [(2, 3)]. During obesity, the overactivation and accumulation of nutrients inside adipose tissue cause the release of different inflammatory mediators. These mediators include tumor necrosis factor α and interleukin 6, beside reduction in the production of adiponectin, predisposing to a pro-inflammatory state and oxidative stress [(4)].The production of interleukin 6 associated with an increase in the synthesis of C-reactive protein in the liver related to inflammation and obesity is always associated with the development of different chronic diseases like atherosclerosis, metabolic syndrome, insulin resistance, and diabetes mellitus [(5)]. Oxidative stress is a state where there is an imbalance between free radicals (unstable molecules) and antioxidants in the body, leading to cell and tissue damage. Oxidative stress is always associated with obesity. Oxidative stress causes elevation of proinflammatory mediators and vice versa [(6)]. Generally, oxidative stress causes damage to different macromolecules within the cells, like proteins, lipids,

and DNA. This leads to encouraging apoptosis, aging, and degenerative malfunction (7).Obesity badly affects different organs within the body; the liver is considered the most affected organ. About 20% to 30% of adults suffer from non-alcoholic fatty liver disease (NAFLD), the primary liver condition linked to obesity [8]. Triacylglycerol buildup inside liver cells is the disease's hallmark. If left untreated, the condition can lead to more severe liver diseases, such as non-alcoholic steatohepatitis, liver fibrosis, cirrhosis, and, less frequently, liver cancer [9] .

The high incidence of NAFLD and its ability to proceed to liver failure, besides its correlation with major cardio-metabolic abnormalities such as type 2 diabetes mellitus (T2DM), the metabolic syndrome, and coronary heart disease (CHD), NAFLD has emerged as a significant public health concern[10] .

Acai is a berry grown on the acai palm tree (Euterpe oleracea), which is native to tropical Central and South America and grows mainly in floodplains and swamps. It produces small flowers that are brown to purple in color. The acai fruit is round, reddish-purple, and 1–2 cm in diameter, with the seeds constituting about 80% of the fruit. Scientists have recently shown an interest in acai berries. This berry has potential medicinal uses in addition to providing several beneficial dietary effects. Acai berry is used for its nutritional and medicinal properties, serving as a staple food and a remedy for conditions like diarrhea, parasites, fever, and skin issues. The indigenous people believed the berries held healing powers, with different parts of the plant used to create infusions, pastes, and medicinal wines for various ailments, including menstrual pain, malaria, and as a tonic for overall well-being, energy, and libido .

Amazonian Indians have been using this fruit for millennia as a natural remedy for many maladies and as a food source. It is said to be a high-energy fruit [11,12]. High concentrations of phenolic substances, including polyphenols and anthocyanins, are found in acai. By altering oxidative stress, inflammation, and autophagy, the bioactive components of açai berry extract offer a variety of pharmacological benefits, including anti-inflammatory and anti-anxiety activities [13]. Studies conducted in vivo show that acai improves the lipid profile, oxidative stress-related parameters, antioxidant enzymes, and non-alcoholic liver steatosis [14]. Apart from its antioxidant properties, anthocyanin also controls lipid metabolism [15].

The US Food and Drug Administration (FDA) has approved the anti-obesity drug orlistat (tetrahydrolipstatin). This drug is a saturated derivative of Streptomyces toxytricini's endogenous lipstatin. Through the reversible inhibition of pancreatic and gastric lipases in the gut, orlistat is used to treat obesity [16]. By converting triglycerides into absorbable free fatty acids and monoglycerides, these lipases are essential for the digestion of dietary fat. These lipases become inactive when orlistat forms a covalent bond with the serine residues in their active sites. Because lipase is inactivated, triglycerides cannot be hydrolyzed, which hinders the absorption of free fatty acids [17] .

The aim of the present study is to evaluate the anti-inflammatory and antioxidant effect of acai berry against liver damage induced by a high-fat, high-carbohydrate diet in rats.

Material and Methods

Chemicals and Drugs

Acia Berry from Carlyle, USA . ALT, AST, total bilirubin, and AFP kit from Sigma-Aldrich, USA . MDA, SOD, and GPX kits from RayBiotech, USA.IL1β, TNFα, TGF alpha and IL6 from TransGen Biotech Co., China

High-Carbohydrate, High-Fat diet

The rats from the experimental groups (except group I) were fed with a high-fat, high-carbohydrate diet rich in lard (17%) and fructose (17%), and drinking water was replaced with a 20% fructose solution (total calories 4,400 kcal/kg, 54% energy from fat)[18] .

Animal Selection

In this study, 48 Wister albino male rats were procured from the Animal House/College of Pharmacy/University of Baghdad. They were managed in accordance with the University of Baghdad's College of Pharmacy's Ethics Committee. Age- and weight-matched rats weighing 200–250 g were kept in an animal home at 22°C with a 12-hour light/dark cycle. The rats were divided into 6 groups, each group with 8 rats: Group I (control group): Rats fed a standard diet for 12 weeks. Group II (induced group): rats receive a high-fat/high-carbohydrate diet for 12 weeks. Group III: rats receive a high-fat/high-carbohydrate diet with 250 mg/kg/day of acai berry extract orally for 12 weeks. Group IV: rats receive a high-fat/high-carbohydrate diet with 500 mg/kg/day of acai berry extract orally for 12 weeks. Group V: rats receive a high-fat/high-carbohydrate diet with 250 mg/kg/day of acai berry extract and 10 mg/kg/day of orlistat for 12 weeks. Group VI: 8 rats receive a high-fat/high-carbohydrate diet with 500 mg/kg/day of acai berry extract and 10 mg/kg/day of orlistat for 12 weeks. At the end of the experiment (24 hours after the last dosing), cervical dislocation was used for animal sacrifice, blood was collected, and the liver was removed for further study .

Measurement of Fat Mass

The Skinfold Thickness-based Method is used in the present study. The method works by measuring the thickness of the subcutaneous fat (fat stored just under the skin) at specific, standardized anatomical sites using a specialized tool called a skinfold caliper.[19]

Biochemical Assessment

The function of the liver was evaluated by measuring different liver enzymes by using the spectrophotometer method according to (Lala V, et al 2023) [20], beside the evaluation of inflammation by ELISA according to (Ikemoto M, *et al*.2001) [21].

Preparation of liver tissue homogenate

After the rat was euthanized by ether diether, the liver was quickly excised and homogenate to measure different antioxidant parameters according to Ali FH, et al. 2015) [22]

Statistical Analysis

By using SPSS V24, numerical data was expressed as mean ±SD. A one-way ANOVA test was used to compare among groups; post hoc Tukey analysis was used to compare the significance between two groups. It was considered significant if the *P-value* was less than 0.05 (*p<0.05*).

Results

Effect of two different doses of Acai Berry extract on weight gain and fat mass

In table (1), group II showed a significant increase in the weight gain and fat mass when compared to group I (p<0.05); at the same time, there was a significant difference when compared among groups (II, III, V) related to the same above parameters *(p<0.05).* In group III, weight gain and fat mass showed a significant decrease when compared to group II (p<0.05). At the same table, there was a significant difference when compared among groups (II, IV, and VI) related to the same above parameters *(p<0.05).* In group IV, weight gain and fat mass showed a significant decrease when compared to group II (p<0.05).

Table 1. Effect of two different doses of Acai Berry extract with and without Orlistat on weight gain and fat mass after 12 weeks

	GROUP I	GROUP II	GROUP III	GROUP IV	GROUP V	GROUP VI
Weight gain (gm)	168.2±15.1	342.5±19. 2*^{aA}	286.2±17. 3^{B}	218.8±19. 3^{b}	192.4±11. 4^{B}	176.5±14.1^{c}
Fat Mass (gm)	164.2±16.3	293.1±13.6*^{a} $_{A}$	241.1±22.1^{B}	219.2±21.1^{b}	181.9±12.5^{C}	171.2±12.1^{c}

Data are expressed as mean ±± SD; n=8 animals in each group.

Group I (control group), **Group II** (induced group) rats receive a high-fat/high-carbohydrate diet. **Group III**: rats receive a high-fat/high-carbohydrate diet with 250 mg/kg/day of acai berry extract. **Group IV:** rats receive a high-fat/high-carbohydrate diet with 500 mg/kg/day of acai berry extract. **Group V:** rats receive a high-fat/high-carbohydrate diet with 250 mg/kg/day of acai berry extract and 10 mg/kg/day of orlistat. **Group VI:** rats receive a high-fat/high-carbohydrate diet with 500 mg/kg/day of acai berry extract and 10 mg/kg/day of orlistat .

*significantly different between groups (I, II) (*P*<0.05).

(a,b,c) is significantly different; the comparison among groups (II, IV, VI) (*P*<0.05).

(A, B, C) is significant different when compared among groups (II, III, V). (*P*<0.05).

Effect of two different doses of acai berry on liver function.

In Table (2), group II showed a significant increase in ALT, AST, total bilirubin, and AFP and a significant decrease in total protein and albumin when compared to group I *(p<0.05).* At the same time, there was a significant difference when compared among groups (II, III, and V) related to the same above parameters *(p<0.05). In* group III, ALT and AST showed a significant decrease when compared to group II (p<0.05); meanwhile, ALT and TSB in group V showed a significant decrease when compared to group III *(p<0.05).* At the same table, there was a significant difference when compared among groups (II, IV, and VI) related to the same above parameters *(p<0.05).* in group IV, ALT, AST, and AFP showed a significant decrease and a significant increase in total protein when compared to group II (p<0.05). meanwhile, ALT, TSB, and AFP in group VI showed a significant decrease, while total protein showed significant increase when compared to group IV *(p<0.05).*

Table 2. Effect of two different doses of Acai Berry with and without Orlistat on liver function after 12 weeks.

	GROUP I	GROUP II	GROUP III	GROUP IV	GROUP V	GROUP VI
AFP (μg/ml)	4.1±0.1	12.5±0. 2*^{aA}	10.2±0. 03^{A}	9.8±0. 03^{b}	8.4±0. 4^{B}	6.5±0.1^{c}
ALT (IU/L)	24.2±1.3	63.1±3.6*^{aA}	41.1±2.1^{B}	37.2±1.1^{b}	33.9±1.5^{C}	26.2±1.1^{c}
AST (IU/L)	21.01±1.2	51.1±2.4*^{aA}	42. 3±1. 5^{B}	36.9±1. 5^{b}	39.6±1.7^{B}	28.1±1.5^{b}
TSB (μmol/L)	0.4±0.02	1.8±0.09*^{aA}	1.4±0.05^{A}	1.1±0. 2^{a}	0.9±0.3^{B}	0.6±0.1^{b}
Total protein (g/dL)	6.2±0.1	2.9±0.2^{*aA}	3.2±0.1^{A}	4.9±0. 6^{b}	4.8±0.8^{B}	5.1±0.3^{c}
Albumin (g/dL)	2.9±0.3	1.1±0.1^{*aA}	1.4±0.3^{A}	1.6±0.7^{a}	2.1±0.6^{B}	2.5±0.9^{b}

Data are expressed as mean ± SD; n=8 animals in each group.
Group I (control group), **Group II** (induced group) rats receive a high-fat/high-carbohydrate diet. **Group III**: rats receive a high fat/high-carbohydrate diet with 250 mg/kg/day of acai berry extract. **Group IV:** rats receive a high-fat/high-carbohydrate diet with 500 mg/kg/day of acai berry extract. **Group V:** rats receive a high-fat/high-carbohydrate diet with 250 mg/kg/day of acai berry extract and 10 mg/kg/day of orlistat. **Group VI:** rats receive a high-fat/high-carbohydrate diet with 500 mg/kg/day of acai berry extract and 10 mg/kg/day of orlistat.
*significantly different compared between group (I, II) (P<0.05);
(a,b,c) is significantly different; the comparison among groups (II, IV, VI) (P<0.05).
(A, B,C) is significantly different when compared among groups (II, III, V). (P<0.05)
AFP: alpha fetoprotein, **ALT**: alanine transaminase, **AST**: aspartate aminotransferase, **TSB**: total serum bilirubin.

Effect of two different doses of Acai Berry extract on different oxidative stress parameters

In Table (3), group II showed a significant reduction in SOD, GPX, and elevation in MDA when compared to group I *(p<0.05*); at the same time, there was a significant difference when compared among groups (II, III, and V) related to the same above parameters *(p<0.05).* In group III, GPX and SOD showed significant increases, while MDA showed a significant decrease when compared to group II *(p<0.05);* MDA in group V showed a significant decrease when compared to group III *(p<0.05).* At the same table, there was a significant difference when compared among groups (II, IV, and VI) related to GPX, MDA, and SOD parameters *(p<0.05).* Group IV, GPX, and SOD showed significant increases, while MDA showed a significant decrease when compared to group II *(p<0.05).*

Table 3. Effect of two different doses of Acai Berry extract with and without Orlistat on different oxidative stress parameters after 12 weeks

	GROUP I	GROUP II	GROUP III	GROUP IV	GROUP V	GROUP VI
MDA (nmol/ml)	3.2±0.8	7.2±0.8*^{aA}	5.3±0.6^{B}	4.1±0.3^{b}	3.9±0.5^{C}	3.4±0.2^{b}
GPX (mg/dL)	2. 7±0.2	1. 9±0.5*^{aA}	4. 1±0.2^{B}	5.9±0.5^{b}	3.8±0.5^{B}	5.2±0.11^{b}
SOD (Unit/ml)	12.2±0.1	8.9±2.1*^{aA}	22.1±1.1^{B}	32.3±1.3^{b}	20.1±1.6^{B}	31.5±1.2^{b}

Data are expressed as mean ± SD; n=8 animals in each group
Group I (control group), **Group II** (induced group) rats receive a high-fat/high-carbohydrate diet. **Group III**: rats receive a high-fat/high-carbohydrate diet with 250 mg/kg/day of acai berry extract. **Group IV:** rats receive a high-fat/high-carbohydrate diet with 500 mg/kg/day of acai berry extract. **Group V:** rats receive a high-fat/high-carbohydrate diet with 250 mg/kg/day of acai berry extract and 10 mg/kg/day of orlistat. **Group VI:** rats receive a high-fat/high-carbohydrate diet with 500 mg/kg/day of acai berry extract and 10 mg/kg/day of orlistat.
*significantly different between groups (I, II) (P<0.05).
(a, b,c) is significantly different; the comparison among groups (II, IV, VI). (P<0.05).
(A, B, C) is significantly different when compared among groups (II, III, V). (P<0.05)
MDA: malondialdehyde, **GPX**: glutathione peroxidase, **SOD**: superoxide dismutase

Effect of two different doses of Acai Berry on different inflammatory parameters

In table 4, group II showed a significant increase in IL1β, TNFα, and TGF alpha when compared to group I *(p<0.05)*, at the same time there was a significant difference when compared among groups (II, III, and V) related to the same above parameters *(p<0.05)*.In group III, IL1β, TNFα, and TGF showed a significant decrease when compared to group II *(p<0.05)* meanwhile, IL1β and TNFα in group V showed a significant decrease when compared to group III *(p<0.05)*. At the same table, there was a significant difference when compared among groups (II, IV, and VI) related to the same above parameters *(p<0.05)*. In group IV, IL1β, TNFα, and TGF showed a significant decrease when compared to group II *(p<0.05)*. Meanwhile, IL1β in group VI showed a significant decrease when compared to group IV *(p<0.05)*.

Table 4. Effect of two different doses of Acai Berry with or without Orlistat on different inflammatory parameters after 12 weeks

	GROUP I	GROUP II	GROUP III	GROUP IV	GROUP V	GROUP VI
TNF-α (pg/ml)	816±140	2726±125*^{aA}	2210±112^{B}	2050±107^{b}	2100±123^{C}	1833±131^{b}
ILB1 (pg/ml)	3. 1±0.2	8. 3±0.3*^{aA}	6.2±0.2^{B}	5.9±0.09^{b}	5.9±0.2^{C}	3.9±0.4^{c}
TGF (pg/ml)	202.1±17.1	452.3±27.4*^{a} ^{A}	316.3±17.3^{B}	289±11.9^{b}	302.4±15.6^{B}	243.2±19.2^{b}
IL-6 (pg/ml)	66.9 ± 2.41	186.9 ±5.1*^{aA}	126.7 ± 2.8^{B}	96.2 ± 3.1^{b}	92.3 ± 6.6^{c}	86.9 ± 1.2^{c}

-Data are expressed as mean ± SD; n=8 animals in each group.

-Group I (control group), **Group II** (induced group) rats receive a high-fat/high-carbohydrate diet. **Group III**: rats receive a high-fat/high-carbohydrate diet with 250 mg/kg/day of acai berry extract. **Group IV:** rats receive a high-fat/high-carbohydrate diet with 500 mg/kg/day of acai berry extract. **Group V:** rats receive a high-fat/high-carbohydrate diet with 250 mg/kg/day of acai berry extract and 10 mg/kg/day of orlistat. **Group VI:** rats receive a high-fat/high-carbohydrate diet with 500 mg/kg/day of acai berry extract and 10 mg/kg/day of orlistat.

*significantly different between groups (I, II) (P<0.05).

(a, b,c) is significantly different; the comparison among groups (II, IV, VI) (P<0.05).

(A, B, C) is significantly different when compared among groups (II, III, V). (P<0.05)

TNF-α: tumour necrosis factor alpha, **ILB1:** interleukin beta 1, **IL6:** interleukin 6, **TGF:** tumour growth factors.

Discussion

In Table (1), the uses of acai berry extracts at two different doses (group III,IV) cause a significant decrease in the weight gain and fat mass as compared to group (II), this finding is completely agree with the previous study in which they found that the uses of acai berry reduce body weight and hyperglycemia, improve lipid profile and attenuated hepatic steatosis besides they found that acai berry extract increase (pAMPK) expression which tightly regulate cellular energy levels (ATP/AMP ratio), physiological stress, and post-translational modifications and increase PPAR-alpha which regulates fatty acid metabolism and is involved in processes like inflammation, energy homeostasis, and nutrient metabolism [23].

After a high-fat and carbohydrate diet led to the advancement of liver injury, the study revealed a substantial spike in the blood level of AFP, AST, ALT, and TSB in group II. These markers are measured to evaluate liver function, any significant elevation of these parameters indicated there are a damage in hepatocyte (hepatotoxicity) which cause leakage of them to the serum which led to their elevation [24,25].

A previous study demonstrated that hepatocyte regeneration, oxidative stress-induced DNA methylation and damage, and biliary epithelial cell proliferation are the three primary potential causes for elevated AFP levels [26]. Additionally, there was a significant decrease in both AST and ALT levels in group III, as well as a decrease in these markers overall (except for TSB in group IV), indicating that an increase in acai berry dose led to a decrease in liver injury and an improvement in liver function because it reduced inflammatory cells , inflammatory factors as TNF-α and IL-6 and liver mass, which in turn led to a decrease in liver injury and a decrease in the concentration of these markers [27].

By lowering these indicators, the inclusion of orlistat in the therapy further enhances liver function since it lessens hepatocyte damage by reducing liver fat storage and, therefore, liver aminotransferase levels. Thus, orlistat and acai berry extract work in concert to reduce liver damage [28]. However, when orlistat was introduced, research on rat models fed a high-fat diet revealed that there was a considerable decrease in the levels of TSB and AFP but no change in the levels of ALT or AST [29]

In rats fed a high-fat and high-carb diet demonstrated a significant increase in MDA and a decrease in the levels of SOD and GPX enzymes in liver tissue homogenate. Oxidative stress is a pathological condition characterized by elevation the concentration of free radicals. Antioxidant enzymes like SOD which dismutation of superoxide anion into normal molecule of oxygen and hydrogen peroxide and GPX which neutralized hydrogen peroxide beside it help in regulate the redox state of cells were significantly decrease with significant increase the lipid peroxidation of cell membrane which associated with significant increase in MDA [30].

According to these findings, obesity brought on by high-fat diets increases oxidative stress in the liver, which is likely a factor in the development of hepatic steatosis and other illnesses [31]. The current study's observations of lower SOD and catalase activity may be related to the rise in oxidative stress indicators. These findings are in line with previous studies, which suggest animals given a high-fat diet may have weakened tissue antioxidant defenses[32-34] . Furthermore, because acai berry extract has dose-dependent antioxidant activity, the study demonstrated that administering it reduced MDA levels and elevated SOD and GPX enzymes. To combat the lipid peroxidation, 500 mg/kg of acai berry extract was adequate [35]. The main active ingredients in acai berries are polyphenols, particularly anthocyanins especially (cyanidin-3-glucoside), flavonoids, and proanthocyanidins, which are powerful antioxidants, Acai's antioxidant properties were confirmed when the Nrf2/HO-1 signaling pathway was modulated, resulting in an increase in antioxidant enzymes, including SOD, CAT and GPX [36].

In the present study, the addition of orlistat to the acai berry extract didn't cause a significant decrease in the oxidative stress condition as compared with groups receiving only acai berry. This finding didn't agree with the previous study that showed the addition of orlistat in the treatment regimen caused a significant decrease in oxidative stress as compared to the induction group [37]. The reason could be due to the decrease in the bioavailability of both acai berry extract and orlistat so there is no synergistic effect after mixing

In the present study, TNF alpha, ILB1, and TGF levels of inflammatory markers were found to be elevated in group II an compared to group I. This finding matches a previous study that found obesity to be a condition of persistent low-grade inflammation linked to inflammatory cells infiltrating adipose tissue and an increase in TNF because of heavy diet in carbohydrates rather than fat [38, 39] .

A previous study showed that the increase in pro-inflammatory markers was that long-chain saturated fatty acids in the blood activated TLR4 [40]. As a result, the NF-κB nuclear translocation caused by the IKK-IκB signaling cascade stimulates the transcription of many pro-inflammatory cytokines and interleukins [41]. Besides, obese patients are found to have high amounts of circulating pro-inflammatory cytokines, including TNF-α, MCP-1, TGF-β, and IFN-γ, as well as interleukins IL-6, IL-1β, IL-18, and IL-8 [42].

The present study showed that administering two different doses of acai berry extract reduced the levels of circulating pro-inflammatory, and that the reduction was dosage dependent as compared to group II. In a previous study, acai berry extract showed a decrease in TNF alpha and ILB1 levels, and the mechanism of the reduction was related to modification of the NLRP3 inflammasome [43]. It also decreased the expression of NF-κβ [44]. In the trial of another previous study, the addition of orlistat to the obesity therapy reduced inflammation and, consequently, inflammatory indicators. This allowed orlistat to function as an adjuvant to the berry extract and enhance its protective potential. [45].

Conclusion

The present study showed that using acai berry extract could enhance liver function may be by reducing of oxidative stress and inflammatory process and protect against hepatotoxicity during heavy diet in fat and carbohydrates.

Acknowledgment

Thanks to the College of Pharmacy/University of Baghdad for invaluable assistance in achieving this study.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethics Statement

The ethical committee in the College of Pharmacy/University of Baghdad reviewed and approved this study. The number of ethical approvals was RECO-22025102A

Conflict of Interest

The authors declare that they have no conflict of interest.

Author Contribution

The authors confirm contribution to the paper as follows: study conception and design: Shihab Hattab Mutalg, data collection: Ali Faris Hassan; analysis and interpretation of results: Ali Faris Hassan, Heba Zaki. draft manuscript preparation: Ali Faris

Hassan. All authors reviewed the results and approved the final version of the manuscript.

References

1. Bradley B, Wissam G, Lizeth C, *et al*, Obesity: A Review of Pathophysiology and Classification, Mayo Clinic Proceedings, 2023,98(12): 1842-1857.
2. Sotak M, Clark M, Suur BE. *et al*, Inflammation and resolution in obesity, *Nat Rev Endocrinol*, 2025,21: 45–61.
3. Hagberg CE, Spalding KL, White adipocyte dysfunction and obesity-associated pathologies in humans, *Nat. Rev. Mol. Cell Biol*, 2024,25:270–289.
4. Makaronidis JM , Batterham RL, The role of gut hormones in the pathogenesis and management of obesity,Curr Opin Physiol, 2019,12 : 1-11.
5. Grunvald E, Shah R, Hernaez R, *et al*,AGA Clinical Practice Guideline on Pharmacological Interventions for Adults With Obesity, Gastroenterology, 2022, 163 (5) : 1198-1225.
6. Ramos-González EJ, Bitzer-Quintero OK, Ortiz G, J.J. et al, Relationship between inflammation and oxidative stress and its effect on multiple sclerosis, Neurología, 2024,39(3):292-301.
7. An X, Yu W, Liu J, *et al*, Oxidative cell death in cancer: mechanisms and therapeutic opportunities, *Cell Death Dis* ,2024,15: 556 .
8. Sahu P, Chhabra P, Mehendale AM,A Comprehensive Review on Non-Alcoholic Fatty Liver Disease, Cureus. 2023,15(12):e50159.
9. Teng ML, Ng CH, Huang DQ, *et al*, Global incidence and prevalence of nonalcoholic fatty liver disease, Clin Mol Hepatol, 2023, 29:S32-S42.
10. Manilla V, Santopaolo F, Gasbarrini A, Ponziani FR, Type 2 Diabetes Mellitus and Liver Disease: Across the Gut–Liver Axis from Fibrosis to Cancer, *Nutrients*, 2023, 15(11):2521.
11. Hemamalini K, A scientific review on: acai berry fruit (Euterpe Oleracea) a potential super fruit of world, Indo American Journal of Pharmaceutical Research, 2021,1: 43-45.
12. Melo PS, Selani MM, Gonçalves RH, *et al* , Açaí seeds: An unexplored agro-industrial residue as a potential source of lipids, fibers, and antioxidant phenolic compounds, *Ind. Crops Prod*, 2021,*161*: 113204.
13. Arnoso BJDM, Magliaccio FM, Araújo CA, *et al*, Açaí seed extract (ASE) rich in proanthocyanidins improves cardiovascular remodeling by increasing antioxidant response in obese high-fat diet-fed mice, Chem. Interact, 2022,351:109721.
14. Pereira RR, Abreu ICME, Guerra JFC, *et al*, Açai (Euterpe oleracea Mart.) upregulates paraoxonase 1 gene expression and activity with concomitant reduction of hepatic steatosis in high-fat diet-fed rats, Oxid Med Cell Longev ,2016:8379105.
15. Tena N, Martín J, Asuero AG, State of the Art of Anthocyanins: Antioxidant Activity, Sources, Bioavailability, and Therapeutic Effect in Human Health, Antioxidants (Basel), 2020,9(5):451.
16. Jain SS, Ramanand SJ, Ramanand JB, Akat PB, Patwardhan MH, Joshi SR, Evaluation of efficacy and safety of orlistat in obese patients, Indian J Endocrinol Metab, 2011,15(2):99-104.
17. Hampl SE, Hassink SG, Skinner AC, Armstrong SC, Barlow SE, et al, Clinical Practice Guideline for the Evaluation and Treatment of Children and Adolescents With Obesity, Pediatrics, 2023 Feb 01;151(2).
18. Birulina JG, Ivanov VV, Buyko EE, *et al* , High-fat, high-carbohydrate diet-induced experimental model of metabolic syndrome in rats, *Bulletin of Siberian Medicine*, 2020,19(4):14-20.
19. Reilly JJ, Wilson J, Durnin JV, Determination of body composition from skinfold thickness: a validation study, Arch Dis Child. 1995 ,73(4):305-10.
20. Lala V, Zubair M, Minter DA. Liver Function Tests. [Updated 2023 Jul 30]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482489/),
21. Ikemoto M, Tsunekawa S, Awane M, *et al* , A useful ELISA system for human liver-type arginase, and its utility in diagnosis of liver diseases, Clin Biochem,2001,34(6):455-461.
22. Ali FH , Intesar T , Maha NH, Evaluation of genotoxicity and effect of petroleum ether extract of Euphorbia lathyris on bone marrow cells: In-vivo study, International Journal of Pharmaceutical Sciences Review and Research, 2015, 32 : 116 -120.
23. Tavares TB, Santos IB, de Bem GF, et al, Therapeutic effects of açaí seed extract on hepatic steatosis in high-fat diet-induced obesity in male mice: a comparative effect with rosuvastatin, J Pharm Pharmacol. 2020 ,72(12):1921-1932.
24. Wang Y, Cui X, Zhang H, et al, Elevated Serum Alpha-fetoprotein Levels in Non-alcoholic Steatohepatitis: Possible Molecular Mechanisms and Potential Clinical Significance, Gene Expr, 2023,22(2):135-140.
25. Hammood AJ, Gharbi WA, Abdul Razzaq SA, Estimation of Liver Enzymes in Patients Infected with Hepatitis B Virus in Baghdad Hospitals, Iraqi Journal of Biotechnology,2022,21(2):1-8.
26. Chen Y, Zhao Y, Feng L, *et al*, Association between alpha-fetoprotein and metabolic syndrome in a Chinese asymptomatic population:

a cross-sectional study, Lipids Health Dis,2016,15:85.
27. Carvalho MMF, Reis LLT, Lopes JMM, *et al*, Açai improves non-alcoholic fatty liver disease (NAFLD) induced by fructose, Nutr Hosp,2018, 35(2):318-325.
28. Zahmatkesh A, Sohouli MH, Shojaie S, *et al*, The effect of orlistat in the treatment of non-alcoholic fatty liver in adolescents with overweight and obese, *Eur J Pediatr* ,2024,183: 1173–1182.
29. Amin HM, Tawfek NS, Abo-El Hussein BK , Abd El-GhanyM.S, Anti-Obesity Potential of Orlistat and Amphetamine in Rats Fed on High Fat Diet, MEJAS,2015, 5(2):453-461.
30. Mohammadi AA, Jazayeri S, Khosravi-Darani K, *et al*, Effects of Probiotics on Biomarkers of Oxidative Stress and Inflammatory Factors in Petrochemical Workers: A Randomized, Double-blind, Placebo-controlled Trial, Int J Prev Med,2015,1:6:82.
31. Ofosu-Boateng M, Shaik F, Choi S, *et al*, High-fat diet induced obesity promotes inflammation, oxidative stress, and hepatotoxicity in female FVB/N mice, Biofactors, 2024,50(3):572-591.
32. Tan BL, Norhaizan ME, Effect of High-Fat Diets on Oxidative Stress, Cellular Inflammatory Response and Cognitive Function, Nutrients, 2019 , 25,11(11):2579.
33. Ulla A, Alam MA, Sikder B, Supplementation of Syzygium cumini seed powder prevented obesity, glucose intolerance, hyperlipidemia and oxidative stress in high carbohydrate high fat diet induced obese rats, BMC Complement Altern Med, 2017,17(1):289.
34. Lee JH, Son CW, Kim MY, Kim MH, *et al*, Red beet (Beta vulgaris L.) leaf supplementation improves antioxidant status in C57BL/6J mice fed high fat high cholesterol diet, Nutr Res Pract, 2009,3(2):114-21.
35. Siracusa R, D'Amico R, Fusco R, *et al*, Açai Berry Attenuates Cyclophosphamide-Induced Damage in Genitourinary Axis-Modulating Nrf-2/HO-1 Pathways, Antioxidants,2022,11: 2355.
36. Impellizzeri D, Cordaro M, Siracusa R, *et al* , Molecular targets for anti-oxidative protection of açaí berry against diabetes myocardial ischemia/reperfusion injury, Free Radic Res, 2023,57(5):339-352.
37. Othman ZA, Zakaria Z, Suleiman JB, Ghazali WSW, Mohamed M, Anti-Atherogenic Effects of Orlistat on Obesity-Induced Vascular Oxidative Stress Rat Model, Antioxidants (Basel), 2021,10(2):251.
38. Ferreira AV, Mario EG, Porto LC, *et al*, High-carbohydrate diet selectively induces tumor necrosis factor-α production in mice liver, Inflammation,2011, 34(2):139-145.
39. Ali DN , Ali FH , Mazin MH , Estimation the Level of Metals (Lead, Cadmium, Copper and Zinc) In Multiple Sclerosis Patients in Basra\ Iraq, Indian Journal of Forensic Medicine & Toxicology, 2020,14(3):1029-1035.
40. Huang S, Rutkowsky JM ,Snodgrass RG, *et al*, Saturated fatty acids activate TLR-mediated proinflammatory signaling pathways, J. Lipid Res,2012, 53:2002-2013.
41. Sun SC, The non-canonical NF-kappa B pathway in immunity and inflammation, Nat. Rev. Immunol,2017,17:545–558.
42. Kirwan AM, Lenighan Y M, O'Reilly ME, *et al*, Nutritional modulation of metabolic inflammation, Biochem. Soc. Trans,2017,45:979–985.
43. Machado AK, Cadoná FC, Assmann CE, *et al*, Has anti-inflammatory potential through NLRP3-inflammasome modulation, Journal of Functional Foods,2019, 56:364-371.
44. Laurindo LF, Barbalho SM , Araújo AC, *et al* , Açaí (Euterpe oleracea Mart.) in Health and Disease: A Critical Review, Nutrients,2023,15:989.
45. Suleiman JB, Nna VU, Zakaria Z, *et al*, Obesity-induced testicular oxidative stress, inflammation and apoptosis: Protective and therapeutic effects of orlistat, Reproductive Toxicology,2020, 95:113-122.

التأثير الوقائي المحتمل للكبد لجرعتين مختلفتين من مستخلص توت الآساي، بمفرده وبالاشتراك مع أورليستات، على السمنة الناجمة عن اتباع نظام غذائي غني بالكربوهيدرات والدهون في ذكور الفئران

شهاب حطاب مطلك[١]، علي فارس حسن[١] وهبه زكي حمودي[١]

١ فرع الأدوية والسموم، كليه الصيدلة، جامعة بغداد، بغداد العراق

الخلاصة

السمنة مرض معقد ومزمن. ولها تأثير سلبي على الصحة العامة ونوعية الحياة وارتفاع معدل الوفيات. الكبد هو أكثر الأعضاء تأثرًا بالسمنة. استخدام المكونات النشطة المختلفة للنباتات والتي كان لها تأثيرات دوائية مختلفة. أحد هذه المكونات هو البوليفينول الذي كان له تأثيرات مضادة للأكسدة ومضادة للالتهابات. وبناءً على ذلك، أصبحت البوليفينول في الوقت الحاضر واحدة من أهم البروتوكولات العلاجية اليوم. كان لمستخلص توت الآساي فوائد دوائية مختلفة بسبب نشاطه المضاد للالتهابات ومضادات الأكسدة. تهدف هذه الدراسة إلى تقييم التأثير الوقائي للكبد لمستخلص توت الآساي في الفئران التي تتغذى على نظام غذائي غني بالدهون والكربوهيدرات. لتحقيق هذا الهدف، تم تقسيم ٤٨ جرذًا ألبينو إلى المجموعة الأولى، حيث تلقت الجرذان

نظامًا غذائيًا طبيعيًا، والمجموعة الثانية: جرذان تتناول نظامًا غذائيًا عالي الدهون والكربوهيدرات، والمجموعتان الثالثة والرابعة: جرذان تتناول نظامًا غذائيًا عالي الكربوهيدرات والدهون مع مستخلص توت الآساي (٢٥٠، ٥٠٠ ملجم/كجم يوميًا) على التوالي، والمجموعتان الخامسة والسادسة: جرذان تتغذى على نظام غذائي عالي الكربوهيدرات والدهون مع ١٠ ملجم/كجم يوميًا من أورليستات و (٢٥٠، ٥٠٠ ملجم/كجم يوميًا) على التوالي من مستخلص توت الآساي. تلقت جميع المجموعات علاجاتها لمدة ١٢ أسبوعًا. في نهاية الدراسة، تم جمع المصل، وأخذ أنسجة الكبد لتحديد وظائف مضادات الأكسدة والالتهابات والكبد. في هذه الدراسة، وُجد ارتفاعٌ ملحوظٌ في مستوى (سوبر أكسيد ديسميوتاز، غلوتاثيون بيروكسيديز) في مُتجانس الأنسجة ($p < 0.05$) وانخفاضٌ ملحوظٌ في مستويات إنزيمات وظائف الكبد و(مالونديالدهيد، عامل نخر الورم ألفا، عوامل نمو الورم، إنترلوكين (B1-عند ($p < 0.05$) المقارنة بين المجموعتين الثالثة والرابعة ومجموعة التحريض. أظهرت الدراسة الحالية أن مستخلص توت الآساي له تأثيراتٌ وقائيةٌ للكبد.

الكلمات المفتاحية: توت الآساي، مضادٌ للالتهابات، مضادٌ للأكسدة، واقيٌ للكبد، أورليستات.