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Full-length Research Article

Ameliorative Effects of Methanol Extract of *Citrullus lanatus* Seed in Hyperlipidaemic Wistar Rats

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Summary: *Citrullus lanatus* (watermelon) is a commonly consumed fruit whose phytochemical constituents have known advantages; however, the seeds of this plant are usually discarded. Hyperlipidaemia is a medical condition characterized by an elevation of any or all lipid profiles and/or lipoproteins in the blood. This study aimed to investigate the haematological effects and lipid-lowering potentials of methanol extract of *C. lanatus* seed (MECLS) in egg yolk-induced hyperlipidaemic male Wistar rats. A total of 40 rats were randomly divided into four groups of ten rats each: Normal control group (NCG), Hyperlipidaemic control group (HCG), and Hyperlipidaemic treated groups (HTG1 and HTG2), which were treated with MECLS at 800mg/kg and 1600mg/kg body weight for 7 days, respectively. Lipid profiles (TC, TG, LDL and HDL) and Haematological parameters (packed cell volume, white blood cell count, red blood cell count, haemoglobin concentration, platelets) of all the animals in each group were determined. The results showed a significant decrease in Total Cholesterol, PCV, WBC, RBC, haemoglobin, and Platelets, with a corresponding significant increase in Triglycerides and HDL following treatment with MECLS in hyperlipidaemic Wistar rats. Treatment of hyperlipidaemia with the methanol extract of *Citrullus lanatus* seeds reduces total cholesterol and causes a reversal of negatively altered haematological parameters resulting from hyperlipidaemia.

Keywords*: Hyperlipidaemia, lipoproteins, Citrillus lanatus, Total Cholesterol, Triglyceride, LDL, HDL.*

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INTRODUCTION

Hyperlipidaemia has been considered the most influential risk factor for coronary heart disease (CHD), a cause of mortality in a high percentage of people around the world (Adegoke *et al.,* 2018; Roth *et al.,* 2020). One of the most common risk factors in patients with cardiovascular disease is dyslipidaemia. Hyperlipidaemia is a common pathological condition distinguished by a selective increase in plasma levels of low density lipoprotein (LDL), total cholesterol (TC) and/or triglycerides (TG) (Jellinger, 2012), which increases the risk of endothelial dysfunction and atherosclerosis (Amit *et al*., 2011), which can manifest clinically as hypertension, coronary heart disease (CHD), myocardial infarction, arrhythmias, stroke or peripheral arterial disease (Shamir and Fisher, 2000; Castilla-Guerra *et al.,* 2009).

Interest in the possible health benefits of various phytochemical constituents such as flavonoids, anthocyanin, ascorbic acid, tocopherol, phenolic compounds, dietary fibre, and carotenoids present in fruits and vegetables, has increased in recent years owing to their potent antioxidant and free-radical scavenging activities, haven been recognized as natural sources of various bioactive compounds (Pennington and Fisher, 2010; Rahman *et al.,* 2013). *Citrullus lanatus* (Watermelon), which is a vine-like flowering plant and belongs to the family *Cucurbitaceae,* is an important vegetable crop in Africa, originally from Southern Africa and can adapt to different environmental conditions (Mandel *et al.*, 2005; Adetutu *et al.,* 2015). While it is commonly consumed, its consumption is usually limited to the fruit. The seeds of *C. lanatus* have been shown to contain phytochemical constituents like alkaloids, flavonoids, tannins, amino acids, carbohydrates, cardiac glycosides, terpenoids, steroids, carotenoids, oils and fats, essential amino acid, vitamins A, B and C, and minerals (calcium, iron, magnesium, potassium, phosphorus and zinc) (Olamide *et al.,* 2011;

Omoboyowa *et al.,* 2015). Atlaş *et al.,* (2011) reported that the juice from watermelon exerts protective effects in the liver, kidney and brain against experimental Carbon tetrachloride (CCL_4) toxicity in rats, which can be attributed to the presence of antioxidants in the juice extract. The bioactive compounds observed to be present in methanol extract of *Citrullus lanatus* seed (MECLS) are known to exhibit medicinal as well as physiological activity (Sofowora, 1993; Adeniyi *et al.,* 2012). This study was designed to analyse the possible haematological and anti-hyperlipidaemic effects of methanol extract of *Citrullus lanatus* seed in hyperlipidaemic conditions.

MATERIALS AND METHODS

Plant Identification and Extract Preparation: *Citrullus lanatus* was purchased from a market in Abakaliki, Ebonyi State, identified and authenticated by a botanist in the Department of Botany, Ebonyi State University, as *C. lanatus* (Identification number: EBSU-H-1120). The seeds of *Citrullus lanatus* were air-dried and pulverized. The crushed Citullus lanatus seeds were subjected to maceration extraction using absolute methanol for total period of 24 hours. The extract was evaporated with a rotary vacuum evaporator to obtain methanol extract of *Citrullus lanatus* seed (Obonga *et al*., 2019).

Experimental Animals: Forty (40) male Wistar rats, weighing between 150g and 180g were bought from FUNAI Animal house, Nigeria. The animals were housed in animal cages with suitable temperature and humidity in the FUNAI Animal House, Ebonyi state, Nigeria. They had free access to food and water throughout the period of the experiment and they were kept under standard laboratory conditions. Handling and use of animals in this study were in accordance with the guiding principles for research involving animals as recommended by the declaration of Helsinki and the Guiding principles in the care and use of animals (Ashal *et al*., 2023).

Experimental Design: Forty (40) male Wistar rats were divided into four (4) groups of 10 rats per group, as follows: Group One: Normal Control Group (NCG), Group Two: Hyperlipidaemic Control Group (HCG), Group Three: Hyperlipidaemic Treatment group 1 (HTG1), were made hyperlipidaemic and treated with methanol extract of *C. lanatus* seed (800mg/kg body weight), for 7 days. Group Four: Hyperlipidaemic Treatment group 2 (HTG2): were also made hyperlipidaemic and treated with (1600mg/kg body weight) methanol extract of *C. lanatus* seed for 7 days.

Induction of hyperlipidaemia in Experimental Rats: Hyperlipidaemia was induced by intraperitoneal administration of egg yolk (0.2ml/10g body weight) for a day (Song *et al*., 2013; Anuwat *et al*., 2017), after which they were sacrificed after 12 hours fasting period to ascertain the attainment of hyperlipidaemia.

Haematological Analysis: At the end of the experiments, the animals were sacrificed by cervical dislocation and blood samples were collected via cardiac puncture, into Ethylene Diamine Tetra Acetic acid (EDTA) bottles. Full blood count was done using Diatron Automated A38-1 Abacus Hematology Analyzer as described by Okeke *et al*. (2023). Results obtained for packed cell volume, red blood cell count, white blood cell count, haemoglobin concentration and blood platelets were recorded.

Lipid Profile Analyses: Low-density lipoprotein (LDL) and high-density lipoprotein (HDL) were assayed using Centronic LDL and HDL kits. Ttiglyceride (TG) levels were assayed using Agappe TG kit using enzyme-linked immunosorbent assay method as described by Danboyi *et al*. (2020). Total cholesterol level was determined spectrophotometrically, using enzymatic colorimetric assay kits (Danboyi *et al*., 2020).

Statistical Analysis: Data are expressed as Mean ± SEM. Results were analysed using a standard statistical software. Comparison of results between the various groups was carried out using ANOVA with statistically significance taken at $p < 0.05$.

RESULTS

The results for lipid profile (Table 1), shows a significant increase in Total Cholesterol in the HCG compared to the control (NCG), followed by a decrease in the HTG1. Triglyceride was significantly increased after induction of hyperlipidaemia (HCG), followed by an increase in other groups. HDL was significantly reduced in HCG compared to NCG, and significantly increased in the treatment groups (HTG1 and HTG2) compared to the NCG. The results also show a significant increase in LDL in all groups compared to the NCG.

The results for haematological parameters (Table 2) shows a significant increase in Packed Cell Volume (PCV) after induction of hyperlipidaemia (HCG), followed by a decrease after treatment (HTG2). Haemoglobin concentration (Hb) was significantly increased in HCG, followed by significant reductions in both HTG1 and HTG2, compared to NCG. White blood cell count (WBC) was significantly increased in HCG, and significantly decreased in the treatment groups (HTG1 and HTG2), compared to NCG. Red blood cell (RBC) and Platelet counts (PLT) were also increased in HCG compared to NCG, and significantly decreased in HTG1 and HTG2 compared to HCG.

Table 1:
Effects of Methanol Extract of *Citullus Lanatus* Seed on the Lipid Profile of various groups.

GROUPS	Total Cholesterol (mmol/l)	Triglyceride (mmol/l)	HDL (mmol/l)	LDL (mmol/l)
Group I (NCG)	**3.82±0.01**	**1.11±0.02**	**1.34±0.01**	**0.55±0.02**
Group II (HCG)	**4.28±0.08#**	**1.51±0.02#**	**1.07±0.02#**	**0.84±0.04#**
Group III (HTG 1)	**3.67±0.06***	**1.69±0.01*#**	**1.30±0.15**	**0.80±0.05#**
Group IV (HTG 2)	**3.91±0.05**	**1.73±0.07*#**	**1.33±0.04***	**0.97±0.05#**

*Values expressed as mean ± SEM. # denotes statistical significance (p<0.05) when compared to NCG. * denotes statistical significance (p<0.05) when compared to HCG*

Table 2
Effects of Methanolic *Citrullus lanatus* Seeds Extract on Haematological Parameters.

GROUPS	PCV (%)	Hb (g/dl)	WBC ($\times10^9$/mm^3)	RBC ($\times10^6$/L)	PLATELET ($\times10^9$/µL)
Group I (NCG)	38.75±0.48	17.17±0.59	6.23±0.18	2.39±0.03	122.00±1.71
Group II (HCG)	42.00±0.82$^{\#}$	19.76±0.30$^{\#}$	6.93±0.21$^{\#}$	2.82±0.05$^{\#}$	158.50±1.29$^{\#}$
Group III (HTG 1)	40.50±1.19	18.75±0.13$^{\#*}$	6.35±0.07*	2.51±0.03$^{\#*}$	138.25±0.85$^{\#*}$
Group IV (HTG 2)	37.00±0.91*	17.64±0.97*	6.33±0.09*	2.43±0.05*	120.75±0.85*

Values expressed as mean ± SEM. $^{\#}$ denotes statistical significance (p<0.05) when compared to NCG. * denotes statistical significance (p<0.05) when compared to HCG.

DISCUSSION

Hyperlipidaemia is a disorder that describes elevated lipid levels within the body (Hill and Bordoni, 2023). It can also be described as an increase in LDL, total cholesterol or triglycerides, and or a decrease in HDL (Su *et al.,* 2021). Hyperlipidaemia has been implicated in cases of hypertension (Wyszynska *et al.,* 2023), coronary heart disease (Jian-zhai *et al.,* 2004), myocardial infarction (Moertensen and Nordestgaard, 2020), arrhythmias (Ivan *et al.,* 2019) and stroke (Shigematsu *et al.,* 2015) amongst others, conditions which might be ameliorated or totally avoided if food crops with medicinal potentials are consumed as a whole, with no parts discarded (Gaire, 2018; Rathore *et al.,* 2024). This study aimed to analyse the possible haematological and anti-hyperlipidaemic effects of methanolic extract of *Citrullus lanatus* Seed (MECLS) in hyperlipidaemic conditions.

Animals in the HCG group exhibited significant hyperlipidaemia compared to the NCG, following infusion with egg yolk. Following treatment with 800mg/kg body weight of MECLS (HTG1) and 1600mg/kg body weight of MECLS (HTG2), the results showed a significant decrease in total cholesterol compared to the HCG, with results similar to that obtained in the NCG. This is in line with the finding of Danboyi *et al.* (2021), that citrulline contained in the seed of *Citrullus lanatus* has anti-dyslipidemic effect. This result is contrary to that of Uto-kando *et al.* (2021), that citrulline does not affect TC and TG.

Increased TC has been linked with increased risk of atherosclerosis (Gaggini *et al.,* 2022), potentially leading to several other conditions such as coronary artery disease, stroke and peripheral arterial disease (Jian-zhai *et al.,* 2004; Shigematsu *et al.,* 2015; Zemaitis *et al.,* 2024). Specifically, an increase in TG has been linked to increased risk of development of pancreatitis (Karalis, 2017).

This study also observed a persistent increase in TG following the induction of hyperlipidemia despite treatment with MECLS. The reason for this increase in TG remains unclear, and this observation counters that of Uto-kando *et al.* (2021), that citrulline has no effect on TG, except proven that this effect is brought about by another active compound contained in the seeds of *Citrullus lanatus.*

The dose-dependent increase in high-density lipoprotein after treatment with MECLS, suggests a positive effect, as increased HDL absorbs cholesterol in the blood, carrying it back to the liver for excretion, thus lowering the TC (Jomard and Osto, 2020). HDL has also been reported to induce endothelial nitric oxide synthase activation, leading to increased production of nitric oxide (Mineo *et al.,* 2003), a known antiatherogenic molecule (Sukhovershin *et al.,* 2015).

This study showed a significant increase in haematocrit, red blood cell count, white blood cell count and blood platelets following induction of hyperlipidaemia (Table 2). This is consistent with previous reports (Alizamir *et al.,* 2018; *Gebrie et al*., 2018; Hashemi *et al*., 2020). Dyslipidemia has also been associated with leucocytosis (Desai *et al.,* 2006; Tsai *et al.,* 2007). Though elevation of blood cell indices has been extensively reported following hyperlipidaemia (Desai *et al.,* 2006; Fessler *et al.,* 2013; Hashemi *et al.,* 2020; Tsai *et al.,* 2007), the mechanism behind remains unknown.

An interesting observation from this study is that the hematological results obtained in the HCG were corrected and brought down to baseline level as seen in the NCG, indicating a correctional effect of MECLS on the effects brought about by hyperlipidaemia. Further studies need to be carried out to ascertain the exact components of MECLS responsible for each effect observed, and to elucidate possible mechanisms.

In conclusion, treatment of hyperlipidemia with MECLS improves some lipid factors, but its effects are more visible in reversal of negatively altered haematological parameters resulting from hyperlipidemia

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