Multidiciplinary Output Research For Actual and International Issue (MORFAI Journal) ISSN (e): 2808-6635
Volumes 4 No. 4 (2025)

CHAYOTE (SECHIUM EDULE JACQ. SWARTZ) EXTRACT AND FRACTIONS IMPROVE MDA LEVELS AND TESTOSTERONE HORMONES IN MALE RATS WITH TYPE 2 DIABETES

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Received	: 30 November 2024	Published	: 31 January 2025
Revised	: 13 December 2024	DOI	: https://doi.org/10.54443/morfai.v4i4.2414
Accepted	: 28 December 2024	Link Publish	: https://radjapublika.com/index.php/MORFAI/article/view/2414

Abstract

This study aimed to analyze the effects of chayote (Sechium edule Jacq. Swartz) extract and fractions on male reproductive function, specifically by observing Malondialdehyde (MDA) levels and testosterone hormones, in a rat model of type 2 diabetes. The study used a laboratory experimental method with a posttest-only controlled group design on male Wistar rats. The rats were randomized into 17 groups, including a negative control group, a positive control group, and groups that received ethanol extract, n-hexane fraction, ethyl acetate, and water of chayote at doses of 50 mg/KgBW, 100 mg/KgBW, and 150 mg/KgBW. The results showed that the ethanol extract, n-hexane fraction, and ethyl acetate of chayote can reduce MDA activity and increase testosterone hormone levels in male white rats (Rattus novergicus) induced by streptozotocin, NA, and HFD. This study suggests that chayote has the potential to be used as a natural ingredient to improve male reproductive function in people with type 2 diabetes.

Keywords: ***Chayote Extract, Diabetes Mellitus, Malonaldehyde, Testosterone Hormone***

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by high blood sugar levels. The International Diabetes Federation (IDF) estimates that the number of people with diabetes will increase to 700 million (10.9%) by 2045, and 21.3 million people in Indonesia by 2030. Optimal male reproductive health, characterized by the quality and quantity of spermatozoa, is intrinsically linked to an individual's holistic well-being, encompassing physical, mental, and social dimensions. Spermatozoa serve as crucial biomarkers in assessing male reproductive function. However, hyperglycemic conditions prevalent in diabetes mellitus can induce oxidative stress, characterized by elevated free radical production. This heightened oxidative stress can precipitate cellular damage, disrupting membrane integrity and potentially leading to apoptosis. Consequently, these detrimental effects can impair the reproductive function of various cells, including those involved in spermatogenesis Complementary and alternative therapies are being explored to manage diabetes and its complications. Chayote (Sechium edule (Jacq.) Swartz), from the Cucurbitaceae family, is a source of natural antioxidants, including flavonoids and proanthocyanins, which have potential anti-diabetic effects. This study investigates the effects of chayote extract and fractions on male reproductive function in a rat model of type 2 diabetes.

LITERATURE REVIEW

Diabetes Mellitus and Male Reproductive Health

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by hyperglycemia stemming from defects in insulin secretion, insulin action, or both. The global prevalence of DM is escalating at an alarming rate, with projections indicating that approximately 700 million individuals will be affected by 2045. This escalating prevalence underscores the urgent need to address DM and its associated complications, including the impact on male reproductive health.

A growing body of evidence suggests a strong link between DM and male reproductive dysfunction. Hyperglycemia, a hallmark of DM, can trigger a cascade of pathophysiological events that disrupt reproductive processes. One of the key mechanisms underlying this dysfunction is oxidative stress, an imbalance between the

production of reactive oxygen species (ROS) and the body's antioxidant defense mechanisms. Oxidative stress can inflict damage upon various cellular components, including lipids, proteins, and DNA, ultimately compromising cellular function and viability. Specifically, within the male reproductive system, oxidative stress can impair spermatogenesis, the complex process of sperm production. Studies have demonstrated that men with DM frequently present with diminished sperm quality, characterized by reduced sperm count, motility, and abnormal morphology. This deterioration in sperm quality can contribute to infertility and a decline in reproductive capacity.

Chayote: A Potential Therapeutic Agent

In the pursuit of alternative therapies to manage DM and its complications, natural products have garnered significant attention. Chayote (Sechium edule Jacq. Swartz), a member of the Cucurbitaceae family, is a widely consumed vegetable that has demonstrated promising medicinal properties. Phytochemical analyses have revealed that chayote is a rich source of bioactive compounds, including flavonoids, proanthocyanins, and other antioxidants. These compounds have been shown to possess various pharmacological activities, such as anti-diabetic, anti-inflammatory, and antioxidant effects. The antioxidant properties of chayote are of particular interest in the context of DM-associated reproductive dysfunction. Antioxidants can scavenge free radicals, mitigating oxidative stress and protecting cells from damage. Studies have shown that chayote extracts can reduce lipid peroxidation, a key indicator of oxidative stress, and enhance antioxidant enzyme activity.

MATERIAL AND METHOD

Research Design

This study used a laboratory experimental design with a post-test controlled group configuration to investigate the effects of chayote (Sechium edule Jacq. Swartz) on MDA and testosterone levels in male white rats (Rattus novergicus) induced by type 2 diabetes mellitus.

Plant Materials

Chayote fruit was obtained through deliberate sampling from Pagar Batu Village, Sipoholon District, North Tapanuli Regency, North Sumatra, Indonesia.

Extraction and Fractionation

Chayote fruit was washed, peeled, and sliced. The slices were air-dried for 15 hours at room temperature and then dried in an oven at 55°C for 72 hours until they reached a constant weight. The dried chayote slices were ground into a fine powder using a grinder.

Extraction: Two kilograms of chayote powder were macerated in 10 liters of 70% ethanol for 3 days with periodic shaking. The mixture was filtered, and the residue was re-extracted with 3 liters of 70% ethanol for 2 days. The filtrates were combined and concentrated using a rotary evaporator at 60°C under reduced pressure. The concentrated extract was then dried in an oven at 40°C until a thick consistency was obtained, resulting in a crude ethanol extract of chayote.

Fractionation: The crude ethanol extract was fractionated using the liquid-liquid partition method. The extract was dissolved in distilled water and partitioned sequentially with n-hexane and ethyl acetate. Each fraction was collected and concentrated using a rotary evaporator. The remaining water layer formed the water fraction. All fractions were stored at 4°C until further use.

Experimental Animals

Fifty-one male Wistar rats (Rattus novergicus), aged 2.5-3 months and weighing 150-220 grams, were obtained from the Animal House of the Faculty of Medicine, Methodist University of Indonesia. The rats were housed in standard cages (40 cm x 30 cm x 13 cm) with wire mesh tops, with a maximum of three rats per cage. The cages were lined with wood shavings as bedding, which was changed twice a week. The rats were maintained under controlled environmental conditions (temperature 25 ± 2°C, humidity 55 ± 10%, and a 12-hour light/dark cycle) and were provided with standard rat chow and clean drinking water ad libidum.

Induction of Type 2 Diabetes Mellitus

Type 2 diabetes mellitus was induced in rats by a combination of a single intraperitoneal injection of streptozotocin (STZ) at a dose of 35 mg/kg body weight (dissolved in 0.1 M citrate buffer, pH 4.5) and nicotinamide (NA) at a dose of 110 mg/kg body weight (dissolved in 0.9% NaCl solution) given 15 minutes before

the STZ injection. After STZ-NA injection, rats were fed a high-fat diet (HFD) consisting of 45% fat, 20% protein, and 35% carbohydrate for 14 days to induce insulin resistance and hyperglycemia.

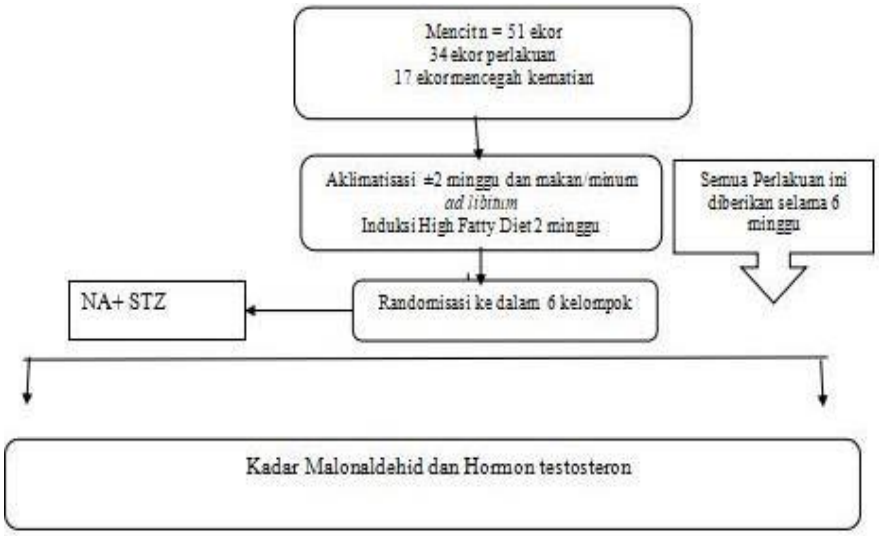

Figure 1.1: Research Flow

RESULTS AND DISCUSSION

Effect of Chayote Extract and Fractions on MDA Levels

The levels of Malondialdehyde (MDA), a marker of lipid peroxidation and oxidative stress, were measured in the serum of rats after 14 days of treatment. The results of the normality test using the Shapiro Wilk test showed that the data were normally distributed, so ANOVA was used to analyze differences in MDA levels. The p-value for MDA activity was 0.001, indicating that the ANOVA showed a significant difference in MDA levels between the control and intervention groups ($p<0.05$) are presented in Table 1.

. **Table 1.** Mean and difference in MDA levels in the control and intervention groups

Group	Mean (nmol/mL)	SD (nmol/mL)	Median (nmol/mL)	Min (nmol/mL)	Max (nmol/mL)	p-value
K0	763	95	800	655	833	
K1	2.068	831	2.276	1.153	2.775	
K2	2.721	209	2.660	2.549	2.953	
K3	2.257	427	2.186	1.870	2.715	
KEE50	1.221	305	1.049	1.041	1.573	
KEE100	1.014	72	996	952	1.093	p<0.001
KEE150	1.106	188	1.208	889	1.222	
KNE50	1.590	359	1.715	1.186	1.870	
KNE100	1.375	639	1.330	759	2.035	
KNE150	1.080	235	999	898	1.345	
KEaE50	1.145	448	1.074	735	1.624	
KEaE100	1.038	214	1.047	818	1.247	
KEaE150	1.133	108	1.164	1.012	1.222	
KWF50	915	172	858	778	1.108	
KWF100	1.278	191	1.339	1.064	1.431	
KWF150	1.981	388	2.046	1.165	2.333	
KM500	665	86	679	572	744	

Note: Control (K0), Rats induced with STZ and HFD (K1), Rats induced with Nicotinamide and HFD (K2), Rats induced with Nicotinamide, HFD and Streptozotocin (K3), Rats induced with nicotinamide, HFD, STZ with 50 mg chayote ethanol extract (KEE 50), Rats induced with nicotinamide, HFD, STZ with 100 mg chayote ethanol extract (KEE 100), Rats induced with nicotinamide, HFD, STZ with 150 mg chayote ethanol extract (KEE 150), Rats induced with nicotinamide, HFD, STZ with 50 mg chayote n-hexane fraction (KNE 50), Rats induced with nicotinamide, HFD, STZ with 100 mg chayote n-hexane fraction (KNE 100), Rats induced with nicotinamide, HFD, STZ with 150 mg chayote n-hexane fraction (KNE 150), Rats induced with nicotinamide, HFD, STZ with 50 mg chayote ethyl acetate fraction (KEaE 50), Rats induced with nicotinamide, HFD, STZ with 100 mg chayote ethyl acetate fraction (KEaE 100), Rats induced with nicotinamide, HFD, STZ with 150 mg chayote ethyl acetate fraction (KEaE 150), Rats induced with nicotinamide, HFD, STZ with 50 mg chayote water fraction (KWF 50), Rats induced with nicotinamide, HFD, STZ with 100 mg chayote water fraction (KWF 100), Rats induced with nicotinamide, HFD, STZ with 150 mg chayote water fraction (KWF 150), Rats induced with nicotinamide, HFD, STZ with 500 mg metformin (KM 500).

Elevated MDA levels are an indicator of oxidative stress, which can damage cells and tissues. The results of this study indicate that the administration of chayote ethanol extract at a dose of 50 mg/kgBW yielded the most significant reduction in MDA levels. This finding aligns with the research conducted by Yasaroh et al. (2021), which demonstrated that Moringa oleifera leaf extract effectively reduced blood glucose levels in diabetic rats. While all treatment groups exhibited a decrease in MDA levels, the group administered metformin at 500 mg/kgBW showed the most substantial reduction. Metformin possesses potent hypoglycemic properties; however, chayote extract may be superior in mitigating oxidative stress and insulin resistance. Chayote contains flavonoids and proanthocyanins, which exhibit antioxidant activity. Flavonoids can donate electrons to free radicals, thereby disrupting chain reactions and preventing cellular damage.

Effect of Chayote Extract and Fractions on Testosterone Hormone Levels

The levels of testosterone hormone were measured in the serum of rats after 14 days of treatment. The results of the normality test using the Shapiro Wilk test showed that the data were normally distributed, so ANOVA was used to analyze differences in testosterone hormone levels. The p-value for testosterone hormone activity was 0.001, indicating that the ANOVA showed a significant difference in testosterone hormone levels between the control and intervention groups ($p<0.05$) are presented in Table 2.

Table 2. Mean and difference in testosterone hormone levels in the control and intervention groups

Group	Mean (ng/dL)	SD (ng/dL)	Median (ng/dL)	Min (ng/dL)	Max (ng/dL)	p-value
K0	454.696	15.125	453.531	440.187	470.370	
K1	243.258	30.567	240.181	214.345	275.246	
K2	269.369	45.048	273.455	222.417	312.235	
K3	289.103	60.151	310.339	221.215	335.755	
KEE50	342.282	31.454	343.285	310.339	373.223	
KEE100	354.763	46.845	356.346	307.147	400.796	p<0.001
KEE150	353.428	38.091	358.162	313.191	388.930	
KNE50	423.168	45.362	419.231	379.903	470.370	
KNE100	380.516	53.005	375.723	330.069	435.755	
KNE150	438.797	56.762	459.899	374.506	481.986	
KEaE50	313.776	17.371	309.123	299.206	333.000	
KEaE100	415.079	9.155	410.920	408.741	425.576	
KEaE150	392.816	9.978	393.204	382.650	402.595	
KWF50	417.738	35.823	434.484	376.609	442.121	
KWF100	423.721	26.605	421.561	398.262	451.341	
KWF150	423.721	26.605	421.561	398.262	451.341	

KM500	439.723	15.944	446.200	421.561	451.409

Note: Control (K0), Rats induced with STZ and HFD (K1), Rats induced with Nicotinamide and HFD (K2), Rats induced with Nicotinamide, HFD and Streptozotocin (K3), Rats induced with nicotinamide, HFD, STZ with 50 mg chayote ethanol extract (KEE 50), Rats induced with nicotinamide, HFD, STZ with 100 mg chayote ethanol extract (KEE 100), Rats induced with nicotinamide, HFD, STZ with 150 mg chayote ethanol extract (KEE 150), Rats induced with nicotinamide, HFD, STZ with 50 mg chayote n-hexane fraction (KNE 50), Rats induced with nicotinamide, HFD, STZ with 100 mg chayote n-hexane fraction (KNE 100), Rats induced with nicotinamide, HFD, STZ with 150 mg chayote n-hexane fraction (KNE 150), Rats induced with nicotinamide, HFD, STZ with 50 mg chayote ethyl acetate fraction (KEaE 50), Rats induced with nicotinamide, HFD, STZ with 100 mg chayote ethyl acetate fraction (KEaE 100), Rats induced with nicotinamide, HFD, STZ with 150 mg chayote ethyl acetate fraction (KEaE 150), Rats induced with nicotinamide, HFD, STZ with 50 mg chayote water fraction (KWF 50), Rats induced with nicotinamide, HFD, STZ with 100 mg chayote water fraction (KWF 100), Rats induced with nicotinamide, HFD, STZ with 150 mg chayote water fraction (KWF 150), Rats induced with nicotinamide, HFD, STZ with 500 mg metformin (KM 500). Diabetes can impair testicular function and testosterone hormone production. The results of this study demonstrate that the n-hexane fraction of chayote at a dose of 150 mg/kgBW yielded the most significant increase in testosterone hormone levels. This observation is supported by research conducted by Ghasani (2016), which indicated that Moringa oleifera leaf extract can improve sperm quality. Moringa oleifera leaves, like chayote, contain flavonoids that act as antioxidants. Nayak et al. (2020) also reported that Moringa oleifera leaf extract can reduce testicular damage and improve the hormonal environment.

CONCLUSION

Administration of ethanol extract, n-hexane fraction, and ethyl acetate fraction of chayote (Sechium edule Jacq. Swartz) demonstrated a significant reduction in Malondialdehyde (MDA) levels in male Wistar rats induced with type 2 diabetes mellitus. This finding suggests that chayote exhibits antioxidant properties, mitigating oxidative stress by scavenging free radicals and protecting cells from damage. Therefore, chayote holds potential as a natural therapeutic agent for ameliorating reproductive dysfunction in male patients with type 2 diabetes

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