PSM Journals

PSM
Biological Research

Research Article 2026 | Volume 11 | Issue 1 | 54-67

Open Access

Article Information

Received: April 14, 2026

Accepted: April 19, 2026

Published: May 1, 2026

Authors' Contribution

All authors conceived and designed the study, as well as made the statistical analysis of data. AA, OH, AAR, and AAA performed the experimental work and wrote the draft. BYHA supervised the performance of experiments, interpreted the results, wrote and edited the manuscript, and made a critical revision. EASA made a critical revision. All authors have approved the final version of the manuscript for publication.

How to cite

Al-Khatib, B.Y.H., Ahmed, A., Hammoud, O., AbdulRahman, A., Al-Shaibani, E.A.S., Al-Subari, A.A., 2026. A Comparison of the Effects of Khat Chewing on Certain Biochemical and Physiological Variables in Males and Females with Type 2 Diabetes in Sana'a City, Yemen. PSM Biol. Res., 11(1): 54-67.

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A Comparison of the Effects of Khat Chewing on Certain Biochemical and Physiological Variables in Males and Females with Type 2 Diabetes in Sana'a City, Yemen

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Abstract:
Diabetes mellitus (DM) is a health condition characterized by high blood glucose levels. Khat (*Catha Edulis*) is a plant commonly cultivated in Yemen and certain East African countries. This study examined the effects of Khat on blood glucose levels and select body parameters in individuals with Type II DM, comparing males and females. The study included 104 individuals, including healthy and diabetic participants, an equal number of males and females. Participants were categorized within each sex as follows: non-diabetic and non-Khat chewers, non-diabetic and Khat chewers, diabetic and non-Khat chewers, and diabetic and Khat chewers. Measurements included fasting blood sugar (FBS), blood pressure, and body mass index (BMI). Blood samples were taken for a complete blood count. BMI results indicated an overweight status among Khat chewers, especially diabetic females (64.28%). FBS was non-significantly decreased in diabetic Khat-chewing males but significantly increased in diabetic-chewing females ($p < 0.01$) compared to non-chewers. Systolic blood pressure was higher across all diabetic groups. In males, Khat caused significant changes ($p < 0.05$) in hemoglobin concentration, total white blood cell count, and monocyte count in diabetic males compared to healthy individuals. Females showed no significant differences in blood parameters across groups, except for a decrease in MCHC among Khat chewers. Khat had no significant impact on lowering blood sugar or blood pressure in diabetic patients of either sex. On the contrary, Khat may aggravate these conditions. Its influence on blood parameters was limited and observed only in males.
Keywords: Khat, Type II Diabetes mellitus, FBS, Blood Pressure, CBC, Daily behaviors.

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INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by a diverse group of conditions associated with elevated blood glucose levels in both fasting and postprandial states (Whiting *et al.,* 2011; Karalliedde and Gnudi, 2016). This disease has emerged as a global pandemic, affecting millions of individuals worldwide and posing significant health challenges that impair quality of life. Diabetes is classified into two types:

1- Insulin-dependent diabetes (Type I): This is an autoimmune disease characterized by a localized inflammatory response in and around the islets of Langerhans, followed by the selective destruction of insulin-producing cells (Duncan *et al.,* 2026).
2- Non-insulin-dependent diabetes (Type II): This is characterized by peripheral insulin resistance and impaired insulin secretion (Whiting *et al*., 2011).

This disorder results from either an absolute or a relative deficiency in insulin secretion or action. Furthermore, long-term hyperglycemia linked to DM is connected to dysfunction and failure of several vital organs, including the retina, kidneys, liver, nervous system, and cardiovascular system (Karalliedde and Gnudi, 2016; Muhammad *et al.,* 2013; Whiting *et al*., 2011).

In 2024, the number of people (aged 20–79) with diabetes, whether diagnosed or not, was estimated at 589 million, with a global adult prevalence of 11.11%. Projections indicate that by 2050, the number of people who developed diabetes will have increased by 44.82% to 853 million, and the prevalence will rise to 12.96%. The Middle East and North Africa region has the highest prevalence of diabetes across all age groups (Genitsaridi *et al*., 2026).

The oxidative stress in diabetes causes overproduction of mitochondrial superoxide in endothelial cells of both large and small vessels, as well as in the myocardium, and leads to many micro and macrovascular complications (Chandra *et al*., 2019). Some plant extracts serve as the protective and curative plant against diabetes mellitus by reducing oxidative stress (Almadiy *et al.,* 2020). Diabetes drugs are used primarily to save life and alleviate symptoms, while secondary aims are to prevent long-term diabetic complications and, by eliminating various risk factors, to increase longevity (Deshmukh and Jain, 2015; Tsushima and Galloway, 2025). The natural remedies are regarded as a valuable source of therapeutic agents (Ashraf et *al.,* 2020; Ullah *et al.,* 2018).

Khat (*Catha edulis*) is an evergreen plant that grows at high altitudes. It is commonly grown throughout the year in the Horn of Africa and Yemen, and known by many names. Unfortunately, chewing khat has become a widespread social habit (Adugna *et al*., 2020). Consumption of various plant-based psychotropic substances has been prevalent among humans since ancient times (Asfaw, 2023). It is estimated that 20 million people worldwide regularly chew Khat leaves to enjoy its stimulating effects (Balint *et al*., 2009). In Yemen, chewing Khat is a common habit; approximately 80-85% of adult males and 10-60% of adult females in Yemen chew Khat at least once a week (Gumaih *et al*., 2019). Khat effects include elevated mood and alertness, euphoria, and increased vigilance. Cathinone, the main element in Khat, reduces hunger similarly to amphetamine, which is why it is thought to have anti-obesity properties. Khat also boosts motor activity, pleasure, and a sense of excitement and activation (Alshoabi *et al*., 2022). It has been found that khat chewing is associated with mood disturbances, alertness, hyperactivity, anxiety, as well as elevated blood pressure, and an increased risk of cancer and heart disease. Additionally, chronic illnesses and psychotic symptoms have been reported to be associated with Khat chewing. Interestingly, Khat chewing has been reported to be associated with developing Type II diabetes and disturbances of glycemic control. Furthermore, Khat chewing has been indicated as a risk factor for anemia among pregnant women due to its impact on their dietary practices, and it can influence birth outcomes (Gumaih *et al*., 2019; Alshoabi *et al*., 2022; Kassaw *et al*., 2022; Gosadi *et al*., 2024). Furthermore, it has been found that Khat affects the digestive system and

may develop cancers such as oral cancer (Alshoabi *et al*., 2022). Esophageal and gastric carcinomas have been observed in Khat chewers in both men and women in Yemen (Alsanosy *et al*., 2020; Alshoabi *et al*., 2022).

Khat contains several phytochemicals such as alkaloids (phenylalkylamines), flavonoids, glycosides, tannins, steroids, triterpenoids, monoterpenes, and volatile aromatic compounds, and other miscellaneous compounds like vitamins, minerals, and amino acids (Getasetegn, 2016; Alsanosy *et al*., 2020). As reported previously, khat leaves and buds contain cathine, cathinone, and methcathinone substances that have amphetamine-like structures and functions. Cathinone is found mainly in young leaves and buds and metabolizes to cathine (+)-nor pseudoephedrine and (-)-nor ephedrine in mature leaves (Alsanosy *et al*., 2020; Alshoabi *et al*., 2022).

The custom of chewing khat has been a persistent issue in Yemeni society, leading to both economic and health-related problems. Some diabetic individuals who chew khat believe that khat helps lower blood sugar levels. Although several studies have investigated this idea, the results remain inconclusive. Therefore, the current study aimed to examine the effect of khat chewing on blood sugar levels and certain body variables in both male and female diabetics, and to explore sex differences.

MATERIALS AND METHODS

Study population and sample size

The present study was conducted in Sana'a city, and the voluntary participants included Type II DM patients attending an outpatient clinic in the Republican Teaching Hospital, for routine investigations, as well as participants from the surrounding environment (neighbors and relatives). This study lasted five months (September 2024- January 2025). The sample size was determined using G. Power System (version 3.1.9.4), in which the calculation was based on the Mean ±SD of PCV% stated in Harish Kumar et al. (2017). All participants were sensitized to the study and asked to sign an informed consent form before the study. This study was conducted according to the principles of the Declaration of Helsinki and was approved by the local Ethical Committee of the Faculty of Science, Sana'a University, Yemen.

This cross-sectional study was conducted on a total of 104 participants who had completed the suitable questionnaires; half (52) of them were males, and half (52) were females. Twenty-six diabetic patients of each sex, known as diabetic patients attending selected diabetes clinics, and 26 healthy volunteers, known as controls (FBS< 140 mg/dL). Control participants were selected randomly and were close matching with patients. The ages of all participants ranged from 35 to 75 years. The main exclusion criteria included Type I DM, pregnancy or lactation, and chronic diseases. Interviews with participants were face-to-face using a pre-tested questionnaire, which included socio-demographic information, lifestyle information, as well as clinical and diabetes-related information.

Study design

This study was designed to include four groups for each sex as follows:

Male groups

- MH- NCK: No-Diabetic & No-Khat-Chewing volunteers (n=12).
- MH- CK: No- Diabetic & Khat- Chewing volunteers (n=14).
- MD- NCK: Diabetic & No-Khat-Chewing volunteers (n=12).
- MD- CK: Diabetic & chewing Khat volunteers (n=14)

Female groups

- FH- NCK: No-Diabetic & No-Khat-Chewing volunteers (n=12).
- FH- CK: No- Diabetic & Khat- Chewing s volunteers (n=14).
- FH- NCK: Diabetic & No-Khat-Chewing volunteers (n=12).

- FH- CK: Diabetic & chewing Khat volunteers (n=14).

Study Measurements

All groups of this study, TII DM patients and healthy individuals, were subjected to the following:

Demographic data

Collect demographic data in a suitable questionnaire form, including age, occupation, anthropometric measurements such as height and weight, disease history, lifestyle, daily behaviors, medication, and other chronic illnesses.

Body Mass Index (BMI)

It was calculated by using the following equation:

[Weight (Kg)/Height (m^2)],

where the weight was measured in kilograms using weighing scales and height was measured in centimeters and converted to square meters.

Blood pressure measurement

Systolic (SBP) and diastolic (DBP) blood pressure were measured by using the electronic pressure device (Ross Max model).

Blood sugar measurement

At least two hours after the last meal, blood samples were collected for Fasting blood sugar (FBS) measurement using a blood glucose monitor and test strips.

Complete blood count (CBC)

Complete blood count (CBC) was measured using a fully automatic hematology analyzer (Rayto Rt-7600 analyzer)

Statistical analysis

All the data were subjected to a normality test before analysis. The results were presented as frequencies and percentages or as mean ± standard deviation of the mean (M± SD). Data were analyzed using GraphPad Prism (version 9.1.1) by applying one-way analysis of variance (ANOVA) to assess the statistical differences between groups. Differences were considered statistically significant at $p < 0.01$.

RESULTS

The baseline clinical characteristics of the studied groups

The results of the baseline clinical characteristics of the studied groups in Sana'a City, Yemen, are presented in Tables 1 and 2.

Age

Twenty-four male participants were under 50 years old, while 28 were over 50 years old (Table 1). For females, 35 participants were under 50 years old, and 17 were above that age (Table 2).

Diabetes duration

In this study, the duration of diabetes among male (Table 1) and female (Table 2) participants was less than 10 years.

Body Mass Index

In the male groups, most participants were within the normal BMI range, but the highest proportion was in the non-chewing khat groups (66.66%), whether healthy or diabetic. Conversely, the overweight BMI range was higher in the khat-chewing groups (42.85%), including both healthy and diabetic individuals (Table 1). In female groups, the normal BMI range was the highest only among healthy non-chewing khat individuals, while the overweight range was most prevalent in both chewing khat groups, healthy (50%) and diabetic (64.28%) (Table 2).

Life behaviors of the studied groups

The results of some life behaviors of the studied groups in Sana'a City, Yemen, are presented in Tables 3 and 4.

Table 1. Frequencies and percentages of the baseline clinical characteristics of the male studied groups.

Clinical characteristics		Groups			
		Non- diabetic Male (MH)		Diabetic Male (MD)	
		MH- NCK (n= 12)	MH- CK (n=14)	MD- NCK (n= 12)	MD- CK (n= 14)
Age (years)	≤ 50	12 (100%)	6 (42.85%)	1 (8.33%)	5 (35.71%)
	≥ 50	0 (00%)	8 (57.14%)	11 (91.66%)	9 (64.28%)
Diabetes duration (years)	<10	-	-	9 (75.00%)	11 (78.57%)
	10 – 20	-	-	3 (25.00%)	2 (14.28%)
	>20	-	-	0 (00%)	1 (7.14%)
BMI (kg/m^2)	Thinness (< 18.5)	2 (16.66%)	0 (00%)	6 (50.00%)	0 (00%)
	Normal (18.5-25)	8 (66.66%)	8 (57.14%)	8 (66.66%)	8 (57.14%)
	Overweight (> 25)	2 (16.66%)	6 (42.85%)	4 (33.33%)	6 (42.85%)

Results are expressed as frequencies and percentages related to the total number of each group, MH-NCK: Male, Healthy, Non-Chewing Khat; MH-CK: Male, Healthy, Chewing Khat; MD- NCK: Male Diabetes, Non-Chewing Khat; MD- CK: Male, Diabetes, Chewing Khat; BMI: Body Mass Index.

Table 2. Frequencies and percentages of the baseline clinical characteristics of the female studied groups.

Clinical characteristics		Groups			
		Non- diabetic Female (FH)		Diabetic Female (FD)	
		FH- NCK (n= 12)	FH- CK (n=14)	FD- NCK (n= 12)	FD- CK (n= 14)
Age (years)	≤ 50	10 (83.33%)	13 (92.85%)	4 (33.33%)	8 (57.14%)
	≥ 50	2 (16.66%)	1 (7.14%)	8 (66.66%)	6 (42.85%)
Diabetes duration (years)	<10	-	-	9 (75.00%)	13 (92.85%)
	10 – 20	-	-	2 (16.66%)	1 (7.14%)
	>20	-	-	1 (8.33%)	0 (00%)
BMI (kg/m^2)	Thinness (< 18.5)	0 (00%)	1 (7.14%)	0 (00%)	0 (00%)
	Normal (18.5-25)	8 (66.66%)	6 (42.85%)	6 (50%)	5 (35.71%)
	Overweight (> 25)	4 (33.33%)	7 (50%)	6 (50%)	9 (64.28%)

Results are expressed as frequencies and percentages related to the total number of each group: FH-NCK: Female, Healthy, Non-Chewing Khat; FH-CK: Female, Healthy, Chewing Khat; FD- NCK: Female, Diabetes, Non-Chewing Khat; FD- CK: Female, Diabetes, Chewing Khat; BMI: Body Mass Index.

Smoking

Most male participants in this study were non-smokers, but the highest proportion of smokers was found in the khat-chewing groups, with 21.42% in healthy participants and 42.84% in diabetics (Table 3). Likewise, most female participants were non-smokers, but interestingly, smoking prevalence was higher in diabetic groups (50% of non-chewers and 42.85% of chewers) compared to healthy groups (0% and 14.85%, respectively) (Table 4).

Sleeping Hours

Most male participants in healthy groups sleep well (6-10 hours), whereas some diabetic individuals sleep well, and others do not (Table 3). Regarding females, most have good sleeping hours (6-10 hours), except for those in the diabetic khat-chewing group, who mostly sleep between 2-5 hours (78.14%) (Table 4).

Exercises

This behavior in male groups was higher in the diabetic non-chewer group (75%), while the lowest was in the diabetic chewer group (35.71%) (Table 3). However, the percentage of exercise was close across the four female groups (Table 4).

Diet

The diabetic groups of both sexes were more compliant with a healthy diet than the non-diabetic groups, especially the non-chewers, with 75% in both sexes (Tables 3 and 4).

Khat chewing times

It was daily in most participants; in healthy individuals, it was 85.71% in males (Table 3) and 92.85% in females (Table 4); in diabetics, it was 92.85% in males (Table 3) and 57.14% in females (Table 4). Notably, the quantities of khat were larger, and the periods of chewing were longer in males than in females, according to the questionnaire information.

Table 3. Frequencies and percentages of some life behaviors of the male studied groups.

Life behaviors		Groups			
		Non- diabetic Male (MH)		Diabetic Male (MD)	
		MH- NCK (n= 12)	MH- CK (n=14)	MD- NCK (n= 12)	MD- CK (n= 14)
Smoking	Yes	0 (00%)	3 (21.42%)	1 (8.33%)	6 (42.85%)
	No	12 (100%)	11 (78.57%)	11 (91.66%)	8 (57.14%)
Sleep Hours	2-5h	0 (00%)	4 (28.57%)	7 (58.33%)	7 (50%)
	6-10h	12 (100%)	10 (71.42%)	5 (41.66%)	7 (50%)
Exercises	Yes	6 (50%)	9 (64.28%)	10 (83.33%)	5 (35.71%)
	No	6 (50%)	5 (35.71%)	2 (16.6%)	9 (64.28%)
Diet	Yes	4 (33.33%)	0 (00%)	9 (75%)	7 (50%)
	No	8 (66.66%)	14 (100%)	3 (25%)	7 (50%)
Khat Chewing Times	Daily	-	12 (85.71%)	-	13 (92.85%)
	Sometimes	-	2 (14.28%)	-	1 (7.14%)

Results are expressed as frequencies and percentages related to the total number of each group: MH-NCK: Male, Healthy, Non-Chewing Khat; MH-CK: Male, Healthy, Chewing Khat; MD- NCK: Male Diabetes, Non-Chewing Khat; MD- CK: Male, Diabetes, Chewing Khat.

Table 4. Frequencies and percentages of some life behaviors of the female studied groups.

Life behaviors		Groups			
		Non- diabetic Female (FH)		Diabetic Female (FD)	
		FH- NCK (n= 12)	FH- CK (n=14)	FD- NCK (n= 12)	FD- CK (n= 14)
Smoking	Yes	0 (00%)	2 (14.85%)	6 (50%)	6 (42.85%)
	No	12 (100%)	12 (85.71%)	8 (66.66%)	8 (57.14%)
Sleep Hours	2-5h	0 (00%)	4 (28.57%)	3 (25%)	11 (78.14%)
	6-10h	12 (100%)	10 (71.42%)	9 (75%)	3 (21.42%)
Exercises	Yes	7 (58.33%)	8 (57.14%)	7 (58.33%)	8 (57.14%)
	No	5 (41.66%)	6 (42.85%)	5 (41.66%)	6 (42.85%)
Diet	Yes	1 (8.33%)	0 (00%)	9 (75%)	7 (50%)
	No	11 (91.66%)	14 (100%)	3 (25%)	7 (50%)
Khat Chewing Times	Daily	-	13 (92.85%)	-	8 (57.14%)
	Sometimes	-	1 (7.14%)	-	6 (42.85%)

Results are expressed as frequencies and percentages related to the total number of each group: FH-NCK: Female, Healthy, Non-Chewing Khat; FH-CK: Female, Healthy, Chewing Khat; FD- NCK: Female Diabetes, Non-Chewing Khat; FD- CK: Female, Diabetes, Chewing Khat.

Clinical measurements among the studied groups

The results of some clinical measurements among the studied groups in Sana'a city, Yemen, are presented in the following figures and tables.

Fasting blood sugar (FBS)

The level of FBS was very similar in both healthy groups, among males and females, and khat showed no significant effect on FBS in healthy individuals. However, a non-significant decrease in FBS was observed in diabetic male khat chewers (Figure 1), while diabetic female

chewers showed a significant increase ($p < 0.01$) compared to non-chewers (Figure 2).

Systolic blood pressure (SBP)

Compared to MH- NCK, all other groups showed an increase in SBP value, which was significant in both diabetic groups in males ($p < 0.05$) (Figure 1). However, in females, it was only elevated in diabetic groups and was significant only in FD- NCK ($p < 0.01$) (Figure 2). There was no significant difference in SBP values between the two diabetic groups, neither in males nor in females.

Diastolic blood pressure (DBP)

In male groups, compared to the MH-NCK, a non-significant increase in DBP value was observed in the MH-CH and MD-CK groups, while a significant increase was seen in the MD-NCK ($p< 0.01$). There was a significant decrease in DBP value in MD-CK compared to MD-NCK ($p< 0.05$) (Figure 1). Conversely, no significant differences were found among all female groups (Figure 2).

Blood variables (Complete blood count)

In male groups, RBC, Hb, and PCV values were close across all groups. However, RBC corpuscular volume and hemoglobin concentration (MCV, MCH, and MCHC) were diminished across all groups compared to the MH-NCK group, with statistically significant differences observed only for MCH and MCHC in both chewing khat groups, healthy and diabetic ($p < 0.05$). The leukocyte counts and differential count showed an increase in all groups compared to the MH-NCK group, but significance was only observed for total WBC count and monocyte count. Notably, the leukocyte count was higher in the chewing khat groups compared to the non-chewing groups. Similarly, platelet counts were elevated in all experimental groups relative to the MH-NCK group (Table 5). In female groups, unlike males, most CBC values were very similar across all groups. However, significance was found only for MCHC in chewing individuals, healthy and diabetic ($p < 0.05$) (Table 6).

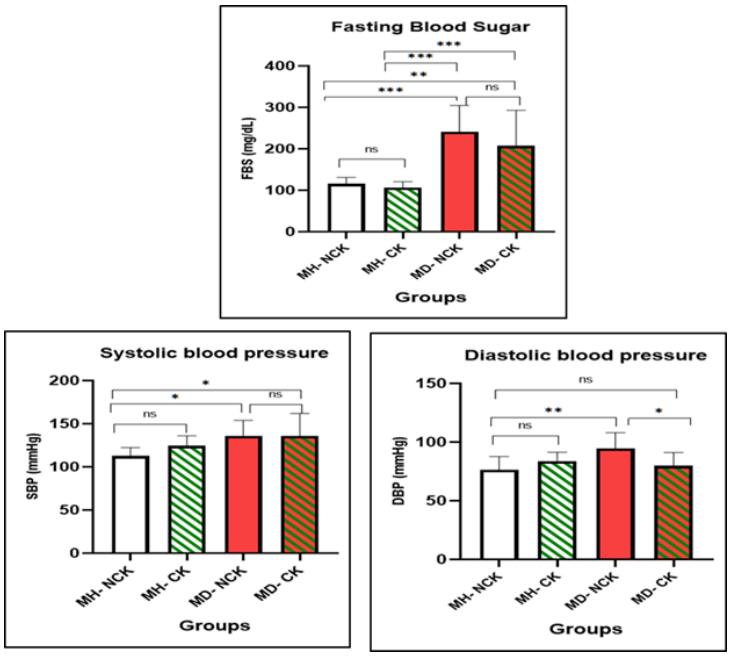

Fig. 1. Comparison of the levels of some clinical measurements among the male study groups.
Results are shown as mean± SD. MH-NCK: Male, Healthy, Non-Chewing Khat; MH-CK: Male, Healthy, Chewing Khat; MD- NCK: Male Diabetes, Non-Chewing Khat; MD- CK: Male, Diabetes, Chewing Khat; FBS: Fasting blood sugar; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; ns: non-significant, *= p< 0.05; **= p< 0.01.

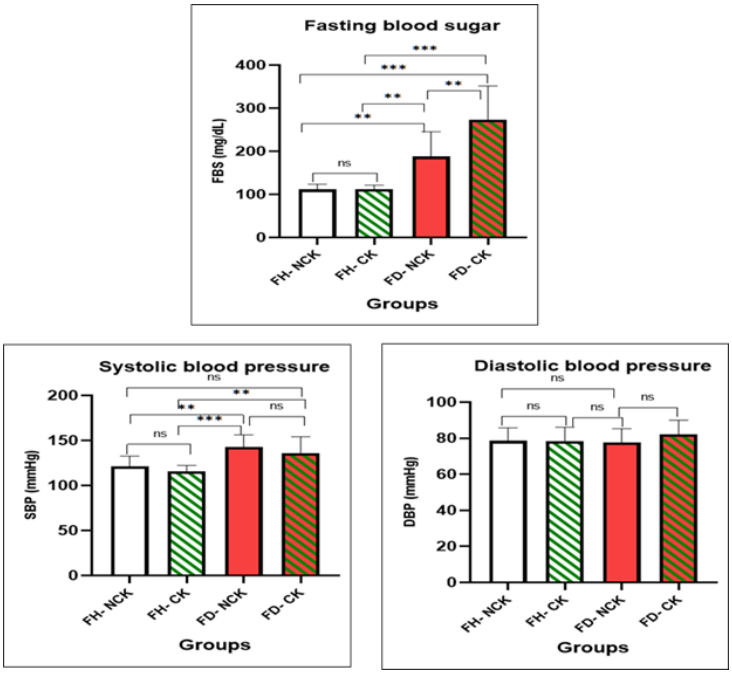

Fig. 2. Comparison of the levels of some clinical measurements among the female study groups.
Results are shown as mean± SD. FH-NCK: Female, Healthy, Non-Chewing Khat; FH-CK: Female, Healthy, Chewing Khat; FD-NCK: Female Diabetes, Non-Chewing Khat; FD- CK: Female, Diabetes, Chewing Khat; FBS: Fasting blood sugar; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; ns: non-significant, *= p< 0.05; **= p< 0.01; ***= p< 0.001.

Table 5. Comparison of blood variables values among the male studied groups.

Clinical Parameters	Groups			
	Non- diabetic Male (MH)		Diabetic Male (MD)	
	MH- NCK (n= 12)	MH- CK (n=14)	MD- NCK (n= 12)	MD- CK (n= 14)
RBC (10^{12}/L)	5.23±1.144	5.50±0.417	5.45±0.342	5.39±0.583
Hb (g/dl)	14.98±1.571	15.24±1.209	15.64±1.227	14.72±1.697
PCV (%)	43.11±5.699	44.17±3.010	46.14±2.090	42.63±4.143
MCV (fl)	87.43±10.17	80.93±4.655	83.58±2.034	80.74±5.805
MCH (pg)	31.16±4.003	27.86±2.209 a *	28.76±1.203	27.31±2.267 a *
MCHC(g/dl)	35.48±0.637	34.33±1.079	34.33±1.331	33.64±0.888 a *
RDW-CV (%)	12.19±0.824	11.65±0.829	11.86±0.804	12.20±0.435
WBC (10^9/L)	5.26±1.503	6.71±1.105	7.20±2.271	7.99±2.522 a *
ANC (10^3/µL)	3.02±1.090	4.57±1.957	3.86±1.320	4.77±1.829
ALC (10^3/µL)	1.83±0.459	2.28±0.560	2.47±0.643	2.52±0.799
AMC (10^3/µL)	0.26±0.094	0.38±0.142	0.41±0.186	0.46±0.211 a *
AEC (10^3/µL)	0.10±0.000	0.15±0.074	0.17±0.096	0.17±0.095
ABC (10^3/µL)	0.01±0.005	0.01±0.005	0.00±0.005	0.00±0.005
Platelets (10^9/L)	262.3±58.90	305.6±56.74	300.9±33.70	306.1±82.93

Results are shown as mean± SD. MH-NCK: Male, Healthy, Non-Chewing Khat; MH-CK: Male, Healthy, Chewing Khat; MD- NCK: Male Diabetes, Non-Chewing Khat; MD- CK: Male, Diabetes, Chewing Khat; FBS: Fasting blood sugar; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; RBC: Red Blood Cell count; Hb: Hemoglobin; PCV: Packed cell volume; MCV: Mean Corpuscular Volume; MCH: Mean Corpuscular Hemoglobin; MCHC: Mean Corpuscular Hemoglobin Concentration; RDW-CV: Red Cell Distribution Width – Coefficient of Variation; RDW-SD: Red Cell Distribution Width – Standard Deviation; WBC: White Blood Cell count; ANC: Absolute Neutrophil Count; ALC: Absolute Lymphocyte Count; AMC: Absolute Monocyte Count; AEC: Absolute Eosinophil Count; ABC: Absolute Basophil Count; a: significant compared to the MH-NCH group, *= p< 0.05.

Table 6. Comparison of blood variables values among the female studied groups.

Clinical Parameters	Groups			
	Non- diabetic Female (FH)		Diabetic Female (FD)	
	FH- NCK (n= 12)	FH- CK (n=14)	FD- NCK (n= 12)	FD- CK (n= 14)
RBC (10^{12}/L)	4.74±0.408	4.71±0.410	4.98±0.469	5.06±0.402
Hb (g/dl)	13.41±1.001	13.04±0.754	13.21±1.392	13.94±1.290
PCV (%)	38.29±2.366	37.77±1.784	39.15±3.223	41.91±2.913
MCV (fl)	81.43±6.765	81.55±3.909	78.33±9.111	81.76±3.405
MCH (pg)	28.54±2.692	28.35±1.794	26.16±3.507	27.54±1.239
MCHC(g/dl)	34.94±0.749	33.67±0.813 a*	34.08±1.549	33.69±0.689 a*
RDW-CV (%)	11.69±0.309	11.62±0.414	12.00±0.459	11.86±0.348
WBC (10^9/L)	6.10±2.256	6.23±1.644	6.08±1.177	6.06±1.667
ANC (10^3/µL)	3.19±1.602	3.60±1.368	3.77±1.442	3.57±1.746
ALC (10^3/µL)	2.30±0.606	2.36±0.516	2.46±0.631	2.40±0.526
AMC (10^3/µL)	0.30±0.145	0.31±0.076	0.36±0.95	0.34±0.118
AEC (10^3/µL)	0.10±0.36	0.10±0.032	0.11±0.043	0.11±0.048
ABC (10^3/µL)	0.01±0.005	0.01±0.005	0.01±0.005	0.00±0.004
Platelets (10^9/L)	296.2±65.78	321.4±68.17	298.2±95.93	273.9±63.8

Results are shown as mean± SD. FH-NCK: Female, Healthy, Non-Chewing Khat; FH-CK: Female, Healthy, Chewing Khat; FD-NCK: Female Diabetes, Non-Chewing Khat; FD- CK: Female, Diabetes, Chewing Khat: FBS: Fasting blood sugar; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; RBC: Red Blood Cell count; Hb: Hemoglobin; PCV: Packed cell volume; MCV: Mean Corpuscular Volume; MCH: Mean Corpuscular Hemoglobin; MCHC: Mean Corpuscular Hemoglobin Concentration; RDW-CV: Red Cell Distribution Width – Coefficient of Variation; RDW-SD: Red Cell Distribution Width – Standard Deviation; WBC: White Blood Cell count; ANC: Absolute Neutrophil Count; ALC: Absolute Lymphocyte Count; AMC: Absolute Monocyte Count; AEC: Absolute Eosinophil Count; ABC: Absolute Basophil Count. a: significant compared to the FH-NCH group. *= $p< 0.05$.

DISCUSSION

Regarding the baseline clinical characteristics in our study, it was observed that the obesity (Overweight) rate was higher in diabetic individuals than in healthy ones, among both males and females. Additionally, this rate was higher among individuals who chewed khat compared to those who did not. This could be due to the extended periods of Khat chewing throughout the day, often without physical activity or other activities. Research linking Khat to obesity is very limited, but a study by Noman et al. (2023) suggested a relationship between Khat chewing and loss of appetite, which can lead to changes in body mass index (BMI). However, this study did not show an increase or decrease in BMI, indicating a need for further research into the relationship between Khat and obesity.

Results of this study indicate that daily positive behaviors, such as abstaining from smoking, engaging in physical exercise, and following a specific diet, were more prevalent among individuals who did not chew Khat and were dedicated to healthy habits. Researchers also observed that individuals with diabetes had disrupted sleep patterns, whereas the healthy groups had well sleep. Additionally, among diabetics, daily positive behaviors were more prevalent among non-chewers of khat than among khat chewers. Our results agree with the results obtained by Surani et al. (2015), who reported that DM exerts a negative effect on patients' sleep quality. Impaired sleep quality disrupts adequate glycemic control, regarded as corner stone in DM management, and leads to many deleterious effects, causing a profound impact on health-related quality of life. A study by Noman et al. (2023) reached the same conclusion, finding that the severity of Khat addiction is associated with an increase in the frequency and intensity of Khat use, worsening of negative mood, and deterioration of subjective sleep quality. Moreover, the study of Luyster and Dunbar-Jacob (2011) indicated that patients with type II diabetes were more likely to score lower on the Pittsburgh Sleep Quality Index (PSQI). PSQI is a validated tool used to measure sleep quality and patterns in older adults. It distinguishes between those with sleep

disorders and those with normal sleep by assessing seven sleep components over one month.

Our results show that males consume Khat for longer periods and in larger quantities than females. This finding was corroborated by another study, which confirmed that females chew Khat for shorter periods and in smaller quantities than males (Nakajima *et al.*, 2017). A study conducted on both sexes attributed the higher Khat consumption among males to differences and variations in gene expression between the sexes (Limenie *et al*., 2020).

In the current study, our results showed that the level of fasting blood sugar in healthy people, males or females, was very close between chewers of khat and non-chewers. While a non-significant rise in blood glucose levels was observed in diabetic males who did not chew Khat compared to those who did. This suggested that Khat might have a blood glucose-lowering effect in males. However, there was a significant increase in blood glucose levels among diabetic females who chewed Khat compared to those who did not. The differences in blood glucose levels between diabetic males and females who chew Khat may be due to the higher Khat consumption and longer chewing durations among males relative to females. Our results about males is matched with a study carried out by Asfaw (2023) who reported that Khat have significant hypoglycemic effect on fasting blood sugar levels of diabetic and healthy Khat chewers. Furthermore, Mengistu et al. (2021) mentioned that chewing Khat significantly reduces glucose levels in type II diabetics, regardless of their health status, compared to non-diabetics. They attributed this reduction in glucose levels in type II diabetics to the significant presence of minerals (magnesium, zinc, iron, chloride, lead, and copper) and ascorbic acid in the Khat leaves consumed. Heymann et al. (1995) in their study suggested that delayed gastric emptying of a semi-solid meal in hepatocellular carcinoma patients, who are khat chewers, may reduce glucose absorption in the intestines and lower blood glucose levels. Conversely to our results of males, another study conducted on Khat chewers demonstrated elevated blood sugar levels in type II diabetics (Alkhormi *et al*., 2021), whereas this study is in accordance with our results in females. Furthermore, it has been found that khat chewing is not associated with improved blood sugar control. Also, a link was found between Khat chewing and type II diabetes, with chewers having a more than three times higher risk of developing the disease compared to non-chewers (Badedi *et al*., 2020). This association may be attributed to the long-term effects of pesticide residues on chronic Khat users (El Hadrani and Al Hoot, 2000).

Our results showed a significant increase in SBP in diabetic patients, both male and female, compared to healthy individuals. Additionally, khat showed no significant effect on SBP when comparing khat chewers with non- chewers, in both healthy and diabetic people. This finding is consistent with the results of Jayed et al. (2023), who observed a transient effect of Khat on blood pressure, lasting for 4 to 5 hours after ingestion. However, morning blood pressure readings did not show any effect of Khat on blood pressure. This transient effect may be attributed to the adverse effects of Khat chewing, including psychoneurological disturbances (Hoffman and Al'Absi, 2010; Ongeri *et al.*, 2019), vasoconstriction of the coronary vasculature (Ali *et al*., 2010), and increased carotid intima-media thickness (Gameraddin *et al*., 2019).

In this study, a non-significant decrease in the MCV value and a significant decrease in the values of MCH and MCHC appeared among male diabetic patients who chewed Khat when compared with the control group. These results are consistent with the results of a study that proved that chewing Khat leads to a significant decrease in hemoglobin concentration, MCV, MCH, and PCV; in addition to a significant increase in platelet count and total WBCs (Al-Absi *et al.*, 2024). It has been found that the khat component includes flavonoid compounds (Getasetegn, 2016; Asfaw, 2023), which are strong inhibitors of iron absorption (Ma *et al*., 2011) because they create insoluble complexes with iron ions in the gastrointestinal lumen, thereby making it inaccessible for absorption (Al-Absi *et al.*, 2024). Besides, as documented by

Al-Dubai et al. (2014), daily Khat chewing is correlated with a decrease in the levels of iron and ferritin in serum, which consequently leads to a decrease in hemoglobin concentration (Al-Absi *et al.*, 2024), which may explain the decrease in MCH, MCV, and MCHC concentration in our study.

Additionally, our results showed a significant increase in the count of WBC cells and monocytes, and a non-significant increase in the platelet count in people with diabetes who chewed Khat when compared to the control group. Interestingly, our study also indicates that the count of WBC and all types of leukocytes was higher in the chewing khat groups compared to the non-chewing groups. These results may be related with stimulated effect of catecholamines that increase the number of leukocytes (Bakovic *et al*., 2013) and increase the exit of platelets from the spleen (Benschop *et al*., 1996). Our results are in accordance with an earlier study reporting a significant increase in total leukocytes in rats administered a crude methanolic extract of *Catha edulis* (Alsalahi *et al*., 2012). In contrast to males, our results did not reveal a distinct variation or difference in blood variables in females, except for MCHC values, which showed a significant increase in chewed Khat females, either healthy or diabetic, in comparison with the healthy, non-chewing group. These findings of females contradict a previous study (Al-Absi *et al.*, 2024) and may be attributed to the shorter duration of khat chewing and the lesser quantity of khat in females compared to males.

CONCLUSION

Based on the findings of this study on individuals with Type II diabetes mellitus, we conclude that:

1. Diabetic non-chewing khat individuals exhibited normal weight and daily positive behaviors more frequently than diabetic chewers.

2. Khat consumption was associated with a non-significant decrease in blood glucose levels in males, while in females, it led to a significant rise in blood glucose levels.

3. Diabetic individuals experienced an increase in systolic blood pressure, but Khat chewing showed no significant effect on this change.

4. Khat caused some changes in blood parameters in males, which were not observed in females.

5. The effect of Khat was related to the quantity and chewing duration. So, it was more apparent in males than in females.

This study was limited by financial constraints; however, we advocate for its continuation with an expanded sample size and varied variables.

ACKNOWLEDGMENT

The authors wish to express their gratitude to the Biological Science Department at the Faculty of Science, Sana'a University, for offering all the general research facilities.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this paper.

Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

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