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Impact of Aqueous *Hibiscus sabdariffa* Extract on Lipid Profile in Women with Subclinical Hypothyroidism: A Study in Al-Nasiriyah City

Wafa S. Abdulredha[1*], Riyadh K. Abdulla[1] and Amal H. Anatheil[2]

[1] *Department of Pharmacognosy and Medicinal Plants, College of Pharmacy, University of Thi-qar, Thi-qar 64001, Iraq*
[2] *Department of Pharmaceutical Chemistry, University of Thi-qar, Thi-qar 64001, Iraq*

*Corresponding author: Email: wafaabdulredha81@utq.edu.iq

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ABSTRACT

Subclinical hypothyroidism (SHT) is a frequently encountered thyroid disorder marked by elevated serum thyrotropin (TSH) levels with normal triiodothyronine (T3) and thyroxin (T4). It is often associated with dyslipidemia, particularly elevated total cholesterol (TC) and low-density lipoprotein (LDL), which increase the risk of cardiovascular disease. *Hibiscus sabdariffa* L. (sour tea) contains anthocyanins and polyphenols known for their lipid-lowering and antioxidant properties. This study aimed to evaluate the effect of *H. sabdariffa* aqueous extract (20 g/100 mL) on lipid metabolism in women with SHT. Fifty participants were enrolled: 10 healthy women (Group 1), and 40 women with SHT, who were subdivided into a control group (Group 2, n = 25) and a treatment group (Group 3, n = 15). Participants in the treatment group consumed two cups of the extract daily for six weeks. Biochemical evaluations of thyroid function and lipid metabolism were carried out before and after the intervention. Results showed that the treatment group demonstrated significant reductions in TC, triglycerides (TG), and LDL levels, with a concurrent increase in high-density lipoprotein (HDL) compared to the control group. Slight improvements in thyroid hormone parameters were also observed. The observed lipid-lowering effects are likely linked to the extract's ability to modulate lipid metabolism and enhance antioxidant activity. In conclusion, daily consumption of *H. sabdariffa* extract may offer a natural, supportive approach for managing dyslipidemia in women with SHT. Further research involving broader participant groups and extended study periods is advised to confirm these findings and explore underlying mechanisms.

Keywords: Cardioprotective properties, Dyslipidemia, *Hibiscus sabdariffa*, Lipid metabolism, Subclinical hypothyroidism (SHT)

INTRODUCTION

Subclinical thyroid dysfunctions are among the most commonly encountered thyroid-related abnormalities and are primarily diagnosed through laboratory evaluation of serum thyrotropine (TSH) levels. In such conditions, free triiodothyronine (T3) and thyroxin (T4) concentrations remain within physiological limits despite deviations in TSH. These disorders are generally categorized into two main forms: subclinical hyperthyroidism and subclinical hypothyroidism (SHT). Subclinical hyperthyroidism is defined by suppressed TSH alongside normal thyroid hormone levels, while SHT is characterized by elevated TSH with normal T3 and T4 values [1, 2].

The prevalence of subclinical thyroid disorders varies according to multiple demographic and environmental factors, including age, ethnicity, geographic distribution, and iodine consumption. Epidemiological data suggest that SHT affects approximately 4% to 10% of the population, whereas the occurrence of subclinical hyperthyroidism is reported in about 1% to 2% of individuals [3]. Thyroid hormones are essential for metabolic processes, particularly those involving lipid homeostasis. They influence hepatic cholesterol biosynthesis by stimulating the activity of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase. Additionally, they regulate lipoprotein lipase, the enzyme responsible for breaking down triglycerides in chylomicrons into free fatty acids and glycerol [4, 5]. Alterations in lipid profiles—particularly elevated total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C)—are frequently observed in patients with SHT [6].

Dyslipidemia, a metabolic condition marked by imbalances in blood lipid concentrations, is strongly associated with increased cardiovascular risk. This condition is typically characterized by elevated levels of TC, triglycerides (TG), and LDL-C, in addition to reduced concentrations of high-density lipoprotein cholesterol (HDL-C). A combination of factors contributes to dyslipidemia, including hereditary predisposition, dietary patterns, smoking habits, and sedentary behavior [7, 8]. In the Iraqi context, thyroid dysfunctions—particularly hypothyroid conditions—are increasingly recognized as public health concerns, with a higher incidence among females and individuals in middle age groups [9-11]. In comparison, data from the United States reveal that thyroid disease prevalence reaches approximately 8.1% among non-Hispanic white populations [12].

Nutritional strategies have been shown to effectively reduce cardiovascular risk factors. Diets rich in fruits, vegetables, whole grains, low-fat dairy, and unsaturated fats, coupled with reduced intake of trans fats, saturated fats, and refined carbohydrates, are strongly correlated with improved cardiovascular outcomes [13]. In recent years, the role of nutraceuticals—especially those containing high levels of antioxidant phytochemicals—has gained considerable attention for their efficacy in improving lipid profiles and managing dyslipidemia [14, 15].

Among the nutraceutical agents studied, *H. sabdariffa*, commonly known as sour tea, has emerged as a promising candidate for lipid regulation. A member of the Malvaceae family, this plant contains a wide spectrum of bioactive components, including mucilage, pectin, anthocyanins, polyphenols, hibiscus acid, and citric acid. These constituents are believed to contribute to its lipid-lowering and

cardioprotective properties [16-21]. Notably, anthocyanins have attracted particular scientific interest due to their broad physiological effects, including their potential to regulate blood pressure and enhance lipid metabolism [22, 23].
Building on this evidence, the present study was designed to explore the efficacy of *H. sabdariffa* extract in modulating lipid parameters in individuals with SHT. By targeting the dyslipidemia frequently associated with thyroid dysfunction, this investigation aims to assess the potential role of *H. sabdariffa* as a complementary therapeutic approach.

MATERIAL AND METHODS

Study Participants

The study included 50 female participants, of whom 10 were classified as healthy and 40 were found to have SHT, based on assessments conducted at the Endocrinology and Oncology Center in Nasiriyah city. Their ages ranged from 25 to 55 years, and the mean body weight was 98 kg.

Preparing *H. sabdariffa* Extract

An aqueous extract of *H. sabdariffa* was prepared using 2000 grams of dried calyces, which were locally obtained from a store in Nasiriyah and finely milled with a laboratory grinder. The extraction involved heating one liter of distilled water to around 90°C in a sterile container, followed by the gradual addition of 200 grams of the powdered plant material, maintaining a 1:10 weight-to-volume ratio. This temperature and ratio are considered optimal for maximizing the yield of active phytochemicals [24]. The mixture was left to steep for an additional 30 minutes to allow full extraction of the bioactive components. Following steeping, the solution was filtered through a fine mesh to remove residual plant material. The final extract was then transferred into a sterilized glass bottle and refrigerated. For best results and to preserve its bioactivity, the extract was used within 24 to 48 hours of preparation.

Study Design and Dose

The study duration was from February 2023 to March 2024. During this period, questionnaires were distributed to the female patients at the Oncology and Endocrinology Center, and individuals interested in participating in the study were identified. Their consent was obtained after they were informed about the study and its objectives. Continuous medical examinations were conducted throughout the 6-week study period to ensure that no complications or disruptions in their health status occurred. This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and the guidelines of the World Medical Association to ensure the respect and protection of all research participants, including both patients and healthy volunteers.
The patient group was divided into two subgroups, resulting in 3 groups as follows:
- Group 1 (G1) = 10 healthy women
- Group 2 (G2) = 25 women with SHT who takes Levothyroxine medication
- Group 3 (G3) = 15 women with SHT who consumed *H. sabdariffa* extract drink + takes Levothyroxine medication.

Two cups of the extract were consumed daily by the participants in group 3 (1 cup in the morning, and 1 cup in the evening) for a duration of 6 weeks.

Data and Laboratory Analysis

Data were collected from the study participants at the beginning and at the end of the 6-week study period. The measurements taken included weight and age. A 3 ml blood sample was drawn from all participants and placed in a centrifuge to obtain the serum, which was then used for analysing the levels of TSH, T_3, T_4, and fT_4 and the lipid profile. The Friedewald formula was used to calculate the LDL level [25].
Chemical analysis of the basic components of *H. sabdariffa* powder was conducted at the Organic Chemistry Laboratory/ College of Pharmacy/ University of Thi-Qar.

Statistical Analysis

All the results are expressed as the means ± S.D. and percentages. The data were statistically analysed via the SPSS program via T-test and ANOVA test. P-value of less than 0.05 was considered statistically significant.

RESULTS

Table 1 shows the proximate composition and functional properties of *H. sabdariffa* powder, which were analysed to determine its nutritional and bioactive components. The results revealed that the moisture content was 10.47%**,** the ash content was 11.64%**,** the crude lipid content was 1.05%**,** the crude fiber content was 1.19%**,** and the protein content was 4.17%**.** Additionally, the functional properties of the powder were evaluated, revealing a total phenolic content of 2.1%**,** antioxidant activity of 9.2%**,** total flavonoid content of 3.89%**,** and total anthocyanin content of 71.5%**.** These findings highlight the nutritional and antioxidant potential of *H. sabdariffa* powder, making it a valuable ingredient in food and pharmaceutical applications.
The mean levels of thyroid hormones in the healthy group were as follows: TSH = 2.56 ± 1.77, T4 = 93.1 ± 6.23, T3 = 1.77 ± 0.49, and fT4 = 23.3 ± 8.42. In the hypothyroid group, the hormone levels were significantly different. The mean levels were as follows: TSH = 7.22 ± 4.64, T4 = 88.29 ± 5.31, T3 = 1.18 ± 0.11, and fT4 = 5.15 ± 1.96. Elevated TSH levels and decreased T4 and fT4 levels reflect the characteristics of hypothyroidism, where the thyroid gland is underactive. Table 2 summarizes the previously mentioned findings.

Table 1 Basic components and functional properties of dried *H. sabdariffa* flower powder

Basic components				
Moisture (%)	Ash (%)	Crude lipid (%)	Crude fiber (%)	Protein (%)
10.47	11.64	1.05	1.19	4.17

Functional properties			
Total phenolic content (%)	Antioxidant activity (%)	Total flavonoids (%)	Total anthocyanin content (%)
2.1	9.2	3.89	71.5

Table 2 Level of thyroid hormones in healthy people and patients with hypothyroidism before the study

Groups	Parameters			
	TSH (mU/L)	T4 (nmol/L)	T3 (nmol/L)	fT4 (UI/L)
Healthy women (N=10)	2.56 * ± 1.77	93.1 * ± 6.23	1.77 * ± 0.49	23.3 * ± 8.42
Subclinical hypothyroidism women (N=40)	7.22 ± 4.64	88.29 ± 5.31	1.18 ± 0.11	5.15 ± 1.96

Data are expressed as mean ± SD, N= number. *Represents significance at P<0.05.

The data presented in Table 3 show the lipid profile parameters (TC, TG, HDL, and LDL) in healthy women and women with SHT. In the healthy group, the mean levels were as follows: TC = 134.4 ± 11.52, TG = 108.1 ± 8.23, HDL = 57.2 ± 6.069, and LDL = 73.7 ± 8.08, which are within the normal reference ranges. In contrast, women with SHT presented significantly higher levels of TC (198.9 ± 8.811), TG (210.475 ± 8.59), and LDL (125.45 ± 4.72), and lower HDL levels (35.975 ± 4.035) compared to the healthy group.

Table 3 Level of lipid profiles in healthy people and patients with hypothyroidism before the study

Groups	Parameters			
	TC (mg/dL)	TG (mg/dL)	HDL (mg/dL)	LDL (mg/dL)
Healthy women (N=10)	134.4 * ± 11.52	108.1 * ± 8.23	57.2 * ± 6.069	73.7 * ± 8.08
Subclinical hypothyroidism women (N=40)	198.9 ± 8.811	210.475 ± 8.59	35.975 ± 4.035	125.45 ± 4.72

Data are expressed as mean ± SD, N= number, TC= Total Cholesterol; TG= Triglyceride; HDL= High Density Lipoprotein; LDL= Low Density Lipoprotein. *Represents significance at P<0.05.

Table 4 presents the mean values and standard deviations of thyroid-related hormones TSH, T4, T3, and fT4 in three groups (G1, G2, and G3). Group 2 exhibited the highest mean TSH level (6.86 ± 2.92 mU/L), significantly higher than both G1 and G3, suggesting potential subclinical or overt hypothyroidism within this group. Correspondingly, G2 showed the lowest levels of T4 (85.76 ± 4.71 nmol/L), T3 (1.17 ± 0.11 nmol/L), and fT4 (22.24 ± 1.96 UI/L), which further supports the likelihood of thyroid hypofunction. In contrast, Group 1 had the lowest TSH (3.48 ± 1.25 mU/L) and the highest levels of T4, T3, and fT4, indicating normal or potentially hyperfunctioning thyroid activity. Group 3 presented intermediate values across all parameters, with hormone levels significantly different from both G1 and G2, possibly representing a subclinical or borderline thyroid state. These findings suggest a gradation in thyroid function among the groups, G3 representing an intermediate state, which indicates a potential beneficial effect of the herbal drink on thyroid function.

Table 4 Level of thyroid hormones for the three groups after the end of the study period

Groups	Parameters			
	TSH (mU/L)	T4 (nmol/L)	T3 (nmol/L)	fT4 (UI/L)
G1 (n=10)	3.48 c ± 1.25	91.1 a ± 5.86	1.96 a ± 0.44	27.3 a ± 5.52
G2 (n=25)	6.86 a ± 2.92	85.76 c ± 4.71	1.17 c ± 0.11	22.24 c ± 1.96
G3 (n=15)	5.21 b ± 1.28	88.6 b ± 3.76	1.34 b ± 0.13	24.2 b ± 2.37

Data are expressed as mean ± SD; Differences in letters a, b, c represent significant differences at P<0.05.

Table 5 shows the lipid profile parameters across the three study groups. In group 1, the mean lipid levels were within normal ranges, with TC = 127.4 ± 11.37, TG = 108.1 ± 8.23, HDL = 57.2 ± 6.07, and LDL = 68.5 ± 7.53. In contrast, group 2 presented significantly altered lipid levels, characterized by elevated TC (195.96 ± 8.77), TG (208.84 ± 9.37), and LDL (125.96 ± 5.06), along with a lower HDL level (36.4 ± 4.23), reflecting the dyslipidemia commonly associated with SHT. However, in group 3, there was a noticeable improvement in lipid parameters compared with those in group 2, with a reduction in TC (183 ± 8.94), TG (175.73 ± 12.31), and LDL (109.47 ± 5.98), along with an increase in HDL (48.27 ± 5.05).

Table 5 Level of lipid profiles for the three groups after the end of the study period

Groups	Parameters			
	TC (mg/dL)	TG (mg/dL)	HDL (mg/dL)	LDL (mg/dL)
G1 (n=10)	127.4 a ± 11.37	108.1 a ± 8.23	57.2 a ± 6.07	68.5 a ± 7.53
G2 (n=25)	195.96 c ± 8.77	208.84 c ± 9.37	36.4 c ± 4.23	125.96 c ± 5.06
G3 (n=15)	183 b ± 8.94	175.73 b ± 12.31	48.27 b ± 5.05	109.47 b ± 5.98

Data are expressed as mean ± SD; Differences in letters a, b, c represent significant differences at P<0.05.

DISCUSSION

The current study explored the influence of *H. sabdariffa* extract (10 g/100 mL), administered twice daily, on lipid parameters in women diagnosed with SHT, and compared the outcomes with those observed in healthy individuals. The results suggest that *H. sabdariffa* may play a beneficial role in regulating lipid metabolism in this patient population. *H. sabdariffa* has long been utilized in traditional medicine due to its wide spectrum of pharmacological properties, including diuretic, antihypertensive, antimicrobial, antioxidant, hepatoprotective, and anti-inflammatory effects. These attributes are largely associated with its high concentration of phytochemicals, including phenolic and organic acids, flavonoids, anthocyanins, and compounds such as citric, malic, hibiscus, hydroxycitric, tartaric, and ascorbic acids [26].

The chemical composition and functional qualities of *H. sabdariffa* powder reinforce its role in promoting health. It possesses moderate moisture, low fat, and a notable fiber content, factors that contribute both to improved storage stability and digestive support. Although its protein content is limited, it can complement dietary protein intake. On a functional level, the abundance of phenolic compounds and anthocyanins imparts significant antioxidant and heart-protective effects through the neutralization of free radicals and reduction of oxidative stress. The results of this study are in agreement with previous literature on the composition of *H. sabdariffa* [27-29].

While research on the role of *H. sabdariffa* in regulating thyroid hormones is still emerging, some findings indicate a possible modulatory capacity. The similarity in structure between specific phenolic and flavonoid compounds and thyroid hormones may allow these substances to bind to intracellular receptors, thereby influencing the feedback regulation of hormone secretion. This mechanism could stimulate the production of thyroxin via the hypothalamic-pituitary-thyroid axis, resulting in lowered TSH concentrations in individuals consuming *H. sabdariffa* [30-32].

Beyond its potential endocrine effects, *H. sabdariffa* has been shown to positively influence lipid metabolism, making it a promising candidate for managing obesity and metabolic dysregulation. Its polyphenolic content acts on multiple metabolic targets, including enzymes, transcription factors, and signaling pathways, contributing to reduced inflammation, improved energy utilization, and better lipid balance [33]. Multiple preclinical and clinical studies support the hypolipidemic action of *H. sabdariffa*. In animal models, administration of aqueous extracts has led to significant reductions in serum triglycerides, total cholesterol, and LDL levels, even under high-fat dietary conditions, while HDL levels often remained stable [34-36]. These lipid-lowering effects are largely attributed to antioxidant mechanisms that protect against LDL oxidation, a key event in atherogenesis.

Mechanistically, *H. sabdariffa* supports cholesterol homeostasis by promoting HDL-mediated reverse cholesterol transport, enhancing hepatic LDL receptor activity, and inhibiting cholesterol absorption. Additional effects include inhibition of HMG-CoA reductase and fatty acid synthase, possibly through activation of AMP-activated protein kinase (AMPK) and down regulation of lipogenic transcription factors [37-39].

Anthocyanins and protocatechuic acid are among the most studied active compounds in this regard. Furthermore, hydroxycitric acid (HCA) in *H. sabdariffa*, especially the (-)-HCA isomer, may reduce triglyceride and cholesterol synthesis by inhibiting ATP-citrate lyase, a key enzyme in lipid biosynthesis [40]. The high anthocyanin content in the plant's calyces is especially associated with its cardiovascular benefits, including blood pressure and lipid control. Alongside polyphenols and hibiscus acid, these compounds exert antioxidant effects that help protect LDL from oxidation and lower the risk of atherosclerosis, a major contributor to cardiovascular disease [41].

CONCLUSION

In conclusion, SHT is common among women in Nasiriyah and is linked to dyslipidemia and higher cardiovascular risk. Daily intake of *H. sabdariffa* (20 g/200 ml), rich in anthocyanins and polyphenols, may help improve lipid profiles and reduce atherosclerosis risk. Its natural hypolipidemic effects make it a promising option for managing thyroid-related lipid disorders. However, further studies are needed to clarify its mechanisms and clinical potential.

Declarations

Ethics Approval and Consent to Participate

The study was registered at College of Pharmacy/ University of Thi-Qar [IQR20230781N23], and informed consent was obtained from all participants.

Consent for Publication

Not applicable.

Availability of Data

All data generated or analysed during this study are included in this published article.

Competing Interests

All authors confirm the absence of any competing interests.

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Author´s Contributions

AH was responsible for the collection, preparation and chemical analysis of the basic components of the aqueous extract of *H. sabdariffa*. WS, and RK interviewed the study volunteers, distributed the research information forms, obtained informed consent, and assessed their health status. WS performed the blood sample and biochemical assessments. The study design, statistical analysis, and manuscript organization were carried out by WS. All researchers reviewed and approved the final version of the manuscript. All authors have read and agreed to the published version of the manuscript.

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