

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

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### ABSTRACT

Subclinical thyroid disorders, particularly subclinical hypothyroidism (SHT), are prevalent conditions characterized by abnormal serum thyrotropin (TSH) levels and normal triiodothyronine (T3) and thyroxine (T4) concentrations. SHT is associated with dyslipidemia, which is characterized by elevated total cholesterol (TC) and low-density lipoprotein cholesterol (LDL), increasing cardiovascular disease risk. *Hibiscus sabdariffa* L. (sour tea) is known for its bioactive compounds, including anthocyanins and polyphenols, which exhibit lipid-lowering and cardioprotective properties. This study aimed to investigate the effects of *H. sabdariffa* extract (20 g/100 ml) on lipid metabolism in women with SHT. A total of 50 participants were recruited, including 10 healthy women (G1) and 40 women with SHT, who were further divided into a control group (G2, n=25) and treatment group (G3, n=15) that consumed two daily cups of *H. sabdariffa* extract for six weeks. Biochemical analyses, including analyses of thyroid hormone levels and lipid profiles, were performed before and after the intervention. Results showed a significant reduction in TC, triglyceride (TG), and LDL levels, along with an increase in high-density lipoprotein cholesterol (HDL) in the intervention group compared with those in the control group. Additionally, slight improvements in serum TSH and thyroid hormone levels were observed. The lipid-lowering effects of *H. sabdariffa* may be attributed to its ability to inhibit lipid synthesis enzymes, increase cholesterol metabolism, and increase antioxidant activity. In conclusion, *H. sabdariffa* extract shows promise as a natural intervention for managing dyslipidemia in SHT patients. Further studies with larger sample sizes and longer follow-up periods are recommended to confirm its therapeutic potential in thyroid-related metabolic disorders.

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

### INTRODUCTION

Subclinical thyroid disorders are among the most prevalent thyroid-related conditions, and are diagnosed through biochemical assessments of serum thyrotropin (TSH) levels. Under these conditions, the concentrations of free triiodothyronine (T3) and thyroxine (T4) remain within the normal range despite an abnormal TSH level. These disorders are classified into two primary types: subclinical hyperthyroidism and subclinical hypothyroidism (SHT). Subclinical hyperthyroidism is characterized by suppressed TSH levels while maintaining normal T3 and T4 concentrations. Conversely, SHT presents with elevated TSH levels, with thyroid hormones remaining within the reference range [1, 2].

The prevalence of thyroid dysfunction in the general population is influenced by various factors, including ethnicity, age, geographic location, and iodine intake. Studies indicate that the prevalence of SHT ranges from 4–10%, whereas subclinical hyperthyroidism occurs in approximately 1–2% of individuals [3]. Thyroid hormones play a pivotal role in metabolic regulation, particularly in lipid metabolism. They facilitate cholesterol synthesis in the liver through the activation of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase. Furthermore, these hormones modulate the activity of lipoprotein lipase, an enzyme that hydrolyses triglycerides from chylomicrons into free fatty acids and glycerol [4, 5]. Notably, SHT has been closely associated with alterations in lipid profiles, specifically elevated total cholesterol (TC) and low-density lipoprotein cholesterol (LDL) levels [6].

Dyslipidemia, a condition characterized by abnormal lipid levels—including increased TC, triglyceride (TG), and LDL levels, along with decreased high-density lipoprotein (HDL) levels—is a recognized risk factor for cardiovascular disease. Several factors contribute to dyslipidemia, including genetics, dietary habits, and lifestyle choices such as smoking and physical inactivity [7, 8]. In Iraq, thyroid disorders, particularly hypothyroidism, have been identified as major public health concerns, with a higher prevalence observed among middle-aged individuals and females [9–11]. Comparatively, studies from the United States indicate that non-Hispanic Caucasians have the highest prevalence of thyroid disease, reaching approximately 8.1% [12].

Dietary interventions have been recognized as effective strategies for mitigating cardiovascular risk factors. Research has highlighted that the consumption of whole grains, fruits, vegetables, dairy products, and unsaturated fats—while reducing trans fats and substituting saturated fats and refined carbohydrates—plays a crucial role in promoting cardiovascular health [13]. Additionally, nutraceuticals, particularly those rich in antioxidant phytochemicals, have been extensively studied for their potential in managing dyslipidemia and improving lipid profiles [14, 15].

One such nutraceutical with significant potential in lipid regulation is *H. sabdariffa* L., which is commonly referred to as sour tea. This plant, which belongs to the Malvaceae family, contains a diverse range of bioactive compounds, including mucilage, pectin, anthocyanins, polyphenols, hibiscus acid, and citric acid. These components contribute to its lipid-modulating and cardioprotective

properties [16-21]. Among these bioactive constituents, anthocyanins have attracted considerable interest because of their extensive biological effects, particularly their ability to improve blood pressure regulation and lipid metabolism [22, 23].

Given these promising properties, the present study aimed to investigate the potential of *H. sabdariffa* extract in regulating lipid levels in patients with SHT, thereby addressing the dyslipidemia often associated with thyroid dysfunction.

## MATERIAL AND METHODS

### Study Participants

The study sample consisted of 50 women, 10 of whom were healthy, while the remaining 40 were diagnosed with subclinical hypothyroidism at the Endocrinology and Oncology Center in Nasiriyah city. Their ages ranged from 25\_55 years, with an average weight of 98 kg.

### Preparing *H. sabdariffa* Extract

To prepare the aqueous extract of *H. sabdariffa*, 2000 g of HS was purchased from a store in Nasiriyah city, and then ground in a mill to obtain a fine powder. Then, one liter of distilled or purified water was first boiled in a suitable vessel. Once the water reached 90°C, 200 g of dried *Hibiscus* flower powder was added at a solid-liquid ratio of 1:10 (g/mL). This ratio and extraction at 90°C for 30 minutes are recommended to obtain the highest content of beneficial ingredients [24]. The mixture was then allowed to steep for 30 minutes to extract the bioactive compounds from the plant material. After the steeping period, the extract was filtered through a fine filter to remove any solid residues. The final extract was stored in a sterilized bottle and kept in a refrigerator until use, preferably within 24 to 48 hours to maintain its potency.

### 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 subclinical hypothyroidism who takes Levothyroxine medication
- Group 3 (G3) = 15 women with subclinical hypothyroidism 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<sub>3</sub>, T<sub>4</sub>, and fT<sub>4</sub> 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  $\pm$  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 =  $2.56 \pm 1.77$ , T<sub>4</sub> =  $93.1 \pm 6.23$ , T<sub>3</sub> =  $1.77 \pm 0.49$ , and fT<sub>4</sub> =  $23.3 \pm 8.42$ . In the hypothyroid group, the hormone levels were significantly different. The mean levels were as follows: TSH =  $7.22 \pm 4.64$ , T<sub>4</sub> =  $88.29 \pm 5.31$ , T<sub>3</sub> =  $1.18 \pm 0.11$ , and fT<sub>4</sub> =  $5.15 \pm 1.96$ . Elevated TSH levels and decreased T<sub>4</sub> and fT<sub>4</sub> 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 * $\pm$ 1.77	93.1 * $\pm$ 6.23	1.77 * $\pm$ 0.49	23.3 * $\pm$ 8.42
Subclinical hypothyroidism women (N=40)	7.22 $\pm$ 4.64	88.29 $\pm$ 5.31	1.18 $\pm$ 0.11	5.15 $\pm$ 1.96

Data are expressed as mean  $\pm$  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 subclinical hypothyroidism. In the healthy group, the mean levels were as follows: TC =  $134.4 \pm 11.52$ , TG =  $108.1 \pm 8.23$ , HDL =  $57.2 \pm 6.069$ , and LDL =  $73.7 \pm 8.08$ , which are within the normal reference ranges. In contrast, women with subclinical hypothyroidism presented significantly higher levels of TC ( $198.9 \pm 8.811$ ), TG ( $210.475 \pm 8.59$ ), and LDL ( $125.45 \pm 4.72$ ), and lower HDL levels ( $35.975 \pm 4.035$ ) 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 * $\pm$ 11.52	108.1 * $\pm$ 8.23	57.2 * $\pm$ 6.069	73.7 * $\pm$ 8.08
Subclinical hypothyroidism women (N=40)	198.9 $\pm$ 8.811	210.475 $\pm$ 8.59	35.975 $\pm$ 4.035	125.45 $\pm$ 4.72

Data are expressed as mean  $\pm$  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 ( $6.86 \pm 2.92$  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 ( $85.76 \pm 4.71$  nmol/L), T3 ( $1.17 \pm 0.11$  nmol/L), and fT4 ( $22.24 \pm 1.96$  UI/L), which further supports the likelihood of thyroid hypofunction. In contrast, Group 1 had the lowest TSH ( $3.48 \pm 1.25$  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 $\pm$ 1.25	91.1 a $\pm$ 5.86	1.96 a $\pm$ 0.44	27.3 a $\pm$ 5.52
G2 (n=25)	6.86 a $\pm$ 2.92	85.76 c $\pm$ 4.71	1.17 c $\pm$ 0.11	22.24 c $\pm$ 1.96
G3 (n=15)	5.21 b $\pm$ 1.28	88.6 b $\pm$ 3.76	1.34 b $\pm$ 0.13	24.2 b $\pm$ 2.37

Data are expressed as mean  $\pm$  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 =  $127.4 \pm 11.37$ , TG =  $108.1 \pm 8.23$ , HDL =  $57.2 \pm 6.07$ , and LDL =  $68.5 \pm 7.53$ . In contrast, group 2 presented significantly altered lipid levels, characterized by elevated TC ( $195.96 \pm 8.77$ ), TG ( $208.84 \pm 9.37$ ), and LDL ( $125.96 \pm 5.06$ ), along with a lower HDL level ( $36.4 \pm 4.23$ ), reflecting the dyslipidemia commonly associated with subclinical hypothyroidism. However, in group 3, there was a noticeable improvement in lipid parameters compared with those in group 2, with a reduction in TC ( $183 \pm 8.94$ ), TG ( $175.73 \pm 12.31$ ), and LDL ( $109.47 \pm 5.98$ ), along with an increase in HDL ( $48.27 \pm 5.05$ ).

**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 $\pm$ 11.37	108.1 a $\pm$ 8.23	57.2 a $\pm$ 6.07	68.5 a $\pm$ 7.53
G2 (n=25)	195.96 c $\pm$ 8.77	208.84 c $\pm$ 9.37	36.4 c $\pm$ 4.23	125.96 c $\pm$ 5.06
G3 (n=15)	183 b $\pm$ 8.94	175.73 b $\pm$ 12.31	48.27 b $\pm$ 5.05	109.47 b $\pm$ 5.98

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

## DISCUSSION

The present study evaluated the effects of *H. sabdariffa* extract (10 g/ 100 ml) applied two times a day on lipid levels in women with subclinical hypothyroidism and compared them with those in healthy women. These findings highlight the potential impact of *H. sabdariffa* in modulating lipid metabolism in hypothyroid patients. *H. sabdariffa* is widely recognized for its diverse pharmacological benefits, including diuretic, choleric, analgesic, antitussive, antihypertensive, antimicrobial, immunomodulatory, hepatoprotective, antioxidant, and anticancer properties. These therapeutic effects are largely attributed to their bioactive compounds, which include phenolic acids, flavonoids, anthocyanins, and organic acids such as citric, hydroxycitric, hibiscus, tartaric, malic, and ascorbic acids. The combined action of these compounds enhances the plant's medicinal value, making it a promising natural remedy for various health disorders [26].

The proximate composition and functional properties of *H. sabdariffa* powder highlight its nutritional and bioactive potential. It has a moderate moisture content that affects shelf life, whereas its low ash content indicates the presence of essential minerals such as calcium, potassium, and magnesium. The powder is low in fat, making it suitable for reduced-fat diets, and contains fiber that supports digestion and satiety. Although it is not a high-protein source, it can supplement dietary protein intake. Functionally, *H. sabdariffa* is rich in phenolic compounds, flavonoids, and anthocyanins, contributing to strong antioxidant, anti-inflammatory, and cardiovascular benefits, while also scavenging free radicals and reducing oxidative stress. The results of the present study are comparable to the composition ratios of *H. sabdariffa* reported in previous studies [27-29].

Despite its broad spectrum of health benefits, research on the effect of *H. sabdariffa* on thyroid hormone regulation remains limited. However, available studies suggest that its phenolic and flavonoid contents may play a role in modulating thyroid function. These compounds have structural similarities to thyroxine hormones and may compete for cytoplasmic receptors, potentially acting as antagonists. This competition could trigger a feedback mechanism, prompting the thyroid gland to increase thyroxine production under the regulation of thyrotropin-releasing hormone (TRH) [30, 31]. Consequently, the increase in thyroid hormones observed in experimental studies may be linked to the stimulatory effect of phenolic and flavonoid compounds on both the thyroid and pituitary glands, resulting in lowering thyroid-stimulating hormone (TSH) levels in subjects consuming *H. sabdariffa* extract [32].

In addition to its influence on thyroid function, *H. sabdariffa* has demonstrated significant lipid-lowering properties, suggesting that it is a potential anti-obesity agent. The polyphenols present in *H. sabdariffa* exhibit multifaceted effects, impacting various metabolic pathways involved in obesity. These compounds contribute to the regulation of energy metabolism, reduction of oxidative stress and inflammation, modulation of transcription factors, control of hormone and peptide activity, inhibition of digestive enzymes, and epigenetic modifications, all of which collectively support their role in managing obesity and related metabolic disorders [33].

Many studies have highlighted the hypolipidemic effects of *H. sabdariffa* extract in both animal models and human clinical trials. Research has demonstrated that administering an aqueous extract of *H. sabdariffa* (10 g/L) significantly reduces serum triglyceride levels by more than 50% in mice subjected to a hypercaloric diet [34]. Similarly, another study confirmed that HSE supplementation at doses of 500 and 1000 mg/kg over six weeks led to substantial decreases in serum cholesterol, triglyceride, and LDL levels in hypercholesterolemic rats, although HDL levels remained unchanged [35]. These findings agree with previous research indicating that the lipid-lowering effects of *H. sabdariffa* result from its ability to reduce lipid profiles in vivo while also exerting potent antioxidant activity, particularly in preventing LDL oxidation [36].

The cholesterol-lowering properties of *H. sabdariffa* can be attributed to several interrelated mechanisms that collectively contribute to the reduction in LDL and total cholesterol levels. One key factor is the increase in HDL, which facilitates the transport of excess cholesterol from peripheral cells to the liver for degradation via the reverse cholesterol transport pathway. This process promotes cholesterol metabolism by inhibiting absorption, interfering with lipoprotein production, and increasing hepatic LDL receptor expression, thereby accelerating LDL clearance from the circulation [37]. Additionally, research suggests that the antihyperlipidemic properties of *H. sabdariffa* are associated with reduced lipid accumulation in hepatocytes through the inhibition of fatty acid synthase and HMG-CoA reductase activity [38]. This effect is mediated via the activation of adenosine monophosphate-activated protein kinase (AMPK) and the downregulation of sterol regulatory element-binding proteins, which further support lipid homeostasis and cholesterol reduction [38, 39].

The lipid-lowering potential of *H. sabdariffa* is associated primarily with its high content of anthocyanins and protocatechuic acid. Additionally, hydroxycitric acid (HCA) isomers, particularly (-)-HCA, exhibit inhibitory effects on citrate lyase, a key enzyme involved in Acetyl-CoA production. By blocking this enzymatic pathway, the biosynthesis of triglycerides and cholesterol is effectively reduced, further reinforcing *H. sabdariffa* as a natural agent for lipid management [40].

The high anthocyanin content in *H. sabdariffa* calyxes is widely regarded as a key factor in their antihypertensive and cholesterol-lowering properties. However, polyphenols and hibiscus acid have also been recognized for their contributions to these effects. Several mechanisms have been suggested to explain the ability of plants to reduce blood pressure and cholesterol levels, with the most widely accepted being their strong antioxidant properties. Anthocyanins help prevent the oxidation of LDL, thereby reducing the risk of atherosclerosis, a major contributor to cardiovascular diseases [41].

## CONCLUSION

In conclusion, subclinical hypothyroidism is common among women in Nasiriyah and is linked to dyslipidemia and higher cardiovascular risk. Daily intake of *Hibiscus 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.

### Funding

This study was funded by the researchers.

### 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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