Progress in Nutrition 2019; Vol.21, N. 1: 225-231 DOI: 10.23751/pn.v21i1.7836

Original article

In Vivo evaluation of therapeutic potential of heart of date palm extract on lipid profile and thyroid hormones in normal male wistar rats

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Summary. *Objective*: Reports exist on the use of *Phoenix dactylifera* as hypolipidemic, hypoglycemic or antioxidant but broad search in the literature revealed absence of studies on the effect of heart of date palm (HDP) on lipid profiles and thyroid hormone and to the best of our knowledge this is the first research carried out to investigate the effect of heart of date palm extract (HDP) on lipid profiles and thyroid hormones. *Method*: Extract of heart of date palm was prepared by mixing 50 gram of finely powdered heart of palm flour with 400 ml distilled water. Sixty healthy male albino rats were divided into ten groups, comprising of six rats in each group. One group was kept as control while other 9 group was divided into three batches of Sukkari, Naboat Saif, Solleg. Each batch has three groups served with 1, 2 and 3 ml of HDP. After the completion of the experimental period (60 days) blood samples were collected from rat's heart. Total Cholesterol, HDL Cholesterol, Triglycerides, Triodothyronine (T3), Thyroxin (T4) and TSH were determined for all groups. *Result:* HDP produced significant beneficial effect in the lipid profile of treated rats by significantly reducing total cholesterol and increasing HDL. LDLc, VLDLc and triglycerides also decreases with most of the treatment with some variations. Value of T3 and T4 significantly decreased, while the value of TSH significantly increased after treatment with HDP. Naboat Saif as compared to other two varieties (Sukkari and Solleg); exhibited better response towards lipid and thyroid hormones. *Conclusion*: This study shows that HDP supplementation may benefit management of lipid profile and thyroid hormones.

Key words: Hormones, cholesterol, triglycerides, dates, thyroxin, lipids

Introduction

Date palm (*Phoenix dactylifera* L.) is a monocotyledonous woody perennial belonging to the Arecaceae family. It is considered as the oldest plant cultivated in hot and dry climate as Arabian Peninsula, Africa, Middle East and Asia and comprises 200 genera and 3000 species (1). Kingdom of Saudi Arabia (KSA) has more than 23 million date palm trees and over 320 varieties with annual earning of over 500 million USD (2). It is one of the most important fruit crop in the KSA (3) and the importance of this kind of trees in that region refers to the nutritional value of the dates which is considered as a major human food (4,5). In today's world scientists and researchers are focusing more on natural plant products all over the world and various results have shown the massive potential of medicinal plants used traditionally (6). Various studies have shown beneficial effect of dates fruits, leaves and pits on health. They are considered to protect against many chronic diseases including cancer and heart diseases (7-9) and possess anti diabetic (10, 11), antimicrobial activity (12, 13), anti-inflammatory effect [14], antidiarrheal effects (15).

Heart of palm is a creamy white cylinder of variable length extracted from several palm genera and species (16, 17). It is a gourmet vegetable basically composed of the apical meristem of the palm and also the part of the young or immature leaves emerging from

the meristem and this edible meristem is normally consumed in soups and salads (16). A study has been done previously on chemical composition, minerals and antioxidants of different kind of hearts of date palm (HDP) from Saudi Cultivars (18) and they reported moisture as the predominant component (ranged from 80.44%-82.82%). Sucrose was predominant in sugar and ranged from 7.65%-82.82%, while the predominant mineral was potassium, sulphur and chloride. Furthermore this study illustrated that solleg had a higher total phenolic and flavonoid contents (56.05 mgGAE/100 gm and 6.82 MG QE/100 gm). Previous study on heart of palm shows that it contains unsaturated fatty acids, minerals (Zn, Fe, Mg, P, Mn, Ca, Cu, Na, K and Se) and crude fiber (19). Synthetic drugs are quiet expensive and shows adverse side effects. In contrast to this natural products are affordable and effective and good remedy in the treatment/management of diseases (20, 21). In addition to nutritional value and antioxidant effect (22, 23) many studies have shown the therapeutic effect of dates (24, 25,26), but to the best of our knowledge this is the first research carried out to investigate effect of HDP consumption (locally called as Al-Guomar) on metabolic response such as lipid profiles and thyroid hormones in male Wistar rats. Due to lack of any data and information on effect of heart of date palm on lipid and thyroid hormone, the authors compared their results with data available on dates fruits, leaves or pits.

Materials and methods

Collection of samples and Preparation

Samples of Sukkari, Naboat Saif, and Solleg (Saudi date palm varieties), consisting of leaves and stems were procured from Agricultural Experimental Station at Derab in Riyadh, King Saud University. HDP was peeled by an experienced staff affiliated to plant production department (Faculty of Food and Agriculture Sciences), considering minimal losses in heart of date palm tissue. After removing plant debris, HDP samples were washed with tap water and then freeze dried (Alpha 1-2 LDplus, Germany) and finely powdered in food grinder (National, MK-G30NR, Japan). Powdered HDP samples were passed to 60 mesh sieves and the flour was stored in air tight container at 4°C for further analysis.

Preparation of heart of palm (HDP) extract

Fifty gram of finely powdered heart of palm flour was mixed with 400 ml distilled water. The mixture was stirred for one hour and then filtered with cheese cloth to obtain a clear filtrate. The extract was prepared daily and used immediately in the rat bioassays (18).

Experimental design

Experimental Animals Center, College of Pharmacy, King Saud University provided sixty healthy male albino rats weighting between 180-200 grams. This study was conducted in accordance with research policies of the King Saud University Research Centre. Rats were housed individually under standard laboratory condition, light and dark cycles of 12h, in a polypropylene cages and allowed free access to commercial diet and water *ad libilum* for two months under strictly controlled pathogen free conditions with room temperature (25±2°C), humidity (50±5%). Commercial rodent chow diet was obtained from grain silos and flour mills, Riyadh Saudi Arabia. Stainless steel oral feeder was used to administer orally heart of palm extract to each rat at fixed time of the day, and with the specified volume of each extract. The initial weights of the rats and the weights every week were recorded. Sixty rats were randomly divided into ten groups, comprising of six rats in each group as discussed in Table 1.

Blood sample Collection

After the completion of the experimental period (60 days) blood samples were collected from heart of each rat after 12 hour fasting in lithium heparin tube. It was centrifuged at 3500 rpm for 10 minutes in megafuge and immediately plasma samples were prepared. After centrifugation supernatant was separated and stored at -80°C (U725-80 Freezers, New Brunswick, Massachusetts, United States) for further analysis.

Biochemical analyses

Lipid profile

High density lipoprotein kit (REF 041) was obtained from United Diagnostic Industry. This method was based on a non HDL precipitation followed by an enzymatic detection. Cholesterol (REF 024) and Triglycerides (REF 059L) kits were also obtained from United Diagnostic Industry. Enzymatic colorimetric

Table 1. Groups of experimental animals

Group No	Sample	No: of rats	Amount of extract consumed (ml)
1	Control	6	3 ml distilled water
2	Sukkari	6	1
3	Sukkari	6	2
4	Sukkari	6	3
5	Naboat Saif	6	1
6	Naboat Saif	6	2
7	Naboat Saif	6	3
8	Solleg	6	1
9	Solleg	6	2
10	Solleg	6	3

method was used for the determination of cholesterol and triglycerides (27, 28).The assays were performed according to the manufacturer's instruction. LDL cholesterol was calculated using following formula (29):
LDL Cholesterol (mg/dl) =Total cholesterol-HDL cholesterol- Triglycerides/5

Thyroid hormone

For the quantitative determination of triodothyronine (T3), thyroxin (T4) and TSH, Chemiluminescent micro particle immune assay was performed in the samples. Architect assays kit used for determination of triodothyronine (T3), thyroxin (T4) and thyroid stimulating hormone (TSH) kit was obtained from Abbot, Ireland (30, 31).

Statistical analysis

SPSS statistical software package was used to analyze the data. Data were expressed as mean ±standard deviation. The differences among the dietary treatment groups were analyzed by one way ANOVA at a significance level of $p \leq 0.05$; and if significant differences were found, a Post-hoc analysis using Duncan's multiple range tests was performed.

Results and discussions

Effect of heart of date palm extract (HDP) on lipid profiles in normal wistar rats

Results of the impact of the consumption of different kind of HDP extract on lipid profiles (total cholesterol HDLc, triglycerides and LDLc) are presented in Table 2. HDP produced significant beneficial effect in the lipid profile of treated rats by significantly reducing total cholesterol and increasing HDL. LDLc, and triglycerides also decreases with most of the treatment with some variations. Maximum effect of HDP treatment on LDLc and triglycerides has been observed in group 7 i.e rats treated with 3 ml extract of Naboat Saif but the least value of total cholesterol was observed in group 6 i.e rats treated with 2ml extract of Naboat Saif. Highest value of HDLc was observed in in group 3 i.e rats treated with 2ml extract of Sukkari.

Table 2. Effect of different kind of heart of palm extract (HDP) on lipid profiles

Group No:	Sample	Total cholesterol (mg/dl)	HDL Cholesterol (mg/dl)	Triglycerides (mg/dl)	LDL Cholesterol (mg/dl)
1	Control	73.11^{a} ±11.098	27.22^{ef} ±2.734	46.33^{e} ±5.368	36.72^{d} ±1.526
2	Sukkari (1ml)	61.61^{e} ±11.723	26.50^{fg} ± 2.526	44.50^{f} ±4.199	34.28^{f} ±1.674
3	Sukkari (2ml)	65.50^{cd}± 10.913	33.83^{a} ±3.148	58.50^{a} ±5.943	40.28^{b} ± 3.045
4	Sukkari (3ml)	65.00^{d} ±6.240	28.50^{d}±2.526	48.17^{d} ± 4.370	35.22^{e} ± 3.622
5	N Saif (1 ml)*	61.50^{e} ± 6.167	30.06^{c}±2.460	51.83^{c} ±4.033	38.89^{c} ±2.055
6	N Saif (2 ml)*	61.06^{e} ± 6.458	30.72^{c} ±2.469	52.33^{c}±4.409	39.17^{c} ± 5.159
7	N Saif (3 ml)*	57.83^{f} ±5.401	25.78^{g} ±2.157	42.50^{g} ±3.365	32.33^{g} ± 2.744
8	Solleg (1 ml)	70.44^{b} ± 7.905	31.89^{b} ±2.139	54.50^{b} ±4.007	41.22^{a}± 3.533
9	Solleg (2 ml)	67.00^{c} ± 10.466	27.39^{def} ±3.147	47.39^{de} ±5.147	34.33^{f} ±1.815
10	Solleg (3 ml)	69.94^{b} ± 9.142	26.78^{efg} ±1.477	44.56^{f} ±2.007	34.61^{f} ± 1.577

Data are expressed as the mean ± standard deviation; Model ANOVA, p values < 0.05 are significant. Superscript abc indicate significant differences among various groups as indicated by ANOVA followed by Duncan's multiple range test. N Saif- Naboat Saif

Effect of heart of date palm extract (HDP) on thyroid hormones in normal wistar rats

Table 3 depicts the thyroid hormone status of control and HDP groups. In control group TSH, T3 and T4 has been found to be 0.017 mg/100 ml, 0.486 mg/100 ml, and 3.90 mg/100 ml respectively. A significant effect of HDP has been found on thyroid hormone. Value of T3 and T4 significantly decreased, while the value of TSH significantly increased after treatment with HDP. Highest TSH (0.060 mg/100 ml) was observed in Sukkari (3ml) group, while lowest T3 and T4 were found in Naboat Saif (2 ml) (0.397 mg/100 ml) and Naboat Saif (3 ml) (3.21 mg/100 ml) respectively.

Discussions

Comprehensive exploration in the review of literature have shown dearth of studies investigating the effect of HDP on lipid profiles and thyroid hormone and to the best of our information this is the first study carried out to identify the effect of HDP extract on lipid profiles and thyroid hormones and such curtail make it difficult to discuss the result but it can be valuable to expand opportunities of thinking and ideas for further research in this field. During the past few decades, the eminence of herbal medicine has attained ground all over the world and witnessed a tremendous surge in acceptance which is mainly due to the faith that besides being cheap and locally available; herbal drugs are safe without any side effects (32, 33, 34). Date palm (Phoenix dactylifera L.) is very significant fruit crops in the palmacea family. Every part of this tree has its own uses. The influence of customary diet on lipid metabolism is a vital factor determining vulnerability to heart disease. Enhanced knowledge of the complexity of nutrient-disease relationships has shifted the framework for CVD prevention from a focus on macronutrient content of diets to foods and dietary patterns (35).

HDL and LDL are the two major groups of plasma lipoproteins involved in lipid metabolism and the exchange of triglycerides and cholesterol, cholesterol ester between tissues (36, 37). Addition of date to the diet of rats decreases plasma triglycerides and cholesterol and it is most likely facilitated by inhibition of absorption of dietary fats, cholesterol and bile acids (38). Erstwhile; studies have revealed that abnormalities of lipid and lipoprotein play substantial part in the pathogenesis and progression of CVD (39, 40). In controlled clinical trials almost 1.5% reductions in the incidence of coronary heart diseases has been observed after just 1% reduction in total and LDL cholesterol concentration (41).

Al Saif et al. (42) reported significant hypolipidemic effect of date diet in rats. Trabzuni et al. (18) in their previous study reported high content of total phenol and total flavonoid and 91%, 88% and 80% DPPH radical scavenging activity of Solleg, Naboat

Table 3: Effect of different kind of heart of palm extract (HDP) on thyroid hormones

Group No	Sample	TSH (mg/100 ml)	T3 (mg/100 ml)	T4(mg/100 ml)
1	Sukkari (1ml)	$0.049^{c} \pm 0.048$	$0.483^{a} \pm 0.061$	$3.42^{ef} \pm 0.357$
2	Sukkari (2ml)	$0.050^{c} \pm 0.004$	$0.446^{b} \pm 0.044$	$3.57^{de} \pm 0.250$
3	Sukkari (3ml)	$0.060^{b} \pm 0.007$	$0.437^{bc} \pm 0.050$	$3.72^{bcd} \pm 0.285$
4	Naboat Saif (1 ml)	$0.017^{a} \pm 0.005$	$0.412^{cd} \pm 0.052$	$3.75^{bcd} \pm 0.199$
5	Naboat Saif (2 ml)	$0.012^{a} \pm 0.005$	$0.397^{d} \pm 0.034$	$3.94^{ab} \pm 0.263$
6	Naboat Saif (3 ml)	$0.023^{d} \pm 0.045$	$0.401^{d} \pm 0.102$	$3.21^{f} \pm 0.236$
7	Solleg (1 ml)	$0.018^{a} \pm 0.010$	$0.446^{b} \pm 0.050$	$3.84^{bc} \pm 0.312$
8	Solleg (2 ml)	$0.027^{d} \pm 0.009$	$0.452^{b} \pm 0.045$	$3.94^{ab} \pm 0.275$
9	Solleg (3 ml)	$0.019^{a} \pm 0.013$	$0.424^{c} \pm 0.053$	$3.64^{cde} \pm 0.429$
10	Control	$0.017^{a} \pm 0.087$	$0.486^{a} \pm 0.051$	$3.90^{ab} \pm 0.201$

Data are expressed as the mean ± standard deviation; Model ANOVA, p values < 0.05 are significant. Superscript abc indicate significant differences among various groups as indicated by ANOVA followed by Duncan's multiple range test.

Saif and Sukkari respectively. Flavonoids in the HDP might also play a role in boosting the activity of lecithin acyl transferase which regulates blood lipids (43). Chaira et al. (44) reported that flesh and pits extracts of date palm fruit have free radical scavenging activities, and the significant effect of palmito extract on serum total lipid level could be attributed to the antioxidant potentials of palmito extract.

In the present study, concentration of HDLc significantly increased and this upsurge may be due to change in HDL composition which increases larger more cholesterol rich lipoprotein called HDLc and decreases the typical protein rich HDL (42). Coronary heart disease is strongly related to decrease in the concentration of high density lipoprotein cholesterol and increase in the LDLc. HDL can act as an acceptor of cellular cholesterol, scavenges extra cholesterol from peripheral tissues by lipid-poor apoA-I and HDL that is mediated by lipid transporter molecules and supply it to the liver for ultimate excretion into the feces as neutral sterols or bile acids and this role of HDL has been shown to be responsible for its athero protective properties (45,46). Long term use of anti hyperlipidemic drugs has been associated with few adverse effects, most importantly gastrointestinal upsets, general weakness, hepatic enzyme elevation and headache (47,48) and so herbal medicines can be better substitute.

Thyroid hormones (thyroxine (T4) and Triiodothyronine (T3)) are involved in the regulation of innumerable body functions such as reproduction, carbohydrate and lipid metabolism and oxygen consumption and any alteration in their normal levels leads to abnormalities (49). Follicular cells from free tyrosine and tyrosine residues of the protein called thyroglobulin synthesizes T4 (50) and almost 80% of the T4 gets converted to T3 by peripheral organs such as the liver, kidney and spleen (51). Trabezuni et al. (18) in their study mentioned that total flavonoids and phenols are the important pharmaceutical compounds of HDP and besides that, it also contains, carbohydrates, calcium salts, magnesium, zinc, potassium and even traces of iodine. The flavonoids can decrease thyroid hormones levels in various ways such as through inhibiting the activation of type 1 deiodinase that is specifically activated by TSH, through inhibiting thyroperoxidase and also by preventing the mineralization of iodine in the thyroid cells (52, 53). Presence of phenolic and flavonoid compounds may reduce both thyroid iodide uptake and thyroid peroxidase activity, which may be the reason for the observed depressing effect of HDP extract on thyroid hormones levels in normal rats. Similar result was reported previously by El Kaslan et al. (54) in normal rats after treatment with date palm pollen. Since HDP includes calcium and magnesium, it can contribute to fabricating and therefore increasing TSH as a mediator of second messenger via calcium-phosphatidylinositol mechanism (55, 56). Meanwhile; thyroid hormones play significant role in the pathogenesis of numerous diseases and any alteration in thyroid hormones levels can have hazardous effects on body physiology so it is necessary to conduct further studies on the effects of plants and their compounds on thyroid hormone secretion rates.

Conclusion

This study revealed that consumption of heart of date of palm as dietary component can be beneficial for lipid or thyroid control but more studies are required to assess its ameliorative role in hyperlipidemic and hyperthyroidism models and to expand vision into its possible mechanism of action and corroboration of these effects on animal and human models.

Acknowledgement

This research project was supported by a grant from the Research Centre of the Female Scientific and Medical Colleges, Deanship of Scientific Research, King Saud University. I would like to express my very great appreciation to Mrs Shaista Arzoo for her assistance in preparation of manuscript.

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