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The effect of herbal treatment of Hyphaene Thebaica (Doum) and Nelumbo Nucifera (Lotus) on Induced Hyperlipidemia and Hypertension in Male Wistar Albino Rats

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Abstract

Hyperlipidemia is a condition in medical terms where any lipid profile or else the lipoproteins are increased in the blood stream. Elevated LDL is risky and the best indicator of atherosclerosis risk. Hypertension is one of the most associated disease with dyslipidemia. For HDL-C, the risk of hypertension is supposed to be increased at such low levels. There are various medicinal plants, which are supposed to be a very important source for upcoming chemical substances which are having the potential for therapeutic effects. There are various phenolic as well as flavonoids substances present in Hyphaene Thebaica (Doum). These ingredients usually work as an antioxidant that are very helpful to provide a control towards hyperlipidemic. Hyphaene Thebaica has antimicrobial, antidiabetic antihypertensive, hypolipidemic and antioxidant effects. Yet another element called as Nelumbo Nucifera (Lotus) is very useful for medicinal purposes in terms of Oriental medicine. These plants are very hypolipidemic, antioxidant activity, antipyretic, antiplatelet activity and hypoglycemic activity.

Objective of the study: to estimate the effects of doum and lotus methanolic extracts on hyperlipidemia, hypertension and diabetes on lipid profile parameters and hypertension parameters like angiotensin converting enzyme and aldosterone.

Material and Methods: The study in this paper was done on fourth rats with the species of Wistar Albino. These rats are divided in to four groups and all are male samples. First one was control group and hyperlipidemia and hypertension induced in three groups. Feeding hyperlipidemic and hypertensive rats with extract of doum in third group and lotus extract in fourth group.

Results: The effect of both extracts on lipid profile parameters, Angiotensin converting enzyme and aldosterone were parallel in significant lowering them. Doum had strong effect on body weight but lotus had strong effect on fasting blood glucose level.

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Conclusion: Doum and Lotus contain flavonoids and phenols which cause lowering in lipid profile, Angiotensin converting enzyme, aldosterone, body weight and fasting blood glucose.

Recommendation: Using the extracts of lotus seeds and doum fruit can be used as adjuvant treatment in hyperlipidemia, hypertension and diabetes.

Key words: Hyperlipidemia, Doum, Lotus, Aldosterone

Introduction

Dyslipidemia is proved to be one of the most important factors which give rise to cardiovascular diseases. Approximately 37% percent of population in Egypt is subjected to have higher blood cholesterol levels as per the observation from various researchers. Many risk factors can be expected to evolve, which are responsible for the development of atherosclerotic cardiovascular diseases; therefore, it becomes essential factor to assess the nature of cardiovascular risk before it becomes imperative [28]. As per the definition stated in the background, Hyperlipidemia is a medical condition which is characterized by the observation of increase any or all lipids profile and lipoproteins in the blood. This estate is also called sometimes hypercholesterolemia or hyper-lipoproteinemia. There are also certain conditions in which a relatively low density of lipoprotein cholesterol is observed. This type of lower density is one of the best indicators for atherosclerosis risk [6]. Investigating it further leads us to Dyslipidemia which is also one of the most state in which large amount of lipids in the blood can be introduced, thereby leading to increased level of cholesterol or also including triglycerides. This can also lead to the low levels of the high-density lipoprotein cholesterol [24]. Hypertension is one of the most associated disease with dyslipidemia. Increased level of serum for TC, LDLC, and cholesterol are supposed to be associated with the probability of improved risk towards hypertension. For HDL-C, risk of hypertension was increased at low levels.

Hypertension and dyslipidemia are investigated by various researchers as to important risk factors that may lead towards cardiovascular diseases. There are certain epidemiological studies that are conducted on population basis. These studies have also reported that an unexpected and gradual increase in the blood pressure of a normal human being or prevalence of the hypertension are also associated with the increased level of lipids in bloodstream [22]. The drugs which are a remedy for the above stated cause comes with several side effects. It is also observed that the consumption of these rock samples which are synthetic in nature may cause hyperuricemia, diarrhea, nausea, myositis, gastric irritation, flushing, dry skin and abnormal liver function. In order to overcome this problem of synthetic drugs, medicinal plants are being studied closely. It is believed that these plants can be a very important and great source for various new chemical substances that can provide potential therapeutic use. More than 80% of the global population scenario depends on various medicines as an input in various developing countries. The use of these traditional folk medicine therapies is very helpful for treating such ailments [26]. Hyphaene Thebaica (Doum) contains certain extracts of the water having specific components like phenolic and flavonoids. These substances can act as an antioxidant that may help for the control of hyperlipidemic. Hyphaene Thebaica has antimicrobial, antidiabetic, antihypertensive, hypolipidemic and antioxidant effects [7]. Doum has pharmacological and nutritional properties [4]. It contains high amount of amino acids valine, leucine, and some non- essential amino acids such as (alanine, aspartic acid, glutamic acid, glycine, serine and proline). It is also was very rich in minerals such as potassium and phosphorous [3]. yet another important species of an aquatic plant termed as Nelumbo Nucifera (Lotus) is very important and useful in various medication purposes. All the parts of the plant can be utilized to provide solutions towards various ailments. They will be helpful enough to synthesize various medicines that can heal many problems as an oriental medicine. These plants are very effective to potential hypolipidemic, antioxidant activity, antipyretic [10], antiplatelet activity [11] and hypoglycemic activity [20].

Materials and Methods

Ethical Approval: This study was carried out in

Research center of Experimental Animal associated to Faculty of Veterinary Medicine– Banha University after the approval of all steps of the experiment with serial N° (000031).

Study Period: The study was carried in the period from March to May 2021.

Plant Materials: Hyphaene Thebaica and Nelumbo Nucifera seeds are obtained from Botanical Market and authorized by plant taxonomist who used it for preparation.

Preparation of plants Extract: The H. Thebaica decoction and N. Nucifera seeds powder (500gm) were presented under reflux of 75% methanol in a glass jar at 70C°. The extracts were filtrated by Whatman apparatus, its filter paper 0.45 micron under pressure. Then at rotatory evaporator at 60C°. Then they were put in methanol 5% with glycerin 0.5% in purified water. The final concentration was each 1 ml contain 750mg of each extract.

Animals: Forty male Wistar Albino rats with average weight between 190-200g (219.10±15.20) were used in this study. They were kept in cages each had 5 with mesh bottom galvanized metal wall boxes under controlled environmental and nutritional conditions amount 25-28 C° and humidity about 55-60% in lab of research center. They were fed standard rat diets and supplied with fresh tap water ad libitum, with a 12-h dark and light cycle. The animals were acclimatized for 2 weeks prior to the beginning of the experiment. Then divided into 4 groups. G1: as a control. G2,3,4: As experimental groups fed by high fat diet and injected weekly by Hydrocortisone and Nondrolone for 4 weeks at doses of Hydrocortisone (succinate sodium 100mg) 1.8mg/kg body weight subcutaneously and Nandurabolin (Nondrolone decarbonate 50mg/ml) 10 mg/kg body weight intramuscular in the gluteal region. Samples were taken from G1 and G2 after rats were sacrificed. Then G3 and G4 continued with high fat diet and daily dose of Hyphaene and Nelumbo respectively by dose 500mg/kg body weight taken by gastric tube for 4 weeks. The group of the rats that were under observed were checked for their symptoms of toxicity as well as mortality. These observations were done for 4 and 24 hours respectively. The control group ate standard diet with energy less than 1830kcal/kg diet and the G2, G3 and G4 ate high fat diets with energy3014 kcal/kg.

Samples Collection: Blood samples were collected from the orbital plexus and intra-cardiac of the rats two times; first time at the end of the first month and second was at the end of the second month. Daily measuring of fasting blood sugar from tail blood by glucometer and daily weight measuring by balance. The serum was separated by centrifugation at 4000 rpm for 20 minutes and then preserved in ice bag to be estimated in the same day.

Biochemical Measurements

1. Lipid profile was determined in all groups, included Total Cholesterol– Triglycerides– LDL-C and HDL-C.
2. Aldosterone hormone.
3. Angiotensin converting enzyme.

Statistical Analysis: The analysis of the data was done based on the SPSS program with version number 23. The record values were expressed as mean and standard deviation (Mean± SD). The one-way analysis of variance (ANOVA) was used to determine the most significant effect of feeding Hyphaene Thebaica and Nelumbo Nucifera. A P-value less than 0.05 (P<0.05) was significant.

Results and Discussion

Table 1: Changes in Serum Concentrations

changes in serum concentrations of Cholesterol in mg/dl.				
Cholesterol	**G I**	**G II**	**G III**	**G IV**
Range	76.8 – 90	110 – 180	76.5 – 83.2	65 – 79
Mean ±SD	82.29 ± 3.85	141.09 ± 24.64	80.24 ± 2.55	72.33 ± 5.07
P value	0.001*			

G I & G II	G I & G III	G I & G IV	G II & G III	G II & G IV	G III & G IV
0.001*	0.722	0.09	0.001*	0.001*	0.175
Changes in serum concentrations of Triglycerides in mg/dl					
TG	**G I**	**G II**	**G III**	**G IV**	
Range	85 – 113	109.5 – 160	100 – 135	95 – 121	
Mean ±SD	102.78 ± 8.44	143.55 ± 15.09	110.83 ± 10.31	105.20 ± 7.77	
P value	0.001*				
G I & G II	**G I & G III**	**G I & G IV**	**G II & G III**	**G II & G IV**	**G III & G IV**
0.001*	0.104	0.619	0.001*	0.001*	0.251

Table 2: Changes in Serum Concentrations of Lipoprotein

Changes in serum concentrations of High-density Lipoprotein (HDL) in mg/dl.					
HDL	**G I**	**G II**	**G III**	**G IV**	
Range	46.2 – 55.4	29.4 – 49	32.5 – 55	41.5 – 54.6	
Mean ± SD	50.02 ± 2.78	41.41 ± 6.25	45.39 ± 5.93	47.06 ± 4.66	
P value	0.005*				
G I & G II	**G I & G III**	**G I & G IV**	**G II & G III**	**G II & G IV**	**G III & G IV**
0.001*	0.049*	0.202	0.089	0.018*	0.468
Changes in serum concentrations of Low-density Lipoprotein (LDL) in mg/dl between control, hyperlipidemic and hypertensive group, Doum group and Lotus group					
LDL	**G I**	**G II**	**G III**	**G IV**	
Range	18 – 24.5	34.7 – 73.35	15 – 23.6	16 – 22.3	
Mean ±SD	21.50 ± 2.37	48.21 ± 13.86	20.63 ± 2.75	19.86 ± 1.77	
P value	0.001*				
G I & G II	**G I & G III**	**G I & G IV**	**G II & G III**	**G II & G IV**	**G III & G IV**
0.001*	0.789	0.615	0.001*	0.001*	0.813

Table 3: Changes in Serum Concentrations Aldosterone Hormone

Changes in serum concentrations of Aldosterone Hormone in pg,/ml					
Aldosterone	**G I**	**G II**	**G III**	**G IV**	
Range	75 – 346	165 – 573	69.1 – 480	108 – 210	
Mean ±SD	169.00 ± 86.88	394.50 ± 139.75	182.91 ± 115.97	155.00 ± 37.91	
P value	0.001*				
G I & G II	**G I & G III**	**G I & G IV**	**G II & G III**	**G II & G IV**	**G III & G IV**
0.001*	0.763	0.762	0.001*	0.001*	0.546
Changes in serum activity of Angiotensin Converting Enzyme (ACE) in U/L					
Angiotensin	**G I**	**G II**	**G III**	**G IV**	
Range	40 – 233	130 – 235	90 – 193	85 – 187	
Mean ±SD	101.50 ± 73.33	190.80 ± 36.08	141.10 ± 33.55	138.50 ± 35.54	
P value	0.002*				
G I & G II	**G I & G III**	**G I & G IV**	**G II & G III**	**G II & G IV**	**G III & G IV**
0.001*	0.071	0.091	0.025*	0.019*	0.903

Table 4:. Changes in Body Weight

Changes in body weight in (grams) between control, hyperlipidemic and hypertensive group, Doum group and Lotus group					
Weight	**G I**	**G II**	**G III**	**G IV**	
Range	190 – 240	160 – 340	180 – 260	192 – 300	
Mean ±SD	219.10 ± 15.20	274.68 ± 39.07	205.88 ± 19.91	222.00 ± 20.85	
P value	0.001*				
G I & G II	**G I & G III**	**G I & G IV**	**G II & G III**	**G II & G IV**	**G III & G IV**
0.001*	0.021*	0.611	0.001*	0.001*	0.005*
Changes in serum concentrations of fasting glucose in mg/dl between control, hyperlipidemic and hypertensive group, Doum group and Lotus group					
Fasting glucose level	**G I**	**G II**	**G III**	**G IV**	
Range	87 – 119	100 – 139	90 – 130	80 – 123	
Mean ± SD	105.20 ± 9.33	131.85 ± 27.26	115.18 ± 11.43	106.68 ± 10.18	
P value	0.001*				
G I & G II	**G I & G III**	**G I & G IV**	**G II & G III**	**G II & G IV**	**G III & G IV**
0.001*	0.007*	0.686	0.001*	0.001*	0.021*

Discussion

Various diseases such as hypertension, diabetes and hyperlipidemia can be healed up with the help of various medicinal plants. These natural plants are one of the most important sources that will be very helpful for primary health care. Amongst the global population approximately 65 to 80% of the human beings in various developing nations rely majorly on these medicinal plants. One of the most consumed beverages across Egypt is Doum. It has a unique property that this medicinal plant is rich in its content of polyphenolic compounds. It can be used as a very effective remedy towards hypertension [12]. Blue lotus was distributed along the Nile River valley. All parts of the plant have valuable therapeutic effects. The bioactive constituents of both plants (doum and lotus) phenols, flavonoids and alkaloids enable them to have multiple therapeutic effects [23].

Previous studies proved the hypolipidemic, antihypertensive and hypoglycemic effects of H. Thebacia and N. Nucifera[14,5,12,7,18,19,8], and[1]. Our results showed that H. Thebacia and N. Nucifera have significant lowering effect to lipid profile that comprises of the complete levels of cholesterol, as well as Triglycerides including low density lipoprotein. The lowering effect of Thebacia agreed with Bayad, 2016 who proved that regular administration of aqueous extract of H. Thebacia for 1or 2 months with 0.5 and 2gmg/kg improve lipids, total cholesterol, Triglycerides. One of the biggest advantages is in the treatment towards hypercholesterolemia. This is more famous amongst Egyptians who have a comparatively low high density of lipoprotein. (HDL-C) is the prevalent lipoprotein abnormality. The two major risk factors responsible are total cholesterol and LDL. Very high levels of total cholesterol can prove to be hazardous for health of human being[29]. In the same context [13] portrayed that triglycerides are one of the major reasons behind the coronary heart disease. They also claimed to be the effective drug for the anti-hypercholesterolemic syndrome. However, these drugs are not useful to reduce the level of triglycerides. However, they concluded that the aqueous extract of Doum is helpful, since it considerably lowers the effect of triglycerides. The results proved significant increase in the level of HDL in the group treated with doum and significant decrease LDL level in the same group which agreed with [14] who proved that supplementation with doum was parallel to reduction of lipoproteins level in the form of decrease LDL and increase in HDL. The results agreed with [16] reported a hypolipidemic effect of doum. [1] proved that the degree meant in the level of

serum TG, TC and LDL with the observed increased level of HDL in rats which have been treated with more levels of the flavonoid H. Thebaica.

Our results showed the significance lowering effect of N. Nucifera on lipid profile include TC, TGs and LDL while significant increasing in HDL. These results agreed with [8] who proved that N. Nucifera has improved lowering effect of lipids in induced diabetic hyperlipidemic rats. Also [21] In his article emphasized that the anti-obesity efficacy, which arrives because of the constituents isolated from N. Nucifera via stimulated lipolysis in mice adipose tissue. N. Nucifera has suppression effect on α-amylase, lipase activity and lipid metabolism and so, lowered lipids in the blood [23]. Also, [18] proved that Lotus showed positive effects on obesity, endocrine system, and lipid metabolism through its effect on TC, TG and LDL. Other results produced by [26] that N. Nucifera had hypolipidemic effect by decreasing TC, TGs, LDL and VLDL and increase HDL in induced hyperlipidemic rats and compared the results with those under treated statins therapy. Our results showed the antidiabetic effect of Doum and Lotus through significant results in groups of rats which treated with daily doses of methanolic extract of doum and lotus but there was significance in results between both groups which indicated the strong antidiabetic effect of Lotus over than Doum. Our results of antidiabetic effect of Doum agree with [15] who proved that plants which include poly-phenolic contents had α-glucosidase inhibitory effect and so had postprandial hypoglycemic effects. Also, our results agree with [7] results that the proper observations for the aqueous extracts of Doum, contributes towards lowering of the blood glucose level. This complete phenomenon can last from one month till two months. The pathogenesis of diabetes mellitus including the chances of managing the oral administration of hypoglycemic herbal treatment have been extensively studied. Our results of antidiabetic effect of N. Nucifera agree with [8] who proved the reduction effect of alcoholic extract of N. Nucifera on blood glucose level in induced diabetic rats. It was found that the level of A1CHb levels in the rats was reduced to a significant amount. This effect was through reversal of insulin resistance or increasing insulin secretion due to its regeneration effect of langerhans β-cells of pancreas. Our results showed significance anti-hyperglycemic effect of both Doum and Lotus, but Lotus was significantly higher in effect than Doum.

Obesity and hyperlipidemia are closely connected and responsible towards the activation of the renin-angiotensin system (RAS) in humans, as it has been observed in various species of diet-induced obese rodents and in several genetic models [32]. The main impact of such issue leads to improvement and sudden increase in the plasma levels of angiotensinogen. This observation was due to adipocyte hypertrophy. Angiotensinogen in the body is produced with the help of the action of renin. This gets converts to angiotensin II (Ang II) with the help of the angiotensin converting enzyme (ACE). The higher level of the Ang II tends to induce large level of contradiction of vascular system and thereby it leads to the increase in blood pressure. The entire process is catalyzed with the ACE whereat tries to breakdown the vasodilator [17], as a result of this phenomenon increase the level of blood pressure is observed as an additional contribution. Various researchers have also implied towards the connection between angiotensin II levels, renin, body mass index (BMI) and ACE as a result of the increase in the adipocytes, which is an important source of these hormones [9] and [30].

In the present study both plants either Doum or Lotus contain different percent of flavonoids, polyphenols and alkaloids which play an important role in lowering ACE which is the key in regulation of blood pressure. Our results showed significant increase in ACE level in induced hyperlipidemic hypertensive group of rats, while with administration of daily doses of Doum extract and Lotus extract there were significant reduction in ACE in serum. Lotus group showed more reduction than Doum group even there was no significant variation between both. The results that we found are also in accordance with [1] and proved that Hyphaene Thebaica had an anti-hyperlipidemic and ACE inhibitory effects. Nelumbo Nucifera is well known to be a traditional treatment for blood pressure higher levels and heat imbalance of the body as per [27]. Our results agree with [31] who proved that active product of N. Nucifera is neferine which inhibits angiotensin II-stimulated

proliferation in vascular smooth muscle cells through hemeoxygenase-1 as well as down-regulating fractalkine gene expression [33]. N. Nucifera decrease the blood pressure through its effect of antioxidant through its role in inhibiting harmful effects of free radicals which participate in developing many diseases like diabetes, cancer, inflammation and atherosclerosis [8].

Our results showed significant lowering aldosterone hormone in group III and IV, but no significance difference between both groups. Group IV(Lotus) showed more lower level than group III (Doum) this agree with the role of Doum and Lotus in lowering blood pressure, these present results are explained with [2] study who proved that Nitric Acid (NO) has a good role in protection and stimulation of suprarenal glands from changes occur with stress, so NO has a stimulation role for secretion of aldosterone hormone. [8] proved that N. Nucifera has a scavenger effect on Nitric oxide and it will cause lowering in aldosterone level and following regulation of blood pressure. Our results showed significant lowering in body weight in both groups treated with Doum and Lotus. Group III(Doum) gives low body weight more than group IV (Lotus). N. Nucifera causes significance decrease in body weight which agree with [8] in the study of the effect of N. Nucifera on the induced diabetic rats by the effect of drugs with increase in its the body weight. It is regulated by the effect of daily dose administrated of N. Nucifera extract. Our results also agree with [1] who proved that H. Thebaica reduced the BMI of the experimental rats fed with high fat diets and treated with extract of H. Thebaica.

Conclusion

Doum and Lotus contain flavonoids and phenols which cause lowering in lipid profile, Angiotensin converting enzyme, aldosterone, body weight and fasting blood glucose.

Ethical Clearance: The researchers were able to ask permission to conduct the study and were given permission to conduct the experiments.

Source of Funding: There was no fund produced from any organization. This work is a self-financed study.

Conflict of interest: The authors declare that there is no conflict of interest.

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