

EFFECTS OF LEAF EXTRACTS OF MORINGA OLEIFERA ON REGULATION OF HYPOTHYROIDISM AND LIPID PROFILE

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ABSTRACT

The aqueous leaf extract of *Moringa oleifera* was evaluated for its ameliorative effect in the regulation of thyroidism in rat model. Male albino rats of 120-150 g were treated orally with doses of 500mg/kg body weight (b.w.) and 250 mg/ kg b.w. of aqueous extract of *Moringa oleifera* leaf. Results show that T3 and T4 were increased and TSH was decreased significantly ($p > 0.05$) at high doses compared to those in the control group. Also, the extract significantly reduced ($p < 0.05$) total cholesterol concentration and low density lipoproteins cholesterol (LDL) concentration in the serum while it had no significant effect on serum High density lipoprotein (HDL) cholesterol concentration at all doses administered when compared with controls. The results of this study suggest that the extract may have beneficial effect on serum cholesterol concentration and a stimulant to thyroid functions.

INTRODUCTION

The hormones produced by thyroid gland enhance protein synthesis and oxygen utilization and these physiologic activities, in turn, influence the basal metabolic rate (BMR) (Boelaert and Franklyn, 2005). The activity of the thyroid gland is predominantly regulated by the concentration of the pituitary glycoprotein hormone, thyroid stimulating hormone (TSH). (Mariotti, 2011). TSH levels are further regulated by the hypothalamus, and also by other regulatory mechanisms, producing a feedback loop so that TSH increases as thyroid hormones decrease and TSH decreases when thyroid hormones increase. Measures of the amount of the thyroid hormones T3 (triiodothyronine) and T4 (thyroxine) in the blood plasma are considered a substantive evaluation of thyroid function (Mariotti, 2011).

Thyroid disease affects about most of the Indian population, but because the disease predominantly strikes middle-aged women, the incidence within this group is rather high. Women are about four times more likely than men to suffer hyperthyroid disorders, eight times more likely to suffer hypothyroidism, and about twice as likely as men to suffer thyroid tumors. Approximately half the cases of thyroid disease involve hyperthyroidism and the other half involves hypothyroidism (Dharmananda, 2012; Saxena *et al.*, 2012).

The current medical therapies for thyroid disorders other than iodine-deficiency goiter are often deemed inadequate because of difficulties in regulating the level of thyroid hormones through use of drugs or an exogenous source of thyroid hormone. As a result, patients often experience only partial relief of the symptoms and those who suffer from hyperthyroidism often have to deal with hypothyroid

conditions following medical destruction of the thyroid gland (Dharmananda, 2012).

Thyroid hormones have significant effects on the synthesis, mobilization and metabolism of lipids. They affect serum cholesterol mainly by altering lipoprotein metabolism (Erem *et al.*, 2006). Overt hypothyroidism is associated with significant increases in circulating concentration of total and low density lipoprotein cholesterol (LDL) (O'Brien *et al.*, 1993). Hypercholesterolemia is favored due to the hormone deficit and to the decreased activity of the lipoprotein lipase (Mansourian *et al.*, 2008). Recently, a large number of clinical studies have indicated that TSH is associated with lipid metabolism and a cluster of cardiovascular diseases (Asvold *et al.*, 2007; Velkoska Nakova *et al.*, 2009). In these studies, the influence of TSH on serum lipids has always been attributed to thyroid hormone levels.

Medicinal plant-based drugs owe the advantage of being simple, effective and exhibit broad spectrum activity and also have continued to play a dominant role in the maintenance of human health since ancient times (Farombi, 2003). Indigenous systems of medicine that use plant-based drugs could provide both concepts of therapy as well as therapeutic agents to complement modern medicine in management of diseases and herbal extracts contain different phytochemicals with biological activity that can be of valuable therapeutic index. Over 50% of all modern clinical drugs are of natural product origin (Stuffness and Douros, 1982) and natural products play an important role in drug development programs in the pharmaceutical industry (Baker *et al.*, 1995). The review of literature revealed that considerable contributions have been made on medicinal plants by many workers (Dadsena *et al.*, 2013; Dandapat *et al.*, 2013; Kullu *et al.*, 2013; Kumar *et al.*,

2013; Kumar *et al.*, 2013a; Mahato *et al.*, 2013; Toppo *et al.*, 2013; Sahu *et al.*, 2013). Medicinal plants are the richest bio-resource of drugs of traditional systems of medicine, modern medicines, nutraceuticals, food supplements, folk medicines, pharmaceutical intermediates and chemical entities for synthetic drugs. It has been suggested that aqueous as well as other extracts from plants used as medicines are potential sources of antiviral, antitumoral (Vlietinck *et al.*, 1995) and antimicrobial agents (Choudhury *et al.*, 2012 a, b; 2013 a, b, c). The leaves of *M. oleifera* are used in folk medicine but their specific impacts on lipid profile and thyroid hormone is not properly known. Keeping this aspect in background the present communication deals with the impact of leaf extract of *M. oleifera* on thyroid hormone and lipid profile of mammalian animal model male albino rats.

MATERIALS AND METHODS

Experimental Animals

Adult albino rats of male sex weighing between 120-150 g procured from authorized suppliers were housed under standard environmental conditions in polypropylene cages at normal room condition in the season ($25 \pm 1^\circ\text{C}$ temperature, $55 \pm 5\%$ humidity and 12 h/12 h light/dark cycle). The animals were allowed free access to drinking water and standard rat feed. The care and handling of rats were in accordance with the protocol approved by Institutional Animal Ethics Committee (process no: 46, page no.137).

Collection of plant material:

The fresh and tender leaves were collected, dried in a shade under $28 \pm 2^\circ\text{C}$ for six to seven days and then crushed into coarse powdery substance by using electric grinder. The coarse powdery substance was dried again and was then sieved to get fine powder using the fine plastic sieve, which was then stored in an air tight bottle in the laboratory until required.

Extract preparation:

50 g of the sieved powder was weighed accurately and subjected to extraction in a Soxhlet apparatus at room temperature using ~350 mL water. The extracts obtained were filtered, concentrated in rotary flash evaporator and maintained at 45°C the percentage yield of the extract was calculated and the dried extract was stored in air tight

container at room temperature for further studies.

Acute toxicity studies

The acute toxicity studies were performed in accordance with the OECD (Organization for Economic Co-operation and Development) guidelines no. 425 (Up and Down Procedure). No death was observed till the end of the study. The test samples were found safe up to the dose of 2000mg/kg and from the results 500 mg/kg was chosen as the maximum dose for further experimentation (WHO.)

Experimental design:

Group 1: Received 1mL of distilled water orally

Group 2: Received 250mg/kg body weight (bw) of *M. oleifera* orally.

Group 3: Received 500mg/kg bw of *M. oleifera* orally

Estimation of thyroid hormones

Estimation of serum T3, T4, TSH was done by chemiluminescence immunoassay method (Demers and Spencer, 2006)

Estimation of Lipid profile

Estimation of total cholesterol, HDL cholesterol, LDL cholesterol and triglycerides was done by cholesterol oxidase - phenol aminoantipyrine method (Rifa and Warnick, 2006)

Statistical analysis

All results were expressed as mean \pm standard error of mean (S.E.M.). Data was analyzed using one-way ANOVA followed by Dunnett's-test. $p < 0.05$ was considered as statistically significant.

RESULTS AND DISCUSSION

The data recorded on thyroid hormone profile in control and *M. oleifera* fed rats are presented in Table -1, 2. The results showed increase in thyroid activity. The TSH level correlated well inversely with T3 and T4 levels. The group which received maximum test dose (500mg/kg bw, 14days) showed maximum percentage increase in hormone concentration of T3 and T4 where as a maximum percentage decrease in TSH levels was observed when compared to the other dose levels, which clearly proves that the response was dose effective and the *M. oleifera* leaf extracts can be used in hypothyroidism condition

Table 1: T3, T4 and TSH concentration for 07 days along with their percent increase (+) or decrease (-) in relation to the control values in male rats

Group	T3(ng/dL)	% increase or decrease	T4(ng/dL)	% increase or decrease	TSH(uIU/mL)	% increase or decrease
Control	30 ± 0.19	-----	2.90 ± 0.86	-----	0.81 ± 0.45	-----
L.D (250mg/kg b.w.)	$61 \pm 0.35^*$	+103	$5.80 \pm 0.66^*$	+100	$0.42 \pm 0.85^*$	-48
H.D (500mg/kg b.w.)	$65 \pm 0.44^*$	+116	$8.50 \pm 0.89^*$	+224	$0.28 \pm 0.87^*$	-65

Values are expressed as mean \pm SEM from the experiments, $n = 6$, $p < 0.05$ relative to control

Table 2: T3, T4 and TSH concentration for 14 days along with their percent increase (+) or decrease (-) in relation to the control values in male rats

Group	T3(ng/dL)	% increase or decrease	T4(ng/dL)	% increase or decrease	TSH(uIU/mL)	% increase or decrease
Control	30 ± 0.19	-----	2.90 ± 0.86	-----	0.81 ± 0.45	-----
L.D (250mg/kg b.w.)	$66 \pm 0.63^*$	+119	$6.45 \pm 0.98^*$	+122	$0.36 \pm 0.72^*$	-55
H.D (500mg/kg b.w.)	$69 \pm 0.66^*$	+130	$8.96 \pm 0.89^*$	+208	$0.24 \pm 0.67^*$	-70

Values are expressed as mean \pm SEM from the experiments, $n = 6$, $* = p < 0.05$ relative to control

Table 3: Lipid profile for 7 days along with their percent increase (+) or decrease (-) in relation to the control values in male rats

Group	Total cholesterol	% increase or decrease	HDL cholesterol	% increase or decrease	LDL cholesterol	% increase or decrease
Control	60±0.05	---	23±0.13	---	18±0.54	---
L.D (250mg/kg b.w.)	59±0.19*	-1.6	25±0.23*	+8.6	17±0.32*	-5.5
H.D (500mg/kg b.w.)	57±0.11*	-5.0	26±0.03*	+13.4	16±0.42*	-11.11

Values are expressed as mean ± SEM from the experiments, n=6, * p<0.05 relative to control

Table 4 : Lipid profile for 14 days along with their percent increase (+) or decrease (-) in relation to the control values in male rats

Group	Total cholesterol	% increase or decrease	HDL cholesterol	% increase or decrease	LDL cholesterol	% increase or decrease
Control	60±0.05	---	23±0.13	---	18±0.54	---
L.D (250mg/kg b.w.)	59±0.43*	-1.9	23±0.24 ^{ns}	-7.5	16±0.69*	11.7
H.D (500mg/kg b.w.)	58.5±0.68*	-3.2	23.02±0.36 ^{ns}	-1.3	16±0.56*	16.8

Values are expressed as mean ± SEM from the experiments, n=6, * p<0.05 relative to control

to normalize hormone levels.

Thyroid hormones play important role on growth and development of the body and regulate metabolism (Huang *et al.*, 2008). So, with an increase in thyroid activity, marked changes in thyroid hormone production, metabolism and action occur. This may result in an increased prevalence of sub-clinical thyroid disease that is associated with thyroid dysfunction (Peeters, 2008). Many factors can influence the concentration of these hormones and therefore disturb the general body metabolism. Thiocyanate from tobacco, smoke, perchlorate and drugs which contain different amounts of iodine can influence the structure and function of thyroid hormones (Steinmaus *et al.*, 2007). Various other studies reported that thyroid disorders vary according to age, genders, ethnic and geographical areas (Lamfon, 2008)

Similar results have been observed in different plant extracts such as Caraway (Dehghani, 2010); Everyouth and Dreamshape (Ohye *et al.*, 2005). Also *Ficus carica* leaf extracts showed similar changes in the levels of T3 and T4, where as TSH level was not investigated (Saxena *et al.*, 2012). Furthermore there are reports where TSH level was inversely correlated with T4 levels but the levels of T3 were variable (Mokshagundam and Barzel, 1993; Chuang *et al.*, 1998; Mansoor *et al.*, 2011). Elevated TSH level directly reflects impaired thyroid hormone production (Saha *et al.*, 2007). The better co-relation of TSH with T4 may be due to the reason that T4 is mainly produce from pituitary gland while only 7% of T3 is secreted. The rest of the T3 production is dependent on the peripheral conversion of T4 to T3 which in turn dependent on many factors including bioavailability of enzyme deiodonase, drugs, disease in which inactive T3 form instead of T3. Age, gender ethnic distributions have been reported to be additional contributing factors by many studies (Nishikawa *et al.*, 1981; Ahmed *et al.*, 2009). Another study showed the effect of *Ocimum sanctum* leaf extract on the changes in the concentration of serum T3, T4 and serum cholesterol were investigated in male mouse. While the serum T4 concentration significantly reduced after drug administration, no marked changes were observed in serum T3 level, T3/T4 ratio and in serum cholesterol level. The study suggested the antithyroid effect of *Ocimum sanctum* leaf (Tripathi and Padamja, 1995).

The data recorded on lipid profile in control and *M. oleifera* fed rats are presented in Table-3, 4). Total cholesterol and LDL levels decreased significantly (p>0.05) where as HDL was

elevated (p<0.05). The relationship between serum lipid parameters and thyroid hormones has been found intensively (De Groot, 1989a, b; Parle *et al.*, 1992; Suzuki *et al.*, 1992; Bauer *et al.*, 1998; Diekman *et al.*, 2000). Studies on this subject, confirm the presence of an inverse relationship between thyroxin serum levels and cholesterol (Ferlito *et al.*, 1975; Hubner *et al.*, 1976; Felicetta, 1987). Other studies demonstrate the influence of iodothyronine on the catabolism of the Very Low Density Lipoprotein (VLDL), showing an increase in LDL and VLDL fractions in untreated hypothyroidism (Muller and Seitz, 1984; Friis and Pederson, 1987).

In some studies it is shown that total and LDL cholesterol are increased in hypothyroidism (Diekman *et al.*, 2000). In a population-based study in older women, in women with high TSH, LDL cholesterol is found 13 % higher, HDL cholesterol 12% lower and total cholesterol, although not statistically significant, 8% higher than women with normal TSH levels (Bauer *et al.*, 1998).

The presence of hypercholesterolemia in clinical hypothyroidism is well established (Erem, 2006). It is also reported that total cholesterol and LDL levels are increased in patients with clinical hypothyroidism (Pearce *et al.*, 2008). This is due to the decreased LDL-receptors' activity, resulting in decreased catabolism of LDL (Abbas *et al.*, 2008). The results in the present study shows that *M. oleifera* extracts is useful in both hypothyroidism as it is increasing the T3 and T4 hormone levels and decreasing TSH as well as in hypercholesterolemia where it is decreasing the total cholesterol.

Although further investigations are required to reveal the exact mechanism of action(s) of thyroid hormone regulation and lipid profile by *Moringa oleifera* leaf extract, the present findings clearly indicate that this extract is stimulant to thyroid functions. However, the authors emphasize that further studies are required to observe the dose dependant effect of leaf extract which might be effective and safe in ameliorating hypothyroidism as well as in dropping the total cholesterol levels.

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