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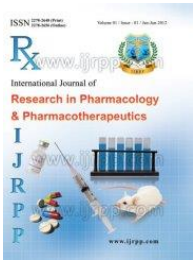

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Hypolipidemic changes in *Kanakalinga karpoorati mezhugu* therapy in Experimental hypothyroid disorder

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ABSTRACT

Kanaka linga karpoorathi mezhugu is a herbomineral drug preparation used in Siddha system of medicine used to treat thyroid disorders and allied ailments. Known risk factors for thyroid disease include autoimmunity, external irradiation of the head and neck, a biosynthetic defect in iodine organification, replacement of the thyroid gland by tumour, and use of certain drugs. There are several forms of herbomineral drugs like Mezhugu, Parpam, Chendooram, Chunnam, Pathangam, Kattu, Kalangu etc have their in own pharmacological system, but needs to meet the global standards. Male albino rats of were used for this present thyro-toxicity study. Animals were provided with normal rats feed and normal water ad libitum. Hypothyoidi condition was induced using methimazole. They were provided with KLK mezhugu in water suspension in test groups. Aanimals were sacrificed, blood was drawn and the serum was separated for biochemical analysis. The result of this study shows the significant thyrotoxicity induced by methimazole was evidenced by increase in serum T3 Triiodothyronine, T4 Thyroxine, TSH secretion due to thyroid cellular necrosis. The administration of KLK mezhugu for 30 days was found able to treat and protect thyroid necrosis against methimazole induced thyroid-toxicity.

Keywords: KLK Mezhugu, Herbomineral siddha drug, Transaminase and Phosphatase, Methimazole

INTRODUCTION

Kanakalinga karpoorathi mezhugu is a herbo-mineral drug preparatiom used in siddha system of medicine used to cure many diseases like,Type of kapha disorder, Abdominal pain, Epilepsy of mental disorders, Urethral discharge, Jaundice, Syphilitic disorder, Burning micturition, 64 varieties of fever, neuralgia with rheumatism, Abdominal swelling, Chronic and severe vatha disorders,, Bronchial asthma, Nenjadaippudan Marpil Kuthu, Kuthirai Valippu (a type of epilepsy). The drug is used in clinical studies for the treatment of thyroid disorders especially hypothyroidism. Thyroid disease is common and disease is more prevalent with increasing age. 5%–9% of adults have subclinical thyroid disease and 0.8%–7.5% have clinical thyroid disease 1–3 in the general population [12] .The thyroid gland secretes 3 hormones- thyroxin (T4), triiodothyronine (T3) and calcitonin. Subclinical thyroid disease is defined by abnormal serum thyroid-

stimulating hormone (TSH) but normal T4 and T3 levels and does not always require treatment, whereas persons with clinical thyroid disease have abnormal serum TSH, T4, and T3 levels and require treatment. Known risk factors for thyroid disease include autoimmunity, external irradiation of the head and neck, a biosynthetic defect in iodine organification, replacement of the thyroid gland by tumour, and use of certain drugs [1]. Other factors associated with an increased risk of thyroid disease include female sex, increasing age, and iodine deficiency [2, 3].

In today's scenario 80% of world's population depends on herbal drugs. According to WHO, Ayurvedic medicines come under traditional medicines and refers to health practices, approaches knowledge and beliefs incorporating plant, animal and mineral based medicines, spiritual therapies, manual techniques and exercises (Yoga and Pranayamam), applied singularly (Herb) or in combination (Polyherb) to treat, diagnose and prevent illnesses or maintain well-beings

Among the traditional systems of medicine in India, Siddha medicine uses more of herbal, mineral and animal products as raw materials in various formulations. The herbs are dispensed in the form of Decoctions, Karkam, Choornam, Pills, Lehyams, Nei, and Manappagu etc. Other forms of drugs include Mezhugu, Parpam, Chendooram, Chunnam, Pathangam, Kattu, Kalangu etc. Siddha formulations over cede the use of herbo mineral and herbo metallic preparations. The usage of these medicines especially the dosage, mode of administration etc. are well documented in traditional literature. To meet the global standards, medicines under the India There are several forms of medications in Siddha system of medicine. They are broadly classified into 32 internal and external therapies. Among the medications, parpams and chendoorams especially made up of metals are widely used in this system.

EXPERIMENTAL

Male albino rats of 8 – 10 weeks of age weighing between 100 and 120g were used for this present thyro-toxicity study. The animals were purchased from Sri Venkateswara Enterprises (Ltd), Bangalore and housed in polypropylene cages. Animals were provided with normal rats feed and normal water *ad libitum*. Animals were divided into three groups of 4 animals. Group I: normal animals provided with usual rat feed and water. Group II: as control animals provided with rat feed and water along with 40mg/kg methimazole in 100ml distilled water and the Group III as Drug treated animals provided with rat feed and water along with methimazole and crude powder of KLK mezhugu in water suspension and the drug followed by it.

At the end of treatment, animals were fasted overnight, anaesthetized with ether and sacrificed by cervical decapitation. Blood was drawn and the serum was separated for biochemical analysis.

Thyroid protective activity was done by assessing the significant changes in body weight, Serum T_3 triiodothyronine, T_4 thyroxine, TSH was determined using ELISA kit method. Albumin level was measured spectrometrically at 600nm and total protein by biuret method a blue purple coloured complex with absorbance at 550nm. Cholesterol and Triglycerides were estimated Friedman and Young method by calorimetric kit method [16]. Lipid peroxide content was assayed by thio-barbituric acid method, catalase estimated calorimetrically. Transaminases activities were estimated by Reitman and Frankel method and which was measured spectrometrically [17]. The acid phosphotases was estimated and the absorbance was read at 405nm. Mean values standard were calculated for all the values carried out [4].

RESULTS AND DISCUSSION

Methimazole (1-methyl-3H-imidazole 2-thione) is an antithyroid drug, methimazole also known as Tapazole or Thiamazole or MMI, and part of the thioamide group. Like its counterpart propylthiouracil, a major side effect of treatment is agranulocytosis. Methimazole molecular formula is $C_4H_6N_2S$. Methimazole inhibits the enzyme thyroperoxidase, which normally acts in thyroid hormone synthesis by oxidizing the anion iodine (I^-) to iodine (I_0), facilitating iodine's addition to tyrosine residues on the hormone precursor thyroglobulin, a necessary step in the synthesis of triiodothyronine (T_3) and thyroxine (T_4). [5]

The result of this study shows the significant thyrotoxicity induced by methimazole was evidenced by increase in serum T_3 Triiodothyronine, T_4 Thyroxine, TSH secretion due to thyroid cellular necrosis. The administration of KLK mezhugu for 30 days was found able to treat and protect thyroid necrosis against methimazole induced thyroid-toxicity.

Table 1: Anti-thyroid effect of KLK mezhuguon T_3, T_4, TSH

Group	Dose	T3 ng/ml	T4 µg/dl	TSH µ/u/ml
Normal	Saline	128.3±10.26	2.33±0.13	3.26±0.21
Control Methimazole treated	40mg/kg	92.76±6.49	4.73±0.28	10.15±0.64
KLK mezhugu	100mg/kg	103.66±6.84	7.775±0.54	8.73±0.69

Each values is the Mean ± SEM of three animals statistically significant from control

In the present experimental study shows that treatment with *KLK mezhugu* crude powder at the dose of 100mg/100g.b.wt, the serum T3 and T_4 was increased from the untreated control animal (methimazole induced). The active thyroid hormone, T3, is one of the most powerful molecules in the human body, affecting every system, every tissue of the body and every aspect of our well-being and health. It increases the mitochondrial energy production. [5]

Thyroid hormones, thyroxine (T_4), and triiodothyronine (T_3) play an important role in all major metabolic pathways. They regulate the basal energy expenditure through their effect on protein, carbohydrate and lipid metabolism. This might be a direct effect or an indirect effect by modification of other regulatory hormones such as insulin or catecholamines [6].

The result of this study shows the significant hypothyrodism induced by methimazole was evidenced by increase in serum T3 and T4 and secretion due to thyro-necrosis. The administration of KLK mezhugu for 30 days was found able to treat and protect thyroid cell or follicles damage against methimazole induced hypothyroidism.

The TSH level is not a measure of thyroid hormone sufficiency in any given patient, either untreated or treated; reliance on the TSH produces both under and over-diagnosis and under treatment. Dysfunctional central hypothyroidism with a normal TSH may be more common than primary hypothyroidism, and TSH-normalizing T4 therapy neither normalizes T3 levels nor restores euthyroidism. The TSH test is useful only for investigating the cause of clinically-diagnosed hypothyroidism. TSH test as the best screening test for the diagnosis of primary hypothyroidism and the best guide for its treatment. If the TSH is elevated, it is a compensatory mechanism; the increased stimulation of the dysfunctional thyroid gland may indeed work to maintain thyroid levels and effects. The TSH response to response to low FT4 levels declines by 80% between ages of 20 and 80 [7].Thus the result shows the increased level of Thyroid Stimulating Hormone (TSH) after the induction of KLK mezhugu in hypothyroidism induced rats.

Concentrations below the reference range usually reflect low albumin concentration, for instance in liver disease or acute infection. Rarely, low total protein may be a sign of immunodeficiency. Normally T3 is bound loosely by serum proteins and hence diffuse much more rapidly into the tissues. Thus the result shows the increased level of albumin and total protein due to the action of the herbal drug KLK mezhugu against the methimazole.

Hypothyroidism is one of the most common causes of hyperlipidemia in humans and animals and it is characterized by excessive cholesterol and TGL levels. There are various factors of increased oxidative stress in hypothyroidism, such as hyperlipidemia, deficient or imbalanced antioxidant system and excessive TSH. Excess TSH levels can cause over-production of oxidants in body and enhanced oxidative stress parameters were found in hypothyroidism [8].

Table: Anti-thyroid effect of KLK mezhugu on Total Protein, Albumin, Cholesterol and TGL.

Group	Dose	Total protein g/dl	Albumin mg/g	Cholesterol mg/dl	TGL mg/dl
Normal	Saline	5.76±0.341	7.89±0.47	48.27±7.87	57.1±4.33
Control Methimazole treated	40mg/kg	6.00±0.396	6.66±0.49	68.96±3.37	67.8±5.42
KLK mezhugu	100mg/kg	6.36±0.400	7.89±0.51	62.06±5.39	39.2±1.80

Each values is the Mean ± SEM of three animals statistically significant from control

Levels of cholesterol and triglycerides will be elevated [9] the impact of subclinical hypothyroidism on lipid parameters is less well-defined. After the 30 days of the treatment with KLK mezhugu against the methimazole the cholesterol and triglycerides shows the normal level.

Thyroid hormones are associated with the oxidative and anti-oxidative status of the organism. Depression of metabolism due to hypothyroidism has been reported to decrease oxidant production and thus protects tissues against oxidant damage. The biological oxidative effects of free radicals on lipids, proteins, and DNA are controlled by a spectrum of antioxidants.

A complex relationship exists between the thyroid gland and the liver in both health and disease. The thyroid status depends not only on thyroxine secretion but also on normal thyroid hormone metabolism. Normal thyroid function, which is essential for normal growth, development and regulation of energy metabolism within cells, is dependent on a normal functioning thyroid and liver axis. After the treatment of *KLK mezhugu* against the methimazole induced hypothyroidism after 30 days it shows significant activity in the level of transaminase and phosphatase.

KLK mezhugu has hypo thyroid protective activity against the methimazole induced thyrotoxic rats. Further studies, are needed to identify the chemical constituents of the herbo mineral drug KLK *mezhugu* that may be responsible for the Thyroid protective activity.

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