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EFFICACY OF *KANAGALINGA KARPOORATI MEZHUGU* IN EXPERIMENTAL HYPOTHYROID DISORDER

V. Elango* and Jeyavenkatesh J

Department of Siddha Medicine, Tamil University, Thanjavur, Tamil Nadu, South India

ABSTRACT

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 [1] .The thyroid gland secretes 3 hormones- thyroxin (T4), triiodothyronine (T3) and calcitonin. *Kanaga linga karpoorathi mezhugu* is a herbomineral 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 rheumatisam, Abdominal s wellin, Chronic and severe vatha disorders,, Bronchial asthma, Nenjadaippudan Marpil Kuthu ,Kuthirai Valippu Type of epilepsy. The drug is used in clinical studies for the treatment of thyroid disorders especially hypothyroidism. 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.

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****Corresponding author***
Dr. V. Elango
Department of Siddha Medicine, Tamil University, Thanjavur, Tamil Nadu, South India

INTRODUCTION

Siddha system of medicine has developed a rich and unique treasure of drug knowledge in which use of various types of herbs, metals, minerals and animal products is very much advocated. Apart from the vast herbal sources some idea about the depth of knowledge the system possesses in the field of mineral. There are 25 varieties of water-soluble inorganic compounds called Uppu. These are different types of alkalies and salts. There are 64 varieties of mineral drugs that do not dissolve in water but emit, vapors when put in fire. Thirty-two of these are natural and remaining are artificial. The system has a classification of metals and alloys, which melts on heating and solidifies on cooling. These include gold, silver, copper, tin, lead and iron. These are incinerated by special processes and are used in medicine. There is a group of drugs that exhibit sublimation on heating and includes mercury and its different forms like red

sulfide of mercury, mercuric chloride and red oxide of mercury etc. Sulphur, which is insoluble in water, finds a crucial place in Siddha materia medica along with mercury for usage in therapeutics and in maintenance of good health. In addition there are drugs obtained from animal sources like milk and milk products, conch and coral etc. In the present study was to investigate the therapeutic efficacy of herbo-mineral drug as KLKM in experimental hypothyroidism.

The word 'Mezhugu' is indicative of soft, semisolid greasy substance, similar to wax. In Tamil language, mezhugu is known as waxy substance which is not sticky when tocuching or pressing. The word 'Kanaka' in Kanakalinga karpura mezhugu denotes 'Gold color' (Sparkling yellow) obtained as an end product after purification and grinding.

This preparations, dosage forms and adjuvants of Mezhugu mentioned in many Siddha classics like Bogar 7000, Bogar saptha kandam, Korakkar Chandra Regai, Urvasi rasa vatha sitka, Anuboga vaithiya navaneetham, Tamil Siddha dictionary by T.V Sampasivam Pillai. Many of these Mezhugu preparations are herbo-mineral origin and they are indicated not only for eradicating diseases and in casualties but also for prevention. This group of drugs is considered very essential since they enter into many alchemical preparations. Many of these mezhugu preparations are added to other simple adjuvants or medicaments like honey, palm jiggery, milk, ghee or manapagu, legium or churanam. Mezhugu is usally a higher order medicine looks like a semi solid greasy substance resourced from herbo mineral origin. A systemic sequential preparation methodology is essential while preparing mezhugu starting from selection, identification, purification and grinding (araippu) or in triturating with particular adjuvants like honey or ghee, results a change in colour of the finished product.

Mezhugu as per Classical texts

Mezhugu is a familiar internal Siddha medicine prepared by grinding or crushing the purified dry powders with ghee, jaggery or honey or oil. The ingredients in mezhugu are herbo mineral in nature and grinded till the greasy consistency occurs.

Kanaga linga karpoorathi mezhugu is a herbomineral 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 rheumatisam, Abdominal s wellin, Chronic and severe vatha disorders,, Bronchial asthma, Nenjadaippudan Marpil Kuthu ,Kuthirai Valippu 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 [1] .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 [2]. Other factors associated with an increased risk of thyroid disease include female sex, increasing age, and iodine deficiency [3,4].

MATERIALS AND METHODS

Animals and Treatment

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 at the dose of 10mg //100 gbww* in water suspension and the drug followed by it.

Collection of Blood Samples

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.

Biochemical Studies

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 colorimeteic kit method [5]. Lipid peroxide content was assayed by thio-barbituric acid method, catalase estimated colorimetrically.

Transaminases activities were estimated by Reitman and Frankel method and which was measured spectrometrically [6]. The acid phosphotases was estimated and the absorbance was read at 405nm. Mean values standard were calculated for all the values carried out [7].

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). [8]. 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 crude powder of *KLK Mezhugu* for 30 days was found able to treat and protect thyroid necrosis against methimazole induced thyroid-toxicity.

Table 1: Anti-hypo thyroid effect of *KLK Mezhugu* on T_3, T_4, TSH

Group	Doses	T3 (ng/ml)	T4 (µg/dl)	TSH (µU/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 Treated	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. [9] (Refer table :1).

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 [10].

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 [11].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 [12].

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.

CONCLUSION

The crude powder of *KLK Mezhugu* has hypo thyroid protective activity against the methimazole induced thyrotoxic rats. Further studies, are needed to identify the chemical constituents of the plant *KLK Mezhugu* that may be responsible for the Thyroid protective activity.

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