

The Effect of Alcoholic Extract of *Physalis alkekengi* on Serum Concentration of Thyroid Hormones in Rats

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Article information	Abstract
<p>Article history: Received: 23 Apr 2011 Accepted: 11 May 2011 Available online: 13 Feb 2012</p> <p>Keywords: <i>Physalis alkekengi</i> Rat Thyroid Stimulating Hormone Pituitary Gland Hyperthyroidism</p> <p>*Corresponding author at: Department of Physiology, Azad University of Arsanjan, Arsanjan, Iran. E-mail: zareiali47@yahoo.com</p>	<p>Background: There are different factors which are effective on maintaining homeostasis, especially by pituitary-thyroid axis hormones. The objective of this study was to examine the effect of <i>Physalis alkekengi</i> plant extract belonging to Solanaceae family on the concentration of the pituitary-thyroid axis hormones.</p> <p>Materials and Methods: This study was conducted on five groups (n=10) of male Wistar rats (with mean weight 210 ± 5g). The control group did not receive any substances, while the reference group received 0.2 ml normal saline daily and the experimental groups received maximum (0.4 g/kg), moderate (0.2 g/kg), and minimum (0.1 g/kg) intraperitoneal (IP) doses of the alcoholic extract for 14 days. At the end of this period, blood samples were drawn and the results were analyzed by SPSS-11.5 software.</p> <p>Results: The results of statistical analysis showed significant increases in plasma concentrations of thyroxin (T4) and triiodothyronine (T3) in the maximum dose group ($p < 0.05$) with no significant changes in plasma concentrations of thyroid-stimulating hormone (TSH).</p> <p>Conclusion: Increases in T3 and T4 levels with no changes in TSH concentration indicate hyperthyroidism euthyroidism in which the levels of thyroid hormones increase while the amount of TSH remains constant. These changes could be due to plasma proteins increase including albumin, which are probably induced by physaline and alkaloids existing in <i>Physalis alkekengi</i>. So, these drug doses do not seem to bring about pathological changes in the pituitary-thyroid axis.</p>

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Introduction

Maintaining body homeostasis is a key factor in human health controlled by various factors and in particular pituitary-thyroid axis, namely, hypothyroidism and hyperthyroidism impose high expenses on the patient as well as health impairments many of which cannot be recovered [1].

Cells and in particular plant cells produce two types of compounds: basic metabolites directly involved in growth and metabolism, and secondary metabolites gained from the basic metabolites.

The most important secondary metabolites include alkaloids, phenolic, essential oils, steroids, and Medicinal plants are highly enriched regarding secondary metabolites. These compounds have deep physiological effects on mammals and have been taken for ages, and even now plant-essence medicines are widely used in modern medicine [2-9].

So far, medicinal plants have been utilized in medicine and treatment of diseases and a whole-scale approach has

recently been established concerning the use of medicines with a natural essence, especially medicinal plants, among people. The plant *Physalis alkekengi* or groundcherry strawberry, called alkekengi in Arabic, is a plant from *Solanum tuberosum* family growing in Europe and Asia. Its fruit is diuretic and laxative and its leaves are nutrient and blood refining, and salve of the leaves is used as skin moisturizer [10].

It belongs to Solanaceae family. Alkaloids and glucocorticoids are among the effective substances in the plants of this family. *Physalis alkekengi* plant fruit also contains lycopene, alkaloids, alcoholic substances, and great amounts of vitamin C. The fruit has ascorbic acid, citric acid, and carbohydrate and the amount of vitamin C in the fruit is more than in lemon (twice times).

Physalis alkekengi plant fruit is prescribed to be taken orally and as diuretic and to treat kidney stones and jaundice. Most of the plants of this family including *Physalis alkekengi* reduce cholesterol level which is not

only for niacin (strong antioxidant) but also for phytonutrients (phenolic compounds, caffeic acid and chlorogenic acid) [10-12].

Thyroid secretes T3 and T4 hormones to regulate body metabolism. So, working on thyroid is of great significance. Among the key factors to control thyroid hormones synthesis and secretion is through regulatory effect of pituitary-hypothalamus hormone axis. Thyroid-Stimulating Hormone (TSH), released from the paraventricular nucleus of hypothalamus, affects anterior pituitary gland and results in TSH secretion [1, 13-15]. T3 and T4 hormones are also secreted cause of TSH [16, 17].

By stimulating the process of transcribing an infinite number of gens, thyroid hormones intensify the production of great amounts of enzymes, structural and carrier proteins, and enhance basic metabolism [18, 19].

Alkaloid compounds stimulate the dose-dependent production of dopamine and serotonin neurotransmitters [12-20]. Thyroid hormones synthesis and secretion control factor is enacted through regulatory effect of pituitary-hypothalamus axis. Tirotopina stimulating hormone released by hypothalamus affects anterior section of pituitary gland and induces the secretion of TSH [21-23]. Thyroid hormones thyroxin and triiodothyronine are also secreted under the effect of THS released by adeno-pituitary gland [17-24].

By stimulating the process of transcribing an infinite number of gens, thyroid hormones intensify the production of great amounts of enzymes, structural and carrier proteins, and enhance basic metabolism [25, 26]. Since *Physalis alkekengi* is widely used, the effect of the plant in several endocrine studies (including spermatogenesis, ovogenesis, blood cholesterol frequencies, liver function, plasma, and also enzymes activity) has been considered [2-9].

However, there have been no studies carried out regarding the effect of *Physalis alkekengi* plant fruit on pituitary-thyroid axis hormonal function so far, so this study is aimed at examining the effect of different *Physalis alkekengi* fruit alcoholic extract doses on plasma levels of pituitary-thyroid axis hormones.



Figure 1. *Physalis alkekengi*

Materials and Methods

In this empirical study, 50 heads of male rats were prepared from the place of animals' propagation and

breeding, Shiraz University of Medical Sciences, and kept under standard temperature and light. Present study was carried out in complying with all ethical codes of working with laboratory animals formulated by the Department of Health Care and Medicine Education.

Before the study, all animals were weighted so that they all were in the same weight range. Mean weight of male rats used in the study was 210 ± 5 g. Total number of the rats was 50 heads first divided randomly into 5 groups of ten.

Control Group 1: did not receive any type of solvent or medicine during the test. *Control Group 2*: received 0.2 ml distilled water a day. *Experimental Group 1, 2 and 3*: respectively received 0.1, 0.2, and 0.4g/kg a day *Physalis alkekengi* fruit alcoholic extract [2, 4]. Standard extracting techniques were used in preparing *Physalis alkekengi* fruit alcoholic extract [2-9].

After providing the plant from the mountains of Alborz zone and around Siahbisheh town and Pol-e Zanguleh in summer and cleaning it, the fruit was ground into powder 500g of which was poured in a closed glass container to which 500ml medical alcohol was added and the mixture was placed on the mixer for 72h so that the effective herbal substances were extracted, then the mixture was filtered with 6000 rmp, centrifuged for 10min, and placed in hot water bath so that its alcohol completely evaporated.

Upon alcohol evaporation, it was in fluid form cause of the water existing in the extract, so it was placed at 40°C near calcium chloride for complete evaporation of the water (Fig. 1). Nevertheless, the extract was not completely dried and powdered for it contained carotenoid and oil compounds, and always had a jelly estate. The extract weight was 15% comparing to dried fruit [3, 5, and 13]. Mean measurements of thyroid hormones and TSH concentration in different groups were statistically analyzed using ANOVA method and Tukey test. Statistical intensity used here was considered F-test and significant ($p < 0.05$).

Results

Regarding T₃ plasma, experimental group receiving *Physalis alkekengi* alcoholic extract (0.4 g/kg) showed a significant increase ($p < 0.05$) comparing to control group, however, the groups receiving the extract doses 0.1, and 0.2g/kg did not show a significant difference comparing to the control group (Table 1).

Regarding T₄, experimental group 3 (receiving *Physalis alkekengi* alcoholic extract (0.4 g/kg)) showed a significant increase ($p < 0.05$) comparing to control group, however, the groups receiving the extract doses 0.1, and 0.2g/kg did not show a significant difference comparing to the control group (Table 1). Regarding the amount of TSH of serum, there was no significance differences observed in any of the receiving groups (Table 1).

Table 1. The comparison between effects of different doses of *Physalis alkekengi* on T_3 , T_4 and TSH concentration in Rats

Parameters Group	T_3 (pg/ml) Concentration Mean \pm SD	T_4 (ng/dl) Concentration Mean \pm SD	TSH (μ IU/ml) Concentration Mean \pm SD
Control	0.76 \pm 0.02	6.9 \pm 0.09	3.75 \pm 0.06
Sham	0.78 \pm 0.04	6.83 \pm 0.09	3.55 \pm 0.07
Experimental group (1) (0.1g/kg)	0.96 \pm 0.04	7.08 \pm 0.03	3.43 \pm 0.08
Experimental (2)(0.2g/kg)	1.02 \pm 0.01	8.88 \pm 0.2	3.85 \pm 0.05
Experimental (3) (0.4g/kg)	1.19 \pm 0.02 *	10.45 \pm 0.08 *	3.48 \pm 0.03

Data presented as mean \pm SEM, * $p < 0.05$ for comparison of each group with control group.

Discussion

Containing alkaloid compounds such as Physalin, *Physalis alkekengi* plant fruit has many medicinal effects including the quality of regulating endocrinal activities [3]. Among the *Physalis alkekengi* plant compounds, Zeaxanthin ester and beta-cryptoxanthin ester can be indicated [27]. An alkaloid known as Physalin T was extracted from a variety of this plant. According to the studies, it is demonstrated that intraperitoneal prescription of the plant fruit aquatic extract in female rats results in longer pro-estrous cycle and Glucose 6-phosphat Dehydrogenase enzyme activity increase in their uteri [18].

Results of the study demonstrated that *Physalis alkekengi* plant fruit extract (0.4 g/kg) has a positive effect on thyroid hormones. Since TSH secretion is stimulated by TRH of paraventricular nucleus of hypothalamus, studies show that some neurotransmitters and neuromediators control the neurons secreting TRH hormone in hypothalamus. Some of these neurotransmetrical structures such as catecholamine (epinephrine, norepinephrine, serotonin, and dopamine) have an increasing role, and some such as 1-interlocine and Gama Amino Butyric Acid (GABA) have a decreasing role [28].

Serotonin increase results in TRH secretion decrease and consequently TSH levels in plasma and, as a corollary, T_3 and T_4 will decrease. Other studies have shown that dopamine results in TSH plasma levels whether as free form or as connected to plasma proteins both by reducing TRH secretion at hypothalamus level and directly preventing from TSH secretion at pituitary level [29, 30]. Dopamine also prevents the anterior pituitary gland from TSH secretion through D2 receptors. It also reduces TSH secretion by stimulating somatostatin secretion as well as T_3 and T_4 plasma levels [31].

Unfortunately, the effect of *Physalis alkekengi* plant extract on catecholamine concentration has not been studied so far. However, studies show that steroid hormones activate some catecholamine systems in central nervous system, yet in the empirical study of *Physalis alkekengi* plant extract effect on estrous cycle and fertility of lab mice and Glucose 6-phosphat Dehydrogenase enzyme activity as well as pituitary-hypothalamus lysil arylamidase, it was determined that the plant contains strong antisteroid compounds. Here, also it is likely that antisteroid compounds existing in the plant extract induce thyroid hormones increase by inhibiting catecholamine

systems in brain, nevertheless further studies are required for determinate conclusion regarding the effect of the plant extract on neurotransmitters concentration [24, 27].

According to the studies, intraperitoneal prescription of *Physalis alkekengi* plant fruit extract induces plasma proteins and albumin increase and also blood cholesterol decrease. Probably, one of the blood cholesterol reduction factors is the increase of the thyroid hormones [2, 3]. As observed in this study, thyroid hormone increase is also probable. Plasma proteins increase leads to plasma thyroid hormones increase because these hormones are carried in blood by plasma proteins including albumin-specific albumin [9].

Some studies demonstrate that the plant fruit have anti-cancer effects in lab mice, and it was showed that the main substance with the effect is citric acid. Some people from different zones of Iran believe that the plant fruit has antifertility effects and according to the studies the plant fruit induces progesterone reduction and consequently lower fertility capability. The fruit decreases the number of fetuses in female rats in serial studies carried out [26].

Results of this study (*Physalis alkekengi* fruit extract effect on pituitary-thyroid axis) suggest that further studies are required on the subject, because T_3 and T_4 levels increase without changes in TSH level indicates hyperthyroidism euthyroidism in which thyroid hormones level increases whereas TSH remains stable. The changes can be emanated from plasma proteins increase including albumin stemmed from the effect of teratogenic compounds of physalin and alkaloids existing in the plant on liver [3,5,29,30]. In sum - despite the thyroid hormones increase - since no tangible TSH level changes are observed, it is unlikely that this medicine (in the given doses) induces pathologic changes in hypothalamus-pituitary-thyroid axis. Presence of glucocorticosteroid compounds in many Solanaceae family species is showed. These compounds decrease the amount of proteins in most tissues and increase plasma concentration of amino acids and also liver and plasma proteins at the same time. On the other hand, teratogenic compounds of physalin and alkaloids existing in the plant extract induce liver cells impairments and finally plasma protein (including albumin) level increase [3, 29,30]. Based on the previous studies, steroid compounds lead to thyroid hormones transferring protein decrease in the serum. So, regarding plasma proteins level increase and the antisteroidal properties of the extract, the increase of thyroid hormones

are justifiable [30]. When thyroid hormones level exceeds the normal level, they prevent from synthesis and secretion of TSH with a negative feedback effect on hypothalamus and pituitary gland [9]. According to the results of the study on thyroid hormones increase, TSH significant invariance seems normal. Results of the previous studies show that *Physalis alkekengi* plant ethanol extract mainly contains glycosidic steroid which is probably of antiestrogenic (antisteroidic) compounds reducing the activities of the enzymes infused by estrogen in several estrogen's target tissues such as uterus, liver, pituitary gland, and hypothalamus [5-9].

Studies demonstrate that estradiol has a dual effect on TSH secretion and thyroid gland activity [32]. Ovarian hormones have both stimulating and inhibitory effects on TSH secretion by pituitary gland. Physiological level of estradiol increases TSH secretion and its secretion is inhibited in the absence of estrogen [16].

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