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*Full Length Research Article*

# The effect of green tea catechins as novel antithyroid compounds in hyperthyroid rabbits induced by levothyroxine sodium

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**Abstract**

**This study was undertaken to extract catechins from green tea leaves. It is to show the curative effect of green tea catechins after a short term daily oral administration for 8 days (200 mg/kg b.w) on serum level of thyroid hormones and thyroid-stimulating hormone in hyperthyroid rabbits induced by levothyroxine sodium (L-T4). Rabbits were divided into 4 groups, 6 rabbits in each group. Group 1 animals received only 3 ml normal saline orally as control group , group 2 was treated with (L-T4) 0.3 mg/kg b .w as hyperthyroidic. The 3rd group hyperthyroidic rabbits were post -treated with green tea catechins extract (200 mg/k g b.w) while the 4th group hyperthyroidic rabbits were post-treated with carbimazole (5 mg / kg b.w). The results indicated high significantly increased (p< 0.001) in serum level of total triiodothyronine (TT3), total thyroxine (TT4) and high significantly stimulating hormone in hyperthyroid rabbits.**

**Key words:** Catechins, Hyperthyroidism, Green Tea

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## INTRODUCTION

Excess secretion of thyroid hormones (hyperthyroidism) is often considered as a causative factor for some of the common health problems such as diabetes mellitus and heart disease, although several scientific studies have been made considering plant extracts in relation to different health problems (Panda and Kar 2003). In the present research, the extract of green tea catechins and its relation to the regulation of thyroid function was studied. Tea is one of the most widely consumed beverages in the world today, second only to water (Yee and Koo 2000). The tea plant, *camellia sinensis* is a member of the Theaceae family.

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Green tea is produced from it leaves by unfermented leaves which would allow fermentation, then dried while, the leaves of black tea is fully fermented (Van *et al*., 1998). It contains a wide assortment of bioactive constituents most of which contain two groups alkaloids and polyphenols. Examples of alkaloids found in tea include caffeine, theobromine and theophylline (Tyler *et al*., 1988). The polyphenols found in tea are classified as catechins which are considered to be bioflavonoids (Balentine *et al*., 1997). The hepatoprotective and other health effects of green tea are believed to be chiefly dependent on the polyphenols content (Miyagawa *et al*., 1997).

## METHODS

### Plant materials

The Chinese green tea was used; the leaves of the green tea were grounded into powder with the help of an electric grinder.

### Preparation of green tea catechins extract

A (20gm) of dried leaves powder was extracted in (500ml) methanol (80%) in water with 3% hydrochloric acid. The sample was refluxed with solvent for 1 h, then filtered. The filtrate was extracted with an equal volume of chloroform to remove caffeine and pigments. The alcoholic layer was extracted with an equal volume of ethylacetate treated with 2% of hydrochloric acid and the ethylacetate layer was concentrated by rotary evaporator at 45˚C and dried at room temperature (John *et al*., 2006). The resultant extract (3gm) was brown and a dry material, the percentage was 15% w/w.

### Experimental Animals

Adult male domestic rabbits weighing (1000-1500) gm were used and housed in individual cages and fed with bran, alfalfa and tap water. The animals were randomly divided into 4 groups, six in each. Each rabbit in the control group was given 3ml of normal saline orally by gastric tube. The second, third and fourth group were treated with a dose of levothyroxine sodium (L-T4) (0.3mg/kg) initially for 12 days to render them hyperthyroidic.

While the second group continued to receive levothyroxine sodium only as hyperthyroidism group, the third group animals were treated with green tea catechins extract (200 mg/kg) and the fourth group of animals were treated with an oral dose of carbimazole (5 mg/kg) along with L- T4 for the last 8 days before termination. Blood samples were taken from the heart of overnight fasted animals after twenty days and serum samples were stored in polyethylene eppendorff tubes at -20ºC until analysis (Panda and Kar 2003).

### Estimation of Total Thyroid Hormones and Thyroid Stimulating Hormone

Total triiodothyronine (TT3), total thyroxine (TT4) and thyroid Stimulating Hormone (TSH) were measured with radioimmunoassay (RIA) kits.

### Statistical Analysis

The results of the present study were analyzed by univarate analysis of variance. The data were expressed as mean±standard deviation (mean±SD). Least significant different test (LSD) was used to test the difference between means (groups) by using statistical program for social science SPSS, $p<0.05$ was considered significant.

## RESULTS

The results indicated high significantly increased ($p< 0.001$) in serum level of triiodothyronine (TT3) and total thyroxine (TT4). Results also indicated high significant decrease ($p< 0.001$) in (TSH) after treatment with L-T4 as compared with control group. The reverse results were observed after treatment with green tea catechins extract and carbimazole as shown in Tables 1, 2 and 3.

## DISCUSSION

The results of the present study shows that the administration of levothyroxine sodium (L-T4) increased the serum total T3 (TT3) and total T4(TT4) levels as compared with control group [ The reference range of total T3 (0.8-1.8ng/ml and total T4 (6.4-8.3 µg/dl) (Jones 1975)] the increase in thyroid hormones level may be due to L-T4 absorbed well by gut, thus increasing level of thyroxine (T4) in circulation, which is then converted into triiodothyronine (T3) by iodothyronine deiodinases (Duntas 2006). The same observation was found in other studies Panda and Kar (2003) and Soukup et al., (2001) observed a high concentration of thyroid hormones after treatment with L-T4. (Kossler *et al*., 1987) induced hyperthyroidism state in rat by thyroxine sodium as well.

**Table 1**. Effect of green tea catechins extract and carbimazole for 8 days on serum level of TT3 in L-T4 induced hyperthyroid rabbits

| Treatments Periods (day) | N | TT3(ng/ml) | | | | | |
|---|---|---|---|---|---|---|---|
| | | Control | Hyperthyroidism | L-T4+Green tea catechins extract | | L-T4+Carbimazole | |
| | | Normal Saline | L-T4 | L-T4 | L-T4+Green tea catechins extract | L-T4 | L-T4+Carbimazole |
| 12 | 6 | 0.83±0.24 | 2.93±0.14 | 2.95±0.14 | - | 3.02±0.06 | - |
| 8 | 6 | 0.82±0.08 | 3.75±0.21***↑ | - | 1.33±0.31***↓ | - | 2.67±0.31***↓ |
| P value | | - | p<0.001 | | p<0.001 | | p<0.001 |

N=number of animals, Mean±SD

**Table 2.** Effect of green tea catechins extract and carbimazole for 8 days on serum level of TT4 in L-T4 induced hyperthyroid rabbits

| Treatments Periods (day) | N | TT3(ng/ml) | | | | | |
|---|---|---|---|---|---|---|---|
| | | Control | Hyperthyroidism | L-T4+Green tea catechins extract | | L-T4+Carbimazole | |
| | | Normal Saline | L-T4 | L-T4 | L-T4+Green tea catechins extract | L-T4 | L-T4+Carbimazole |
| 12 | 6 | 4.76±0.68 | 15.33±3.55 | 17.33±2.94 | - | 16.33±2.42 | - |
| 8 | 6 | 4.85±0.67 | 20.76±0.80***↑ | - | 6.44±0.48***↓ | - | 9.34±0.16***↓ |
| P value | | - | p<0.001 | | p<0.001 | | p<0.001 |

**Table 3**. Effect of green tea catechins extract and carbimazole for 8 days on serum level of TSH in L-T4 induced hyperthyroid rabbits

| Treatments Periods (day) | N | TT3(ng/ml) | | | | | |
|---|---|---|---|---|---|---|---|
| | | Control | Hyperthyroidism | L-T4+Green tea catechins extract | | L-T4+Carbimazole | |
| | | Normal Saline | L-T4 | L-T4 | L-T4+Green tea catechins extract | L-T4 | L-T4+Carbimazole |
| 12 | 6 | 0.42±0.02 | 0.22±0.03 | 0.21±0.02 | - | 0.21±0.02 | - |
| 8 | 6 | 0.46±0.02 | 0.20± 0.02*** ↓ | - | 0.30±0.03***↑ | - | 0.28± 0.03***↑ |
| P value | | - | p<0.001 | | p<0.001 | | p<0.0 1 |

Thyroid–stimulating hormone (TSH) considered the most important regulator of thyroid function, rapidly increases the rates of release and synthesis of thyroid hormones (Schell-Frederick and Dumont 1970). It is secreted from the anterior pituitary gland, thus rising levels of T3 and T4 reduce the secretion of TSH negative feedback mechanism as observed in our data that high significance decreased in serum level of Thyroid–stimulating hormone after treatment with thyroxine sodium and remained within the reference range [0.2-4.2 µIU/ml] (Farling 2000). Anderson *et al*., (2002) and Toft (2001) observed an increase in hyperthyroidism serum thyroid hormones with low serum Thyroid–stimulating hormone levels. Also, Christ-Crain *et al*., (2004) referred that the treatment with L-T4 decreased TSH level. However, when 200 mg/kg of green tea catechins extract was administered with L-T4, it reversed the concentration as evidenced by a marked decrease in the level of both the thyroid hormones, indicating the antithyroidic nature of the extract.

This decrease in thyroid hormones level may be due to inhibit thyroid peroxidase. Divi and Doerge (1996) found that dietary flavonoids were potent inhibitors of thyroid peroxidase. It may be due to inhibite reactive oxygen species which result in hyperthyroidism because hyperthyroidism is a hypermetabolic state accompanied with an increase in the total consumption of oxygen which again results in an increased formation of reactive oxygen species (Karbownik and Lewinsk 2003). It may also be due to inhibite 5'-iodothyronine deiodinase activity, Ferreira *et al*., (2002) found that deiodinase activity was significantly inhibited by flavonoids, because

antioxidant activity of catechins may affect the peripheral conversion of thyroid hormones by way of deiodination (Cabrera *et al*., 2006; chaurasia and Kar 1997).

Synthesis of thyroid hormone requires iodination of tyrosyl residues. This iodination is catalyzed by thyroid peroxidase and the conversion of T4 to T3 occurs via deiodinase so that thyroid–stimulating hormone level is increased as compared with hyperthyroidism group to stimulate thyroid cells and to secretion thyroid hormone (Hassi *et al*., 2001; Sakamoto et al., 2001).

Flavonoids have antithyroid effect and dietary administration of the green tea extract catechins induce goiters in normal rats. Antithyroid drugs are effective in controlling hyperthyroidism because they inhibit thyroid hormone production (Mclyer et al., 1996). In this study, carbimazole was used as an antithyroid drug because of its few side effects (Brennan and Jones 2005).

High significance decreased in serum level of total T3 and total T4 after treatment with carbimazole beclause the carbimazole inhibit the oxidation of iodide to iodine by competing with iodide as a substrate for peroxidase and interferes with the iodination of tyrosine and the coupling of iodotyrosines (Davies 1972). Therefore thyroid-stimulating hormone level increased as compared with hyperthyroidism group. As observed, carbimazole was used by other researchers for the same purpose (Wilson et al., 1996).

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