PROTECTIVE EFFECT OF CURCUMIN AND QUERCETIN ON THYROID FUNCTION IN SODIUM FLUORIDE INTOXICATED RATS

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SUMMARY: This study was conducted to evaluate the protective potential of the polyphenols curcumin and quercetin on thyroid function in sodium fluoride intoxicated rats. Seventy eight-week-old male Wistar rats receiving a standard diet and regular drinking water were divided into seven groups of 10 each. Group I served as the untreated control. Groups II, III, IV, and V were treated intraperitoneally for 7 days, respectively, with 10 or 20 mg/kg body weight of curcumin or quercetin, followed by 600 mg/L of sodium fluoride in their drinking water for 7 days. Group VI rats were administered 10 mg/kg body weight of vitamin C intraperitoneally for 7 days followed by 600 mg NaF/L in their drinking water for 7 days as a comparison group. Group VII rats were treated only with the same concentration of NaF in their drinking water for 7 days as a further control. After fatal anesthesia with ketamine and xylazine, blood samples were collected by retro-orbital puncture, and the serum levels of thyroxine and triiodothyronine were measured by radioimmunoassay. Pretreatment especially with the higher dosages of curcumin and quercetin, and also vitamin C prior to fluoride exposure effectively kept the serum thyroid hormone levels near the normal range.

Keywords: Curcumin; Fluoride-intoxicated rats; Oxidative stress; Quercetin; Thyroid function; Thyroid hormones; Vitamin C.

INTRODUCTION

The central nervous system in mammals may be disturbed by thyroid gland dysfunction,[1-3] increased corticosteroid hormone,[4] poor nutrition,[5] exposure to X-rays,[6] and various chemicals, including fluoride (F).[7,8] Chronic F toxicity, mainly in the form of dental and skeletal fluorosis from F in water and food, is a global public health problem. Although at one time the function and structure of the thyroid gland were believed to be essentially unaffected by 1 ppm F in drinking water,[9] thyroid dysfunction is now known to occur even with relatively low levels of F intake.[10] Decreased blood serum thyroxine (tetraiodothyronine, T4) and triiodothyronine (T3) have been associated with diminished thyroid function.[11] Thus Yu found a decreased level of T4 in serum and an increased thyroid-stimulating hormone (TSH) in residents of a fluorosis endemic area where the iodine level in urine (162.7±48.7 µg/24 hr) suggested a sufficient iodine intake.[12]

Thyroid hormones are vital for optimal postnatal maturation in animals, especially for the central and peripheral nervous systems[1,2,13-15] and the skeleton.[16-18] Maturation in the cerebellar cortex of the rat is markedly influenced by thyroid hormone levels. Hypothyroidism and anemia have be shown to occur not only with antithyroid drugs but also with F intoxication.[19] To help prevent F intoxication, many non-enzymatic antioxidants possess protective effects against

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toxicity induced by F. Non-enzymatic antioxidants, such as quercetin and curcumin (Figure 1), can also act to overcome the oxidative damages by being part of antioxidant mechanisms.

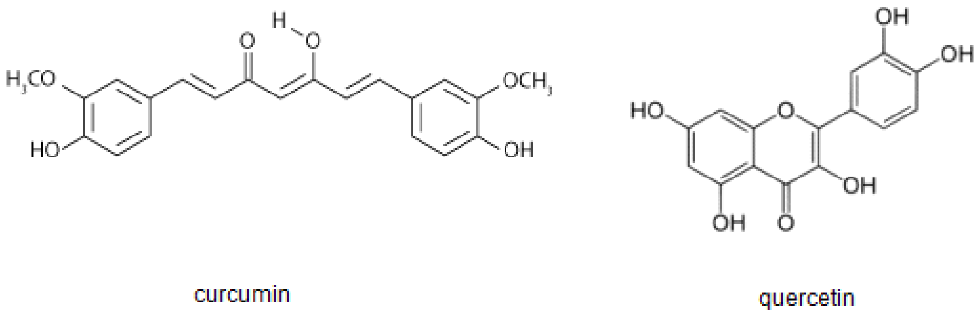

Figure 1. Chemical structures of curcumin and quercetin.

Studies have found that polyphenolic compounds like quercetin and curcumin can reduce or prevent oxidative damage caused by toxicants and oxidative materials.[20,21] Hence the aim of the present study was to evaluate possible protective effects of quercetin and curcumin against oxidative stress induced by F on thyroid function in rats.

MATERIALS AND METHODS

Animals: Our study was performed on 8-week-old male Wistar rats (*Rattus norvegicus albinus*) weighing 220–250 g, housed in ventilated animal rooms at 24 ± 2°C with a 12-hr light/dark cycle and 60 ± 5% humidity. The rats were fed a standard laboratory animal feed manufactured by Pasture Institute, Tehran, Iran. Milipore deionized drinking water was provided *ad libitum*. Experiments were performed between 10:00 and 14:00. All experiments were performed following the norms of the ethical committee of the University of Mazandaran, Babolsar, which are in accordance with the national guidelines for animal care and use.

Treatments: The rats were randomly divided into seven groups of 10 animals each. Group I was kept as a normal control receiving 0.5 mL of isotonic saline intraperitoneally (ip) for 7 consecutive days, and rats in groups II and III, and IV and V were administered quercetin and curcumin (10 and 20 mg/kg body weight) ip for 7 days followed by exposure to NaF (600 ppm = 271 ppm F ion) in their drinking water for next 7 days. Rats in group VI as a positive control were given vitamin C (10 mg/kg body weight) ip for 7 days followed by 600 ppm NaF in their drinking water for the next 7 days. At the same time, rats in group VII as a further control were treated with 600 ppm NaF in their drinking water. After the last application, the rats were fatally anesthetized with ketamine (60 mg/kg) and xylazine (5 mg/kg) administered intramuscularly. Blood samples were collected by retro-orbital puncture in plain plastic tubes.[22]

Estimation of thyroxine and triiodothyronine: Serum total thyroxine (T4) and triiodothyronine (T3) levels were estimated by radioimmunoassay using a commercially available Cis-Bio RIA Kit. All assays were performed in triplicate.

Statistical analysis: Results are presented as means ± S.D. Differences between group means were estimated using a one-way analysis of variance followed by Duncan's multiple range tests. Results were considered statistically significant when $p < 0.05$.

RESULTS AND DISCUSSION

As seen in Figures 2 and 3, the effects of 600 ppm NaF (271 ppm F ion) in the drinking water of the rats for one week significantly decreased the serum levels of the thyroid hormones thyroxine (T4) and triiodothyronine (T3) to 0.95 ± 0.076 μg/mL and 88 ± 1.64 ng/dL, respectively.

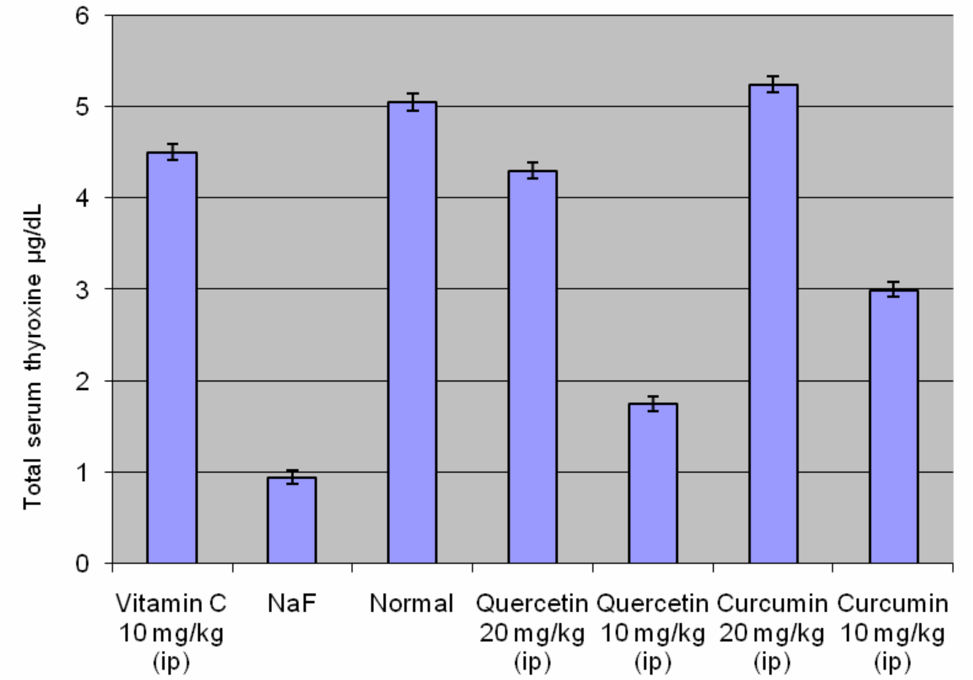

Figure 2. Effect of polyphenolic compounds on serum total thyroxine levels in sodium fluoride intoxicated rats. There are no significance differences between the curcumin 20 vs. the saline (normal) group ($p > 0.05$). However, there are significant differences between the saline, curcumin 10, quercetin 20, quercetin 10, and vitamin C groups vs. the NaF group ($p < 0.001$).

However, after a one-week pretreatment ip with the 20 mg/kg bw dosages of curcumin and quercetin, and also with 10 mg ip vitamin C/kg bw, the serum T4 and T3 levels remained close to normal after exposure to 600 ppm NaF in the drinking water for one week. Pretreatment ip for one week with 20 mg curcumin/kg bw actually increased the serum total T4 level to 5.25 ± 0.089 μg/mL, which was significantly higher ($p < 0.05$) than in the normal control level and highly significantly ($p < 0.001$) greater than in the NaF control. Similarly, one-week pretreatment with 20 mg quercetin/kg bw and 10 mg vitamin C/kg bw increased the serum T3 triiodothyronine level more than in the normal group, but not significantly so ($p > 0.05$). Lesser but definite effects were seen with the pretreatment 10 mg/kg bw dosages.

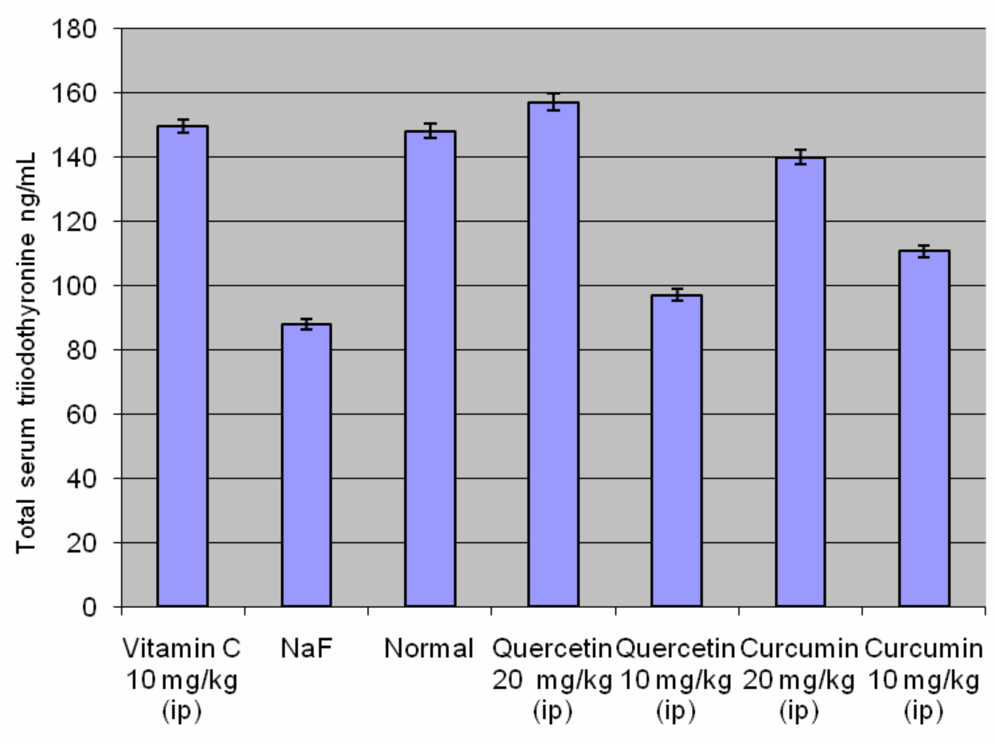

Figure 3. Effect of polyphenolic compounds on serum total triiodothyronine levels in sodium fluoride intoxicated rats. There are no significance differences between the curcumin 20, quercetin 20, and vitamin C groups vs. the saline (normal) group ($p > 0.05$). However, there are significant differences between the NaF, curcumin 10, and quercetin 10 groups vs. the saline group ($p < 0.001$).

During aerobic metabolism, along with exposure to various environmental agents including radiation and redox cycling substances,[23,24] free radicals such as superoxide anion, hydrogen peroxide and hydroxyl radical are generated *in vivo* due to sequential reduction of oxygen. In diseases like diabetes, and cardiovascular and neurodegenerative disorders, free radicals have been shown to play important role as mediators or in the progress of the disease.[25,26] Oxidative stress occurs when production of free radicals exceeds the body's natural antioxidant defense systems and damages deoxyribonucleic acid, proteins, and lipids.[22,27-29] Antioxidant defense systems activate free radical scavengers to protect the body against oxidative injury. Various studies report that F intoxication through drinking water can cause thyroid dysfunction.[30-32] Results from the present work indicate that pretreatment with curcumin and quercetin or with supplemental vitamin C provides protective effects against NaF-induced thyroid dysfunction in young adult male rats.

In conclusion, this study has demonstrated that the two polyphenolic compounds, curcumin and quercetin, exert impressive protection against thyroid dysfunction in rats induced by F in their drinking water. By implication, these results indicate that these polyphenolic compounds might have therapeutic value in human clinical studies. In any event, further studies are clearly desirable.

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