Possible Stimulatory Effect of Quercetin on Secretion of Selected Pituitary Hormones

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Abstract
Quercetin is found in various types of foods such as apples, red onions, grapes, berries, citrus fruits, cherries, broccoli, tea etc. It is characterized by antioxidative, anti-carcinogenic, bacteriostatic and anti-inflammatory effects on the animal organism. The aim of our study was to examine its effect on endocrine system of the rabbit *in vivo*. Twenty healthy adult female rabbits were divided into four groups (control group and three experimental groups). Various concentrations of quercetin (10, 100 and 1000 µg/kg body weight) were intramuscularly administrated to rabbits in experimental groups during 30 days. A sensitive, biochemical method, ELISA was used to determine the concentrations of selected hormones (follicle-stimulating hormone - FSH, luteinizing hormone – LH, prolactin – PRL) after 30 days of administration. Non-significant differences between groups were found after application of different quercetin concentrations. Stimulatory effect was observed on FSH secretion by higher dose of quercetin. Similarly, LH and PRL increased at concentration 100 µg/kg and 1000 µg/kg. Our results indicate the possible effect of quercetin on secretion of selected pituitary hormones.

Keywords: quercetin, hormone, FSH, LH, PRL

1. Introduction

Quercetin is found in various types of foods such as apples, red onions, grapes, berries, citrus fruits, cherries, broccoli, tea, etc. [1]. It is also present in medicinal plants - *Ginkgo biloba*, *Hypericum perforatum* a *Sambucus canadensis* [2, 3]. Two of its most abundant resources are onions and shallots, while its content in different parts is diverse [4]. Average quercetin income, which has been reported ranges from 6 to 31 mg per day [5].
Quercetin can develop beneficial effects on health. This includes protection against various diseases such as osteoporosis, some types of cancer, lung and cardiovascular diseases, but also anti-aging effect. It belongs to the health-promoting substances, especially due to its ability to absorb highly reactive species such as peroxynitrite and hydroxyl radical. Thus, numerous studies have been performed to collect scientific evidence for these claims, as well as information of the exact mechanism of action and potential toxicological aspects of flavonoids [6].
The ability to suppress the proliferation of a wide variety of cancers and to inhibit glycolysis, macromolecular synthesis and enzymatic activity belongs to many biological activities of quercetin [7]. It also owns an antibacterial activity against Bacillus cereus, *Salmonella enteriditis*, *monocytogenesa Listeria*, *Pseudomonas putida* [8].

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In vivo studies suggest quercetin may act against neurodegeneration with a focus on cognitive effects, ischemia, traumatic injury [9].

Follicle stimulating hormone (FSH) and luteinizing hormone (LH) are secreted by basophil cells of anterior pituitary gland and play an important role in the production of gonadal hormones and regulation the reproduction process [10]. Coordinated secretion and activity of FSH and LH is essential for regulation of ovarian and testicular function. Prolactin (PRL) is a polypeptide produced by the anterior pituitary. Its main effect is to stimulate breast-feeding after birth. During pregnancy, prolactin prepares the mammary gland for lactation together with other hormones - estrogen, progesterone, cortisol and insulin [11].

The aim of our study was to investigate the effect of quercetin on the endocrine system of rabbit *in vivo*. We focused on the assessment of endocrine profile in plasma of female rabbits focusing on follicle stimulating hormone (FSH), luteinizing hormone (LH) and prolactin (PRL).

2. Materials and methods

Animals

Twenty healthy adult female rabbits (body weight 4.0 ± 0.2 kg) were divided into four groups (control group and three experimental groups – E1, E2 and E3). Various concentrations of quercetin (E1 – 10 µg/kg, E2 – 10 µg/kg and E3 – 1000 µg/kg body weight) were intramuscularly administrated to rabbits in experimental groups during 30 days (3 times a week). A sensitive, biochemical method, ELISA was used to determine the concentrations of selected hormones (follicle-stimulating hormone - FSH, luteinizing hormone – LH, prolactin – PRL) after 30 days of administration.

Blood sample collection

Blood samples from *vena auricularis* were taken to EDTA-treated tubes from all animals after 30 days of experiment. Blood plasma was obtained from whole blood by centrifugation at 3000 rpm for 10 min. at 20 °C. The clear supernatant (plasma) was then separated from the pellet and kept frozen until analysis.

ELISA (Enzyme linked immunosorbent assay)

Quantification of hormones after quercetin administration was performed using ELISA method. ELISA assays (Dialab, Wiener Neudorf, Austria) were performed according to the manufacturer's instructions and the color intensity was inversely proportional to the concentration of hormones in the sample.

Statistical Analysis

The significance of differences between the control and experimental groups was evaluated by One-Way ANOVA (Dunnett´s multiple comparison test) using the statistical software GraphPad Prism 3.01 (GraphPad Software Inc., San Diego, CA, USA). Differences were compared for statistical significance at the level $P \leq 0.05$.

3. Results and discussion

Very wide range of biological effects of quercetin was confirmed in many of reported results [12]. This flavonoid can provide an antibacterial, antiviral, anti-inflammatory, analgesic, antiallergic, hepatoprotective, cytostatic, apoptotic, estrogenic and antiestrogenic properties [12, 13]. It reduces tissue damage by oxidation [14]. Flavonoids in the human diet may reduce the risk of various cancers, particularly breast and prostate (those affected by hormones) and may also be the prevention of menopausal symptoms [13].

In our work, we examined the possible impact of quercetin on hormonal profile of female rabbits.

Application of quercetin indicated increased secretion of FSH (Figure 1) between the control and experimental groups, suggesting a possible effect on folliculogenesis.

A similar non-significant increasing tendency of secretion was recorded in LH (Figure 2), however, the highest concentration of LH occured in E2 group (100 µg/kg of quercetin).

We have not observed significant differences in the secretion of prolactin (Figure 3) between the control and the experimental groups.

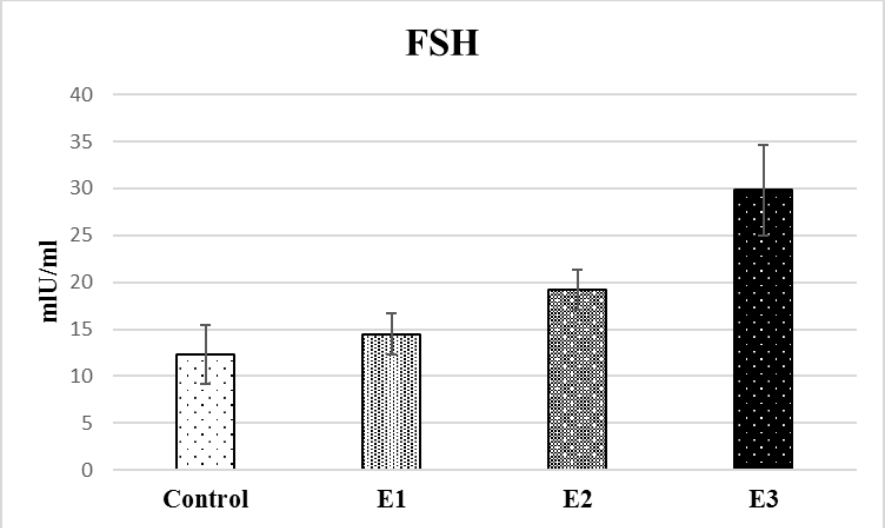

Figure 1. Blood plasma levels of FSH (mean ± SD). The level of significance was set at *$P < 0.05$.

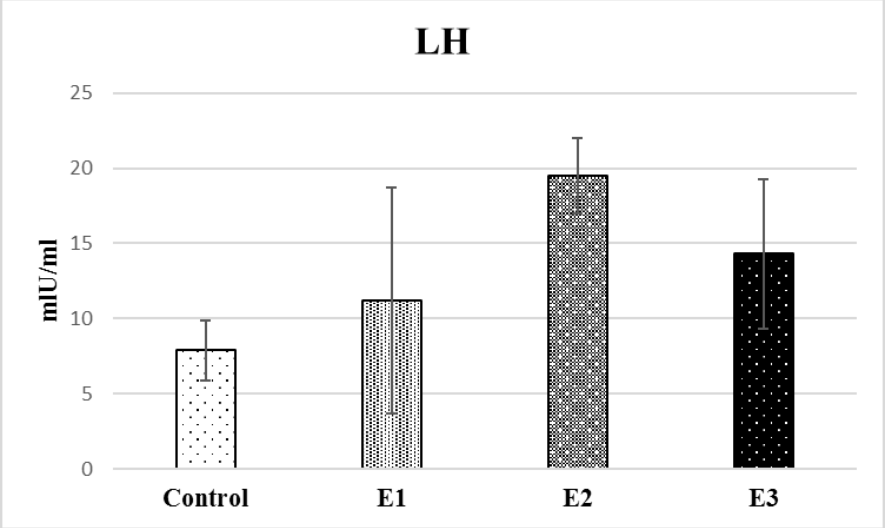

Figure 2. Blood plasma levels of LH (mean ± SD). The level of significance was set at *$P < 0.05$.

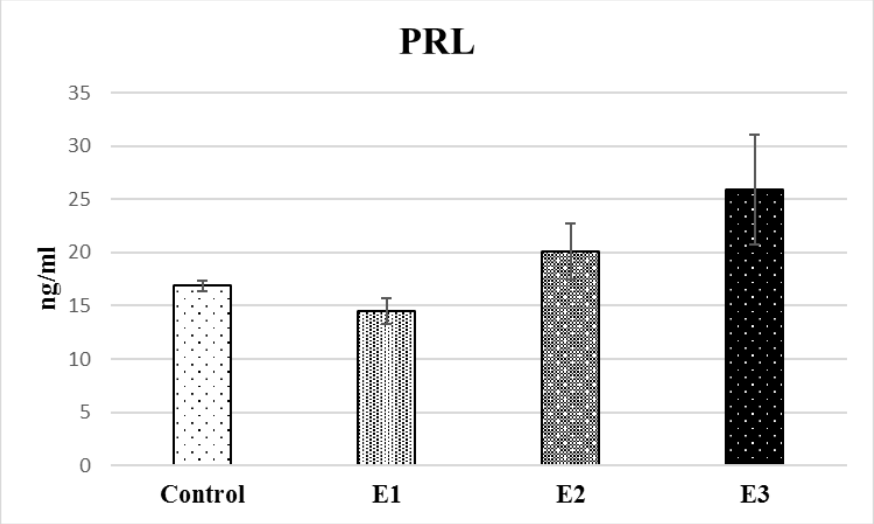

Figure 3. Blood plasma levels of PRL (mean ± SD). The level of significance was set at *$P < 0.05$.

Khaki et al. [15] administered onion juice to animals to test the effects of flavonoids on the parameters of spermatozoa, serum levels of FSH, LH and testosterone concentrations. As a result, the concentration of LH was significantly increased ($P<0.05$) in the groups which were fed by fresh onion juice. In the experimental and control groups in FSH hormone, there was no difference. Chen et al. [16] investigated the effects of phytoestrogens genistein, resveratrol and quercetin on steroidogenesis and cell proliferation in mice. They observed reduced secretion of progesterone caused by genistein and resveratrol administration. On the contrary, quercetin increased the secretion of progesterone.

Davis et al. [17] indicate that quercetin can inhibit the membrane receptors (Ca^{2+}-ATPase) of thyroid hormones - low levels of quercetin stimulated and high concentrations inhibited the receptor activity. We can suppose quercetin may affect other hormones of the endocrine system of animals, thus the anterior pituitary hormones.

4. Conclusions

After application of different concentrations of quercetin, we have observed no statistically significant differences of hormones between groups. However, increasing concentrations of the administered compound stimulated the secretion of FSH as well as LH and PRL at 100 μg/kg and 1000 μg/kg respectively.

The results suggest a possible effect of quercetin on the secretion of pituitary hormones. However, further investigation in a larger number of animals is needed.

Acknowledgements

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