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Alterations in Serum Oestrogen and Progesterone Levels in Prolonged Administration of Garlic (*Allium Sativum*) Ingestion to Female Wistar Rats

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ABSTRACT

With reported advances in the Hypocholesterolaemic, anticoagulative, antihypertensive, hepatoprotective, anti-tumour and hypoglycemic properties of *Allium Sativum* (Garlic), reports on the effect(s) of chronic garlic ingestion on serum oestrogen and progesterone levels of female wistar rat remain scanty. Current study investigated the changes in serum oestrogen and progesterone levels due to prolonged administration of Garlic to female wistar rats. Twenty (20) adult female Wistar rats of the albino variant (of between 160 - 230g) were procured and acclimatized for two weeks, following which they were divided into 4 groups of 5 rats each. While Group 1 received standard rat diet and water *ad libitum*, Groups 2, 3 and 4 served as the experimental groups; and were respectively fed with varied garlic doses of 250, 500 and 750 (mg/kg body weight). Following period of administration, blood samples were obtained from each rat and serum assayed by biochemical means (using the enzyme linked immunosorbent assay - ELISA) for changes in oestrogen and progesterone levels. Upon analysis, Using the one way analysis of variance (ANOVA), Study found a statistically insignificant ($p < 0.05$) effect of garlic (*Allium sativum*) on oestrogen and progesterone levels after 6 weeks period of chronic administration of garlic to animals irrespective of the dose administered. In conclusion, garlic has no significant duration or dose dependent effect on serum oestrogen and progesterone changes.

Keywords: Garlic, Oestrogen, Progesterone

INTRODUCTION

With speculative health benefits of garlic consumption for over a century, many different cultures have recently recognized the potential use of garlic in the prevention and treatment of different diseases. Recent studies support the effects of garlic and its extracts in a wide range of applications, with several of such implicating it to possess cholesterol reduction, anticoagulative, antihypertensive, hepatoprotective, anti-tumour and hypoglycemic effects [1&2].

Even though Garlic is known to reduce serum cholesterol in both male and female subjects [3&4], However, cholesterol is needed in the biosynthesis of sex hormones, including the female sex hormones; oestrogen and progesterone.

Garlic products such as diallyl trisulfide have been reported to have spermicidal effects [5]. Ebomoyi and Ahumibe, (2010) reported that garlic consumption can significantly reduce serum testosterone level, a direct effect on the common pathway of oestrogen synthesis. Based on their study, garlic can inhibit steroidogenesis (steroid production) in two ways: (a) interference in the transfer of free cholesterol to mitochondria of Leydig cells, which is

an important step in steroidogenesis, and (b) disrupting the conversion of cholesterol to testosterone by affecting the activity of key regulatory enzymes in steroidogenesis. Also, green garlic can damage Leydig cells, which are responsible for secretion of testosterone and estrogen [6&7].

While garlic extract is known to lower blood cholesterol levels (in both humans and animals) and inhibits cholesterol biosynthesis [8], the production of testosterone is not related to cholesterol metabolism [9], rather, it is dependent on the modulation of steroidogenic enzymes. For example, the conversion of cholesterol to biologically active testosterone is a multistep enzyme process (including enzymes that control the transfer of cholesterol from outer to inner mitochondrial membranes) [8]. Apparently, garlic extract stimulates the secretion of gonadotropins and ovarian hormones through activation of pituitary gland, promotion of exit from the Golgi cells, cell cycle, and increased ability of binding to oestrogen receptors [10]. This might be one reason for the observed increase in progesterone level. After administration of garlic extracts to albino wistar rat within a 12 weeks period, [7] observed a significant fall in rat blood glucose levels at the end of 3-6 or 9-12th weeks of study which was consistent with earlier reports that oral administration of garlic extract significantly decreased blood glucose levels [11].

Garlic may have insulin-like properties [4] and therefore directly reduce blood glucose levels by stimulating glycogenesis and inhibiting gluconeogenesis and glycogenolysis in hepatic and muscle cells; it may increase beta cells in the pancreas by activating regeneration of these cells [5], or the fibre of the plant may also interfere with carbohydrate absorption, thereby affecting blood glucose [8]. The body weights of rats in both the control and the experimental groups increased at the end of the 12th week of study compared to the controls. This shows that garlic administration did not affect body weight in the rats. Since garlic reduces serum cholesterol and showed the same effect on serum testosterone, therefore, there is need to further explore its effects on serum oestrogen and progesterone levels in order to give an insight for further research on its mechanism of action.

Aim of Study

Current study was undertaken to investigate the effects of prolonged garlic administration on serum oestrogen and progesterone levels, using wistar rats as experimental model. Specifically, study determined the possible effects of prolonged garlic feeding (duration effect) on oestrogen and progesterone levels. Study also investigated the interplay between serum oestrogen progesterone and blood cholesterol levels due to chronic garlic administration to Wistar rats.

Materials and Method

Study Design:

Rats were divided into 4 groups of 5 each; Groups 1, 5 served as control group, and Groups 2, 3 and 4; served as the experimental groups with varied garlic (*Allium sativum*) doses. Food and water was given to the animals *ad libitum* during the acclimatization period (2 weeks) and throughout the 6 weeks of the experiment. Prior to the study, the rats were weighed, and then they were administered with garlic (250, 500 and 750 mg/kg body weight) every morning at 10.00 am for a period of 6weeks using an orogastric tube [12]. At the end of 6 weeks, the animals were weighed again after which they were sacrificed. The rats' serum oestrogen and progesterone were then analysed at the end of the experimental period. Blood (5 ml) was collected from the abdominal aorta of the rats and serum oestrogen and progesterone were analysed using Elisa [13].

Resources and Sources:

Local cultivar of garlic (*Allium sativum*) was purchased from the local market and authenticated by expert botanist (Dr. H. A. Akinnibosun) at the Department of Plant Biology and Biotechnology, University of Benin where a sample was deposited at the herbarium of that department. The garlic sample was then hand-peeled and sun-dried for 6 hours and then refrigerated for future use. Twenty adult female Wistar albino rats (weighing 160 - 230g) obtained from the Animal House of the Faculty of Pharmacy, University of Benin, were used for the study. The rats were housed in plastic cages in the animal house of the Faculty of Pharmacy, University of Benin, and allowed to acclimatize for a period of two weeks prior to the study.

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Preparation of Plant Sample and Extraction of Bioactive Components

Dried garlic cloves (600g) were crushed with mortar and pestle and then weighed. The crushed garlic was exposed to air for 10 - 15 min so that there will be conversion of alliin to allicin (active substance in garlic) by the enzyme allinase. The crushed garlic was then mixed with 600ml distilled water and left for 24 h to macerate [14]. Resultant mixture was then filtered, while obtained extract was used for serum oestrogen and progesterone experiment [6&7].

Dosage Calculation

Stock solution: one (1) gram of garlic extract in 10mls of water, which is 10g of garlic extract in 100mls of water. The dose for individual rat per body weight was calculated as follows;

dose x weight/1000 = (x) mg

1ml =100mg of garlic extract.

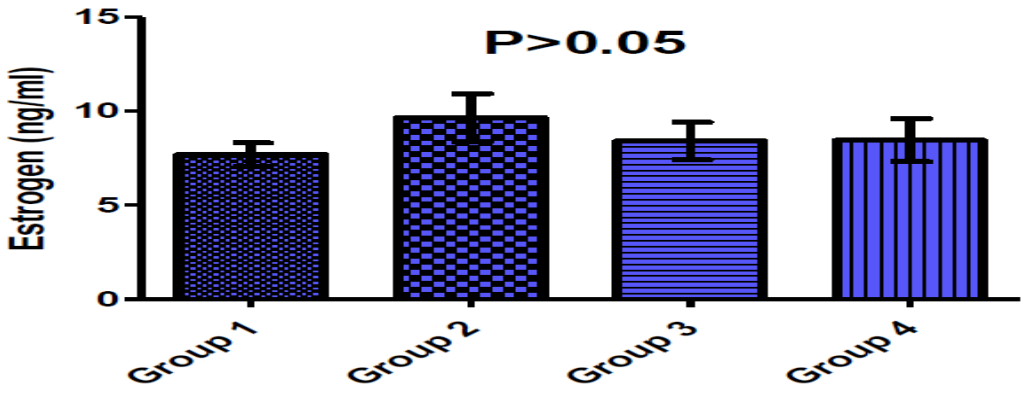
Therefore, 100mg/ml = (x) ml.

Analytical Approach

All results were presented as Means ± SEM. Statistical analyses were carried out using Graph pad prism 5.0. Analysis of variance (ANOVA) was used to compare the differences between the groups. p-value < 0.05 was considered significant.

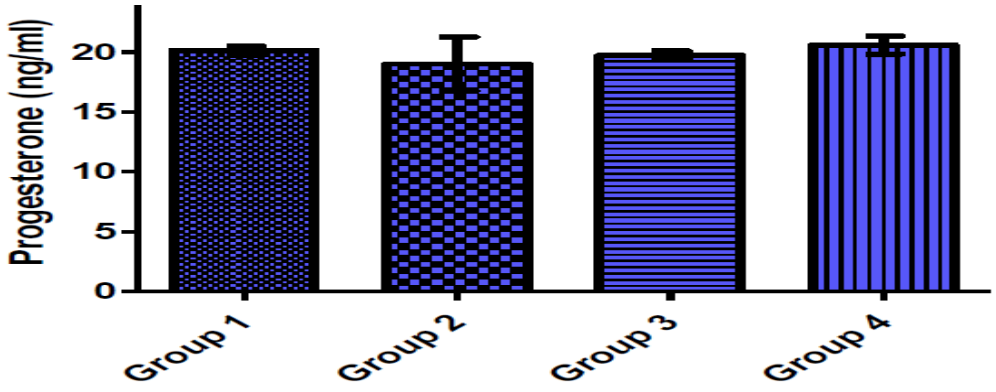
Results

Figure I: Serum Oestrogen level of female rats treated with garlic at different doses



As shown from above figure, there was an insignificant change in serum oestrogen level in the treated groups compared with the control (p < 0.05). Although there was a slight increase observed in group 2, it was however not significant.

Figure II: Serum Progesterone level of female rats treated with garlic at different doses



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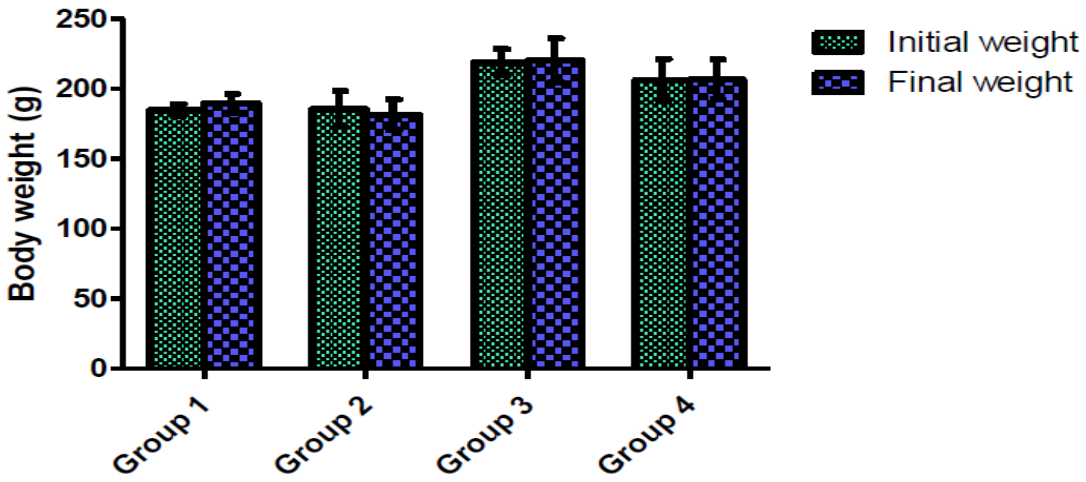
As shown in Figure II (above), there was also no significant change in serum progesterone level in the treated groups compared with the control ($p < 0.05$). There was a slight decrease observed in group 2, which returned back to the control level in group 3 and then slightly increased again in group 4. These changes were however not statistically significant.

Figure III: initial and final body weight of female rats treated with garlic at different doses.



From the above figure, there was no significant change between the initial and the final body weight in the treated and the control groups ($p < 0.05$). Groups 3 and 4, showed a slight increase although not significant. The observed increase in Groups 3 and 4 was due to normal growth of the rats.

Discussion

Current study focused on examining the effect(s) of chronic garlic ingestion on the female hormones, oestrogen and progesterone, the question here is, does garlic have the same effect on these cholesterol-linked hormones as it does on blood cholesterol level? Although garlic is a cholesterol reducing agent even in female [15&16] garlic has no significant effect on the female reproductive hormones oestrogen and progesterone.

As reported by Ebomoyi and Ahumibe (2010), garlic consumption can significantly reduce serum testosterone level. This was reported to perhaps be due to a direct effect on the common pathway of oestrogen synthesis. It was reported that garlic can inhibit the manufacture of steroids in two ways: (a) interference in the transfer of free cholesterol to mitochondria of Leydig cells, which is an important step in steroidogenesis, and (b) disrupting the conversion of cholesterol to testosterone by affecting the activity of key regulatory enzymes in steroidogenesis. Also, green garlic can damage Leydig cells, which are responsible for secretion of testosterone and oestrogen [6-10]. Although the testosterone lowering effect of garlic appears to be well established, it doesn't seem to have any effect on oestrogen.

While garlic extract is known as a lowering factor in blood cholesterol levels (in both human and animal) and inhibits cholesterol biosynthesis [17], the production of testosterone is not related to cholesterol metabolism [18], rather, it is dependent on the modulation of steroidogenic enzymes. For example, the conversion of cholesterol to biologically active testosterone is a multistep enzyme process (including enzymes that control the transfer of cholesterol from outer to inner mitochondrial membranes) [19]. This may also be the case with the effect of garlic on oestrogen and perhaps progesterone.

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It is possible that garlic exerts its effect by reducing the sensitivity of oestrogen to its receptor as reported by Kyung-Ho *et al* (2016) [20]. In their research titled "Differential pro-apoptotic effect of allicin in oestrogen receptor-positive or -negative human breast cancer cells. They reported that allicin is known to induce apoptosis and inhibit tumorigenesis in various carcinoma cells. However, the precise mechanism of allicin-induced apoptosis remains unclear in human breast cancer cells.

They reported that ERα−MDA-MB-231 cells were more sensitive to allicin-induced apoptosis as compared with ERα+MCF7 cells. They also reported that allicin induced reactive oxygens species (ROS)-mediated and caspase-dependent apoptosis in MDA-MB-231 cells, but not in MCF7 cells. Collectively, their findings suggest that allicin induces differential apoptotic pathways through MAPK activated by ROS-dependent or -independent signalling pathway in breast cancer cells. On progesterone, garlic also showed no significant effect, and this confirms the report of Behnaz (2013) [21] that garlic extract have fewer effects on female reproductive system.

Conclusion

This study shows no significant effect of *Allium sativum* on oestrogen and progesterone following a 6week chronic period of ingestion ($p < 0.05$) irrespective of the different garlic doses. Nutritional status is a major factor controlling fertility in humans. Poor nutrition results in delayed puberty, aberrant oestrous cycles, lowered conception rates, reduced birth weight and ovarian follicular growth. Endocrine and metabolic signals that regulate follicular growth are also expected to influence oocyte development either through changes in hormones/growth factor concentrations in follicular fluid or via granulose-oocyte interactions [22&23].

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