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Original Article

A Comparative Study Between Effects of Some Antioxidants on Levels of Hormones in Male Rabbits

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ABSTRACT

Backgrounds: *A. Muricata* is a genus of tropical fruit trees belonging to the family Annonaceae, that contains chemical compounds exhibiting antitumor, pesticidal, antiviral and antimicrobial effects, thus signifying several potentially beneficial applications. Ginger such as zingerone, gingerdiol, zingibrene, gingerol and shogaols have shown antioxidant activities. Panax ginseng is one of the most widely used medicinal plants for the treatment of various diseases. This study was aimed to compare the effects of these antioxidants on levels of some hormones in male rabbits. **Methods**: Animals were assigned to one of four treatment groups: control group, 100 mg A. muricata, 100 mg ginger or 100 mg ginseng/kg BW. Testosterone, estradiol and progesterone hormone concentrations were assayed by using commercial kit. **Results**: Overall, the three plants show similar effect on different measured parameters. Results obtained showed that treatment with A. muricata, ginger or ginseng caused significant ($P<0.05$) increase body weight, relative testes weight, testosterone, progesterone, estradiol, T_3 and T_4 in serum of blood compared to control. A. muricata and ginseng were more effective than ginger. **Conclusion.** Treatment of rabbit with A. muricata, ginger or ginseng has ameliorative effects on the fertility, hormonal status and may have curiously applications in regenerative.

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INTRODUCTION

Common cancer prevention agents have been proposed to have advantageous impacts on wellbeing and on distinctive malady states, such as neurodegenerative and cardiovascular infections, diabetes and cancer [1]. The utilize of normal plant antioxidant items to handle distinctive infections has exceptionally old roots; well, sometime recently the improvement of present-day pharmaceutical with manufactured drugs and cancer prevention agents. A part of the organic exercises of characteristic cancer prevention agents have been credited to their capacity to rummage responsive oxygen species (ROS) that neutralize oxidative stretch. Within the final a long time, a huge number of thinks about have recommended that their classical hydrogen-donating antioxidant movement is improbable to be the sole clarification for their impacts [2]. To begin with of all, characteristic cancer prevention agents are subjected to abroad digestion system *in vivo* that alters their redox possibilities. Besides, the concentration of common cancer prevention agents and their

metabolites in vivo are lower than that ordinarily utilized in vitro. Collecting prove recommends that the cellular impacts of characteristic cancer prevention agents may too be interceded by their intuitive with particular proteins central to intracellular signaling cascades, their balance of the expression and movement of key proteins, their affecting of epigenetic instruments or their balance of the intestine microbiota [3-6].

A. muricata L., commonly known as soursop, graviola, guanabana, paw-paw and sirsak, may be a part of the Annonaceae family comprising roughly 130 genera and 2300 species [7]. It is local to the hottest tropical zones in South and North America and is presently broadly disseminated all through tropical and subtropical parts of the world, counting India, Malaysia and Nigeria [8]. All parcels of the *A. muricata* tree, comparative to other Annona species, counting *A. squamosa* and *A reticulata* are broadly utilized as conventional can offer assistance give fundamental supplements and components to the human body [9].

The identification of antioxidants from natural products has become a matter of great interest in recent studies for their noteworthy role in nullifying the destructive effects of ROS [10]. The antioxidant activity of the *A. muricata* leaves was found to be stronger than *A. squamosa* and *A. reticulata* species as shown through different in vitro models, such as ABTS, nitric oxide and hydroxyl radicals [11]. The seeds and leaves of the plant are reported to possess enzymatic antioxidants, including catalase and superoxide dismutase, and non-enzymatic antioxidants, including vitamin C and E [12]. Padma and colleagues appeared that the ethanolic extricate of the *A. muricata* stem bark caused a decrease in lipid peroxidation actuated by cold immobilization push within the brain and liver of rats, showing the adaptogenic potential of this plant [13,14]. The stem bark extricates (200 mg/kg) moreover appeared defensive impacts against oxidative stretch initiated by carbon tetrachloride in rats and altogether expanded the oxidant levels and serum chemical exercises to near normal [15]. These findings strongly suggest the potential use of *A. muricata* as a natural source of antioxidants.

Ginger rhizome (*Zingiber officinale R.*, family: Zingiberaceae), is used worldwide as a spice. Both antioxidative and androgenic activity of *Z. officinale* were reported in animal models. All major active ingredients of *Z. officinale*, such as Zingerone, Gingerdiol, Zingibrene, gingerols and shogaols, have antioxidant activity [16,17]. Ginger has been demonstrated to have various pharmacological activities such as antiemetic, antiulcer, anti-inflammatory, antioxidant, anti-platelet, glucose and lipid-lowering, cardiovascular and anti-cancer activities [18]. Although several pharmacological effects of ginger have been studied, the relative potencies of major standard non-volatile pungent compounds of ginger – [6]-gingerol, [8]-gingerol, [10]-gingerol and [6]-shogaol – and their molecular mechanisms in antioxidant and anti-inflammatory activities have not been reported yet [19]. Ginger too has capsaicin, curcumin and limonene as well as proteolytic chemicals. Furthermore, it is one of the leading carrier herbs and it seem offer assistance in stomach related assimilation by up to 200% [20]. Other than, other analysts appeared that ginger oil has dominative defensive impact on DNA harm actuated by H_2O_2 and might act as a forager of oxygen radical and may be utilized as an antioxidant [21]. Antioxidants protect DNA and other important molecules from oxidation and damage, and can improve sperm quality and consequently increase fertility rate in men [22], enhanced sperm healthy parameters in rats [23] and rabbits [24].

Ginseng, which may be a plant having diverse species has been well examined, particularly the *'Panax'* specie, and has been detailed to have antioxidant properties, upgrade resistant work and amalgamation of nitric oxide [25]. Traditionally, ginseng is being used as an aphrodisiac and it has been reported that *Panax* ginseng enhances nitric oxide synthesis in corpora cavernosa endothelium; and ginsenosides, a major component of ginseng,

improves acetylcholine-induced and transmural nerve stimulation-activated unwinding related with expanded tissue cyclic guanosine monophosphate [26]. A study reported that *Panax* ginseng increased serum levels of luteinizing hormone (LH) and follicle stimulating hormone (FSH) which increased spermatogenesis in the rats [27]. Rats that received 5% ginseng experienced increase in blood testosterone level with reduced prostate weight [28]. Be that as it may, whereas plant species are connected in animals' generation for purposes other than generation, the regenerative impacts of these plants on the creatures is of vital thought, particularly when breeding creatures are included and considering that numerous plants and plant items have been detailed to hinder spermatogenesis in different creature species [29]. Making strides the rabbit generation industry in Nigeria, which has been respected as emanant or simple [30]. It is conceivable that Panax ginseng may upgrade regenerative capacities of rabbit bucks as detailed in mice and rodents treated with Panax ginseng [31]. Earlier studies on *Panax* ginseng with rabbits recorded significant increases in serum levels of follicle stimulating hormone (FSH), testosterone (T), triiodothyronine (T_3), and tetraiodothyronine (T_4) of treated rabbit bucks, whereas drain abdicate was altogether diminished in rabbit does managed Panax ginseng extricates [30,32]. This study was aimed to compare between effects of three plants (*A. muricata*, Ginger and Ginseng) on levels of some hormones in male rabbits.

METHODS

A. muricata leaf (powder) (maximum international company, Brasil) was purchased from local pharmacy. Each capsule contains 0.3125 g powder and the content of each capsule was dissolved in corn oil just before use. Each capsule contains 3 g powder and the content of each capsule was dissolved in corn oil just before use. Ginger was gotten from Predominant Nourishment and Detailing by Jarrow Equations, Los Angeles, USA. Ginseng root extract (Gift from pharmaceutical company, Libya). Develop male Modern Zealand White rabbits (6 months old) and starting weight of (3.401 ± 28.24 Kg) were utilized. Animals were individually housed in cages and weighed weekly throughout 12-weeks.

The first group was used as control. While, groups 2, 3 and 4 were treated with *A. muricata*, ginger or ginseng 100 mg/kg BW respectively [33-35]. Rabbits were orally administered their respective doses for 3 months. At the end of the exploratory period, body weight of rabbits was recorded. Animals were sacrificed by decapitation and testes were immediately removed and weighed then the organs weight ratio was calculated. The relative weight of organs (%) was calculated as g/100g body weight. Serum was obtained by centrifugation of blood samples at 860×g for 20 min, and was stored at (–20°C) until used for analysis. Testosterone, estradiol and progesterone hormone concentrations were assayed by using commercial kit supplied by Coat – A – Count testosterone RIA, from Diagnostic Systems Laboratories (DSL), from Texas, USA. FSH, LH, T_4 and T_3 levels hormone concentrations were assayed by using commercial kit that was supplied by Coat - A - Count, from Los Angeles, USA.

Where applicable, statistical analysis was carried out in Minitab software (version 17). Statistical significance was assessed using ANOVA analysis with Tukey multiple comparison test after detection normal distribution to the data and appropriate $P < 0.05$ consider significant.

RESULTS

Table 1 representing body weight (BW) and relative weight of testes of male rabbits (control and treated with *A. muricata*, ginger or ginseng). The current results indicated that treatment with *A. muricata*, ginger or ginseng caused significant ($P<0.05$) increase in BW and relative weight of testes in male rabbits compared to control animals. In same table, results were found significantly increase ($p<0.05$) in testosterone and progesterone in treated groups

compared to control. However, level of estradiol was significantly decreased in ginger group.

Table 2 exhibited levels of serum T_3, T_4, SFH and LH of male rabbits treated with *A. muricata*, ginger or ginseng. Results indicated that treatment with *A. muricata* caused significant ($P<0.05$) increase in levels of T_3 and LH. Ginger was not caused significant difference in levels of four hormones. Meanwhile treatment with ginseng was caused significant increase in levels of T_3, T_4 and FSH.

Table 1. Table 1.Body weight (BW) and relative weight of tests, levels of testosterone, progesterone and estradiol of control male rabbits and rabbits treated with A. muricata, ginger or ginseng.

Parameters	Groups			
	Control	*A. muricata*	Ginger	Ginseng
BW (gm)	3.30±0.114^{b}	3.49±0.978^{ab}	3.42± 0.083^{ab}	3.53±0.206^{a}
Testes (g/100gm)	3.10±0.518^{c}	7.08±0.047^{a}	4.05±0.689^{bc}	6.11±1.00^{ab}
Testosteron (ng/ml)	1.59±0.083^{b}	2.40±0.299^{a}	2.63±0.345^{a}	2.80±0.458^{a}
Estradiol (mg/dl)	9.14±0.027^{b}	9.36±0.060^{a}	7.50±0.159^{c}	9.15±0.076^{b}
Progesteron e (g/dl)	7.68±0.087^{c}	8.21±0.220^{ab}	8.43±0.253^{a}	8.07±0.263^{b}

Values are expressed as means ± SEM; n = 5 for each treatment group. Mean values within a row not sharing a common superscript letter (a, b, c) were significantly different, p<0.05.

Table 2. Serum triiodothyronine (T_3), thyroxin (T_4), serum follicle-stimulating (FSH) and luteinizing hormone (LH) of Control male rabbits and treated rabbits with A. muricata, ginger or ginseng.

Parameters	Groups			
	Control	*A. muricata*	Ginger	Ginseng
T_3 (ng/dl)	1.71±0.07^{b}	2.04±0.229^{a}	1.81±0.0508^{b}	1.87±0.13^{ab}
T_4 (ug/dl)	1.15±0.027^{c}	1.35±0.0500^{b}	1.35±0.050^{b}	3.41±0.194^{a}
FSH (mIU/ml)	0.81±0.017^{a}	0.80±0.019^{a}	0.80±0.019^{a}	0.82±0.026^{a}
LH (mIU/ml)	0.79±0.02^{b}	0.93±0.086^{a}	0.78±0.006^{b}	0.76±0.019^{b}

Values are expressed as means ± SEM; n = 5 for each treatment group. Mean values within a row not sharing a common superscript letter (a, b, c) were significantly different, p<0.05.

DISSCUSION

The protective antioxidant mechanisms maintain the cellular oxidation-reduction potentials required for normal metabolism and to prevent free radical attack of amino acids, proteins, and the lipid components of cell membranes necessary for functional and structural integrity of cells and tissues [36].

Treatment with *A. muricata*, ginger or ginseng was caused increment in BW and relative tests weight. Treatment with *A. muricata* or ginseng was caused increment in level of testosterone and progesterone in blood serum all through the 12-week exploratory period of bucks treated comparing to control group. The increase BW observed in the present study due to treatment with ginger is agreements with [37,38]. Also, reported significant increase in body weight gain (14.4%) of broilers fed ginger [39]. They reported that increase in BW gain of the broilers fed ginger indicates the positive nutritive effects of this natural feed additive. There was significant increase testis weight could therefore be due to the increased androgen biosynthesis as evidenced by a significant increase in serum testosterone levels in the experimental rabbits. Study has shown that the level of testosterone was positively correlated with the weight of testis, epididymis, seminal vesicle and prostate glands [40]. The increase in testes weight of rabbits treated with ginger is consistent with the report of [41] who observed an increase in the testicular weight of rats treated with *Z. officinale* for 8 days with a concomitant increase in testosterone level. It is plausible that the increased weight of the testes reflects a dual effect of increased testosterone levels and sperm contained in these organs.

Ginger rhizome contains a wide assortment of both antioxidative [16] and androgenic action [41]. The major dynamic phenolic fixings disconnected from *Z. officinale* have antioxidant action [42]. Treatment with ginger caused an increase in plasma testosterone concentration. This result is in agreement with the finding of [43] who suggested that ginger administration also increased the level of testosterone. The positive effect of ginger extract on male sex

hormone was in harmony with study reported that administration of ginger for twenty days significantly increased testosterone, FSH and LH levels in rats which could be attributed to the androgenic activity of ginger that increased the α-glycosidase enzyme in epididymis, and fructose sugar in seminal vesicle [44]. Also, an increase in serum testosterone level suggests a possible androgenic property of ginger. Thyroid hormones homeostasis can be disrupted by variety of xenobiotics, this disruption was found to be associated with thyroid follicular cell hypertrophy, hyperplasia, and the development of thyroid tumors in rats. Thyroid toxicants affect circulating concentrations of thyroid hormones by either direct action on the thyroid gland or by increasing peripheral elimination of the thyroid hormones [45]. Treatment with ginger caused an increase in plasma T_3 and T_4. These results are in agreement with the finding reported that ginger has stimulating effect on thyroid gland and subsequent it is contraindicated in women with subacute thyroiditis [46].

From our result with ginseng, it caused significantly increased in all parameters (Table 1 and 2). Ginseng-specific saponins (ginsenosides) were considered as the major bioactive compounds for the metabolic activities of ginseng [47]. Ginseng roots showed up to encourage survival and neurite expansion of refined cortical neurons [48]. Ginseng has been illustrated to have a broad run of pharmacological impacts on the regenerative, cardiovascular, endocrine, and safe frame works. Its ability to diminish fatigue, enhance blood circulation, aid menopausal symptoms, boost immune function, and enhance concentration has been verified in certain countries [49]. Ginseng infusion was found to have a great impact on patients with persistent heart disappointment and administrative impact on thyroid hormones [50]. Moreover, treatment with Panax ginseng before, during or after acrylamide treatment reduced or partially antagonized increased serum serotonin, corticosterone, T_3, T_4, TSH, estradiol, progesterone and plasma adrenaline induced by acrylamide towards the normal values of controls [51]. The thyroid hormone T_3 exhibits an extensive range of physiological functions, which were related to the regulation of thermogenesis, metabolism, systemic vascular resistance, heart rate, renal sodium reabsorption and blood volume [52]. Thyroid hormones were found to control the expression of proteins included in all steps of lipid digestion system driving to the improvement of subjective and quantitative changes of lipids in thyroid illness [53]. Taken together, these results suggest that ginseng species may have direct actions on the anterior pituitary gland and/or on the hypothalamic dopaminergic mechanisms [54].

The male sex steroid, testosterone, is synthesized in the Leydig cells under the control of LH, which is produced by the anterior pituitary [55]. Testosterone levels are strongly correlated with libido and studies with Panax ginseng in rats have been reported to significantly increase blood testosterone levels. Ginsenoside Rb1 found in ginseng has been reported to increase the secretion of LH by acting directly on the anterior pituitary gland [56]. It is additionally known for its antimicrobial activities, antiparasitic, antimalarial and insecticidal activities [57.58]. From our result with *A. muricata* caused significantly increased in all parameters. Our results were in argumenta with study in rats [59, 60]. The research on *A. muricata* has identified more than 40 compounds with anti-cancerous properties, capable of killing cancer cells [61,62]. It is also known for its antimicrobial actions, antiparasitic, antimalarial and insecticidal actions [57, 58].

CONCLUSION

In conclusion, treatment of rabbit with *A. muricata*, ginger or ginseng as ameliorative effects on the fertility, hormonal status and may have curiously applications in regenerative.

Disclaimer

The article has not been previously presented or published, and is not part of a thesis project.

Conflict of Interest

There are no financial, personal, or professional conflicts of interest to declare.

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