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Research Article

DOSE DEPENDENT INHIBITORY EFFECT OF *LAGENARIA SICERARIA* FRUIT POWDER ON FSH AND LH HORMONES IN MALE WISTAR RATS

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Abstract:

Male Wistar rats were received 300, 500 and 1000 mgkg⁻¹ body weight of the LSFP for 08 weeks for estimating the dose dependent effect on FSH and LH hormones. Material and methods: male Wistar rats [190–220 g] were divided into four groups as control, low dose [300 mgkg⁻¹], medium dose [500 mgkg⁻¹] higher dose [1000 mgkg⁻¹]. Such doses of LSFP suspended in gum acacia [2%] were orally administered. 24 h after the last day dosing blood samples were withdrawn by retro orbital method for estimation of serum FSH and LH hormone level. Gonadal morphology of testis was estimated by testicular index for any changes. Control group findings were compared with higher dose treatment groups. Results: Serum FSH and LH level was significantly reduced in 1000 mgkg⁻¹ LSFP dose as compared with control group male rats, which was evidenced in testicular index morphology. Conclusion: significant decrease in serum FSH and LH level and testicular index were observed at the dose 1000 mgkg⁻¹ of LSFP, while no changes were observed at the doses 300 mgkg⁻¹ and 500 mgkg⁻¹ when compared to male control group rats. The phytochemical analysis depicted major chemical constituents as 5-alpha-reductase enzyme inhibitors [oleic acid, linoleic acid, steric acid and palmitic acid] phytosterols [β -sitosterol, campesterol, fucosterol], flavonoids, alkaloids. The observed results may due to the presence of 5-alpha-reductase enzyme inhibitors or phytosterols.

Key Words: FSH; LH; testicular index; hypothalamo-pituitary-gonadal axis; gonadotropin-releasing hormone

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INTRODUCTION:

There is perhaps no function more important in life than reproduction of the species. Reproduction in humans and animals is a natural process that more often than not proceeds without problem. To date, there is an ongoing scientific investigation on some of the reported therapeutic & medicinal properties of the plant. Indian medicinal plants have traditionally been used for enhancing sexual function including libido & fertility. Just recently, the role of the plant in improving reproductive function has been the focus of interest. This account to the fact that male infertility is one of the problems faced by 10% of couples in society & within a population; the incidence rate for male infertility is approximately 1 out of 136 individuals.

Sex hormones are known to regulate the reproductive functions and characteristics in both male and female organisms [1]. plant derived chemicals that influence endocrine activities in both humans & animals have received a great deal of attention due to their possible beneficial as well as adverse effects. Some of these plants are known to possess their effect through their action on hypothalamo-pituitary-gonadal axis. Several phytochemicals such as phytosterols (β -sitosterol), 5α -reductase enzyme inhibitors, flavonoid, alkaloids, saponins, glycosides, are known to possess stimulatory or inhibitory effects on the reproductive functions. Plants with estrogenic property can directly influence pituitary action by peripheral modulation of FSH and LH, decreasing secretion of these hormones and blocking ovulation [2,3]. Gonadotropin - Releasing Hormones (GnRH) are responsible for controlling reproductive functions in males. The hypothalamus secretes it into the pituitary gland. The pituitary gland secretes LH hormone after receiving a GnRH from the hypothalamus. LH stimulates Leydig cells of testes to produce testosterone. Testosterone helps FSH to make Sertoli cells, in the seminiferous tubules to make immature sperm to a mature sperm. GnRH activity is essential for reproductive function, and its pulsatile manner of secretion is critical to its activity. Additionally, FSH, LH, and prolactin are essential for reproductive function, and fertility is abolished in their absence. Deprived secretion of FSH and LH results in failure of gonadal function. This state is typically depicted in males as failure in production of normal sperm count. Conditions with very low FSH secretions are: loss of muscle and body hair, Kallmann syndrome (Decreased functioning of the glands that produces sex hormones), Hypothalamic suppression, Hypopituitarism, Hyperprolactinemia. The reduced serum sex hormone profile depicts suppression of reproductive functions. Thus

assessment of serum sex hormone is therefore very useful tool in evaluating the reproductive integrity in both animals and humans [1]. So the aim of present research was to determine the dose dependent effect of LSFP on serum FSH and LH level and testicular index in male Wistar rats.

MATERIALS AND METHODS:**Collection of plant material**

The fruits of *Lagenaria siceraria* (Molina) standley were collected from local market in Maharashtra, India. The plant was authenticated by Department of Botany, Rashtra Sant Tukadoji Maharaj Nagpur University, Nagpur (Voucher specimen no. 9257).

Preparation of fruit powder

The small flakes of fruit were shed dried on tray dryer and processed in pulveriser to make powder.

Selection and Description of experimental animals

Male Wistar rats [190-220 g] were used for the experiment. The rats were having free access to food and water, with a natural light-dark cycle, acclimatized for two weeks before experiments. The experimental protocol was approved by the Institutional Animal Ethics Committee [IAEC] and the laboratory animals were cared according to the guidelines of CPCSEA, Ministry of Forests and Environment, Government of India [registration number 729/02/a/ CPCSEA]. Acute toxicity study/ [LD₅₀ determination] was done as per the acute toxic class method/OECD-423 guidelines and 1/10th of LD₅₀ cut off dose [5000 mgkg⁻¹] was taken as therapeutic dose which was 500 mgkg⁻¹.

Experimentation

Male Wistar rats were grouped in four with 10 rats in each group as, Control group [vehicle only], Lower dose group [300 mgkg⁻¹ of LSFP], Medium dose group [500 mgkg⁻¹ of LSFP], Higher dose group [1000 mgkg⁻¹ of LSFP].

LD₅₀ cut off dose [5000 mgkg⁻¹] was found to be safe and 1/10th of LD₅₀ cut off dose was taken as therapeutic dose for subsequent pharmacological screening. LSFP suspended in 2% gum acacia was administered daily orally for 08 weeks, except that control group was received (vehicle) 2% gum acacia only. 24 h. after the administration of last dose animals were weighed and euthanized for collection of blood samples by retro orbital method in heparinized tubes. After 15 min, centrifuged for 20 min at 3000 rpm and serum samples were collected. Estimation of serum FSH and LH level was done at Metropolis diagnostics lab Mumbai. At autopsy testis were dissected out, adherent tissues were removed

and weighed up to the nearest 0.001 g. and estimated for gonadal morphology [3]. As Testicular index [TI] [4,5,6]. This was calculated for each rat [testis length X Testis Width/body weight]. TI reflects spermatogenesis and FSH and LH production.

RESULT AND DISCUSSION:

Serum FSH and LH levels and testicular index were significantly decreased in 1000 mgkg^{-1} of LSFP dose treated male rats compared to control group male rats. While no changes were observed at the doses 300 mgkg^{-1} and 500 mgkg^{-1} when compared to male control group rats. It might be contributed to the dysregulation of hypothalamic-pituitary-gonadal

(HPG) axis or by estrogen agonist β -sitosterol might be contributing for negative feedback mechanism [7,8]. In the male, gonadotrophin releasing hormone (GnRH) secreted from the hypothalamus stimulates secretion of luteinizing hormone (LH) and follicle stimulating hormone (FSH) from the pituitary. LH and FSH regulate testicular activity. LH stimulates leydig cells to produce testosterone. FSH acts on sertoli cells to stimulate germ cell spermatogenesis. FSH also stimulates secretion of inhibin, which together with testosterone (and oestradiol) are involved in regulating GnRH secretion from the hypothalamus.

Table 01: Effect of LSFP on serum FSH level in male rats

Gr	Treatment	Dose	FSH (mIU/ml)
I	Control	--	1.09 \pm 0.17
II	Low dose group	300 mgkg^{-1}	1.01 \pm 0.14
III	Medium dose group	500 mgkg^{-1}	0.96 \pm 0.09
IV	Higher dose group	1000 mgkg^{-1}	0.54 \pm 0.07*

The values are given as $\text{MEAN} \pm \text{SD}$ of five rats in each group. * indicates significant ($p \leq 0.05$) when control group was compared with Higher dose treatment groups. One-way ANOVA followed by Dunnett's multiple comparison tests.

Table 02: Effect of LSFP on serum LH level in male rats

Gr	Treatment	Dose	LH (mIU/ml)
I	Control	--	<0.07
II	Low dose group	300 mgkg^{-1}	<0.07
III	Medium dose group	500 mgkg^{-1}	<0.06
IV	Higher dose group	1000 mgkg^{-1}	<0.04*

The values are given as $\text{MEAN} \pm \text{SD}$ of five rats in each group. * indicates significant ($p \leq 0.05$) when control group was compared with treatment groups. One-way ANOVA followed by Dunnett's multiple comparison tests.

Table 03: Effect of LSFP on Testicular Index in male rats

Gr	Treatment	Dose	Testicular Index
I	Control	--	0.88 \pm 0.08
II	Low dose group	300 mgkg^{-1}	0.85 \pm 0.1
III	Medium dose group	500 mgkg^{-1}	0.84 \pm 0.06
IV	Higher dose group	1000 mgkg^{-1}	0.61 \pm 0.07*

The values are given as $\text{MEAN} \pm \text{SD}$ of five rats in each group. * indicates significant ($p \leq 0.05$) when control group was compared with Medium & Higher dose treatment groups. One-way ANOVA followed by Dunnett's multiple comparison tests.

CONCLUSION:

Significant reduction in serum FSH, LH hormones and testicular index at the dose 1000 $mg\ kg^{-1}$ of LSFP, while no significant changes at lower doses of LSFP when compared to male control group rats. From the phytochemical analysis ^[9], it was found that the major chemical constituent present were flavonoids, phytosterols (β -sitosterol, campesterol, fucosterol), alkaloids, 5-alpha-reductase enzyme inhibitors (linoleic acid, oleic acid, palmitic acid, and steric acid). On the basis of evidences from serum hormonal estimation and testicular index it is possible that the presence of phytosterols, 5-alpha-reductase enzyme inhibitors may be responsible for the observed results. Further pharmacological and biochemical investigation are needed to find out the other active constituent responsible for the observed results and to elucidate its exact mechanism of action.

Conflict-of-Interest

No Conflict-of-Interest

Ethical matter

The experimental protocol was approved by the Institutional Animal Ethics Committee [IAEC] and the laboratory animals were cared according to the guidelines of CPCSEA, Ministry of Forests and Environment, Government of India.

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