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Journal Name:	International Journal of Biochemistry Research & Review
Manuscript Number:	2014_IJBcRR_13433
Title of the Manuscript:	Contraceptive Effect of Ethanol Extract of <i>Dioscorea villosa</i> Tuber on Reproductive Hormones of Female Wistar Rats
Type of the Article	Original Research Article

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
<u>Compulsory</u> REVISION comments	Abstract - Lines 12-14: "The extract at all doses significantly ($p < 0.05$) decreased the levels of serum luteinizing hormone (LH). However, the extract at 200 and 400 mg/kg body weight did not significantly ($p > 0.05$) alter the concentration of LH in the serum of the animals when compared with the control": you are supposed to compare results from experimental groups (B, C and D) with those from the control group (A). So what is your control group when serum levels of LH decrease? - Lines 19-20: "The extract at all doses significantly ($p < 0.05$) increased the serum follicle stimulating hormone (FSH) concentration in the treatment groups. Administration of the extract at	The control group when serum levels of LH decreased increased. It has been compared with the control group (A). When FSH serum levels decreased, the serum levels of FSH in the groups increased.



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	100 and 200 mg/kg body weight did not significantly ($p>0.05$) alter the concentration of FSH in the serum of the animals when compared with the control”: when FSH serum levels decrease what is the control group? With which group are you comparing this result? - FSH is known to induce the proliferation and maturation of ovarian follicle cells which produce estrogens and particularly estradiol as they are growing. So how do you explain the fact that your extract decreased serum levels of estradiol but increase serum levels of FSH?	The results of the treatment groups (B, C, and D) were compared with the control group. Administration of the extract at 400 mg/kg body weight which significantly increased the serum FSH in the rats compared to the control group might have caused the slight increase in serum estrogen level which was observed at 400 mg/kg body weight, which compared favourably with the control. The decreased serum estradiol concentration at 100 and 200 mg/kg body weight might point to the fact that <i>Dioscorea villosa</i> extract will only have an effect on serum estradiol concentration when administered at a high dose (400 mg/kg body weight). Following the result/findings from the study, the extract at 400 mg/kg body weight which caused increase in serum FSH levels also caused the slight increase in serum estrogen level which was observed at 400 mg/kg body weight, which compared favourably with the control. This was only obtained with the 400 mg/kg
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	Introduction - Lines 61-71: from “It is an herbaceous twining ... chemically converted to progesterone contraceptives and cortisone [18]”: Please delete all. - Lines 84-86: “Therefore, the present study was designed to investigate the contraceptive effect of the ethanolic extract of <i>Dioscorea villosa</i> tuber on reproductive hormones of female albino rats”: this is not enough to justify your work! Is this plant traditionally used as a contraceptive? What prompted you to carry out this study?	body weight of the extract. Therefore, this is in line with your statement that “FSH is known to induce the proliferation and maturation of ovarian follicle cells which produce estrogens and particularly estradiol as they are growing”. Lines 61-71 reported the occurrence, prevalence and botanical description of the plant as it relates to its potential of being an oral contraceptive. Therefore, for these reasons of ours, the authors crave your indulgence to let it remain. Yes, the plant is traditionally used as a contraceptive. We obtained this information from our pilot/preliminary study on ethnobotanical survey. In life sciences, such claims by traditional medical practitioners are not accepted until there is scientific evidence to either substantiate or refute this purported claim. This was what prompted us to carry out this study. Findings from the study made us to conclude that the plant has a potential of being a potent oral contraceptive.
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	Material and method - 2.1.1 Plant materials and authentication: please provide the voucher number of that plant! Results - Lines 161-164: Compared with the distilled water treated control animals, the extract at all doses significantly ($p < 0.05$) decreased the concentration of luteinizing hormone (LH) in the serum of the animals (Figure 1). The extract at 200 and 400 mg/kg body weight did not significantly ($p > 0.05$) alter the concentration of LH in the serum of the animals (Figure 1): not clear!!! It is impossible to observe this in your figure. Reformulate! In that figure (figure 1) what is meaning of “a, b and c”? These letters refer to what? Correct throughout the manuscript.	Voucher specimen number of the plant has been provided. It was a mistake on our part. The 200 and 400 bars are supposed to carry superscript “a” and “a” since they did not significantly ($p > 0.05$) alter the concentration of LH in the serum of the animals. Only the extract at 100 mg/kg body weight decreased serum LH level when compared with the control which should carry superscript “b” (Figure 1). “a, b and c” was used to express the level of significance (difference) between the treatment groups and the control group.
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	- Lines 184-185: with which group are you comparing your result? You cannot say that the extract significantly increased FSH serum levels at all tested doses but the effect was not statistically significant at 100 and 200 mg/kg BW. If so, then there was no significant increase at all tested doses! Please revise such kind of statement throughout the manuscript. Discussion - Lines 230-232: your results show that the extract at 400 mg/kg BW markedly increased FSH serum concentration but did not significantly affect estradiol levels. Explain why, since FSH is supposed to stimulate ovarian follicle cell proliferation and therefore to stimulate estradiol synthesis.	The treatment groups (B, C and D) were compared with the control group. Only the extract at 400 mg/kg body weight increased the serum FSH level. The extract at 100 and 200 mg/kg body weight did not significantly alter the serum FSH levels when compared with the control. The decreased serum estradiol concentration at 100 and 200 mg/kg body weight might point to the fact that <i>Dioscorea villosa</i> extract will only have an effect on serum estradiol concentration when administered at a high dose (400 mg/kg body weight). Following the result/findings from the study, the extract at 400 mg/kg body weight which caused increase in serum FSH levels also caused the slight increase in serum estrogen level which was observed at 400 mg/kg body
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	- Lines 241-244: What do you mean by “D. villosa will only have <u>an effect</u> on serum estradiol concentration when administered at a high dose”? The decrease of the serum concentration of estradiol at 100 and 200 mg/kg BW is also an effect! - Lines 244-245: please give more information’s about this statement: “The extract increased the serum FSH levels at 400 mg/kg body weight by	weight, which compared favourably with the control. The increase in serum FSH level at 400 mg/kg body weight was only specific for the 400 mg/kg body weight which caused corresponding increase in serum estradiol level. This was only obtained with the 400 mg/kg body weight of the extract. Therefore, this is in line with your statement that “FSH is known to induce the proliferation and maturation of ovarian follicle cells which produce estrogens and particularly estradiol as they are growing”. It means that increase in serum FSH level at 400 mg/kg body weight was only specific for (have an effect on) the “high dose” of 400 mg/kg body weight which caused corresponding increase in serum estradiol level. We did not investigate the effects of <i>D. villosa</i> tuber extract on the production of GnRH or on the mRNA expression of GnRH in the hypothalamus. We were only
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	stimulating the hypothalamus to release high quantities of GnRH". Did you investigate the effects of D. villosa extract on the production of GnRH or on the mRNA expression of GnRH in the hypothalamus? You should explain why a substance that increases FSH serum concentrations and decreases LH serum concentrations may be used as an oral contraceptive. - Line 248: what do you mean by "consequential"?	attributing the increase in serum FSH level at that dose of the extract to stimulation of the hypothalamus to release high quantities of GnRH. This is in view to providing biochemical explanation on the increase in serum FSH level at the 400 mg/kg body weight of the extract. The increase in serum FSH concentration by the extract at 400 mg/kg body weight coupled with the decrease in serum LH concentration by the extract at 100 mg/kg body is taken as an "alteration" in female reproductive hormone concentration. This alteration (hormonal imbalance) "may" trigger disruption of ovulation. This may result in impairment of oestrous/menstrual cycle which would then hamper conception/pregnancy. Therefore, the substance "extract" may be employed as an oral contraceptive. The "consequential" means that the extract which caused alteration(s) in female hormonal level might have "adverse
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		effect” on the maturation and ovulation of follicles which may further impair fertility, implantation and pregnancy in female rats.
<u>Minor</u> REVISION comments	If there any ethical issue, please clarify.	The last sentence of Section 2.2.3 mentioned and explained the provisions contained in the departmental ethical committee. This ethics were adopted in the present study.
<u>Optional/General</u> comments		