

PART 1:

PART 2:

Created by: EA



SDI FINAL EVALUATION FORM 1.1

* Reviewer's comment: Your results just indicate an ovarian resistance towards gonadotropines (FSH) stimulation. Maybe the extract increased ovarian cell resistance towards FSH stimulation. This resistance may prevent ovulation. This may be the mechanism whereby the extract induces its contractive effect. And in further studies you may investigate the effects of this extract on the ovarian expression of FSH receptors.

Introduction

- Reviewer's comment: Lines 84-86: "Therefore, the present study was designed to investigate the contraceptive effect of the ethanolic extract of *Dioscorea villosa* 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?

* Authors' feedback: 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 used as a potent oral contraceptive.

*Reviewer's comment: This information is very important. The empirical use of the plant is what prompted you to carry out this study in order to bring a scientific proof to the presumable contraceptive effect of that plant. I think this should be added in the manuscript.

Discussion

- Reviewer's comment: Lines 241-244: What do you mean by "D. villosa will only have an effect 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!

* Authors' feedback: 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.

* Reviewer's comment: Then what is the pharmacological relevance of this result? Just talk about the ovarian resistance as your results in general show that the extract increases serum levels of FSH but decreases/or did not significantly affect serum levels of estradiol.

- Reviewer's comment: Lines 244-245: please give more information about this statement: "The extract increased the serum FSH levels at 400 mg/kg body weight by 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

Your comment that the extract increased ovarian cell resistance towards FSH stimulation as it affects ovulation is welcomed. This has been incorporated in the manuscript as the possible mechanism of contraceptive action of the extract. Your suggestion to investigate the effect of the extract on the ovarian expression of FSH receptors in further studies has been noted and will be worked on.

This "very important information" to bring a scientific proof to the presumable contraceptive effect of the plant has been added to the manuscript.

Like you requested, we have added the issue of "ovarian resistance" to the manuscript, since our results in general show that the extract increases serum levels of FSH but decreases/or did not significantly affect serum levels of estradiol.



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the mRNA expression of GnRH in the hypothalamus? * Authors' feedback: 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 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 a view to providing biochemical explanation on the increase in serum FSH level at the 400 mg/kg body weight of the extract. * Reviewer's comment: This is too speculative. Just delete this sentence. This will not compromise the quality of your manuscript. - Reviewer's comment: You should explain why a substance that increases FSH serum concentrations and decreases LH serum concentrations may be used as an oral contraceptive. * Author's feedback: 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. * Reviewer's comment: This should clearly appear in the manuscript either in the discussion or in the conclusion, and also in the abstract.	We have deleted the sentence. This has been clearly written in the abstract, discussion and conclusion.
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