Review Form 1.6

Journal Name:	**Journal of Pharmaceutical Research International**
Manuscript Number:	**Ms_JPRI_82272**
Title of the Manuscript:	**Role of Bisphenol A in regulation of arrival of sexual maturity and fertility in male albino 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.
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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)*
Compulsory REVISION comments	We found some unclear issues in this manuscript. Here are the comments: 1. For the abstract, please add the significancy level ($p < 0.05$ etc.) and the correlation coefficient (R^2=1 etc) for every result statements to show the significant findings of this study. 2. In the introduction part, the author has mentioned that, "*Despite, wide-range of research in early life exposure of BPA, its specific role in arrival of sexual maturity was loosely attended."* Please add and clearly explain about the "Research gap" or the difference of this study and the others. What is the urgency to conduct this study? 3. Please add the material section and completely mention the chemical reagents that are used for the step by step in this study (e.g. reagent for histopathological analysis) 4. Please complete and add the information about the origin, the sex and the number and also the replication per experimental group of animal that is used in this study. 5. In the etichal approval, please complete this statement with the number of etichal approval certificate. 6. In the methodology section, please add more information about the administration route of bisphenol A and the preparation of bisphenol A solution step. 7. In the experimental design section, the author has mentioned that, *"A parallel sham control group was used, animals of these groups were administered with vehicle only."* Please clarify about the vehicle term in this study. 8. The Parameter section can be merged with the Methodology section and Please add the citation for all method that is used in this study, especially for fertility test and histopathological analysis. 9. Please make the figure 1-3 and the figure caption are more informative (e.g. add the note in the figure caption about the meaning of significancy level (*, **, ***) and the data representation with the used statistical analyses method and also please add the error bar on the all graph. For the figure 3, please complete the axis and ordinate title of the curve. 10. In the discussion part, the author explained that "*higher doses did show higher decline in testicular weight gain comparing to control. It also emerged that higher doses of BPA (i.e. 25 and 50 mg/kg) had minimum impact on reduction in testicular weight gain when compared with low dose (i.e. 5 mg/kg). One of the possible reasons for this could be low bioavailability of BPA."* This is an intresting finding from this study. If this condition is caused by low bioavailability of BPA, the effect still be linier correlation with the dose. Although, the biovailability of BPA is lack, the higher administration means the higher concentration too in the systemic. So, please add the other possible explanation for this finding.	1. Thank you for the comment, Modifications as suggested by the reviewer was inserted in the text. 2. Thank you for the detailed review, A sentence has been inserted in text to justify the phrase. 3. Thank you. A Section 2.7.1 has been added in the text with added information. 4. Thank you, Origin, scientific name, sex, age, and housing conditions have been explained in Section 2.2 Experimental Animals. Total number of animals in each group and further division in sub-group has been clarified in the Section 2.4 Experiment Design. 5. Thank you for the comment, an ethical approval number has been added in the text Section Ethical Approval. 6. Thank you, A sentence was added in the Section 2.4 Experimental Design clarifying preparation of BPA solution and mode of administration. 7. Thank you for detailed review, vehicle used for the study is now inserted in the text. 8. Thank you, the Parameter section has been merged with the Methodology Section, and suggested citation have been added. 9. Thank you, Level of significance and base group for comparison has now been added in the legend text for Figure 1-2. Axis title has been added in Figure 3, title has been re-ordinated according to the legend. 10. Thank you for kind review, another explanation for the aforesaid quoted text has been added in the text.
Minor REVISION comments	Please add and clearly explain for our below questions in the discussion part to make this manuscript be more informative: 1. What is the mechanism of action of bisphenol A leading to delayed sexual maturity and fertility? Is there correlation with the hormonal system? Please elaborate completely. 2. In the introduction part, the author stated that *"Bisphenol A, a potent endocrine disrupting chemical, has been associated with precocious puberty in girls, indicating direct or indirect influence in modulation of ovaries and uterus.".* This statement is interesting issue, why is the effect of bisphenol A can be different between male and female? Modulation effect in female and inhibition effect in male. Then, the author has also mentioned that *"Bisphenol A has been associated with reduced testicular*	1. Thank you, Second paragraph of the introduction have mentioned that 'BPA is an endocrine disrupter'. The hypothesis of delayed sexual maturity was exclusively used in this study thus previous study to corroborate with this statement was unavailable. 2. Thank you, Due to BPA's androgen receptor antagonist and estrogenic property previous study have noted negative impact on the male reproductive system and precocious effect on female. Reprogramming effect can be observed in both gender without discrimination, though this information is generally known and definitely available, it was not included in the text. 3. Thank you, Last three lines of discussion elaborates how results of this study implicate by providing BPA's role in testicular growth and

	weight by multiple studies [1,16,18]. Earlier study has noted gonadal tissues to be sensitive target for reprogramming effect of key hormones [31]. Woldemeskel (2017) explained that testicular weight is sensitive to toxicity, specifically due to perturbation in rapidly dividing germ cells [47].” What are these effect can observe too in the female reproductive system? Please compare. 3. What the implicative information for the readers based on this results study? 4. Explain briefly and clearly the further experimental planning related to findings in this study.	Spermatogenesis. 4. Thank you for the detailed review, A sentence has been added in the last paragraph of discussion explaining how results of this study can lead to further studies.
Optional/General comments	The reviewed manuscript discusses about the effect of bisphenol A on the sexual maturity and fertility in rats.Tough manuscript looks very interesting and provides the beneficial information for peoples, especially about bisphenol A in the daily life. However, some modification and clarification are needed to improve the quality of manuscript before it published.	Thank you for the valuable comments, we have made sincere attempt to make changes accordingly.

PART 2:

	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)*
Are there ethical issues in this manuscript?	*(If yes, Kindly please write down the ethical issues here in details)*	Reviewer’s comments were extremely helpful, we have made changes in the manuscript and highlighted texts accordingly.