Journal Name:	Asian Journal of Research and Reports in Endocrinology
Manuscript Number:	**Ms_AJRRE_65450**
Title of the Manuscript:	**Comparative Effects on Wistar Rat's Thyroid Gland, Serum Selenium and Iodine Concentration of Bisphenol A, Carbimazole and Thyroxine**
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	Results - Clinical observations: Can the authors be more accurate when they say that "rats from group 2 showed nervous signs"? Did they use specific tests to measure this? What kind of signs did they detect? - Can the authors include the % of increase/decrease in T3, T4 and TSH in the text? - Section "3.4 Thyroid histopathology" needs to be redone. 1) It is essential to include images of control animals. 2) For every group (1, 2, 3 and 4) images of both sexes should be included. Currently there are no images of group 1 animals and no males of group 4. 3) Scale bars should be included in the images. 4) The figure legend should specify what the arrows are pointing to. 5) I suggest generating a panel with all the images, for example: Image Group1 male / Image Group1 female Image Group2 male / Image Group2 female Image Group3 male / Image Group3 female Image Group4 male / Image Group4 female 6) Right now, as it is written in the text, it gives the impression that the alterations in the thyroid gland were observed in 1 animal per group: "In the thyroid gland of a female rat", "in a female rat of the same group 3", "were observed also in a male rat". If the observations were only present in 1 individual, the findings are not representative of the whole group. If this is the case, it should be clearly stated, as it would suggest that the BPA and carbimazole treatments used in this study do not necessarily lead to thyroid gland structural alterations. It is essential to show images and describe the observations that a whole group share in common. If the observations were present in all the individuals, please correct the text accordingly. 7) It should be clearly mentioned if observations in male and females were the same or whether different alterations were observed across sexes. Discussion: - Unfortunately, I do not have full access to reference 21, however, I have serious doubts that this is the correct reference. This is a "review that compiles findings on the application of P2 receptor antagonists" and within the references of those review I cannot find one assesses exposure of BPA. Please, double check. In any case this review should not be cited, and the original research article should be cited instead. - I think reference 22 might be incorrect since this assesses low concentrations of serum triiodothyronine as a good marker for long-term mortality in hemodialysis patients and not neonatal treatment with BPA. - The authors do not discuss the inconsistent results of previous studies where "BPA exposure at 40 mg/kg for 15 days increased T4 levels" and the current findings where BPA exposure at 20 mg/kg for 4 weeks decreased T4 levels.	

	- Both deiodinase type 1 and 2 are selenocysteine containing enzymes, that catalyze deiodination of T4 to T3. So: “The authors found that selenium is needed for hepatic conversion of thyroxine (T4) to 3,3,5-triiodothyronine (T3) and that type 1 and 2 iodothyronine deiodinases, identified as a selenocysteine containing enzymes, catalyze~~s~~ deiodination of (T4) to biologically active thyroid hormone T3. - and thus play an important role in thyroid hormone metabolism ~~in rats and cattle~~. Type 1 and 2 deiodinases play an essential role in all mammals (including humans) not just in rats and cattle. They are even present in amphibians and fish. So, please, remove “in rats and cattle”.	
Minor REVISION comments	Introduction: - Bisphenol A (BPA), an estrogenic endocrine-disrupting chemical **(EDC) is** used to manufacture… - **In** the environment, it can be… Material and methods: - It is not stated if group 1, 3 and 4 were also treated by oral gavage. All animals should have been treated by oral gavage (even controls by administrating saline) to have comparative results. Please, state. -“Group 3 (same as group 2) received cabimazole”. Group 3 cannot be as group 2 as this last one was given BPA. - Where all groups treated for 4 weeks? This sould be made clear. - In “2.3 histopathological methods” sectioned at 5m should be 5µm. Results - Changes in the concentration of T3, T4 and TSH are presented - TSH concentration decreased (P<0.01) in group 4 while a significant increase (P<0.05) was observed in group 2 which received 20µg /kg body weight/day of BPA. - TSH of group 3 was not significantly increased, but the value was a slightly higher than in the control. - Table (2): Concentration of serum selenium and iodine in BPA, carbimazole and Thyroxine treated Wistar rats Discussion: - where ~~the~~ thyroid gland microscopic and functional alterations were observed. - This was evidenced by the decreased concentration of T4 and T3 with a significant increase of TSH in serum of BPA-treated animals, in addition to degeneration of the thyroid follicles with lymphocytic infiltration. - I am not what authors want to say in with the sentence “However, most studies suggested the use of traumatic protocols and methods for hormone dosage or the induction methodology using rats as animal model. For unknown reasons resistance to induction of hypothyroidism in mice was described [27].” Please clarify in text. - Carbimazole has been the drug of choice in some patients (which kind of patients?) because it may have fewer side effects, such as less frequent gastrointestinal tract problems [28]. - The relation between selenium and iodine has been well studied ~~by~~ [31] [32].	
Optional/General comments	- I strongly suggest changing the title for “Comparative Effects of Bisphenol A, Carbimazole and Thyroxine on Wistar Rat’s Thyroid Gland and Selenium and Iodine Serum Concentrations” - For section “3.4 thyroid histopathology” would if be possible to quantify the thyroid follicular area and compare it to control values?	

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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)*	

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