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Journal Name:	Asian Journal of Research in Biochemistry
Manuscript Number:	**Ms_AJRB_50942**
Title of the Manuscript:	**Effect of Oral intake of Sodium Benzoate on Serum Cholesterol and Proinflammatory cytokine (Tumor necrosis factor alpha [TNF-α] and Interleukin-6 [IL-6]) levels in the heart tissue of Wistar rats**
Type of the Article	**Original Research Article**

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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	The authors have done the experimental analysis of sodium benzoate in the Wistar rats, but certain clarifications are requested as follows 1. The authors described the effects of oral sodium benzoate in concentrations of 150, 250 and 500 mg/kg body weight to reduce cholesterol as in Figure 1 and proinflammatory cytokines as in Figure 2. The effects of reduction in proinflammatory markers are more marked in Figure 2 compared to Figure 1. Question? Is there any side effects observed in this study? 2. In lines 34-36, it is stated as sodium benzoate is used in the treatment of hepatic metabolic defects associated with hyperammonemia in urea cycle disorder. Suggestion The authors are requested to put some insights on hepatic and renal parameters assessment also both in Wistar rats and human beings, especially in diseased states to find out its effects 3. In lines 36-38, it is stated as 2% solution of sodium benzoate in drinking water is safe for lifelong treatment in mice without any noticeable side effects Question? Whether such concentration is applicable to humans and find out the safe concentration to implement it in the water supply of human population and its beneficial effects- assessment requested. 4.In lines 44-47, the upper limits of sodium benzoate allowable in food varies 0.1% in United States with a range 0.15 to 0.25% and in European countries, it is 0.015 to 0.5%. The authors are requested to assess whether the sodium benzoate in this range reduce the cholesterol and proinflammatory cytokines in human beings as a trial to implement its usage in therapeutic levels in addition to their efforts done on Wistar rats. 5. Lines 165-211—good. The authors narrated the biochemistry mechanism of action of sodium benzoate in an appreciable manner. 6. In lines 200-202, it is stated as inflammation was shown to be a prominent hallmark of ventricular hypertrophy. In lines 215-218, it is stated as sodium benzoate has a novel anti-inflammatory role. Suggestion Assessment of reduction in ventricular hypertrophy is requested during sodium benzoate administration, especially by Echocardiography assessment of	Fig 1 shows serum cholesterol levels of sodium benzoate administered animals. Fig 2. Shows proinflammatory marker in heart tissue. These are two different parameters. But all connected due to the inflammatory pathway. 1. The only noticeable side effect is a decrease in body weight of animals. 2. Line 34-36, was sited as a reference on sodium benzoate usage in the clinical practice for the treatment of childhood hyperammonemia. A publication on AFSJ, with manuscript no 2019/AFSJ/50650 talks about sodium benzoate effects on electrolytes and liver marker enzymes in wistar albino rats. This present study is a pilot study on the effect of sodium benzoate on serum cholesterol, Interleukin-6 and TNF-alpha of heart tissues in wistar albino rats. In another study we may focus on effect in human beings. Thanks for your suggestion. 3. Line 36-38, is sited with references on a previous study by Toth, 1984. This study is an animal study and isn't designed to determine if 2% concentration can be applicable in humans. Maybe another study will determine that. 4. Lines 44-47, is reported from European commission, 1995. Thanks for the request. but this can be evaluated in a next study for humans, to determine its therapeutic effect at those concentrations. 5. Lines 165-211. Thanks for the commendation. 6. Lines 200-202, during inflammatory processes, there is production of cytokines after the activation of NF-kB. IL-6 and TNF-alpha are both implicated in cardiac hypertrophy. Ref 34-37 are references sited for the statement. Thanks for your suggestion, but this study only covered analysis of serum cholesterol, and proinflammatory cytokine levels in the heart tissue of wistar albino rats. Sodium benzoate inhibition of the rate limiting enzyme (HMG-CoA reductase)in the cholesterol biosynthetic pathway, inhibits cholesterol synthesis, as well as the farnesyl pyrophosphate and geranyl geranyl pyrophosphate, these two are substrates for farnesylation reaction for the activation of the ras proteins for the activation of mitogen activated protein kinase for the activation of NF-kB, which leads to the production of cytokines. This pathway just stated is the inflammatory pathway, so sodium benzoate inhibition of the rate limiting enzyme functions in an inhibitory manner of this inflammatorypathway, by preventing the activation of NF-kB. Further study will concentrate on more indepth determination

	pathological hypertrophy and failing heart with a measurement of proinflammatory markers to correlate with its reduction of hypertrophy and control of failure symptoms in humans by administering sodium benzoate in therapeutic concentration. It is very much interested to review this paper further, if the authors do some efforts for the application of sodium benzoate to the human beings in addition to Wistar rats to implement it in the therapeutic range in pathological conditions such as ventricular hypertrophy and failure, hepatic and renal disorders in addition to hypercholesterolemia.	of heart activity. This as I stated earlier is a pilot animal study and shows the effect of sodium benzoate on serum cholesterol and Interleukin-6 and TTNF-alpha levels in heart tissue of wistar albino rats. Thanks for your suggestions, we will consider human study in our next analysis
Minor REVISION comments		
Optional/General comments		

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)***	