



SDI Review Form 1.6

Journal Name:	Journal of Advances in Medical and Pharmaceutical Sciences
Manuscript Number:	Ms_JAMPS_28571
Title of the Manuscript:	Hepatoprotective activity of Nigella sativa oil against Antitubercular drug-induced Hepatotoxicity in 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:

(<http://www.sciencedomain.org/page.php?id=sdi-general-editorial-policy#Peer-Review-Guideline>)



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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	1. The similar work is already published by many other researchers in various journals e.g. 1. Jadhav, R. and Mateenuddin, M., 2013. Effect of Nigella Sativa Oil on Hepatotoxicity Induced by Antitubercular Drugs in Albino Rats. Indian Medical Gazette—APRIL, 147. 2. Jaswal, A., Sharma, M., Raghuvanshi, S., Sharma, S., Reshi, M.S., Uthra, C. and Shukla, S., 2016. Therapeutic Efficacy of Nigella Sativa Linn. against Antituberculosis Drug- Induced Hepatic Injury in Wistar Rats. Journal of Environmental Pathology, Toxicology and Oncology, 35(1). 3. Jaswal, A., Sinha, N., Bhadauria, M., Shrivastava, S. and Shukla, S., 2013. Therapeutic potential of thymoquinone against anti-tuberculosis drugs induced liver damage. Environmental toxicology and pharmacology, 36(3), pp.779-786. 4. Hassan, A.S., Ahmed, J.H. and Al-Haroon, S.S., 2012. A study of the effect of Nigella sativa (Black seeds) in isoniazid (INH)-induced hepatotoxicity in rabbits. Indian journal of pharmacology, 44(6), p.678. Please give good relevant answer why you elect this already published work for your research studies.	1. This work was chosen in the year 2011 when this type of work was not done and also these types of drugs were not used at that time. There were rare report of this type of activity in that region. 2. The result was not done histologically but was observed under the simple microscope. Facilities were not available for histological studies.



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	2. In section 1.4 (Grading of Liver) author mentioned "The specimens were dehydrated in ascending grades of ethanol and cleared in xylene and then embedded in paraffin wax. Sections of about 5 µm were cut and then stained with hematoxylin and eosin for examination by light microscopy." But results lack Histological slides. 3. Number of scientific studies show that Antitubercular Drugs decrease the body weight due to their toxic effects. But the results shown by the author is contraindicated as table 1 shown that there is increase in the body weight of the rats. Please follow the give below research paper for the same. 1. Usmani, A., Mujahid, M., Khushtar, M., Siddiqui, H.H. and Rahman, M., 2016. Hepatoprotective effect of Anacyclus pyrethrum Linn. against antitubercular drug-induced hepatotoxicity in SD rats. Journal of Complementary and Integrative Medicine. 2. Kalra, B.S., Aggarwal, S., Khurana, N. and Gupta, U., 2007. Effect of cimetidine on hepatotoxicity induced by isoniazid-rifampicin combination in rabbits. Indian Journal of Gastroenterology, 26(1), p.18. 4. In the Result Section author mentioned that NS shown anti-inflammatory and anti-necrotic effect but in the research protocol there is no such parameters which provide the scientific evidence related to their anti-inflammatory and anti-necrotic effect. In other words author only perform Liver profile parameters but not inflammatory markers which predict that their formulation of NS has only hepatoprotective activity not the anti-inflammatory and anti-necrotic. If author is able to support their statement than please mention the	3. There is no significant increase in the body weight, if little weight has increased may be due to serosis or due to inflammation of the liver which decreased in the presence of NSO. 4. Anti-inflammatory and anti-necrotic effect was not observed. It was only with the help simple microscope and naked eye we could see there was anti-inflammatory and anti-necrotic effect. 5. Pre or post treatment schedule of the protective drug is now mentioned in the manuscript and also the day of sampling and dissection is now mentioned in the article 6. Statistical analysis was performed using ONE-WAY ANNOVA which has been written in the article.
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	detained results of inflammatory markers test. 5. Author fail to explain about the pre or post treatment schedule of the protective drug and if possible please mention pictorial design of whole treatment schedule which include the total period of treatment time and on which day sampling and dissection was done. 6. In section 1.5 (Statistical analysis) author fail to mention about the ANOVA test that is which ANOVA test was used either ONE-WAY or TWO WAY. 7. In section 1.2 please mention the refence from where you elect the toxic dosage of the Isoniazid and Rifampicin. 8. In legends of Fig 1 there is spelling mistake of Rifampicin drug and there is a need of formatting in this Figure 9. In introduction section please try to mention the detailed Mechanism of action of Isoniazid and Rifampicin that how they produce hepatotoxicity with the help of Diagram. 10. Please Cite latest references in the manuscript as all the cited references are very old. 11. Please mention the method of administration of drug in brief. 12. Why only female rats are elected? 13. Please mention the abbreviation of LSD in table No. 2	Significant difference among the treatments is now calculated using Duncan's multiple range test which has been added to the article. 7. In different articles different dosage of the drugs are shown which shows the hepatotoxic activity. Since the results for the said dosage was already given and results are shown in the literature. On the basis of these already mentioned results we increased the dosage to see if Nigella sativa shows the hepatoprotective activity or not. This is the basis of the selection of dosage of these drugs. 8. In fig 1 Rifampicin is corrected now 9.the mechanism of action of Isoniazid and Rifampicin is already mentioned in the discussion section, why we need to repeat this in the introduction section. 10. New references are now cited in the text 11. Drugs were administered into the rats with the help of oral feeding tubes 12. The rats which were available in the university happen to be female. There was no intention to take only female rats.
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	14. Please rewrite the following sentences: Table 2. Effect of Nigella. sativa on marker enzymes and total bilirubin in the serum of control and drug administered rats. (Pg 9) The Liver with and without treatment were dissected out immediately, chilled (Pg 7) collected by retro orbital puncture from all the animals without using any anticoagulant using a 2 ml syringe under light ether anesthesia and the blood was allowed to clot for 30 minutes at room temperature. (Pg 6) (Table 1) was coadministered with Rifampicin + Isoniazid, it resulted in the decrease of these marker enzymes and maintained these enzymes at normal levels in the serum of rats compared to the only Rifampicin + Isoniazid administered rats thus indicates the hepatoprotective action of Nigella sativa. (Pg 9) 15. If possible then author should perform some inflammatory markers test of liver homogenates and some anti oxidant parameters (Reduced glutathione, LPO test etc.)	Appropriate diet means the necessary diet for the growth of the rats. They have all the necessary nutrients in the diet. 13. Abbreviation of LSD is mentioned in Table as per suggestion 14. In Table 2. Effect of Nigella. sativa on marker enzymes and total bilirubin in the serum of control and drug administered rats has been now rewritten The sentence 'The Liver with and without treatment were dissected out immediately, chilled (Pg 7' is now rewritten. The sentence 'collected by retro orbital puncture from all the animals without using any anticoagulant using a 2 ml syringe under light ether anesthesia and the blood was allowed to clot for 30 minutes at room temperature. (Pg 6)' has been rewritten as per the suggestion. '(Table 1) was coadministered with Rifampicin + Isoniazid, it resulted in the decrease of these marker enzymes and maintained these enzymes at normal levels in the serum of rats compared to the only Rifampicin + Isoniazid administered rats thus indicates the hepatoprotective action of Nigella sativa. (Pg 9)' is now rewritten as per the suggestion 15. Sir, it is not possible now to do this work again as this study was done in the year 2011.
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Minor REVISION comments	1. Need lot of correction related to grammatical and sentence errors. For example need arises 3) production of blood clotting factors and amino acids including those used to fight against infection 4) processing and storage of iron which is necessary for the production of red blood cells 5) etc... 2. Please cite reference in the first paragraph of the introduction section. In the discussion part on page 10 author stated that "which could be the reason in our study that the <i>N. Sativa</i> and honey reduced the toxicity of these harmful drugs. Generation" But in the present study there is no any explanation of honey in the research protocol. 3. Please rewrite the conclusion section and make it more informative.	1. Grammar and sentence errors has been corrected as per suggestion. In the sentence honey is now removed 3. Conclusion section has been rewritten and is more informative now as per the suggestion of the reviewer.
Optional/General comments	Lack of connectors' in between the paragraph as there is a lack of connection in the introduction section.	