Peer Review File

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Reviewer A

-The author used 40 TB patients' urine samples in the test of total RMP concentration and another 75 TB patients' samples in the confirmatory experiment. How to guarantee the universality of the two experimental results? If the following 75 patient samples were used to test the total rifampin concentration in urine, while the previous 40 patient samples were used for confirmatory tests, would the results still be consistent? It may be necessary to test the total RMP concentration of 75 TB patients' urine samples, so the data will be more convincing.
Reply 1: Thank you for your suggestion. The issue you mentioned may exist, which is also a difficult issue to avoid in clinical research. Although we cannot supplement the data of these 75 individuals, we collected samples for testing within the same time frame after patients took medication, and the basic information of the selected patients was also limited. Therefore, we believe that this meets the consistency requirements of clinical research.
Changes in the text: NONE.

-The author found that when the total concentration of RMP in urine is higher than a certain threshold, it would interfere with some test results. The author should try to use some other methods to reduce or even avoid the interference of RMP on the results, and add this aspect to the discussion in order to improve the innovation of the article.
Reply 2: Thank you for your suggestion. We are currently trying various methods to reduce this impact, but the results are not ideal. Once the results are available, we will publish them as a new paper and send them to the relevant test strip manufacturers for clinical practice.
Changes in the text: NONE.

-In this paper, the experimental subjects selected in the experiment have taken at least two other anti-TB drugs besides rifampin. How can the author exclude the influence of other drugs on the experimental results? Some patients who received other drugs for TB but used rifampicin should be rolled in as negative control cases.
Reply 3: Thank you for your suggestion. Rifampicin is the main drug for tuberculosis, and it is rare for people not to use this drug unless there are strong adverse reactions.
Changes in the text: NONE.

-Methods; Page 3, line 9 and 15, the abbreviation RMB should be RMP.
Reply 4: Thank you for your suggestion. The abbreviation RMB have changed into RMP.
Changes in the text: Page 3, line 11 and 17, the abbreviation RMB have changed into RMP

-Discussion; Page 8, line 1, data clerical error, the total RMP concentration range of 88–76 ug/ml should be 88–376 ug/ml.
Reply 5: Thank you for your suggestion. We have changed.

Changes in the text: Page 8, line 3, the “88–76 ug/ml” have changed into “88–376 ug/ml”.

Reviewer B

Wang et al demonstrated the finding of interference of Oral Rifampin in Urine Dipstick interpretation in those patients with pulmonary TB. While their findings add additional information to the literature, this manuscript merits a revision for improvement.

Major comments:

What’s the purpose of doing two different approaches – in vitro interference assays and confirmatory test? This is understable that the in vitro assay was used to establish the standard curve and threshold. But beyond that, both approaches use the same test kits/procedures to measure the False positive effect of RMP (dRMP) in the UDT. Additional clarification is much needed. Along that line, why two groups of patient populations – 40 vs. 75?? Why can’t the samples from one group used for both? Are any part of 40 patients in the 75?? That needs to be clarified in text as well.
Reply 1: Thank you for your suggestion. 40 patients are not the part of the 75. We have clarified in text.
Changes in the text: Page 5, line 1.

While the authors focused on the false positive UDT effect (different analytes on the UDT) based on the RMP concentration, very little is mentioned about the effect based on the time course (i.e., post-RMP dose – 2-6 hrs vs. 12hrs etc) until the conclusion. What happened to the time course differences?
It’s also suggested to make a summary graph of different analytes affected at different concentrations of RMP at different time courses.
Reply 2: Thank you for your suggestion. We have to admit that this is our design flaw, but it does not affect the overall results of our paper. If such data is supplemented, it will take at least 2 years, so we will conceptualize new research later and add this new content to it.
Changes in the text: None.

Pg 2 Line 25: What about dRMP? when does it reach its peak in the urine?
Reply3: Thank you for your suggestion. This was not our research content, so we did not conduct research.
Changes in the text: None.

Pg 2 Line 34: anti-interference ability of Arkray’s auction sticks? “Elaborate” anti-interference ability. What does it mean there?
Reply 4: Thank you for your suggestion. Anti interference ability is a capability of the urine test strip itself, which can counteract the influence of certain drug metabolites and other metabolites in the body, ensuring the accuracy of the results.
Changes in the text:Pg 3- Line 5-7.

Pg 4- Line 31-33: Do any of the 75 patients have any urinary symptoms for concern of UTI? Same thing for the 40 patients as well?
Reply 5: Thank you for your suggestion. The issue is a difficult issue to avoid in clinical research. We collected samples for testing within the same time frame after patients took medication, and the basic information of the selected patients was also limited. Therefore, we believe that this meets the consistency requirements of clinical research.
Changes in the text: NONE.

Pg 4 Line 31 and Pg 3 Line 11: 40 vs. 75 patients: see above comment about these two groups of patient populations. Why not use one group and use the same sample for both approaches? How can you ensure that the findings/conclusion from both groups for in vitro vs. confirmatory are conformed to each other, not because of two different patient populations?
Reply 6: Thank you for your suggestion. The issue is a difficult issue to avoid in clinical research. We collected samples for testing within the same time frame after patients took medication, and the basic information of the selected patients was also limited. Therefore, we believe that this meets the consistency requirements of clinical research.
Changes in the text: NONE.

What about some of those TB patients on RMP treatment who developed UTI? It will also be more powerful to add a UTI patient group (i.e. known positive UDT as baseline) and a spike in RMP/RDMP or test with the samples from RMP-treated TB patients. This will also answer how RMP interferes in TB patients with the presence of UTI symptoms.
Reply 7: Thank you for your suggestion. This was a good idea, however, this was not our research content, so we did not conduct research.
Changes in the text: NONE.

Pg 7 Line 24-25: Be specific about each analyte being affected. Use of “such as” indicates vagueness and generalization. How many of the exact analytes (and what are they) are false positive? Were they randomly false pos at different concentrations of RMP reaching 150ug/mL? If so, mention it.
Reply 8: Thank you for your suggestion. The “such as” was a mistake in our statement. We have changed “such as” into “including”.
Changes in the text: Pg 7 Line 27.

Discussion: Oral Rifampin is not just used as part of TB regime. It’s also used to treat prophylaxis or post-exposure of Brucella etc, for a long course. Suggest adding a Comment/previous lit on the potential interference of Rifampin on UDT in those patients with Rifampin therapy for other infectious diseases.
Reply 9: Thank you for your suggestion. In fact, we are not concerned about what diseases to treat. What we are concerned about is the impact of metabolites from taking drugs on urine testing indicators. Therefore, adding other diseases is a good suggestion, however, not adding them will not affect the conclusion
Changes in the text: NONE.

Minor comments:

Pg 3: line 3-5: Suggest including a statement stating a brief finding of the study as a conclusion to the introduction.
Reply 10: Thank you for your suggestion. We have added the conclusion to the introduction.
Changes in the text: Pg 3: line 8-11.

Pg3 Line 18: how long were the samples stored?
Reply 11: Thank you for your suggestion. We have added samples store Sample storage time. The maximum storage time was 90 days.
Changes in the text: Pg 3: line 25.

Pg 3 Line 24: 500mg/L – is it RMP or dRMP or what is the mixture? Clarify.
Reply 12: Thank you for your suggestion. 500mg/L – is urine sample. We have changed.
Changes in the text: Pg 3: line 32.

Pg 3: Line 30: Thawing in waterbath for how long?
Reply 13: Thank you for your suggestion. Thawing in waterbath for 5 minutes.We have changed.
Changes in the text: Pg 4: line 5-6.