**Dear Dr. Bojan Radak**

Vinča Institute of Nuclear Sciences, Belgrade

Response to Dr. Bojan Radak’s comments are written in violet

Bojan Radak, sub-editor made comments in red.

Thank you for your useful comments and suggestions about our manuscript. We have modified the revised manuscript accordingly and the detailed corrections are listed below point by point:

ADDITIONAL COMMENTS

Please indicate the page numbers for suggested corrections.
Please, be as specific as possible if major correction by the author(s) is recommended! :
For English Improvement: Line 29-31, line 64(researches =?), line 71, line 102-103. Etc

\* We checked and corrected the language/Grammar mistakes with Foreign Language Institute of Mersin University.

\*\* Unfortunately, it does not appear so. However, it will be down to the main Editor to decide.

 \*\*\*Actually we checked the grammar in the whole of the revised manuscript. Also, we checked it again upon the request from Dr. Bojan RADAK and corrected some mistakes such as: line 45-47, line 47-48, line 50-51, line 53, line 55, line 57, line 61, line 64-65, line 66-67, line 70, line 88, line 98, line 101-105, line 115, line 124, line 130-131, line138-139, line 140, line 143, line 153, line 164-167, line 173, line 183 *etc*.

REPORT:
The manuscript “Solubility and degradation of paracetamol in subcritical water” by Z. Emire et. al. describes enhancement in the solubility of paracetamol drug in subcritical water (at 403K) and degradation of the drug in the presence of O2 and H2O2 (at 30 Bar). However, the work described in the manuscript seems premature at this stage to be published in this journal. Following are the major and minor comments about the manuscript.

\*This is an original and scientifically favourable work that should benefit the readers. Water sources that contaminated with paracetamol can be effectively cleaned and potential risks can be eliminated and solubility of paracetamol presented in detailed along with theoretical solubility equations through this work.

So, this manuscript should be published in such a qualified journal after all corrections and improvements.

\*\* Thank you for pointing out the importance of your manuscript, but nobody questioned it.

\*\*\*Thanks for the notice. We had tried to clarified the importance of the related work.

1. MINOR COMMENTS

a. English throughout the manuscript needs improvement.

For example Line 29-31, line 64(researches =?), line 71, line 102-103. Etc

\* We checked and corrected the language/Grammar mistakes with Foreign Language Institute of Mersin University.

b. In Experimental part “How the pressure was fixed at 30 bar with oxygen and nitrogen using O2 and using H2O2”. Please reframe the sentence so that following questions may not arise.
What was the ratio of oxygen and Nitrogen? What was the need of Nitrogen when Oxygen is also being used? In case of H2O2 what was the need for Oxygen and nitrogen?

\* We rewrited the related sentences and clearly explained the aim of using oxygen and nitrogen gases (Line 101-104).

\*\* I am sorry, but the sentence is eirther grammatically incorrect, or there is a mixup in explaining. Nitrogen cannot be an oxidizing agent, and you did use plural when mentioning both nitrogen and hydrogen peroxide in one sentence. In the next sentence, you are also using plural for no obvious reason.

I asumed that grammar was your problem, and not a mixup, so I deliberately changed the sentences to this (check it out and let me know if that is what you meant):

"The pressure was maintained at 30 bar with nitrogen, and 0.035 mL of H2O2 were used as oxidizing agent in each degradation experiment to keep the water in liquid form. In the other batch of degradation experiments, the pressure was maintained at 30 bar with oxygen, which also acted as an oxidizing agent at that instance."

\*\*\* We notice through your comment that we had used the plural form of “oxidizing agent” in our previous revised manuscript. Sorry for this mistake. We replaced related sentences with your revised sentences given in above comments with a minor modification. These sentences are more clear in the last revised manuscript.

c. In Experimental part for HPLC analysis which column was used? There is no mention of it.

\*Actually, we already mentioned HPLC analysis and column used in our manuscript (please look at line 85-86)

d. Table II and III needs to mention values for the degradation of paracetamol without any oxidant.

\*We corrected Table II and Table III in our revised manuscript (Line170 and Line 176)

2. MAJOR COMMENTS

a. Line 38 and 39 of text says “.......relatively safe at lower doses.” and Line 42 and 43 of text says “Paracetamol has been found in sewage treatment plant with concentrations up to 6 ppb and 10 ppb in neutral waters.”

The work described in this manuscript has taken only one concentration (5 ppm) which is 103 times higher. How is the study relevant? It is suggested that for the degradation experiments some more concentrations approaching ppb level should be considered.

\* Taking the literature into consideration, lots of work specified the risk of the environmental or aquatic medium that contain hazardous materials in low doses. However, they used solutions contain higher concentrations of target materials. ( M. Shakir, M. Faraz, M. A. Sherwani, S. I. Al-Resayes, J. Lumin. 176 (2016) 159; H. Wang, Y. Liu, J. Jiang, Chemosphere 155 (2016) 583 ).

For example, 65 ppb of acetaminophen has been detected in surface water and the concentration of acetaminophen might be much higher in pharmaceutical industry wastewater. However, authors were used Stock solutions of acetaminophen prepared in pure water at 100 ppm (H. Wang, Y. Liu, J. Jiang, Chemosphere 155 (2016) 583 ).

In addittion, this is a model work which aqueous solution that artificially prepared. Working with concentration in ppb levels contains some difficulty in experimental and analysis stage, too.

\*\* Experimental difficulties cannot be an excuse, but practicallity and relevance can. Please try to present your argument about using higher concentrations somewhere in the text, and inform me where and how you did so.

\*\*\* It is wtitten in line 42-43 as: "Paracetamol has been found in sewage treatment plant with concentration up to 6 ppb and 10 ppb in natural waters.7,11,12” Even so, we used a stock 5 ppm aqueous paracetamol solution (line 99).

We had tried to explain this by illustrating some literature references that used solutions contain higher concentrations of target materials, in spite of the fact that aquatic medium containing these materials in lower doses. It is a regular situation that hazardous materials can be exist in too high concentration in the exit waste of management which is different in the aquatic environment far from the management. For instance, we must employ a degradation/removal process directly to the exit water of a management/industry, not to the water of sea or underground. Furthermore, we know that concentration of exit water is always higher than other water samples (sea, river or underground water).

The sentence “Working with concentration in ppb levels contains some difficulty in experimental and analysis stage” is not the main reason of working in higher concentration but added an extra explanation that cause a difficulty in the analysis stage.

b. Result and Discussion part describes five equations for the approximation models and have developed a sixth equation which varies dramatically for 393 and 403K temperatures.

What is the need to show the result in main manuscript with first five equations when they do not match the result obtained. They can be shown in supplementary information if authors find it relevant.

\*We have tried the five theoretical equations to our results to determine the best one that appropritate with results. When we obtained that none of the five equations were not appropriate, we modified the equations and obtained the new one which predicts mole fraction solubility of paracetamol correctly. This is a standart procedure which was applied in lots of literature work as stated in our references numbered 13, 14, 15 and 23.

\*Table one clearly shows the results obtained with all of the equations. These results are a part of the RESULTS sections..

\*\* I will accept that, just do not call them, as they clearly seem to be empirical, or approximative, as you mentioned.

\*\*\* We corrected this in our last revised manuscript (line 11-line 75)

There is no theoretical discussion or its practical relevance about how equation 6 was arrived. Please include the same.

\*Generally actual/previously created equations are modified using specific coefficients (using Microsoft Excell ) in theoretical equations works and obtained equations are analysed for consistency with experimental results.

Can equation be modified further so as to fit results from temperature 393 and 403 K.

\* We pointed out in line 122-123 that mole fraction solubility of paracetamol decreased dramatically at 413 K due to possible degradation of paracetamol at the higher temperature as shown in figure 1. Otherwise, high tempreture decrease the solubility of paracetamol, even at 393 and 403 K.

c. The authors should make use of “Supplementary Information (SI)” facility that is available with most of the journals including this one to make your claims’ about the work strong. For example, besides suggested above important HPLC graphs of the solubility and degradation of the drug along with standard drug can be uploaded in SI.

\* There are over 100 HPLC chromatograms (for degradation and solubility of paracetamol for each in triple). In addition, previous articles (references 13, 14, 15 and 23) did not give HPLC chromatograms as Suplementary Information. However We uploaded some of HPLC chromatograms as Supplementary Information in our revised submission. After all, if editor request some others of them we can includ.