3 Reviewer

The manuscript by Bogdanov describes the anticancer and antiphytopathogenic activity of fluorinated isatins and their water-soluble hydrazone derivatives. Author has synthesized series of benzylated isatin derivatives in good yield and screened for their cytotoxicity against two cancer cell lines (M-HeLa & HuTu-80) and one normal human hepatocyte. Some of the synthesized compounds showed moderate activity with moderate selectivity. Furthermore, the cell death mechanism associated with apoptosis due to mitochondrial membrane dissipation and stimulation of ROS species production in tumor cells. In addition to this, author has prepared few water soluble pyridinium isatin hydrazine derivates and which shows antagonistic effect against phytopathogens of bacterial and fungal origin. This reviewer is recommending this manuscript for the publication in IJMS after minor revision.

Response: Thank you very much for the helpful summary and positive evaluation of this work!

1. Scheme 1 is one pot or two step reaction?

   Answer. The reaction shown in Scheme 1 is a two-step one-pot as the intermediate sodium salt undergoes further alkylation without isolation.

2. In fig.3 please provide appropriate number or name.

   Answer. As recommended by the reviewer, Figures 3 and 4 have been revised.

3. For Table 1 caption, author should provide the incubation time.

   Answer. As recommended by the reviewer, Table 1 caption has been corrected.

4. Is there any reason why author did not evaluate the compounds 7a-c for their anticancer activity?

   Answer. We have previously studied the anticancer activity of these compounds. However, these hydrazones and some of their analogs did not show such activity; therefore, it was not studied in this work. At the same time, we have shown that isatin ammonium hydrazones have a high potential as compounds exhibiting antimicrobial activity against anthropo- and phytopathogens. Therefore, the anticancer activity of hydrazones 7a-c was not studied in this article.

5. General synthetic procedure for the synthesis of 3a-f and 4a-e can be rewritten, it is quite unclear to reader.

   Answer. As recommended by the reviewer, this paragraph has been more detailed.

6. Author has prepared several fluorinated isatin derivatives and all are well characterized. However, 19F NMR data is missing in the experimental. Author can provide 19F NMR data for at least active compounds.

   Answer. As recommended by the reviewer, this data have been more detailed.

Author can check this manuscript for typo error before revision.

Answer. The manuscript has been double checked for typos and errors.