Dear Reviewer,

We would like to express our sincere appreciation for your careful attention to our manuscript and for the suggested improvements and valuable comments. We have revised the manuscript according to your remarks. Please find below the detailed description of the revision with our point-by-point answers.

Reviewer: The paper describes an investigation of cyanoarylporphyrazine and its iron complex as a photosensitizer (PS). The PS and iron complex were then studied for cellular toxicity, uptake and fluorescence properties. The paper is well-written and very easy to follow. The results are clearly presented, and conclusions are supported by the results. Characterization and analysis appear to be well-organized and systematic too.

Point 1: The major concern is about the originality/novelty of this work. The synthesis of iron complex of cyanoarylporphyrazine is neither very difficult task nor it very interesting from synthetic aspect.

Response 1: In the present work, the synthesis of the iron complex of tetra(2-naphthyl)tetracyanoporphyrazine (**FePzNPh**) is described for the first time and a comparative analysis of the photophysical and photobiological properties of the porphyrazine free base and its iron complex is carried out, with emphasis on the effect of iron on the studied properties. In particular, the spectral properties were studied, the quantum yield of fluorescence and photobleaching was determined, the dynamics of accumulation and photodynamic activity in relation to tumor cells in culture were studied.
We believe that the ease of obtaining compounds, including **FePzNPh** studied in this work (single-stage synthesis, mild conditions), is an additional advantage, as it provides reproducibility, easy production scalability, low product cost, and reliable quality control. We believe that interest in the synthesis of such compounds lies in the field of prospects for its practical implementation for production.

Point 2: Additionally, it is expected that iron complexation enhances the photodynamic therapy for the generation of toxic hydroxyl radicals by Fenton reaction (as described by the authors in the discussion). However, this was not observed by the authors and inadequate explanation was provided.

I believe this work can be accepted after addressing the concerns about novelty and significance of iron complexation in photodynamic activity.

Response 2: The presence of iron at the center of the photosensitizer macrocycle strongly affects its photochemical, photophysical, and photobiological properties [1], such as water solubility, triplet state lifetime, intersystem crossing efficiency, quantum yield and fluorescence lifetime, and photostability [2–3]. Because of this, the photobiological properties also change. It is these considerations that motivate our work.

In addition, in the presence of iron in the macrocycle, the development of the Fenton reaction can be expected. We have covered this aspect in the discussion (Lines 415-420 in the revised version of the manuscript). Our interest was also aroused by recent publications on the role of iron-catalyzed enhancement of the antitumor effect due to the induction of ferroptosis as an immunogenic cell death, which can effectively suppress tumor resistance to therapy [4]. However, this mechanism requires a separate study and is beyond the scope of the article.

References:

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