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Prof. Dr. Marcus Tullius Scotti and Prof. Dr. Luciana Scotti
Editor-in-Chief

We want to thank you and the reviewers for giving us the opportunity to revise our manuscript entitled “**3-Hydroxytanshinone Inhibits the Activity of Hypoxia-Inducible Factor 1- α by Interfering with the Function of α -enolase in the Glycolytic Pathway.**” (molecules-2974696)
We appreciated the thoughtful comments. Please find our responses to the reviewers’ comments below.

► Reviewer 1’s comments:

Abstract:

The authors used many undefined abbreviations. Also, you should define for the reader that tanshinones are traditional Chinese medicine with multiple variety of therapeutic effects.

A: As recommended, we have added a list of abbreviations in the part of manuscript and tanshinone has been explicitly defined as a traditional Chinese medicine in the abstract section.

In the section of discussion, the authors did not discuss the issue of bioavailability and hydrophobicity of tanshinones and possible chemical structure modification to be tried at preclinical and clinical levels. An issue of great importance.

A: Thank you for this important suggestion. We have added the reviewer's comments to the discussion section.

What is their cytotoxicity on normal cells?

A: Thank you for your thorough review. A test was performed to assess the cytotoxic effects of tanshinone using Human Umbilical Vein Endothelial Cells (HUVECs). No toxicity was detected at the concentrations utilized in the study. Moreover, it was found that tanshinone demonstrated no toxicity in human bone marrow-derived endothelial progenitor cells (EPCs) at concentrations up to 30 μ M, as reported in the articles. Based on these findings, it can be inferred that tanshinone does not exhibit toxicity towards normal cells.

Reference

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We heartily thank you and the reviewers again and hope that the revised version of our manuscript is now acceptable for publication in *Molecules*. We are looking forward to your positive response. Thank you.

sincerely yours,

Sik-Won Choi, Ph.D.