Reviewer #1:
Scientific Quality: Grade B (Very good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Minor revision
Specific Comments to Authors: The paper is concise, logically written, and organized. The hypothesis and corresponding conclusion are clear, followed by a detailed and well-depicted scientific methodology. In order to further improve scientific value the Discussion/Conclusion section could also tackle the following questions: 1.Taking into account myriads of other anti-cancer mechanisms of action for Physcion in other cancer cell types , as well as established promotion of chemosensitivity, what would be the author's opinion about the potential effectiveness of Physcion in other targeted therapies resistances 2. Could numerous established anticancer mechanisms for Physcion (antineoplastic, anti-inflammatory, antiangiogenic, and antiproliferative) suggest that PIM1-regulated glycolysis is not the only mechanism underlying sorafenib sensitivity

Response: Thank you for your kind advice. It is possible that Physcion affects other targeted therapies resistances, and that PIM1-regulated glycolysis may not be the only mechanism underlying therapeutic sensitivity. We have stated this in discussion section.

Reviewer #2:
Scientific Quality: Grade C (Good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Accept (General priority)
Specific Comments to Authors: This is an interesting study about the physcion in hepatocellular carcinoma. The study is well designed and the findings are interesting. Discussion is good, and references are updated. The authors should make a carefully editing to the manuscript, and update the figures.

Response: Thank you for your kind advice. We have carefully edited the article.

Reviewer #3:
Scientific Quality: Grade B (Very good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Minor revision
Specific Comments to Authors: Aerobic glycolysis is a well-recognized

hallmark of cancer cells, and it is critical for cancer initiation and development. It is worthy of note that a recent study reported that sorafenib impaired OXPHOS and promoted glycolysis in HCC. The physcion acts as a suppressor of metastasis and plays a pivotal role in chemosensitization. However, the effect of physcion during sorafenib resistance has not been studied yet. In this study, the authors designed the research to investigate the effect of physcion on the sensitivity of HCC cells to sorafenib. The research is well performed. The methods are described in detail, and the results are very interesting.

Minor comments:

1. The statistical methods should be described in the method section.

Response: Thank you for your kind advice. We have completed the statistical methods in the method section.

2. How about the limit of this research? Please make a discussion about it.

Response: Thank you for your kind advice. We have added the limitation of current study in the discussion section.

3. The quality of the images should be improved.

Response: Thank you for your kind advice. We have provided images with high quality during revision.

4. Some minor language polishing should be corrected.

Response: Thank you for your kind advice. We have carefully revised the manuscript and corrected language mistakes.