Reviewer’s report

Title: Potential therapeutic role of Tridham in human Hepatocellular Carcinoma through induction of p53 independent Apoptosis

Version: 1 Date: 6 August 2013

Reviewer: Aditi Roy

Reviewer’s report:

The manuscript provides a relatively comprehensive study of the mechanism of action of TD in Huh 7 cells. The question posed by the authors is well defined. Methods are appropriate, well described and figures are clear and informative. However, my most major concern is the readability of the manuscript in its current form. The authors should pay closer attention to correct construction. There are also too many run on sentences to point out in this manuscript. These issues could be easily addressed with a careful editing and perhaps the input of a scientific writer.

Minor Essential Revisions

1. Abstract, Paragraph 1: “……antiproliferative and antiapoptotic” should be “……antiproliferative and pro-apoptotic”

2. Abstract, Paragraph 3: “Viability…” should be “Viability studies…..”

3. Background, Paragraph 1: Although the study was performed for Bad there is no reference of it in this section or even as part of Discussion. The significance of Bad & the results with it needs to be mentioned to explain pro-apoptotic MOA of TD.

4. Please provide reference information on the therapeutic potential of Prosopis cineraria component of TD/ address this aspect which is missing in the manuscript.

5. Please be consistent on how you would like to cite Terminalia chebula - either as “Terminalia chebula” or “T. chebula”; also cytochrome c as either “cytochrome c” or “cytochrome C” all through.

6. Background, Paragraph 5: The presentation of literature review of the therapeutic properties of TD could be more organized, discussing each component in sequence followed by presentation of information that is common to more than one component in TD.

7. Results, Induction of apoptosis by activation of caspase-3: “Expression of Caspase 3 gene was found to be up regulated in both Western blot (Figure 6)
and colorimetric assay (Figure 7). The figure represents data obtained by flow cytometry.

Please correct the construction of the legend too. “Effect of TD on cell cycle analysis ..” is not an accurate representation.

8. Discussion, Paragraph 1: “However, instead of using individual herbal drugs, for treating multiple diseases, a combinational therapy is currently gaining higher importance [44] elicit..”

Please replace “treating multiple diseases” by “treating diseases with multiple indications”

9. Discussion, Paragraph 2: Please discuss the implications of vacuolation of the cytoplasm with relevant supporting reference(s).

10. Discussion, Paragraph 5: Please cite reference in support of the text “....DNA ladder formation, characteristic of apoptosis ....”

11. Discussion, Paragraph 6: “The mitochondrial membrane translocation of Bax from cytosol has been reported in response to various death stimuli [51-54]”. is not an accurate representation.

12. Discussion, Paragraph 7: “.....cytochrome C thus, forming a pore in the outer membrane of mitochondria...”. Please replace “thus” with “by”

13. Please be consistent with font style. Certain segments of the text are in italics.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.