Reviewer's report

Title: Identification of a potent herbal molecule for the treatment of breast cancer

Version: 1 Date: 2 September 2008

Reviewer: Farrukh Afaq

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In this manuscript the authors have investigated the effect of (8'Z)-3-pentadec-10-enyl-benzene-1,2-diol (PDBD) isolated from polyherbal mixture on estrogen-receptor positive and (ER+) and estrogen-receptor negative (ER-) breast cancer cells. Growth inhibiting effects of PDBD were more pronounced both in ER+ and ER- breast cancer cells as compared to normal mammary epithelial cells. Furthermore, treatment of breast cancer cells with PDBD resulted in inhibition of Akt signaling and its downstream target such as NF-κB activation, IAP proteins and Bcl2 expression. In addition, activation of JNK/p38 MAPK-mediated pro-apoptotic signaling was observed in both ER+ and ER- breast cancer cells after PDBD treatment. Based on this, these investigators propose that PDBD is a natural product worthy of consideration for development in breast cancer. While this manuscript is of potential interest, substantial criticisms are raised that temper enthusiasm for this manuscript. Any revised manuscript should adequately address the following points:

1) The authors should use normal mammary epithelial (184A1) cells instead of using immortalized mammary epithelial (MCF-10A) cells to determine the growth inhibitory effect of PDBD.

2) The purity of PDBD is not discussed in the manuscript.

3) Are the dosages of PDBD used in cell culture studies pharmacologically achievable in the in vivo setting of treated experimental animal models? If these dosages are unable to be achieved, the clinical relevancy of these in vitro studies is questioned.

4) The data in terms of time points shown in Table 1 do not correlate with that discussed in results section. It is also not clear that at this time point when all the cells were dead than how come the authors have analyzed the arrest of cells in different phases of the cell cycle.

5) The manuscript in general is not properly prepared and presented.

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.