Reviewer’s report

Title: Zuo Jin Wan, reverses P-gp mediate Multidrug resistance by inhibiting the activation of PI3K/Akt/NF-kappaB pathway

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Reviewer: Shinya Wakusawa

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This paper deals with demonstration of involvement of PI3K/Akt/NF-kB signaling pathway in anti-MDR action of the formula of Zuo Jin Wan. Authors provide several important and interesting evidences concerning its molecular mechanism of action. However, this paper merely has shown the action of Zuo Jin Wan did not discrepant with the action of its component herbs or main pharmacologically active ingredients. In addition, this paper contains several weak and questionable points.

Major

1. Figure 1 showed increased cytotoxicity by ZJW of L-OHP in MDR cells. How was in HCT116 cells.

2. In several results, cells were exposed to LY294002 for 2 hrs. Is it true that P-gp has declined within 2 hrs (Fig 3A)? If ZJW down-regulates MDR through inhibiting PI3K/Akt signaling pathway, the exposure time of LY and ZLW should be same, namely 2hr or 48 hr.

How was the effect of another inhibitor wortmannin?

3. In Discussion “In our study, a remarkable activation of phosphorylation AKT and NF-kB was detected in HCT116/L-OHP cells, which also have up-regulation of P-gp.”

Where those data are shown? Authors have to show those data in Figure 3 and 4.

4. ChIP assay data shown in Figure 5 indicates association of NF-kB with ABCB1 gene. How was in HCT116 cells, and how was the effect of Zuo Jin Wan.

5. Though authors think that Zuo Jin Wan reverses P-gp-mediated MDR by inhibiting expression of P-gp. Does not Zuo Jin Wan compete for transport of L-OHP?

6. Student t-test should not be used for comparison of multiple groups.

Level of interest: An article of limited interest

Quality of written English: Acceptable

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.