Reviewer’s report

Title: The 4-aminopiperidine series has limited anti-tubercular and anti-staphylococcus aureus activity

Version: 1 Date: 11 December 2014

Reviewer: Michio Kurosu

Reviewer’s report:

The 4-aminopiperidine series has limited antitubercular and anti-staphylococcus aureus activity

The team explored SAR of 4-aminopiperidine derivatives against M. tuberculosis. 4-Aminopiperidines were reported to exhibit antimycobacterial activity (ref 3, Tuberculosis 2009, 89:334-353). The compound 4 was reported to be >90% Mtb growth inhibition at 10 ug/mL concentrations. The reported 4-aminopiperidines possesses the N-benzyl-N-phenethyl-1-aryl-4-aminopiperidin core structure. Table 1 summarizes SAR data of selected 11 molecules where the R group was diversified. The team resynthesized the compound 4, but 4 did not show antimycobacterial activity at the reported concentrations (MIC 4 ug/mL reported, >20 ug/mL observed in this article). I believe the data reported in Tuberculosis 2009 were MIC of library molecules (unpurified). These new evidences imply that impurity of crude 4 was more active than the pure form. Table 2 and 3 illustrated ineffective anti-TB molecules based on 4-aminopiperidine and 4-carboxylpiperidine. The team identified that 1 has the MIC of 10 ug/mL. I felt that this article was poorly articulated SAR data. Because the compound 1 showed a reasonable MIC for Mtb, the efforts described here are reasonable SAR performance. Conclusion should appeal the identification of a new 4-aminopiperidine, rather than non-pursuable of this series.

Comments:

• The activities against Mtb and S. aureus were reported. Activity of S. aureus destruct construction of article. If the team include data for Gram-negative and cytotoxicities, it would increase quality of this article. I suggest remove the data of S. aureus and evaluate the selected molecules (i.e 1) against series of bacteria.
• Conclusion should be elaborated towards positive sense.
• The compounds in Table 3 are not organized rationally.
• Synthetic protocol for 1 should be included.
• Add more references
• Title is not appropriate: “anti-staphylococcus activity” should not be in title.
• Grammatical errors should be corrected.
• The author should rewrite this article; the current version is very unattractive.
Level of interest: An article of limited interest

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.