Reviewer #1:

1. Authors developed QSAR equation and validated it using test set. However, there is no explanation how they divided training set and test set. If the selection of compounds for training set is random then it does not meet the journal standards. Explanation is required in this regard.

2. For the QSAR Eq.1: Inter correlation between the descriptors is not stated. This is more crucial when Chi indices and No. of rotatable bonds is repeated in the Equation.

3. A model over fits if it includes more descriptors than required. To prove the lack of over fitting for the QSAR model the authors should check: Number of data points/number of descriptors = 4. Which means you cannot use six descriptors to explain 21 compounds. Explanation is needed in this regard.

4. In Table 3, Simple quadratic and simple cubic models have same value. Explanation is needed for this result.

5. Please provide the details/figure about the quality of protein structure (Ramachandran plot) which authors have modeled.

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6. Authors state as follows: The active site contains important and highly conserved amino acids like His111, Asp214, Glu276, His348 and Asp349. The above statement infers that the alpha glucosidase inhibitor should also bind in the active site and exhibit interactions with the His111, Asp214, Glu276, His348 and Asp349 amino acids. In contrast, in the results section, authors state that their compound is potent by exhibiting hydrogen bonds with His239, His245, His279, and Thr275. They also claim that the potent compound is having Pi-Pi stacking and Pi-cation interaction with Phe 311 and Lys 155 (Figure 6a). Please explain how a compound can be potent without binding in active site/key residues/conserved amino acids.

Page no. 9 Second paragraph, the following line needs clarity/explanation:
7. On the other hand, His279 forms hydrogen bonding with catalytic residue His279 which is believed to have some reducing effect in the enzyme's activity.

In the synthesis part:

8. Further several hydrazides of phenyl and substituted phenyl derivatives were shown to exert histone diacetylase activity. Similarly chromene ether derivatives also showed HDAC activity. Hence it remains to be seen whether these compounds reported here would interfere in DNA transcription pathways. The selectivity of the synthesized compounds towards alpha glucosidase needs to ascertained.

9. However the metabolic instability of these compounds makes them vulnerable and it remains to be seen whether they would cause any toxicity as the breakdown products will be hydrazines known for their toxic effects.

10. Moreover for alpha glucosidase activity, the structure activity relationship studies from literature reveal that it is essential to have 5,6,7-trihydroxyflavone structure. However the present manuscript does not contain any of the substituents on the flavone ring that does not augur well with the hypothesis of alpha glucosidase inhibition.

Reviewer #2:

1. Authors have to clarify the basis of synthesizing the flavones hydrazones being active as <alpha>-glucosidase inhibitors.

In this study two important moieties known for their inhibitory activity against *a*-glucosidase had been studied. Flavone moiety that is well known for its antidiabetic activity was being combined with hydrazone moiety which is also known for it's a-glucosidase inhibition activity to see if these hybrid compounds could improve the activity.

2. Regarding the QSAR study, it is not possible to develop a QSAR model with 10 descriptors for 21 molecules. Maximum 4 descriptors may be considered for model development. The validation results on the test set should also be mentioned.

We appreciate the reviewer's comment on these important issue and therefore we had studied further on the qsar model to remove some of the descriptors. The validation test result had been mentioned in the manuscript as being suggested by worthy reviewer.

3. Apart from 2D-QSAR authors are suggested to perform 3D-QSAR on the alignment of the most active compound 5 as well as docking analysis to obtain the important steric, hydrophobic and electronic features controlling the <alpha>-glucosidase inhibitory properties. 3D-QSAR results should be validated by 2D-QSAR and vice-versa.

We appreciate the reviewers suggestion to include the 3D-QSAR study. However we are currently developing the 3D-QSAR model to be used to design new compounds for another study.

4. The homology modeling was done between 3A4A and MAL12 but the docking was performed on 3W37. Please clarify.

The protein 3W37, which contains crystal structure for acarbose, was only used to validate the docking method. This is in reference to a paper by Muhammad Yar (M. Yar, M. Bajda, L. Shahzadi, S. A. Shahzad, M. Ahmed, M. Ashraf, U. Alam, I. U. Khan, A. F. Khan. Novel synthesis of dihydropyrimidines for a-glucosidase inhibition to treat type 2 diabetes: In vitro biological evaluation and in silico docking, Bioorg. Chem. 54 (2014) 96-104.) which claims that the active site of 3W37 is highly conserved and can be used for validation purpose.