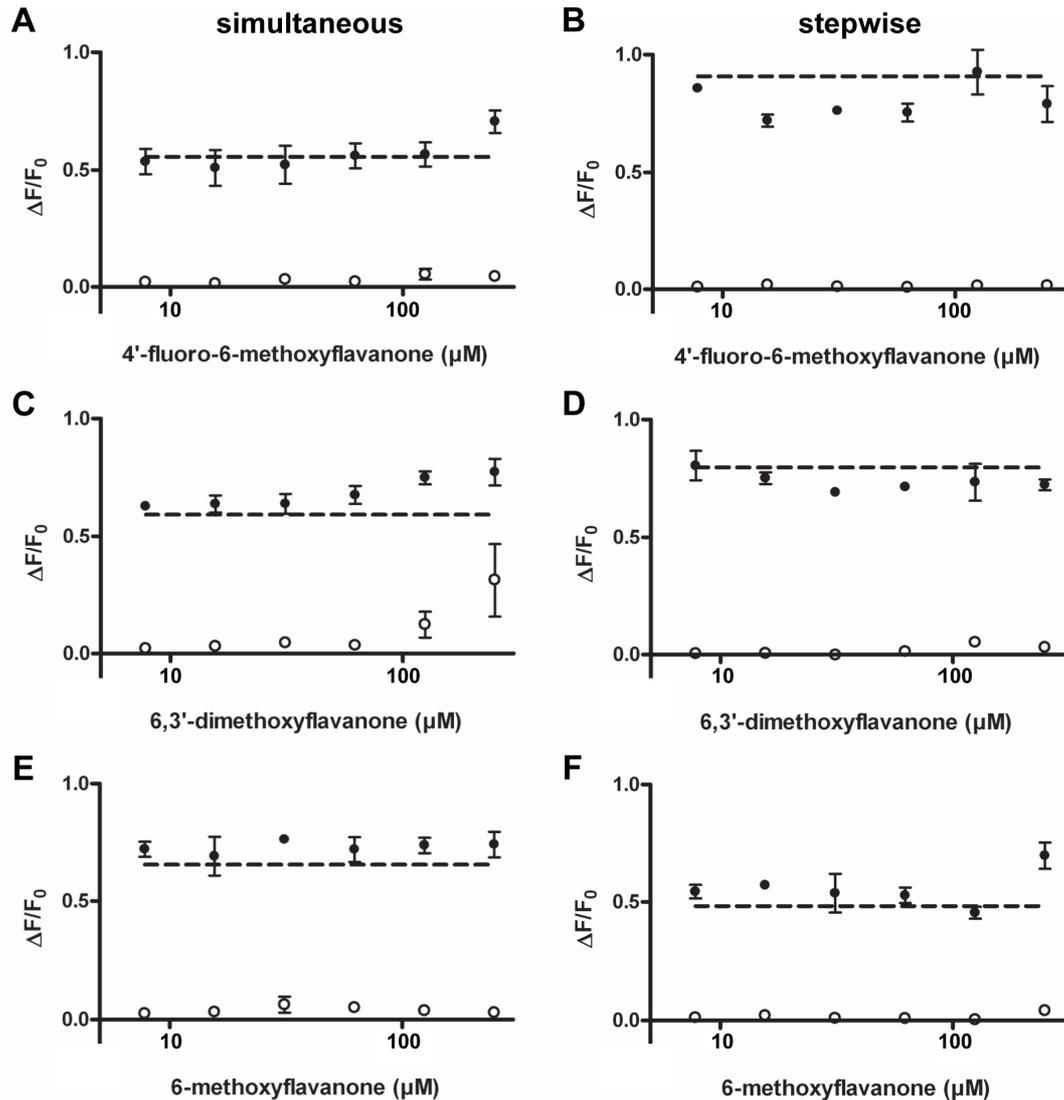


**File S3** Investigation of identified inhibitors on hTAS2R16.

To investigate whether the hTAS2R39 inhibitors 6,3'-dimethoxyflavanone (**3**), 4'-fluoro-6-methoxyflavanone (**6**), and 6-methoxyflavanone (**11**) were able to inhibit a bitter receptor not known for flavonoid activation, hTAS2R16 was selected for inhibition experiments. Measuring dose-response curves of the hTAS2R16 agonist salicin under the conditions used in this study revealed an EC<sub>80</sub> concentration of 10 mM salicin on hTAS2R16. The results in **Figure S3** show that no inhibition of hTAS2R16 occurred.



**Figure S3.** Inhibition of response of 10 mM salicin (---) on hTAS2R16 (induced (●), non-induced (○)) by 4'-fluoro-6-methoxyflavanone (**6**) after simultaneous addition (**A**) and stepwise addition (**B**), by 6,3'-dimethoxyflavanone (**3**) after simultaneous addition (**C**) and stepwise addition (**D**), and by 6-methoxyflavanone (**11**) after simultaneous addition (**E**) and stepwise addition (**F**).