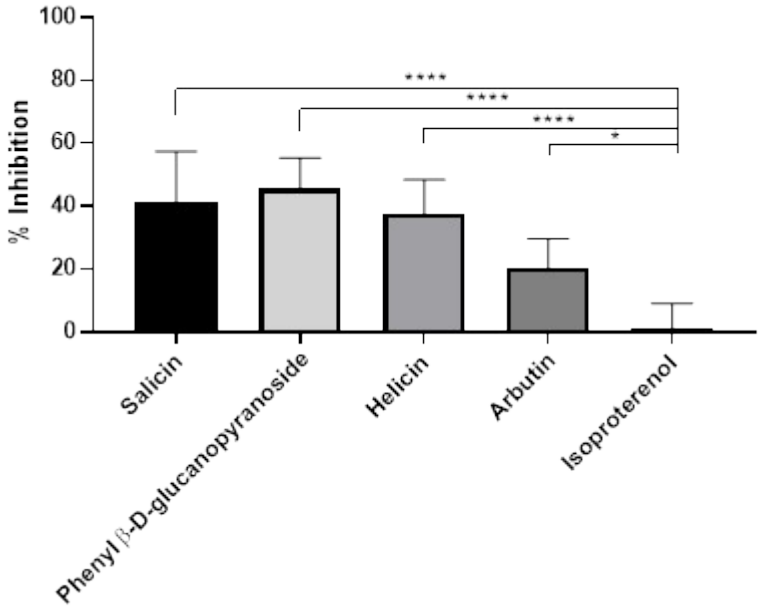
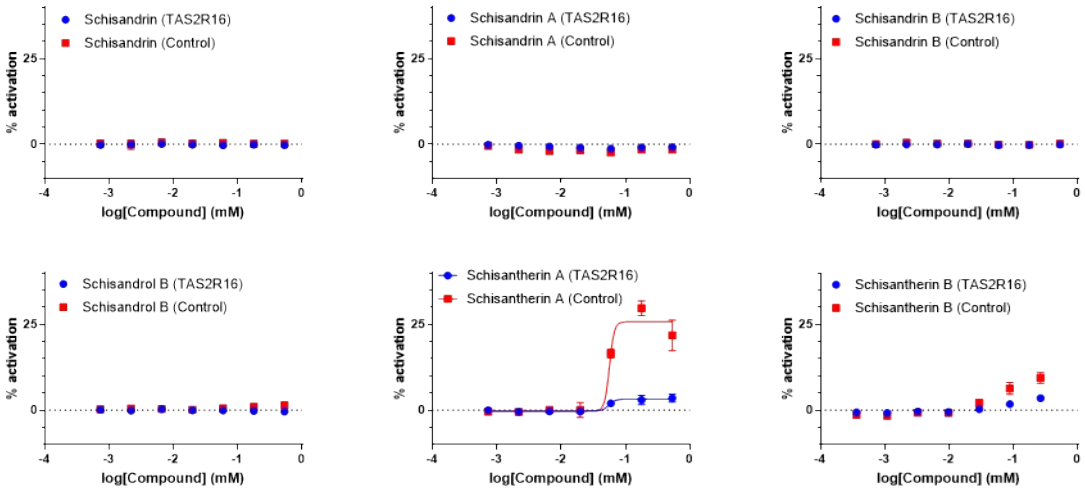
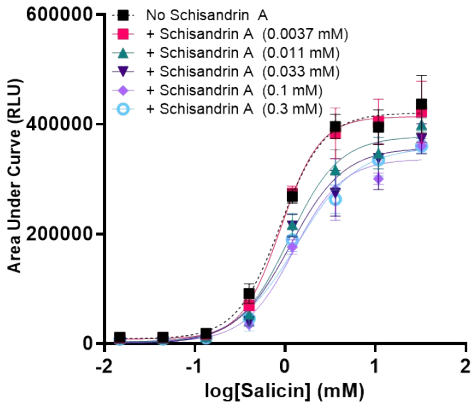
Supplementary Figures



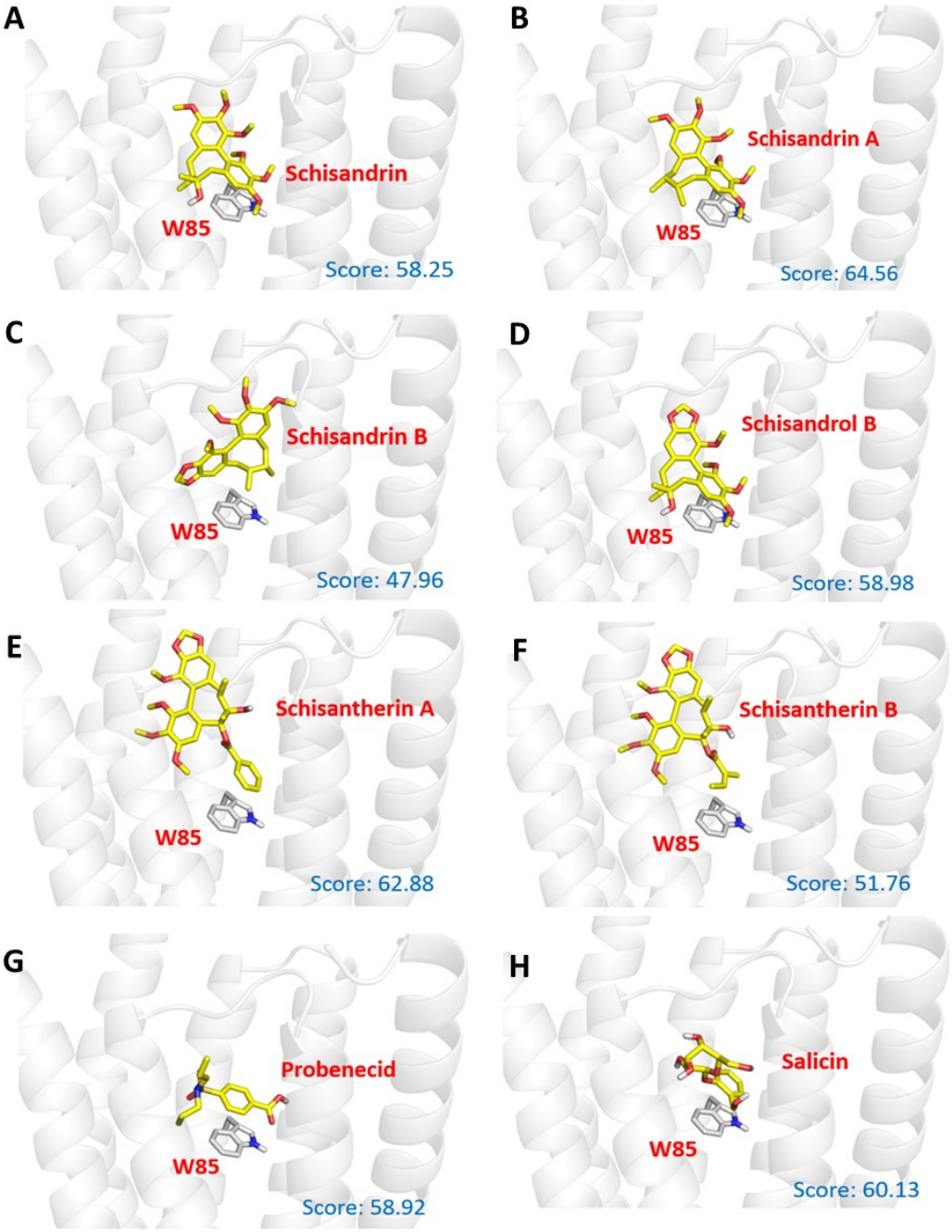
Supp. Fig. 1. Schisandrin A (**A**), was tested at 0.5 mM for inhibitory activity against salicin-like glycosides (helicon, arbutin, phenyl b-d-glucanopyranoside) which are known TAS2R16 agonists, and isoproterenol, an adrenergic receptor agonist. While Schisandrin A is able to inhibit the TAS2R16 agonist effects, it has no inhibitory effect on TAS2R16-expressing cells stimulated with isoproterenol. Data is presented as an average of at least 6 experimental replicates. Error bars are S.D.. Bonferroni's multiple comparisons test was employed to determine statistical significance of Schisandrin A inhibition of TAS2R16 activation by TAS2R16 agonists against a non-TAS2R16 specific stimulant, isoproterenol. Four asterisks (****) indicate $p \leq 0.0001$. One asterisk (*) indicate $p \leq 0.05$.



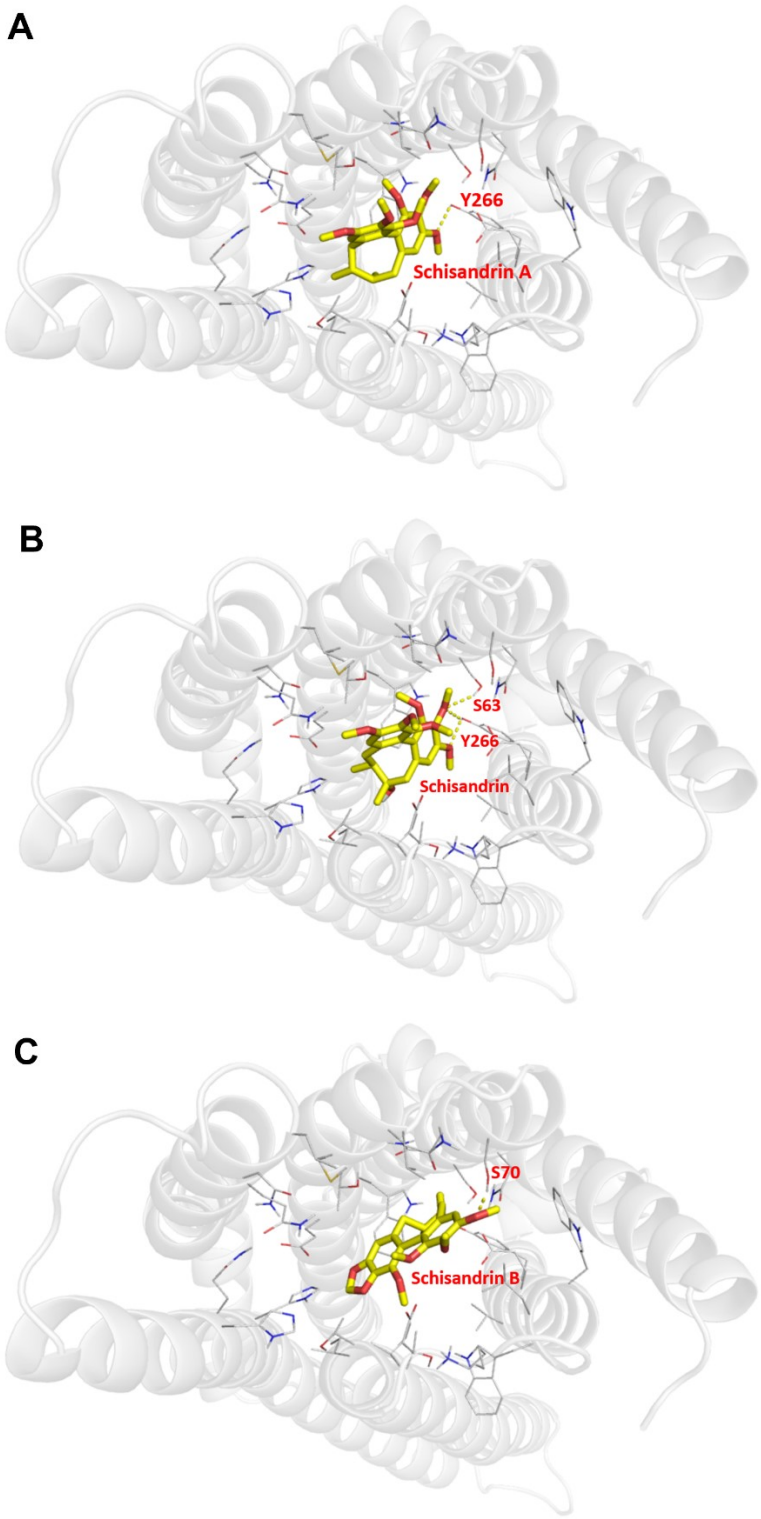
Supp. Fig. 2. Dose response studies of schisandra lignans against cells expressing hTAS2R16 or against control cells expressing only gust44-clytinII. Percent activation is calculated with reference to the maximum activation achieved with known activators salicin (2 mM) for TAS2R16, Gα16-gust44 and clytin II expressing cells, and isoproterenol (0.05 μM) for Gα16-gust44 and clytin II expressing cells (control). The data were fitted in GraphPad Prism using a four-parameter logistic fit. Data presented is the average of at least three experimental replicates. Error bars are S.D..



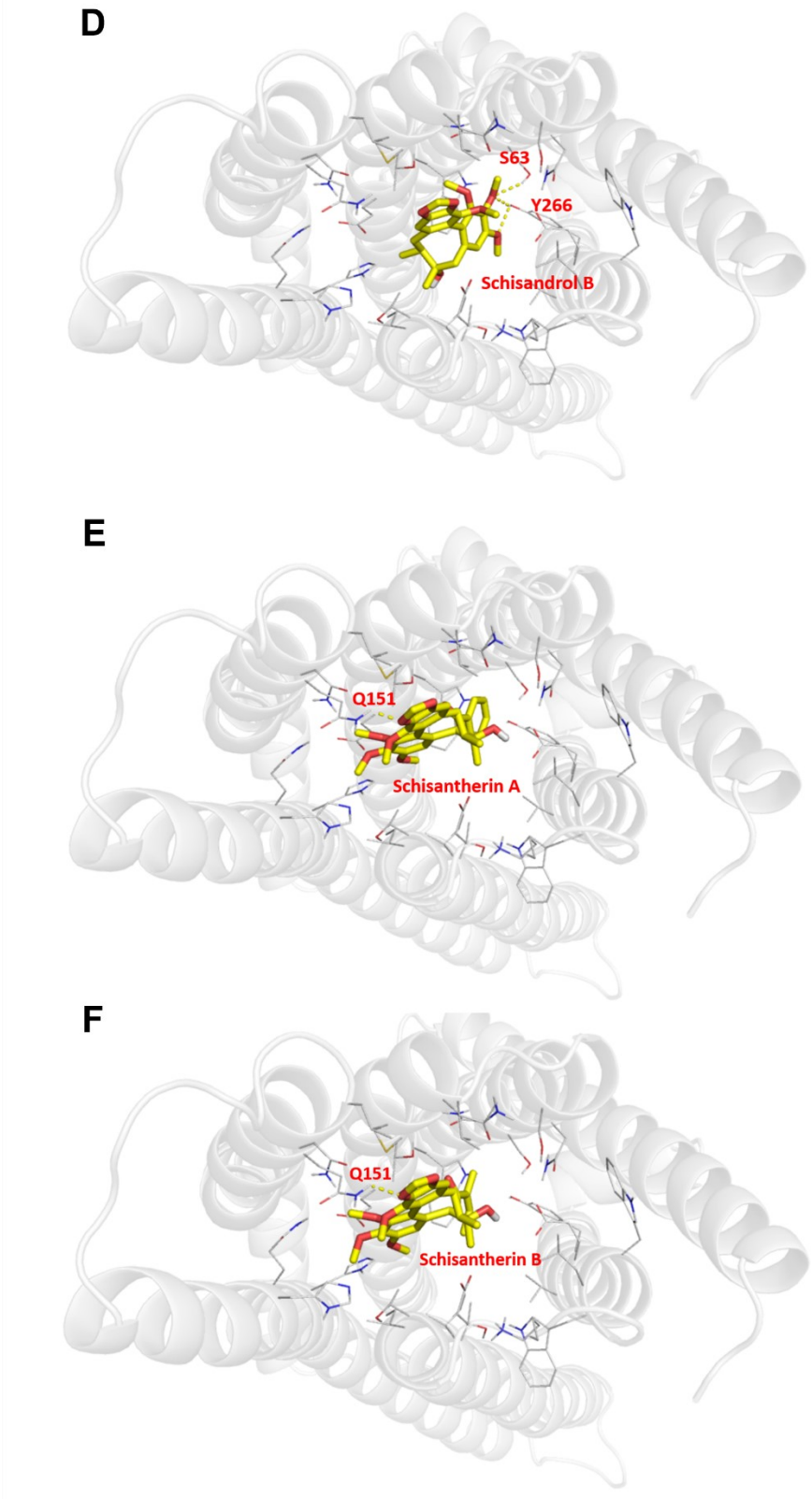
Supp. Fig. 3 Dose response curves of salicin against cells expressing hTAS2R16 in the presence of increasing amounts of schisandrin A. The data were fitted in GraphPad Prism using a four-parameter logistic fit. Data presented is the average of at least two experimental replicates. Error bars are S.D..



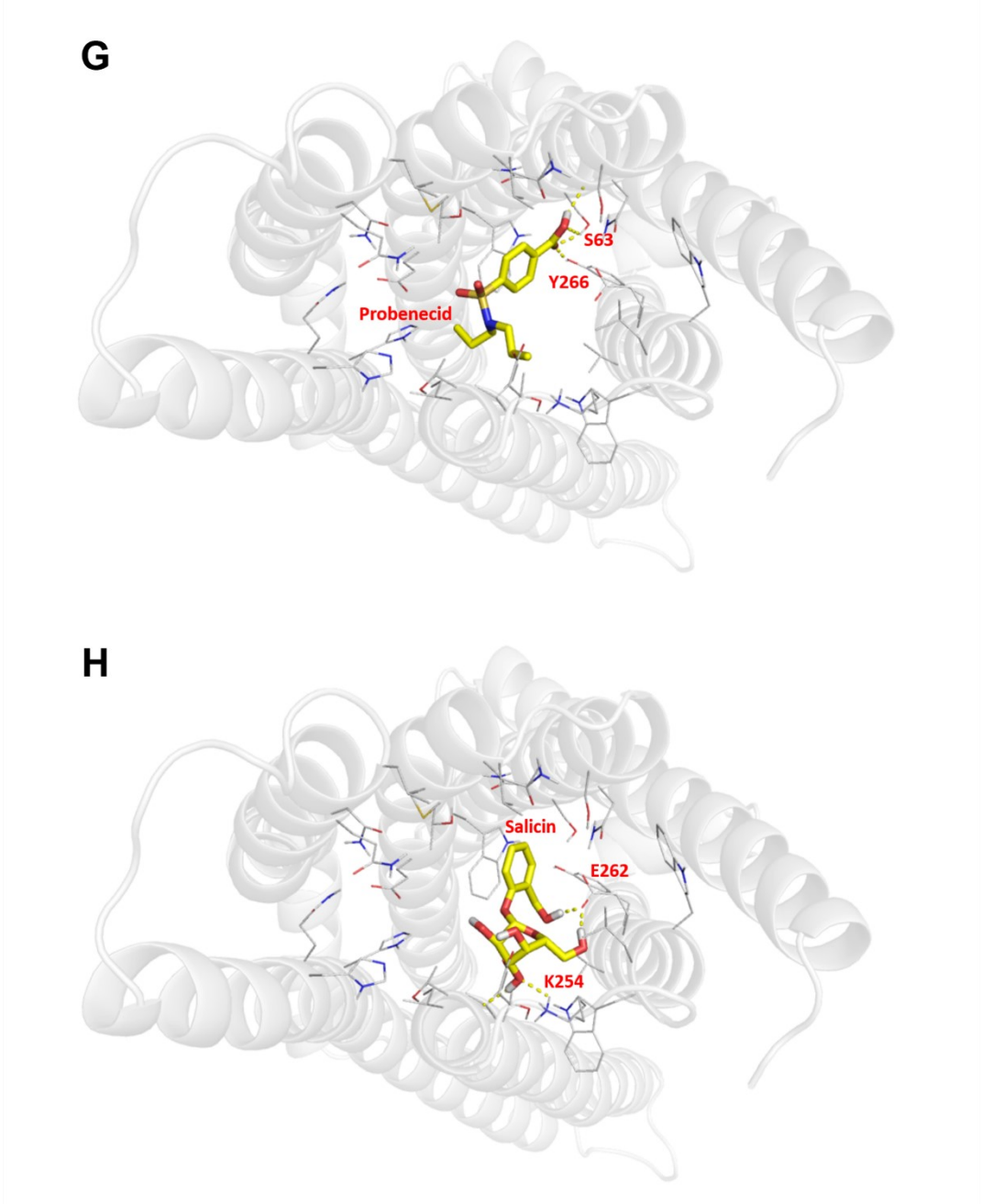
Supp. Fig. 4. The sideview of the best docking solution for *Schisandra* lignans **1** – Schisandrin (**A**), **2** – Schisandrin A (**B**), **3** – Schisandrin B (**C**), **4** – Schisandrol B (**D**), **5** – Schisantherin A (**E**), **6** – Schisantherin B (**F**), and two reference ligands salicin (**G**) and probenecid(**H**). Notes: (1) for clarity, only the key residue W85 on hTAS2R16 is shown; (2) score refers to the docking score from molecular docking simulations; (3) a typical parallel pi-pi interaction between phenyl rings is formed in **A, B, D, E, G, H.**



Supp. Fig. 5. The top view of the best docking solution for *Schisandra* lignans **1** – Schisandrin (**A**), **2** – Schisandrin A (**B**), **3** – Schisandrin B (**C**), **4** – Schisandrol B (**D**), **5** – Schisantherin A (**E**), **6** – Schisantherin B (**F**), and two reference ligands salicin (**G**) and probenecid (**H**). For clarity, only the binding pocket residues and ligands are shown.



Supp. Fig. 5 Continued. The top view of the best docking solution for *Schisandra* lignans **1** – Schisandrin (**A**), **2** – Schisandrin A (**B**), **3** – Schisandrin B (**C**), **4** – Schisandrol B (**D**), **5** – Schisantherin A (**E**), **6** – Schisantherin B (**F**), and two reference ligands salicin (**G**) and probenecid (**H**). For clarity, only the binding pocket residues and ligands are shown.



Supp. Fig. 5 Continued. The top view of the best docking solution for *Schisandra* lignans **1** – Schisandrin (**A**), **2** – Schisandrin A (**B**), **3** – Schisandrin B (**C**), **4** – Schisandrol B (**D**), **5** – Schisantherin A (**E**), **6** – Schisantherin B (**F**), and two reference ligands salicin (**G**) and probenecid (**H**). For clarity, only the binding pocket residues and ligands are shown.