

Supplementary data

The specific binding and promotion effect of azoles to human aldo-keto reductase 7A2

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Table S1. Kinetic parameters of effect of voriconazole on AKR7A2 enzyme activity with SSA as a substrate

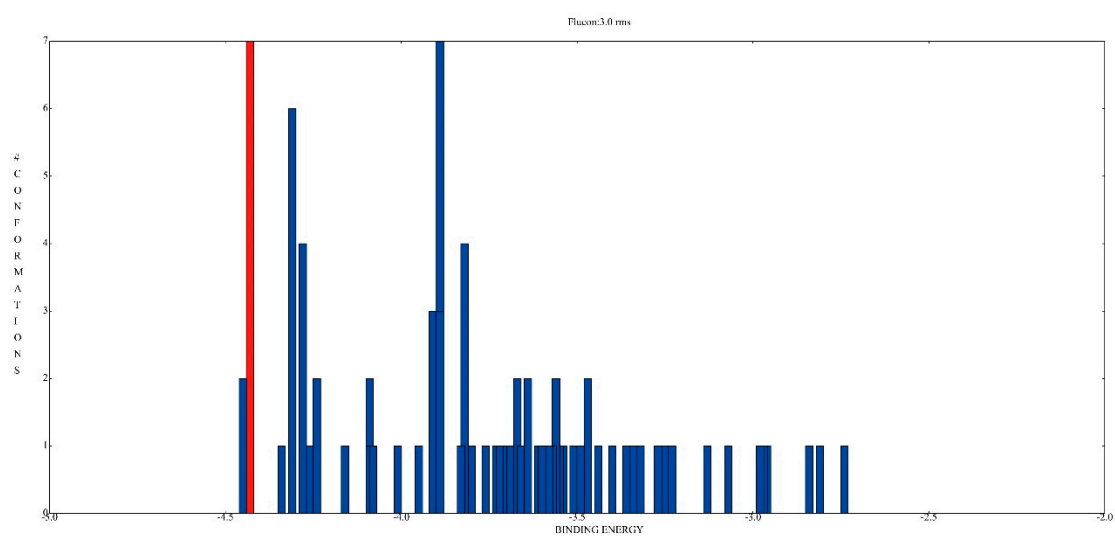


Figure S2 The cluster distribution of fluconazole docking into AKR7A2.
The red column represents some conformers binding at the entrance of the substrate pocket

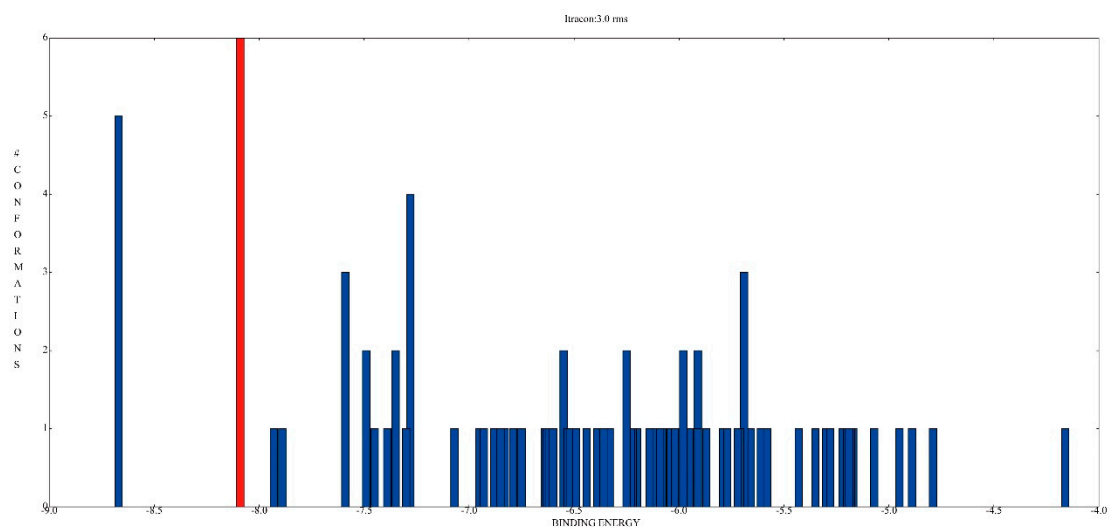


Figure S3 The cluster distribution of itraconazole docking into AKR7A2.

The red column represents some conformers binding at the entrance of the substrate pocket

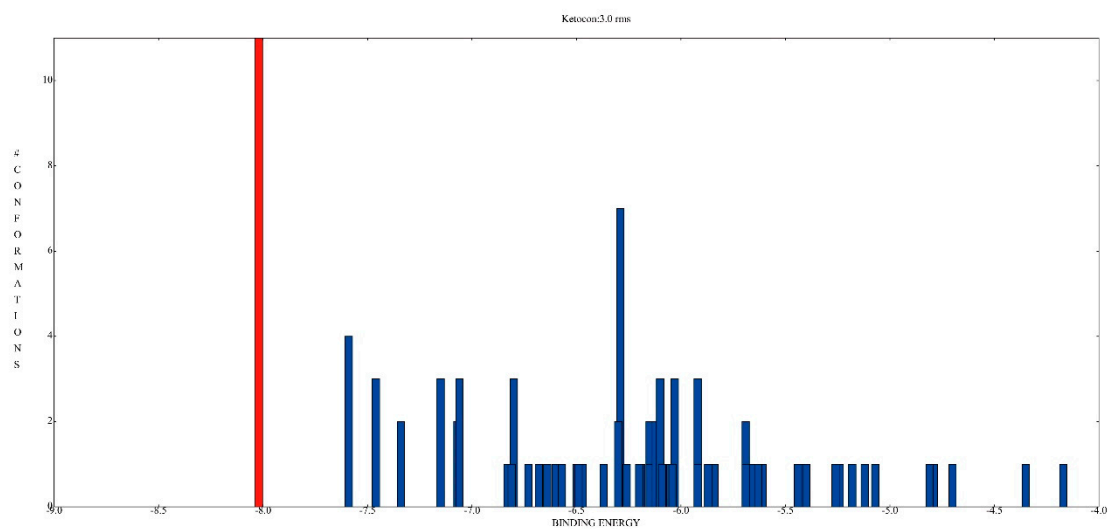


Figure S4 The cluster distribution of ketoconazole docking into AKR7A2.
The red column represents the conformers binding at the entrance of the substrate pocket

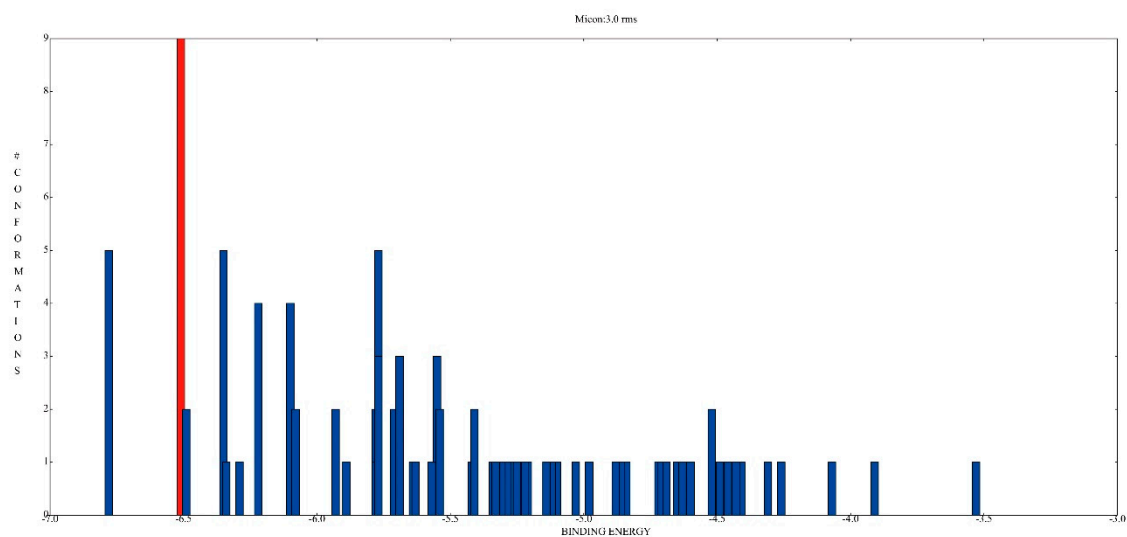


Figure S5 The cluster distribution of miconazole docking into AKR7A2.
The red column represents some conformers binding at the entrance of the substrate pocket

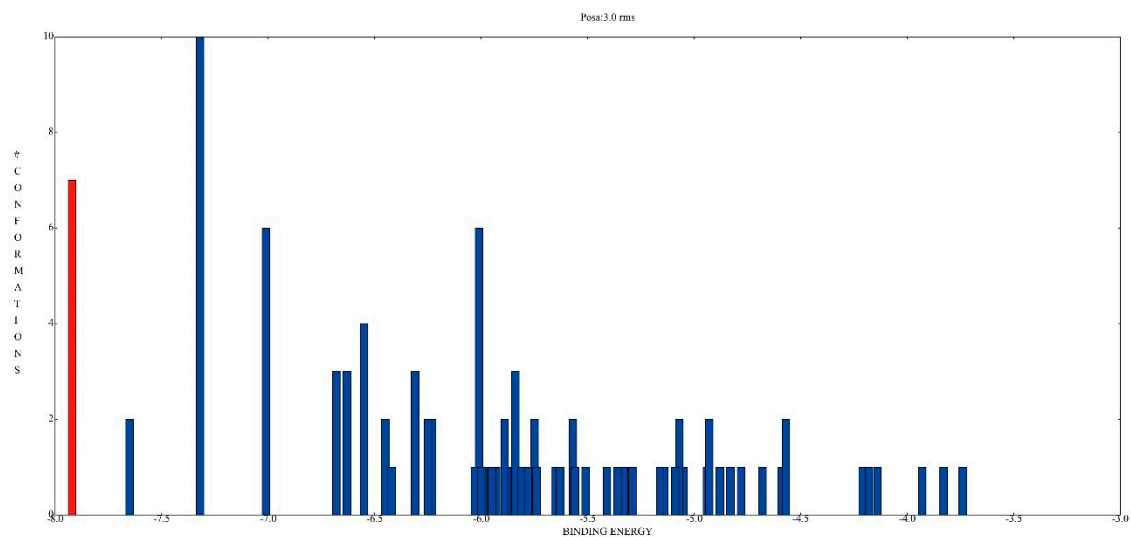


Figure S6 The cluster distribution of posaconazole docking into AKR7A2.

The red column represents the conformers binding at the entrance of the substrate pocket

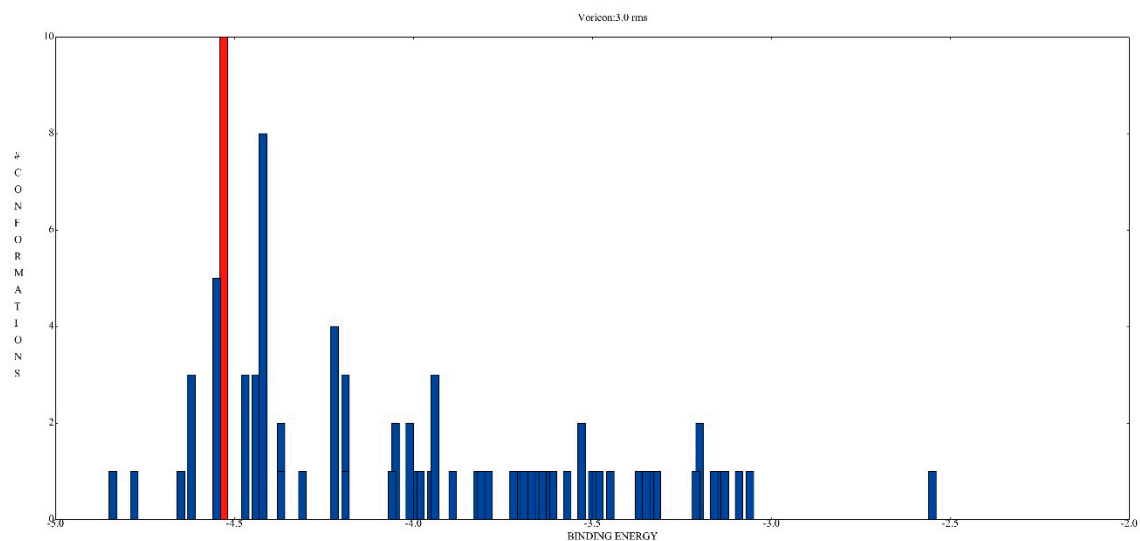


Figure S7 The cluster distribution of voriconazole docking into AKR7A.
 The red column represents the conformers binding at the entrance of the substrate
 pocket

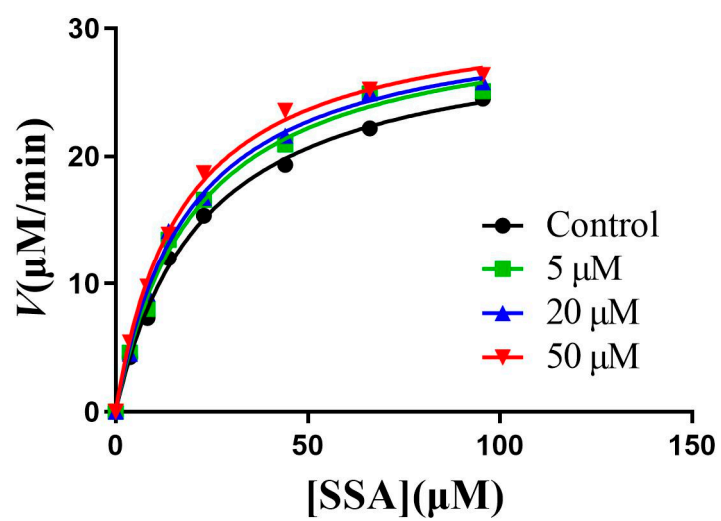


Figure S8 The Michaelis-Menten equation fittings of SSA catalyzed by AKR7A2 in the absence or presence of voriconazole

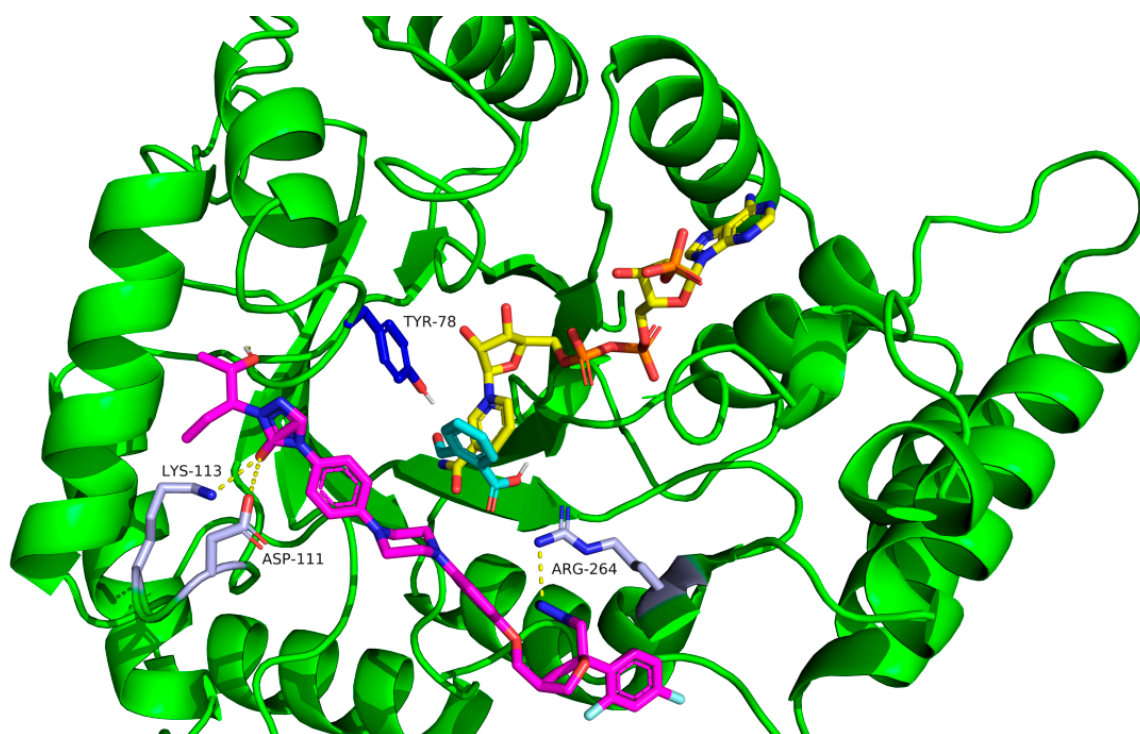


Figure S9 The interactions of posaconazole with the residues in the substrate pocket.

The simulations were performed with flexible docking by setting Tyr-78 as the flexible residue. Protein backbones are represented as green ribbon format. 2-CBA is depicted in cyan sticks, NADPH is depicted in yellow sticks, and posaconazole is depicted in purple sticks. The active center Tyr-78 residue is depicted in blue sticks.

Color scheme: red for oxygen atoms, blue for nitrogen atoms, and orange for phosphorus atom. Hydrogen bonds are shown as yellow dashed lines. Asp-111, Lys-113, and Arg-264 can form hydrogen bonds with posaconazole.

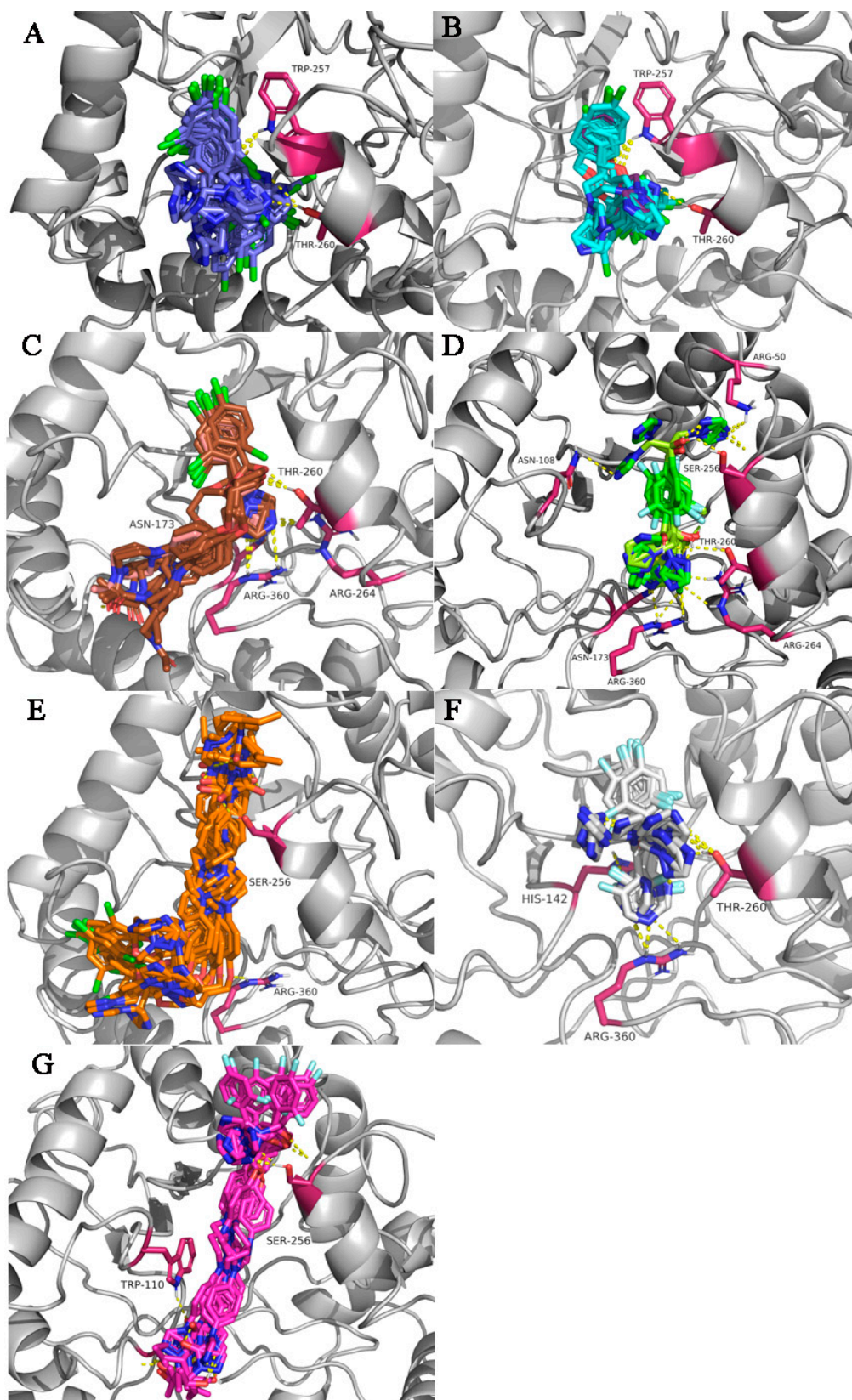


Figure S10 The hydrogen bonds between the azoles and the residues in AKR7A2.
A. Miconazole, B. Econazole, C. Ketoconazole, D. Fluconazole, E. Itraconazole, F.
Voriconazole, G. Posaconazole

Table S1. Kinetic parameters of effect of voriconazole on AKR7A2 enzyme activity with SSA as a substrate

Protein/drug	Drug concentration (μM)	K_m (μM)	k_{cat} (min ⁻¹)	k_{cat}/K_m (min ⁻¹ *μM ⁻¹)	Normalized Value (k_{cat}/K_m)
AKR7A2	0	22.65 ± 1.23	74.98 ± 1.48	3.31	1.00
voriconazole	5	20.44 ± 1.63	77.83 ± 2.26	3.81*	1.15
voriconazole	20	18.99 ± 1.02	78.36 ± 1.44	4.13**	1.25
voriconazole	50	17.30 ± 0.88	79.54 ± 1.33	4.60***	1.39

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. The data represents the mean ±SD of at least three replicates and were analyzed by GraphPad Prism 8.0.