Figure S1. Training set and text set for pharmacophore model generation.

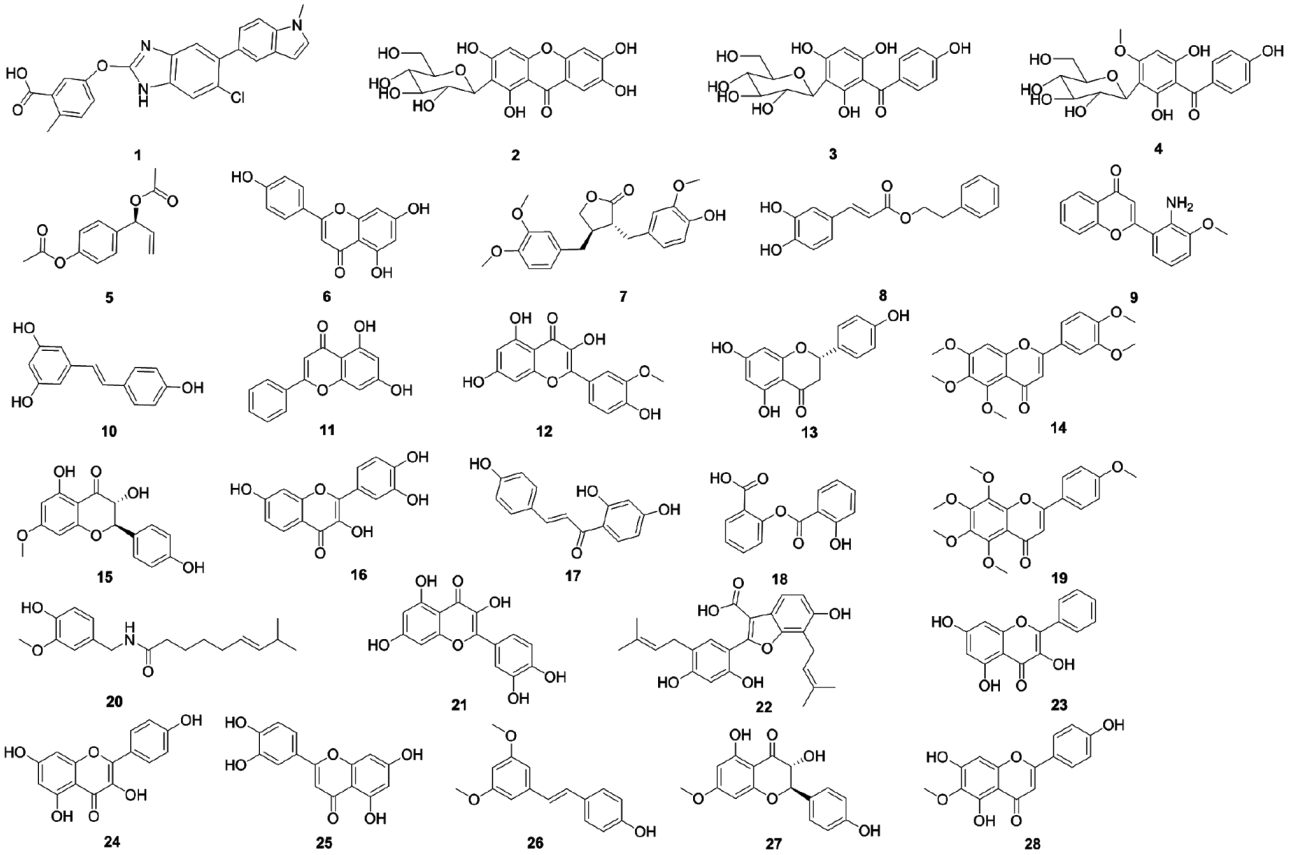

Figure S2. Top list of hit compounds (score value >50 kcal/mol).

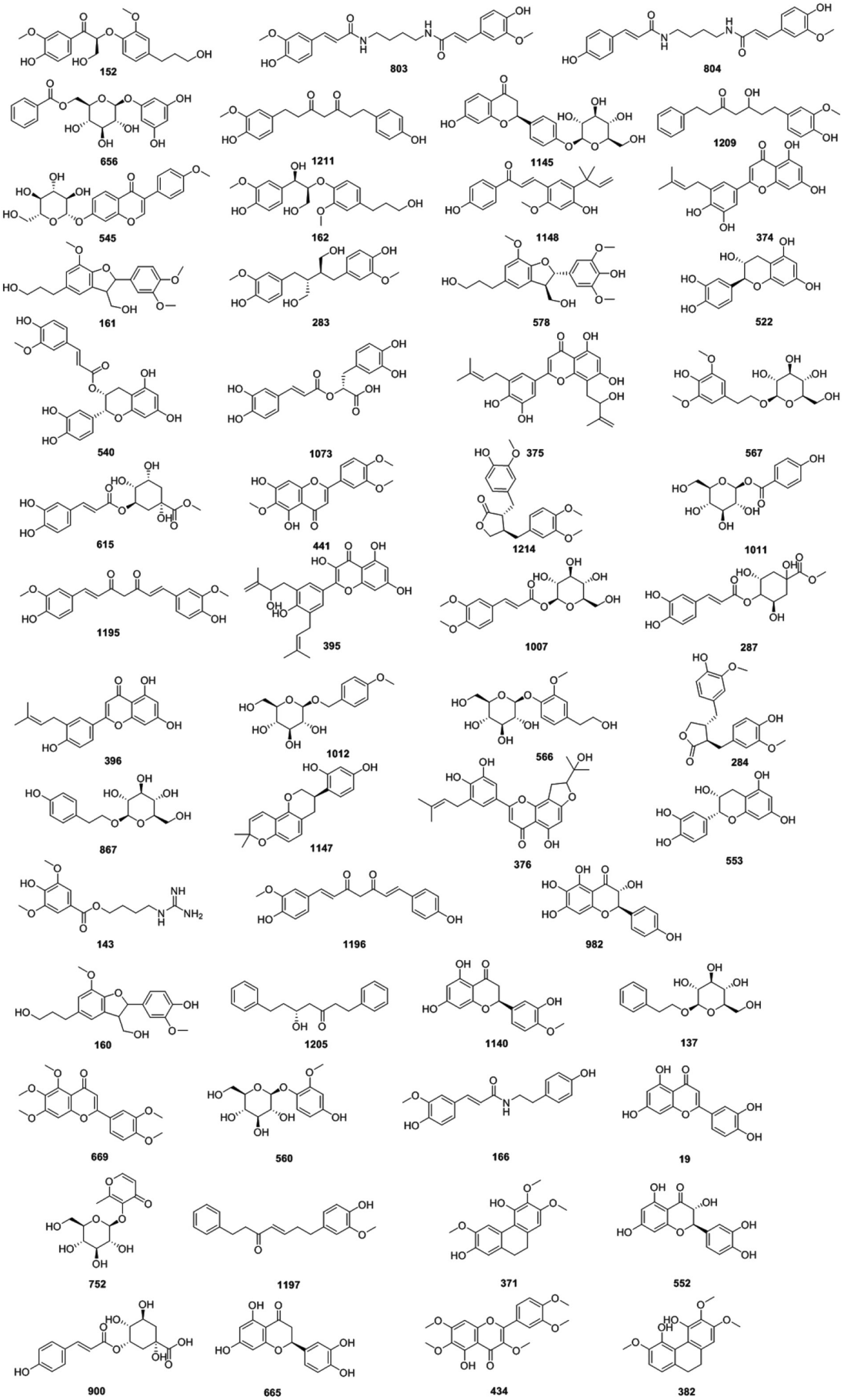

Table SI. Training set and text set for pharmacophore model generation.

| First author, year | Compound no. | (Refs.) |
|---|---|---|
| Xiao *et al*, 2013 | 1[a,b] | (1) |
| Zhang *et al*, 2013 | 2[a] | (2) |
| Zhang *et al*, 2013 | 3[a] | (2) |
| Zhang *et al*, 2013 | 4[a] | (2) |
| Yaku *et al*, 2013 | 5[a] | (3) |
| Huang *et al*, 2015 | 6[a] | (4) |
| Han *et al*, 2016 | 7[a] | (5) |
| Yu *et al*, 2011 | 8[a] | (6) |
| Castilla-Madrigal *et al*, 2017 | 9[a] | (7) |
| Gu *et al*, 2018 | 10[a] | (8) |
| Choi *et al*, 2016 | 11[a] | (9) |
| Dong *et al*, 2014 | 12[a] | (10) |
| Nyane *et al*, 2017 | 13[*] | (11) |
| Yong *et al*, 2015 | 14[a] | (12) |
| Zhang *et al*, 2010 | 15[c] | (13) |
| Yong *et al*, 2015 | 16[a] | (12) |
| Zhang *et al*, 2013 | 17[a] | (14) |
| Smith *et al*, 2016 | 18[a] | (15) |
| Yong *et al*, 2015 | 19[c] | (12) |
| Medina-Contreras *et al*, 2017 | 20[c] | (16) |
| Krishnamoorthy *et al*, 2017 | 21[c] | (17) |
| Nguyen *et al*, 2010 | 22[c] | (18) |
| Song *et al*, 2017 | 23[c] | (19) |
| Varshney *et al*, 2018 | 24[c] | (20) |
| Jiménez-Sánchez *et al*, 2017 | 25[c] | (21) |
| Ko *et al*, 2015 | 26[c] | (22) |
| Zhang *et al*, 2010 | 27[c] | (13) |
| Wang *et al*, 2015 | 28[c] | (23) |

[a]Training set, [b]Initial ligand 991 in 4CFE; [c]Test set.

Table SII. Generated ten pharmacophore models.

| No. | Features | Rank | Direct Hit | Partial Hit | Max fit |
|---|---|---|---|---|---|
| 01 | ZHH | 112.738 | 111111111111111111 | 000000000000000000 | 3 |
| 02 | ZHH | 112.738 | 111111111111111111 | 000000000000000000 | 3 |
| 03 | RHH | 111.642 | 111111111011111111 | 000000000100000000 | 3 |
| 04 | RHH | 108.762 | 111111111111111111 | 000000000000000000 | 3 |
| 05 | RHH | 108.762 | 111111111111111111 | 000000000000000000 | 3 |
| 06 | RHH | 101.295 | 111111111011111111 | 000000000100000000 | 3 |
| 07 | RHH | 101.258 | 111111111011111111 | 000000000100000000 | 3 |
| 08 | RHH | 101.258 | 111111111011111111 | 000000000100000000 | 3 |
| 09 | RHH | 100.404 | 111111111011111111 | 000000000100000000 | 3 |
| 10 | ZHH | 99.149 | 111111111111111111 | 000000000000000000 | 3 |

Z, hydrophobic region feature; H, hydrogen bond acceptor lipid; R, ring aromatic.

Table SIII. Top list of hit compounds (score value >50 kcal/mol).

| Compound no. | Compound name | CDOCKER interaction energy, kcal/mol | Formula | PubChem CID/CAS no. |
|---|---|---|---|---|
| 152 | Acotarin D | 64.2332 | $C_{20}H_{24}O_7$ | 2306174-08-1 |
| 803 | (E,E)-Terrestribisamide | 63.872 | $C_{24}H_{28}N_2O_{26}$ | 5321825 |
| 804 | N-p-Coumaroyl-N'-feruloylputrescine | 60.2194 | $C_{23}H_{26}N_2O_5$ | 44241259 |
| 656 | 6'-Benzoate phloroglucinol 1-β-D-glucopyranoside | 59.2064 | $C_{19}H_{20}O_9$ | 2407648-32-0 |
| 1211 | Demethoxycurcumin | 58.5833 | $C_{20}H_{18}O_5$ | 5469424 |
| 1145 | Liquiritin | 57.6091 | $C_{21}H_{22}O_9$ | 503737 |
| 1209 | 5-Hydroxy-7-(4-hydroxy-3-methoxyphenyl)-1-phenyl-3-heptanone | 57.2732 | $C_{20}H_{24}O_4$ | 5318228 |
| 545 | Ononin | 56.276 | $C_{22}H_{22}O_9$ | 442813 |
| 162 | 7S,8R-Erythro-4,7,9,9'-tetrahydroxy-3,3'-dimethoxy-8-O-4'-neolignan | 56.1007 | $C_{20}H_{26}O_7$ | 13893597 |
| 1148 | Licochalcone-A | 55.7685 | $C_{21}H_{22}O_4$ | 5318998 |
| 374 | Epimedokoreanin D | 55.6196 | $C_{20}H_{18}O_6$ | 5315125 |
| 161 | 3-[2-(3,4-Dimethoxyphenyl)-3-(hydroxymethyl)-7-methoxy-2,3-dihydrobenzofuran-5-yl]-1-propanol | 55.1088 | $C_{21}H_{26}O_6$ | 4639677 |
| 283 | (-)-Secoisolariciresinol | 55.0016 | $C_{20}H_{26}O_6$ | 11552274 |
| 578 | (7S,8R)-3,3',5-trimethoxy-4',7-epoxy-8,5'-neolignan-4,9,9'-triol | 54.7096 | $C_{21}H_{26}O_7$ | 56838440 |
| 522 | (-)-Catechin | 54.2336 | $C_{15}H_{14}O_6$ | 73160 |
| 540 | Malaferin C | 54.1877 | $C_{25}H_{22}O_9$ | 71596193 |
| 1073 | Rosmarinic acid | 54.0327 | $C_{18}H_{16}O_8$ | 5281792 |
| 375 | 2-[3,4-Dihydroxy-5-(3-methylbut-2-enyl)phenyl]-5,7-dihydroxy-8-(2-hydroxy-3-methylbut-3-enyl)chromen-4-one | 53.9136 | $C_{25}H_{26}O_7$ | 131676094 |
| 567 | 2-(4-Hydroxy-3,5-dimethoxyphenyl)ethyl-β-D-glucopyranoside | 53.9011 | $C_{16}H_{24}O_9$ | 76308955 |
| 615 | Methyl 5-O-caffeoylquinic acid methyl ester | 53.8888 | $C_{17}H_{20}O_9$ | 6476139 |
| 441 | 5,7-Dihydroxy-3',4',6-trimethoxyflavone | 53.8865 | $C_{19}H_{19}O_7$ | 5273755 |
| 1214 | Arctigenin | 53.7069 | $C_{21}H_{24}O_6$ | 64981 |
| 1011 | p-Hydroxybenzoyl-β-D-glucopyranoside | 53.6545 | $C_{13}H_{16}O_8$ | 14132342 |
| 1195 | Curcumin | 53.6135 | $C_{21}H_{20}O_6$ | 969516 |
| 395 | 3'-(2-Hydroxy-3-methyl-3-butenyl)-4',3,5,7-tetrahydroxy-5'-prenylflavone | 53.1348 | $C_{25}H_{26}O_7$ | 1812887-75-4 |
| 1007 | 3,4-Dimethoxycinnamyl-β-D-glucopyranoside | 52.7184 | $C_{17}H_{22}O_9$ | 21581586 |
| 287 | 4-O-Caffeoylquinic acid methyl ester | 52.6425 | $C_{17}H_{20}O_9$ | 71720840 |
| 396 | 3'-Prenylnaringenin | 52.5223 | $C_{20}H_{18}O_5$ | 5315396 |
| 1012 | 4-Methoxybenzyl-β-D-glucopyranoside | 52.4808 | $C_{14}H_{20}O_7$ | 10685601 |
| 566 | 3-Methoxyphenethyl-alcohol-4-O-β-D-glucopyranoside | 52.2909 | $C_{15}H_{22}O_8$ | 23815379 |
| 284 | (-)-Arctigenin | 52.1262 | $C_{20}H_{22}O_6$ | 119205 |
| 867 | Salidreoside | 52.0402 | $C_{14}H_{20}O_7$ | 159278 |
| 1147 | Glabridin | 52.023 | $C_{20}H_{20}O_4$ | 124052 |
| 376 | 2-(3,4-Dihydroxy-5-(3-methylbut-2-en-1-yl)phenyl)-5-hydroxy-8-(2-hydroxypropan-2-yl)-8,9-dihydro-4H-furo[2,3-h]chromen-4-one | 51.9827 | $C_{25}H_{26}O_7$ | 2196202-19-2 |
| 553 | (-)-Epicatechin | 51.8918 | $C_{15}H_{14}O_6$ | 72276 |
| 143 | Leonurine | 51.8901 | $C_{14}H_{21}N_3O_5$ | 161464 |
| 1196 | Desmethoxy curcumin | 51.6991 | $C_{20}H_{18}O_5$ | 5469424 |
| 982 | (2R,3R)-3,5,6,7,4'-Pentahydroxyflavanonol | 51.6525 | $C_{15}H_{12}O_7$ | 101353295 |
| 160 | Dihydrodehydrodiconiferyl alcohol | 51.4808 | $C_{20}H_{24}O_6$ | 4365980 |
| 1205 | (R)-5-Hydroxy-1,7-diphenyl-3-heptanone | 51.4631 | $C_{19}H_{22}O_2$ | 46213118 |
| 1140 | Hesperidin | 51.3406 | $C_{16}H_{14}O_6$ | 72281 |
| 137 | Phenethyl-β-D-glucopyranoside | 51.1543 | $C_{14}H_{20}O_6$ | 11289099 |
| 669 | 5,6,7,3',4'-Pentamethoxyflavone | 51.1409 | $C_{20}H_{20}O_7$ | 145659 |

Table SIII. Continued.

| Compound no. | Compound name | CDOCKER interaction energy, kcal/mol | Formula | PubChem CID/CAS no. |
|---|---|---|---|---|
| 560 | Isotachioside | 51.1143 | $C_{13}H_{18}O_8$ | 15098566 |
| 166 | N-trans ferulic acid casein amide | 51.0104 | $C_{18}H_{19}NO_4$ | 5280537 |
| 19 | Luteolin | 51.0005 | $C_{15}H_{10}O_6$ | 5280445 |
| 752 | 2-Methyl-3-O-β-D-glucopyranosyl-pyran-4-one | 50.6335 | $C_{12}H_{16}O_8$ | 5316639 |
| 1197 | 7-(4"-Hydroxy-3"-methoxyphenyl)-1-phenyl-4E-heptene-3-one | 50.5732 | $C_{20}H_{22}O_3$ | 5318278 |
| 371 | 3,6,7-Trimethoxy-9,10-dihydrophenanthrene-2,5-diol | 50.5535 | $C_{17}H_{18}O_5$ | 14135385 |
| 552 | (+)-Taxifolin | 50.2719 | $C_{15}H_{12}O_7$ | 439533 |
| 900 | 3-O-Trans-coumaroylquinic acid | 50.2104 | $C_{16}H_{18}O_8$ | 11078262 |
| 665 | 2S-Eriodictyol | 50.1198 | $C_{15}H_{12}O_6$ | 440735 |
| 434 | Artemetin | 50.0462 | $C_{20}H_{20}O_8$ | 5320351 |
| 382 | 4,5-Phenanthrenediol, 9,10-dihydro-2,3,6-trimethoxy-9,10-Dihydrophenanthrene | 50.0364 | $C_{17}H_{18}O_5$ | 25141334 |

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