# Virtual screening campaigns and ADMET evaluation to unlock the potency of flavonoids from *Erythrina* as 3CL$^{pro}$ SARS-COV-2 inhibitors

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Tabel S1. Binding energy values based on virtual screening

| Group I | Compound Name | Binding Energy (kcal/mol) |
|---|---|---|
| | **Flavones** | |
| 1 | 6-Prenylapigenin | -8.76 |
| 2 | Luteolin | -7.79 |
| 3 | Vogelin C | -8.01 |
| 4 | Vogelin J | -9.53 |
| 5 | Carpachromene | -8.81 |
| 6 | Atalantoflavone (Limonianin) | -9.32 |
| 7 | Neocyclomorusin | -10.99 |
| 8 | Salvigenin | -8.05 |
| 9 | Tetramethylisoscutellarein | -7.98 |
| 10 | Sinensetin | -7.65 |
| 11 | Vitexin | -11.27 |
| 12 | Isovitexin | -9.66 |
| 13 | Isovitexin-2″-β-D-glucopyranoside | -4.02 |
| 14 | Apigenin-7-O-rhamnosyl-6-C-glucoside | -10.89 |
| 15 | Vicenin-1 | -11.79 |
| 16 | Vicenin-2 | -10.9 |
| 17 | Isoorientin | -9.73 |
| 18 | Diosmetin-6-C-glucoside | -9.58 |
| **Group II** | **Flavonols** | **Binding Energy (kcal/mol)** |
| 19 | 3,7,4′-Trihydroxyflavone | -8.81 |
| 20 | Kaempferol-3-O-(2″-O-β-D-glucopyranosyl-6″-O-α-L-rhamnopyranosyl-β-D-glucopyranoside) | -13.23 |
| 21 | Kaempferol-3-O-β-Dglucopyranosyl- (1 → 2)-β-D-glucopyranoside | -6.78 |
| **Group III** | **Flavanones** | **Binding Energy (kcal/mol)** |
| 22 | Liquiritigenin | -8.28 |
| 23 | Isobavachin | -9.14 |
| 24 | Glabrol | -9.96 |
| 25 | Erythribyssin K | -8.45 |

| | | |
|---|---|---|
| 26 | Liquiritigenin-5′-O-methyl ether | -8.35 |
| 27 | 7,3′,4′-Trihydroxyflavanone | -8.5 |
| 28 | 5′-(2-Hydroxy-3-methylbut-3-enyl) abyssinone II | -10.88 |
| 29 | 7-Hydroxy-4′-methoxy-3′-(3- hydroxy-3-methyl-trans-but-1-enyl)-5′-(3-methylbut-2-enyl) flavanone | -11.22 |
| 30 | Abyssinone I | -8.77 |
| 31 | Abyssinone II | -9.28 |
| 32 | Abyssinone III | -10.43 |
| 33 | Abyssinone IV | -10.63 |
| 34 | Abyssinone-IV-4′-O-methyl ether | -10.37 |
| 35 | Erylatissin C | -8.8 |
| 36 | 5-Deoxyabyssinin II | -9.88 |
| 37 | 7-Hydroxy-4′-methoxy-3′-(3- methylbut-2-enyl) flavanone | -9.3 |
| 38 | 2(S)-5′,7-Dihydroxy-[2″,2″-(3″- hydroxy)-dimethylpyrano]-(5″,6″:3′,4′)flavanone | -9.0 |
| 39 | 2(S)-5′,7-Dihydroxy-[2″,2″-(3″- hydroxy)-dimethylpyrano]-(5″,6″:3′,4′)flavanone | -9.2 |
| 40 | Erythribyssin G | -10.58 |
| 41 | Erythribyssin I | -8.86 |
| 42 | Erylivingstone I | -7.97 |
| 43 | Naringenin | -8.43 |
| 44 | Isosakuranetin | -8.38 |
| 45 | Eriodictyol | -8.67 |
| 46 | Homohesperetin | -8.97 |
| 47 | 3′-Prenylnaringenin | -9.7 |
| 48 | Licoflavanone-4′-O-methyl ether | -9.49 |
| 49 | Abyssinone V | -10.9 |
| 50 | Abyssinone-V-4'-O-methyl ether | -10.56 |
| 51 | 6-Prenylabyssinone V | -11.23 |
| 52 | Iespedezaflavanone B (Euchrestaflavanone A) | -10.3 |
| 53 | 5-Hydroxysophoranone | -10.7 |
| 54 | Burttinonedehydrate | -10.84 |
| 55 | Burttinone | -11.34 |

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|---|---|---|
| 56 | Erycaffra D | -11.42 |
| 57 | Erycaffra F | -11.93 |
| 58 | Sigmoidin A | -11.38 |
| 59 | Sigmoidin B | -9.63 |
| 60 | 3′-O-Methylsigmoidin | -9.55 |
| 61 | 4′-O-Methylsigmoidin | -10.25 |
| 62 | Sigmoidin C | -9.04 |
| 63 | Sigmoidin D | -8.84 |
| 64 | Sigmoidin E | -10.09 |
| 65 | Sigmoidin F | -10.62 |
| 66 | Sigmoidin G | -9.23 |
| 67 | 2(S)-5,5′,7-Trihydroxy-2′-prenyl- (2″,2″-dimethylpyrano)-(5″,6″:3′,4′) flavanone | -11.15 |
| 68 | 2(S)-5,5′,7-Trihydroxy- [2″(5″- hydroxy)-methylpyrano]- (5′′,6″:3′,4′)flavanone | -9.47 |
| 69 | 2(S)-5,7-Dihydroxy-3′-methoxy- [2″(5″-hydroxy)-methylpyrano]- (5″,6″:3′,4′) flavanone | -9.7 |
| 70 | 2(S)-5,7-Dihydroxy-[(5″,6″:3′,4′)- (2″,2″-dimethylpyrano)-(5‴,6‴:5′,6′)]-(2‴,2‴- dimethylpyrano)flavanone | -10.27 |
| 71 | Erysenegalone (Erythrisenegalone) | -10.53 |
| 72 | Citflavanone | -9.45 |
| 73 | Lonchocarpol A (Senegalensein) | -11.19 |
| 74 | Lonchocarpol C | -11.75 |
| 75 | Lonchocarpol D | -11.21 |
| 76 | Lupinifolin | -10.49 |
| 77 | Fuscaflavanones A1 | -10.84 |
| 78 | Fuscaflavanones A2 | -10.95 |
| 79 | Fuscaflavanones B | -10.41 |
| 80 | Abyssinin I | -8.89 |
| 81 | Abyssinoflavanone II (Abyssinin II) | -9.38 |
| 82 | Abyssinin III | -10.42 |
| 83 | Abyssinoflavanone IV | -10.61 |
| 84 | Abyssinoflavanone V | -8.66 |
| 85 | Abyssinoflavanone VI | -10.11 |

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|---|---|---|
| 86 | Abyssinoflavanone VII | -10.84 |
| 87 | 2(S)-5′-(2-Hydroxy-3-methylbut-3-enyl)licoflavone-4′-O-methyl ether | -10.73 |
| 88 | 2(S)-5,7-Dihydroxy-5′-prenyl- [2″,2″-(3″-hydroxy)-dimethylpyrano]-(5″,6″:3′,4′) flavanone | -10.36 |
| 89 | 2(S)-5,7-Dihydroxy-5′-methoxy- [2″,2″-(3″-hydroxy)-dimethylpyrano]-(5″,6″:3′,4′) flavanone | -9.48 |
| 90 | 2(S)-5,7-Dihydroxy- [2″,2″-(3″,4″-dihydroxy)-dimethylpyrano]-(5″,6″:3′,4′) flavanone | -9.68 |
| 91 | 2(S)-5,7-Dihydroxy-5′-prenyl [2″,2″-(3″,4″-dihydroxy)-dimethylpyrano]-(5″,6″:3′,4′) flavanone | -10.45 |
| 92 | 2(S)-5,5′,7-Dihydroxy-6′-prenyl [2″,2″-(3″,4″-dihydroxy)-dimethylpyrano]-(5″,6″:3′,4′) flavanone | -11.2 |
| 93 | 2(S)-5,5′,7-Trihydroxy-[2″,2″-(4″-chromanone)-dimethylpyrano]-(5″,6″:3′,4′) flavanone | -9.24 |
| 94 | (2S)-5,7-Dihydroxy-5′-prenyl-2″-(4″-hydroxyisopropyl)-dihydrofurano [1″,3″:3′,4′] flavanone | -10.72 |
| 95 | (2S)-5,7-Dihydroxy-5′-methoxy-2″- (4″-hydroxyisopropyl)-dihydrofurano [1″,3″:3′,4′] flavanone | -9.3 |
| 96 | (2S)-5,7,5′-Trihydroxy-2″-(4″-hydroxyisopropyl)-dihydrofurano [1″,3″:3′,4′] flavanone | -9.61 |
| 97 | (2S)-5,7-Dihydroxy-5′-prenyl-2″- (4″-hydroxyisopropyl)- 3″-hydroxy-dihydrofurano [1″,3″:3′,4′] flavanone | -10.76 |
| 98 | (2S)-5,7,5′-Trihydroxy-2″-(4″-hydroxyisopropyl)-3″-hydroxy-dihydrofurano [1″,3″:3′,4′] flavanone | -9.69 |
| 99 | (2S)-5,7,5′-Trihydroxy-6′-prenyl-2″-(4″-hydroxyisopropyl)-3′′- hydroxy-dihydrofurano [1″,3″:4′,5′] flavanone | -11.13 |
| 100 | Addisoniaflavanone I | -11.04 |
| 101 | Addisoniaflavanone II | -11.55 |
| 102 | Addisoniaflavanone III | |
| 103 | 5,7-Dihydroxy-3′,4′-dimethoxy-5′-(3-methylbut-2-enyl) flavanone | -9.45 |
| 104 | Erylivingstone A | -8.79 |
| 105 | Erylivingstone B | -9.32 |
| 106 | Erylivingstone C | -10.1 |
| 107 | Erylivingstone D | -10.12 |
| 108 | Erylivingstone E | -9.6 |
| 109 | Erylivingstone F | -10.13 |

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|---|---|---|
| 110 | Erylivingstone G | -9.07 |
| 111 | Erylivingstone H | -9.34 |
| 112 | Hamiltone A | -8.39 |
| 113 | 6-Methoxyhamiltone A | -7.78 |
| **Group IV** | **Chalcones** | **Binding Energy (kcal/mol)** |
| 114 | Isobavachalcone | -9.58 |
| 115 | Isoliquiritigenin | -8.63 |
| 116 | Licoagrochalcone A | -9.22 |
| 117 | Abyssinone VI | -10.81 |
| 118 | Abyssinone-VI-4-O-methyl ether | -10.34 |
| 119 | Butein | -8.9 |
| 120 | 3-O-Methylbutein | -8.47 |
| 121 | 5-Prenylbutein | -9.7 |
| 122 | Abyssinone A | -9.07 |
| 123 | Abyssinone B | -9.76 |
| 124 | Abyssinone C | -9.47 |
| 125 | Abyssinone D | -9.42 |
| 126 | 2,4,4'-Trihydroxychalcone | -8.74 |
| 127 | 6′-Hydroxy-2′,3′,4′,4-tetramethoxychalcone | -7.45 |
| **Group V** | **Isoflavans** | **Binding Energy (kcal/mol)** |
| 128 | Eryzerin C | -11.42 |
| 129 | 4′,7-Dihydroxy-2′-methoxy-3′-(3-methylbut-2-enyl) isoflavan | -11.49 |
| 130 | Eryzerin D | -10.54 |
| 131 | Eryzerin C | -9.28 |
| 132 | Eryvarin T | -8.29 |
| 133 | Erythribidin A | -9.38 |
| 134 | Phaseollinisoflavan | -9.34 |
| 135 | 2′-Methoxyphaseollinisoflavan | -8.76 |
| 136 | Erylivingstone J | -9.53 |
| 137 | Erylivingstone K | -9.32 |
| 138 | 2′,7-Dihydroxy-3′ -(3-methylbut-2- enyl)-2‴,2‴-dimethylpyrano [5″,6″:4′,5′] isoflavan | -10.21 |

| Group VI | Isoflav-3-enes | Binding Energy (kcal/mol) |
|---|---|---|
| 139 | Erypoegin A (Burttinol C) | -9.44 |
| 140 | Erypoegin B (Burttinol B) | -8.95 |
| 141 | Burttinol A | -9.1 |
| 142 | 7,4′-Dihydroxy-2′,5′-dimethoxyisoflav-3-ene | -8.45 |
| 143 | Bidwillol A | -9.08 |
| 144 | Eryvarin H | -8.46 |
| 145 | Eryvarin I | -8.85 |
| 146 | Eryvarin O | -9.45 |
| **Group VII** | **Isoflavanones** | **Binding Energy (kcal/mol)** |
| 147 | Vestitone | -8.14 |
| 148 | Eriotrichin B (Bidwillon A) | -10.52 |
| 149 | Prostratol C | -9.3 |
| 150 | Erythribyssin E | -9.23 |
| 151 | Erythribyssin J | -9.75 |
| 152 | Orientanol D | -9.9 |
| 153 | Orientanol F | -10.43 |
| 154 | 5,2',4'-Trihydroxy-6-prenyl-2‴,2‴dimethyldihydropyrano[5‴,6‴] isoflavanone | -10.36 |
| 155 | 5-Deoxyglasperin F | -9.07 |
| 156 | 5-Deoxylicoisoflavanones | -9.11 |
| 157 | Sigmoidin H | -9.33 |
| 158 | Sigmoidin I | -9.38 |
| 159 | Sigmoidin J | -9.42 |
| 160 | Bidwillon B | -11.32 |
| 161 | 2,3-Dihydro-2′-hydroxyneobavaisoflavanone | -9.41 |
| 162 | Eryvellutinone | -9.97 |
| 163 | Eryzerin A | -11.01 |
| 164 | Eryvarin B | -11.58 |
| 165 | Eryvarin M | -8.02 |
| 166 | Eryvarin N | -9.33 |
| 167 | Eryvarin V | -10.64 |

| | | |
|---|---|---|
| 168 | Eryzerin B | -11.93 |
| 169 | Erycaffra E | -9.26 |
| 170 | 5,7-Dihydroxy-2′,4′,5′trimethoxyisoflavanone | -7.93 |
| 171 | Orientanol E | -12.04 |
| 172 | 2,3-Dihydro-2′-hydroxyosajin | -11.17 |
| 173 | Erythraddison III | -9.22 |
| 174 | Erythraddison IV | -9.42 |
| 175 | 2,3-Dihydropratensein | -9.35 |
| 176 | 5,7,3′-Trihydroxy-4′-methoxy-6,5′di(γ,γ-dimethylallyl) isoflavanone | -10.55 |
| 177 | (R)-saclenone | -8.58 |
| 178 | 5,3′-Dihydroxy-4′-methoxy-5′-γ,γ-dimethylallyl-2′′,2′′-dimethylpyrano[5,6:6,7] isoflavanone | -9.9 |
| 179 | 5,3′-Dihydroxy-2′′,2′′-dimethylpyrano-[5,6:6,7]-2′′′,2′′′-dimethylpyrano [5,6:5,4] isoflavanone | -9.73 |
| 180 | 2,3-Dihydroauriculatin | -11.3 |
| 181 | 5,4-Dihydroxy-2-methoxy-8-(3,3- dimethylallyl)-2,2-dimethylpyrano [5,6:6,7] isoflavanone | -10.9 |
| 182 | Glyasperin F | -9.24 |
| 183 | Licoisoflavanones | -9.11 |
| 184 | Vogelin A (Lysisteisoflavanone) | -9.37 |
| 185 | Erypoegin C (Vogelin B) | -9.41 |
| 186 | Erypoegin D | -9.2 |
| 187 | Erypoegin G | -9.22 |
| 188 | Vogelin D | -10.44 |
| 189 | Auriculatin 4'-O-glucoside | -11.62 |
| **Group VIII** | **Isoflavones** | **Binding Energy (kcal/mol)** |
| 190 | Daidzein | -7.73 |
| 191 | 8-Prenyldaidzein | -9.74 |
| 192 | Neobavaisoflavone | -8.66 |
| 193 | Erysubin F | -10.78 |
| 194 | Eryvarin S | -11.58 |
| 195 | Erythraddison II | -11.74 |
| 196 | 2′,7-Dihydroxy-4′-methoxy-5′-(3-methylbut-2-enyl) | -9.33 |

| | | |
|---|---|---|
| | isoflavone | |
| 197 | Calycosin | -7.91 |
| 198 | 5-Deoxy-3'-prenylbiochanin A | -9.02 |
| 199 | Erylatissin A | -9.14 |
| 200 | Erylatissin B | -9.52 |
| 201 | Corylin | -9.1 |
| 202 | Bidwillon C | -9.07 |
| 203 | Erythrinin A | -8.67 |
| 204 | Genistein | -8.1 |
| 205 | 6-Hydroxygenistein | -8.26 |
| 206 | 6,8-Diprenylgenistein | -11.97 |
| 207 | Wighteone (Erythrinin B) (6-Prenylgenistein) | -9.78 |
| 208 | Lupiwighteone (8-Prenylgenistein) | -10.21 |
| 209 | Isowighteone (3′-Isoprenylgenistein) | -9.0 |
| 210 | Isolupabigenin | -11.23 |
| 211 | 6,8-Diprenylorobol | -12.18 |
| 212 | 3′-O-Methylorobol | -8.11 |
| 213 | 5,4′-Dihydroxy-7-methoxy-3′-(3-methylbuten-2-yl) isoflavone | -9.02 |
| 214 | 5,2′,4′-Trihydroxy-7-methoxy-5′-(3-methylbuten-2-yl) isoflavone | -9.22 |
| 215 | Cajanin | -8.15 |
| 216 | 3′-Formyl-5,4′-dihydroxy-7- methoxyisoflavone | -8.24 |
| 217 | 5,4′-Dihydroxy-7-methoxy-3′-(3-methyl-2-hydroxybuten-3-yl) isoflavone | -8.74 |
| 218 | 5-Hydroxy-3′′-hydroxy-2′′,2′′-dimethyldihydropyrano [5′′,6′′:3′,4′] isoflavone | -9.17 |
| 219 | 4′-Hydroxy-5,7-dimethoxyisoflavone | -8.24 |
| 220 | Vogelin E | -9.37 |
| 221 | Vogelin F | -9.47 |
| 222 | Vogelin G | -11.29 |
| 223 | Ficuisoflavone | -9.24 |
| 224 | 5′-Prenylpratensein | -9.22 |
| 225 | 3′-(3-Methylbut-2-enyl) biochanin | -9.03 |

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|---|---|---|
| 226 | Piscerythrinetin | -9.02 |
| 227 | 2′-Hydroxy-5′-methoxybiochanin A | -8.24 |
| 228 | 5′-Formylpratensein | -8.32 |
| 229 | 5,7-Dihydroxy-4′-methoxy-3′-(2,3-dihydroxy-3-methylbutyl) isoflavone | -9.22 |
| 230 | Schliebenone A | -9.21 |
| 231 | Schliebenone B | -8.95 |
| 232 | Schliebenone C | -9.52 |
| 233 | 5,4'-Dimethoxy-3'-prenylbiochanin A | -8.93 |
| 234 | Laburnetin | -9.36 |
| 235 | Indicanine D | -9.31 |
| 236 | Alpinumisoflavone | -8.99 |
| 237 | 4-O-Methylalpinumisoflavone | -8.58 |
| 238 | 5,4′-Dimethoxy alpinumisoflavone | -8.48 |
| 239 | Indicanine C | -8.8 |
| 240 | Indicanine E | -9.37 |
| 241 | Parvisoflavone B | -9.6 |
| 242 | Warangalone (Scandenone) | -11.3 |
| 243 | Auriculasin | -11.4 |
| 244 | Auriculatin | -11.15 |
| 245 | Warangalone 4′-O-methyl ether | -10.64 |
| 246 | Robustone | -8.56 |
| 247 | M-Wi-2 | -9.15 |
| 248 | Erythgianin A | -9.85 |
| 249 | 4′,7-Dihydroxy-2′′,2′′- dimethylpyrano [5′′,6′′:5,6] isoflavone | -9.89 |
| 250 | Osajin | -10.08 |
| 251 | Derrone | -8.9 |
| 252 | Isoderrone | -8.98 |
| 253 | Isochandalon | -9.77 |
| 254 | Erysubin A | -9.79 |
| 255 | Erysubin B | -9.51 |
| 256 | 5,4′-Dihydroxy-2′-methoxy-8-(3,3- dimethylallyl)-2′′,2′′-dimethylpyrano [5,6:6,7] isoflavone | -11.62 |

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|---|---|---|
| 257 | 5,7,4′-Trihydroxy-6-(3″,3″-dimethylallyloxiranylmethyl) isoflavone | -10.71 |
| 258 | Erymildbraedin A | -9.61 |
| 259 | 5,4-Dihydroxy-8-(3,3- dimethylallyl)-2-methoxyisopropylfurano [4,5:6,7] isoflavone | -11.81 |
| 260 | Erymildbraedin B | -11.84 |
| 261 | Erysenegalensein D | -11.78 |
| 262 | Erysenegalensein E | -11.83 |
| 263 | Isoerysenegalensein E (Lysisteisoflavone) | -11.73 |
| 264 | Erysenegalensein F | -11.03 |
| 265 | Erysenegalensein G | -11.03 |
| 266 | Erysenegalensein K | -10.35 |
| 267 | Erysenegalensein L | -10.65 |
| 268 | Erysenegalensein M | -10.82 |
| 269 | Erysenegalensein N | -11.78 |
| 270 | Erysenegalensein O | -9.93 |
| 271 | 5,7,4′-Trihydroxy-6-(2″-hydroxy3″-methylbut-3″enyl) isoflavone | -9.83 |
| 272 | Erypoegin K | -9.81 |
| 273 | Senegalensin | -11.9 |
| 274 | Erythrinin C | -9.75 |
| 275 | Hydroxyerythrinin C | -9.83 |
| 276 | 8-Prenylerythrinin C (Isosenegalensein) (Euchrenone b10) | -11.67 |
| 277 | Vogelin H | -12.15 |
| 278 | Vogelin I | -11.56 |
| 279 | Eriotriochin | -11.88 |
| 280 | Erythraddison I | -11.33 |
| 281 | Panchovillin | -8.29 |
| 282 | 7-Demethylrobustigenin | -7.86 |
| 283 | 7-O-Methylluteone | -9.56 |
| 284 | 2,3-Dehydrokievitone | -10.07 |
| 285 | 8-Prenylluteone | -11.7 |
| 286 | 4′-Hydroxyisoflavone-7-O-β-D-glucopyranoside | -10.2 |

| | | |
|---|---|---|
| 287 | 4′-Hydroxyisoflavone-7-O-α-L-rhamnosyl/ (1 →6)-β-ᴅ-glucopyranoside | -11.31 |
| 288 | Derriscanoside B | -3.21 |
| **Group IX** | **Pterocarpans** | **Binding Energy (kcal/mol)** |
| 289 | Demethylmedicarpin | -7.51 |
| 290 | Sophorapterocarpan A (Homoedudiol) | -8.63 |
| 291 | Phaseollidin | -8.55 |
| 292 | 1-Methoxy phaseollidin | -8.58 |
| 293 | Erythrabyssin II | -10.07 |
| 294 | 1-Methoxyerythrabyssin II | -10.29 |
| 295 | Calopocarpin | -9.25 |
| 296 | 3,9-Dihydroxy-4-prenylpterocarpan | -8.78 |
| 297 | Eryvarin J | -10.14 |
| 298 | Eryvarin K | -8.76 |
| 299 | Erythribyssin B | -7.57 |
| 300 | Erythribyssin C | -9.2 |
| 301 | Medicarpin | -7.57 |
| 302 | Sandwicensin | -8.61 |
| 303 | Erycristin | -10.12 |
| 304 | 3-Hydroxy-10-(3-hydroxy-3-methylbutyl)-9-methoxypterocarpan | -8.83 |
| 305 | 3-Hydroxy-10-(2,3-dihydroxy-3-methylbutyl)-9-methoxypterocarpan | -9.02 |
| 306 | Dolichins A and B | -8,74 |
| 307 | Erybraedin A | -9.48 |
| 308 | Erybraedin B | -9.38 |
| 309 | Erybraedin C | -8.83 |
| 310 | Erybraedin D | -8.84 |
| 311 | Erybraedin E | -8.74 |
| 312 | Erybraedin F | -7.78 |
| 313 | Erystagallin C | -9.62 |
| 314 | Erylysin A | -9.72 |
| 315 | Erylysin B | -8.92 |

| | | |
|---|---|---|
| 316 | Erylysin C | -9.79 |
| 317 | Shinpterocarpin | -8.54 |
| 318 | Orientanol B | -8.24 |
| 319 | Orientanol C | -9.39 |
| 320 | Neorautenol | -9.2 |
| 321 | Isoneorautenol | -9.07 |
| 322 | 8-Methoxyneorautenol | -7.87 |
| 323 | Phaseollin | -8.78 |
| 324 | Folitenol | -9.9 |
| 325 | Erythribyssin L | -9.63 |
| 326 | Erythribyssin D | -9.21 |
| 327 | Erythribyssin M | -9.21 |
| 328 | Erysubin C | -7.7 |
| 329 | Erysubin D | -10.3 |
| 330 | Fuscacarpan A | -9.37 |
| **Group X** | **6α-Hydroxypterocarpans** | **Binding Energy (kcal/mol)** |
| 331 | Cristacarpin (Erythrabissin I) | -9.2 |
| 332 | Erystagallin A | -10.06 |
| 333 | Demethylerystagallin A | -10.24 |
| 334 | Erystagallin B | -10.26 |
| 335 | Eryzerin E | -9.54 |
| 336 | Fuscacarpan B | -8.64 |
| 337 | Fuscacarpan C | -8.63 |
| 338 | Erypoegin I | -9.17 |
| 339 | Erypoegin J | -9.68 |
| 340 | Orientanol A | -9.28 |
| 341 | Erysubin E | -8.83 |
| 342 | Eryvarin A | -8.88 |
| 343 | Erythribyssin A | -9.79 |
| 344 | Hydroxycristacarpone | -9.91 |
| **Group XI** | **Pterocarpenes** | **Binding Energy (kcal/mol)** |
| 345 | Erycristagallin | -9.64 |

| | | |
|---|---|---|
| 346 | Erypoegin E | -9.08 |
| 347 | Erypoegin H | -9.81 |
| 348 | Eryvarin D | -9.56 |
| 349 | Eryvarin E | -9.73 |
| 350 | Eryvarin W | -10.49 |
| 351 | Erythribyssin O | -9.15 |
| **Group XII** | **Coumestans** | **Binding Energy (kcal/mol)** |
| 352 | Coumasterol | -7.89 |
| 353 | 4-Hydroxycoumasterol | -8.15 |
| 354 | Sigmoidin K | -9.73 |
| 355 | Isosojagol | -9.88 |
| 356 | Erythribyssin N | -9.57 |
| **Group XIII** | **3-Arylcoumarins** | **Binding Energy (kcal/mol)** |
| 357 | Indicanine A | -8.58 |
| 358 | Indicanine B | -9.21 |
| 359 | Robustic acid | -8.57 |
| **Group XIV** | **Coumaronochromones** | **Binding Energy (kcal/mol)** |
| 360 | Erysenegalensein J | -10.35 |
| **Group XV** | **2-Arylbenzofurans** | **Binding Energy (kcal/mol)** |
| 361 | Latissimbenzofuran | -7.56 |
| 362 | 2-(5′-Hydroxy-3″-methoxyphenyl)- 6-hydroxy-5-methoxybenzofuran | 8.69 |
| 363 | Vignafuran | -7.86 |
| 364 | Eryvarin L | -7.61 |
| 365 | Eryvarin P | -7.65 |
| 366 | Eryvarin Q | -8.79 |
| 367 | Eryvarin U | -8.53 |
| 368 | Glyinflanin H | -8.71 |
| 369 | Burttinol D | -9.21 |
| 370 | Erypoegin F | -8.83 |
| 371 | Erythribyssin F | -9.34 |
| 372 | 2′-O-Demethylbidwillol B | -9.37 |

| | | |
|---|---|---|
| 373 | Addisofuran A | -9.44 |
| 374 | Addisofuran B | -9.07 |
| 375 | Kanzonol U (Glabrocoumarone A) | -8.65 |
| **Group XVI** | **3-Aryl-2,3-dihydrobenzofurans** | **Binding Energy (kcal/mol)** |
| 376 | Erythribyssin H | -7.5 |
| 377 | Eryvarin R | -7.81 |
| **Group XVII** | **Biflavonoids** | **Binding Energy (kcal/mol)** |
| 378 | Bis-Sigmodiol | -11.49 |

Table S2. swissADME

| Compound No | Compound | Molecular weight | Hydrogen Bond acceptor | Hydrogen Bond donor | Mlogp | Violation | Druglikeness |
|---|---|---|---|---|---|---|---|
| 7 | Neocyclomorusin | 436.45 | 7 | 3 | 1.37 | 0 | Yes |
| 11 | Vitexin | 431.37 | 10 | 6 | -2.25 | 0 | Yes |
| 14 | Apigenin-7-O-rhamnosyl-6-C-glucoside | 562.25 | 13 | 9 | -3.29 | 3 | No |
| 15 | Vicenin-1 | 562.25 | 13 | 9 | -3.29 | 3 | No |
| 16 | Vicenin-2 | 578.52 | 14 | 10 | -4.04 | 3 | No |
| 20 | Kaempferol-3-O-(2′′-O-β-ᴅ-glucopyranosyl-6′′-O-α-L-rhamnopyranosyl-β-ᴅ-glucopyranoside) | 756.6 | 20 | 12 | -5.49 | 3 | No |
| 28 | 5′-(2-Hydroxy-3-methylbut-3-enyl) abyssinone II | 408.49 | 5 | 3 | 2.55 | 0 | Yes |
| 29 | 7-Hydroxy-4′-methoxy-3′-(3- hydroxy-3-methyl-trans-but-1- enyl)-5′-(3-methylbut-2-enyl) flavanone | 422.51 | 6 | 5 | 2.76 | 0 | Yes |
| 32 | Abyssinone III | 390.47 | 4 | 1 | 3.38 | 0 | Yes |
| 33 | Abyssinone IV | 392.49 | 4 | 2 | 3.38 | 0 | Yes |
| 34 | Abyssinone-IV-4′-O-methyl ether | 406.51 | 4 | 1 | 3.59 | 0 | Yes |
| 40 | Erythribyssin G | 408.49 | 5 | 2 | 2.63 | 0 | Yes |
| 49 | Abyssinone V | 392.49 | 4 | 2 | 3.38 | 0 | Yes |
| 50 | Abyssinone-V-4'-O-methyl ether | 422.51 | 5 | 2 | 3.03 | 0 | Yes |
| 51 | 6-Prenylabyssinone V | 476.60 | 5 | 3 | 3.74 | 0 | Yes |
| 52 | Iespedezaflavanone B (Euchrestaflavanone A) | 408.49 | 5 | 3 | 2.82 | 0 | Yes |

| Compound No | Compound | Molecular weight | Hydrogen Bond acceptor | Hydrogen Bond donor | Mlogp | Violation | Druglikeness |
|---|---|---|---|---|---|---|---|
| 53 | 5-Hydroxysophoranone | 476.60 | 5 | 3 | 3.74 | 0 | Yes |
| 54 | Burttinonedehydrate | 438.51 | 6 | 3 | 2.21 | 0 | Yes |
| 55 | Burttinone | 438.51 | 6 | 3 | 2.21 | 0 | Yes |
| 56 | Erycaffra D | 454.51 | 7 | 4 | 1.41 | 0 | Yes |
| 57 | Erycaffra F | 454.51 | 7 | 4 | 1.41 | 0 | Yes |
| 58 | Sigmoidin A | 424.49 | 6 | 4 | 2.28 | 0 | Yes |
| 61 | 4′-O-Methylsigmoidin | 370.40 | 6 | 3 | 1.50 | 0 | Yes |
| 64 | Sigmoidin E | 406.47 | 5 | 2 | 2.82 | 0 | Yes |
| 65 | Sigmoidin F | 422.47 | 6 | 3 | 2.28 | 0 | Yes |
| 67 | 2(S)-5,5′,7-Trihydroxy-2′-prenyl- (2′′,2′′-dimethylpyrano)- (5′′,6′′:3′,4′) flavanone | 422.47 | 6 | 3 | 2.28 | 0 | Yes |
| 70 | 2(S)-5,7-Dihydroxy-[(5′′,6′′:3′,4′)- (2′′,2′′-dimethylpyrano)- (5′′′,6′′′:5′,6′)]-(2′′′,2′′′-dimethylpyrano)flavanone | 420.45 | 6 | 2 | 2.28 | 0 | Yes |
| 71 | Erysenegalone (Erythrisenegalone) | 406.47 | 5 | 2 | 2.82 | 0 | Yes |
| 73 | Lonchocarpol A (Senegalensein) | 408.49 | 5 | 3 | 2.82 | 0 | Yes |
| 74 | Lonchocarpol C | 408.49 | 5 | 2 | 2.90 | 0 | Yes |
| 75 | Lonchocarpol D | 424.49 | 6 | 3 | 2.08 | 0 | Yes |
| 76 | Lupinifolin | 420.50 | 5 | 2 | 3.03 | 0 | Yes |
| 77 | Fuscaflavanones A1 | 422.47 | 6 | 2 | 2.41 | 0 | Yes |

| Compound No | Compound | Molecular weight | Hydrogen Bond acceptor | Hydrogen Bond donor | Mlogp | Violation | Druglikeness |
|---|---|---|---|---|---|---|---|
| 78 | Fuscaflavanones A2 | 422.47 | 6 | 2 | 2.41 | 0 | Yes |
| 79 | Fuscaflavanones B | 420.45 | 6 | 2 | 2.01 | 0 | Yes |
| 82 | Abyssinin III | 420.45 | 6 | 2 | 2.01 | 0 | Yes |
| 83 | Abyssinoflavanone IV | 382.41 | 6 | 3 | 1.72 | 0 | Yes |
| 85 | Abyssinoflavanone VI | 366.41 | 5 | 2 | 2.26 | 0 | Yes |
| 86 | Abyssinoflavanone VII | 424.49 | 6 | 4 | 2.01 | 0 | Yes |
| 87 | 2(S)-5′-(2-Hydroxy-3-methylbut-3-enyl)licoflavone-4′-O-methyl ether | 438.51 | 6 | 3 | 2.21 | 0 | Yes |
| 88 | 2(S)-5,7-Dihydroxy-5′-prenyl- [2′′,2′′-(3′′-hydroxy)-dimethylpyrano]-(5′′,6′′:3′,4′) flavanone | 424.49 | 6 | 3 | 2.08 | 0 | Yes |
| 92 | 2(S)-5,5′,7-Dihydroxy-6′-prenyl [2′′,2′′-(3′′,4′′-dihydroxy)-dimethylpyrano]-(5′′,6′′:3′,4′) flavanone | 456.49 | 8 | 5 | 0.76 | 0 | Yes |
| 97 | (2S)-5,7-Dihydroxy-5′-prenyl-2′′- (4′′-hydroxyisopropyl)- 3′′-hydroxy-dihydrofurano [1′′,3′′:3′,4′] flavanone | 440.49 | 7 | 4 | 1.28 | 0 | Yes |
| 99 | (2S)-5,7,5′-Trihydroxy-6′-prenyl-2′′-(4′′-hydroxyisopropyl)-3′′- hydroxy-dihydrofurano [1′′,3′′:4′,5′] flavanone | 456.49 | 8 | 5 | 0.76 | 0 | Yes |
| 100 | Addisoniaflavanone I | 424.49 | 6 | 3 | 2.08 | 0 | Yes |
| 101 | Addisoniaflavanone II | 442.50 | 7 | 5 | 1.28 | 0 | Yes |
| 117 | Abyssinone VI | 392.49 | 4 | 3 | 3.70 | 0 | Yes |
| 118 | Abyssinone-VI-4-O-methyl ether | 406.51 | 4 | 2 | 3.90 | 0 | Yes |

| Compound No | Compound | Molecular weight | Hydrogen Bond acceptor | Hydrogen Bond donor | Mlogp | Violation | Druglikeness |
|---|---|---|---|---|---|---|---|
| 128 | Eryzerin C | 394.50 | 4 | 3 | 3.73 | 0 | Yes |
| 129 | 4′,7-Dihydroxy-2′-methoxy-3′-(3-methylbut-2-enyl) isoflavan | 340.41 | 4 | 2 | 2.95 | 0 | Yes |
| 130 | Eryzerin D | 392.49 | 4 | 2 | 3.73 | 0 | Yes |
| 138 | 2′,7-Dihydroxy-3′ -(3-methylbut-2- enyl)-2‴,2‴-dimethylpyrano [5″,6″:4′,5′] isoflavan | 392.49 | 4 | 2 | 3.73 | 0 | Yes |
| 148 | Eriotrichin B (Bidwillon A) | 354.40 | 5 | 3 | 2.04 | 0 | Yes |
| 153 | Orientanol F | 368.42 | 5 | 2 | 2.26 | 0 | Yes |
| 154 | 5,2',4'-Trihydroxy-6-prenyl-2‴,2‴dimethyldihydropyrano[5‴,6‴] isoflavanone | 368.42 | 5 | 2 | 2.26 | 0 | Yes |
| 160 | Bidwillon B | 406.47 | 5 | 2 | 2.82 | 0 | Yes |
| 163 | Eryzerin A | 408.49 | 5 | 3 | 2.82 | 0 | Yes |
| 164 | Eryvarin B | 422.51 | 5 | 2 | 3.03 | 0 | Yes |
| 167 | Eryvarin V | 422.47 | 6 | 3 | 2.01 | 0 | Yes |
| 168 | Eryzerin B | 408.49 | 5 | 2 | 2.63 | 0 | Yes |
| 171 | Orientanol E | 424.49 | 6 | 4 | 2.28 | 0 | Yes |
| 172 | 2,3-Dihydro-2′-hydroxyosajin | 422.47 | 6 | 3 | 2.28 | 0 | Yes |
| 176 | 5,7,3′-Trihydroxy-4′-methoxy-6,5′di(γ,γ-dimethylallyl) isoflavanone | 438.51 | 6 | 3 | 2.48 | 0 | Yes |
| 180 | 2,3-Dihydroauriculatin | 422.47 | 6 | 3 | 2.28 | 0 | Yes |

| Compound No | Compound | Molecular weight | Hydrogen Bond acceptor | Hydrogen Bond donor | Mlogp | Violation | Druglikeness |
|---|---|---|---|---|---|---|---|
| 181 | 5,4-Dihydroxy-2-methoxy-8-(3,3- dimethylallyl)-2,2-dimethylpyrano [5,6:6,7] isoflavanone | 436.50 | 6 | 2 | 2.48 | 0 | Yes |
| 188 | Vogelin D | 422.51 | 5 | 2 | 3.03 | 0 | Yes |
| 189 | Auriculatin 4'-O-glucoside | 584.61 | 11 | 6 | -0.03 | 3 | No |
| 193 | Erysubin F | 390.47 | 4 | 2 | 3.20 | 0 | Yes |
| 194 | Eryvarin S | 390.47 | 4 | 2 | 3.20 | 0 | Yes |
| 195 | Erythraddison II | 406.47 | 5 | 3 | 2.64 | 0 | Yes |
| 206 | 6,8-Diprenylgenistein | 406.47 | 5 | 3 | 2.64 | 0 | Yes |
| 208 | Lupiwighteone (8-Prenylgenistein) | 338.35 | 5 | 3 | 1.64 | 0 | Yes |
| 210 | Isolupabigenin | 422.47 | 6 | 4 | 2.09 | 0 | Yes |
| 211 | 6,8-Diprenylorobol | 422.47 | 6 | 4 | 2.09 | 0 | Yes |
| 222 | Vogelin G | 422.47 | 6 | 3 | 1.90 | 0 | Yes |
| 242 | Warangalone (Scandenone) | 404.46 | 5 | 2 | 2.64 | 0 | Yes |
| 243 | Auriculasin | 420.45 | 6 | 3 | 2.09 | 0 | Yes |
| 244 | Auriculatin | 420.45 | 6 | 3 | 2.09 | 0 | Yes |
| 245 | Warangalone 4′-O-methyl ether | 418.48 | 5 | 1 | 2.84 | 0 | Yes |
| 256 | 5,4′-Dihydroxy-2′-methoxy-8-(3,3-dimethylallyl)-2″,2″- dimethylpyrano [5,6:6,7] isoflavone | 420.45 | 6 | 3 | 1.83 | 0 | Yes |
| 257 | 5,7,4′-Trihydroxy-6-(3″,3″-dimethylallyloxiranylmethyl) isoflavone | 408.44 | 6 | 3 | 4.61 | 0 | Yes |

| Compound No | Compound | Molecular weight | Hydrogen Bond acceptor | Hydrogen Bond donor | Mlogp | Violation | Druglikeness |
|---|---|---|---|---|---|---|---|
| 259 | 5,4-Dihydroxy-8-(3,3- dimethylallyl)-2-methoxyisopropylfurano [4,5:6,7] isoflavone | 434.48 | 6 | 2 | 1.96 | 0 | Yes |
| 260 | Erymildbraedin B | 418.44 | 6 | 2 | 1.76 | 0 | Yes |
| 261 | Erysenegalensein D | 438.47 | 7 | 5 | 1.29 | 0 | Yes |
| 262 | Erysenegalensein E | 422.47 | 6 | 4 | 1.83 | 0 | Yes |
| 263 | Isoerysenegalensein E (Lysisteisoflavone) | 422.47 | 6 | 4 | 1.83 | 0 | Yes |
| 264 | Erysenegalensein F | 436.45 | 7 | 3 | 1.37 | 0 | Yes |
| 265 | Erysenegalensein G | 420.45 | 6 | 2 | 1.90 | 0 | Yes |
| 266 | Erysenegalensein K | 378.37 | 6 | 3 | 1.39 | 0 | Yes |
| 267 | Erysenegalensein L | 436.45 | 7 | 4 | 1.29 | 0 | Yes |
| 268 | Erysenegalensein M | 420.45 | 6 | 3 | 1.83 | 0 | Yes |
| 269 | Erysenegalensein N | 438.47 | 7 | 5 | 1.29 | 0 | Yes |
| 273 | Senegalensin | 422.47 | 6 | 3 | 1.90 | 0 | Yes |
| 276 | 8-Prenylerythrinin C (Isosenegalensein) (Euchrenone b10) | 422.47 | 6 | 3 | 1.90 | 0 | Yes |
| 277 | Vogelin H | 422.47 | 6 | 3 | 1.90 | 0 | Yes |
| 278 | Vogelin I | 438.47 | 7 | 4 | 1.1 | 0 | Yes |
| 279 | Eriotriochin | 464.55 | 6 | 3 | 2.23 | 0 | Yes |
| 280 | Erythraddison I | 468.50 | 8 | 4 | 0.51 | 0 | Yes |
| 285 | 8-Prenylluteone | 422.47 | 6 | 4 | 2.09 | 0 | Yes |

| Compound No | Compound | Molecular weight | Hydrogen Bond acceptor | Hydrogen Bond donor | Mlogp | Violation | Druglikeness |
|---|---|---|---|---|---|---|---|
| 286 | 4′-Hydroxyisoflavone-7-O-β-D-glucopyranoside | 416.38 | 9 | 5 | -1.11 | 0 | Yes |
| 287 | 4′-Hydroxyisoflavone-7-O-α-L-rhamnosyl/ (1 → 6)-β-D-glucopyranoside | 430.40 | 9 | 4 | -0.89 | 0 | Yes |
| 294 | 1-Methoxyerythrabyssin II | 422.51 | 5 | 2 | 3.37 | 0 | Yes |
| 329 | Erysubin D | 422.60 | 5 | 2 | 2.59 | 0 | Yes |
| 333 | Demethylerystagallin A | 408.49 | 5 | 3 | 2.90 | 0 | Yes |
| 334 | Erystagallin B | 438.51 | 6 | 3 | 2.56 | 0 | Yes |
| 350 | Eryvarin W | 390.47 | 4 | 2 | 3.58 | 0 | Yes |
| 360 | Erysenegalensein J | 436.45 | 7 | 3 | 1.88 | 0 | Yes |
| 378 | Bis-Sigmodiol | 680.74 | 10 | 4 | 1.85 | 1 | Yes |

Table S3. pkCSM absorption

| Compound No | Compound | Water solubility | Caco2 permeability | Intestinal absorption (human) | P-glycoprotein substrate | P-glycoprotein I inhibitor | P-glycoprotein II inhibitor |
|---|---|---|---|---|---|---|---|
| 7 | Neocyclomorusin | -4.312 | 1.253 | 100 | Yes | No | Yes |
| 11 | Vitexin | -3.422 | 0.582 | 64.706 | Yes | No | No |
| 14 | Apigenin-7-O-rhamnosyl-6-C-glucoside | -2.905 | -0.372 | 41.287 | Yes | No | No |
| 15 | Vicenin-1 | -2.917 | -0.184 | 34.82 | Yes | No | No |
| 16 | Vicenin-2 | -2.913 | -0.272 | 25.193 | Yes | No | No |
| 20 | Kaempferol-3-O-(2′′-O-β-D-glucopyranosyl-6′′-O-α-L-rhamnopyranosyl-β-D-glucopyranoside) | -2.889 | -0.599 | 3.141 | Yes | No | No |
| 28 | 5′-(2-Hydroxy-3-methylbut-3-enyl) abyssinone II | -4.647 | 0.929 | 91.765 | Yes | Yes | Yes |
| 29 | 7-Hydroxy-4′-methoxy-3′-(3- hydroxy-3-methyl-trans-but-1- enyl)-5′-(3-methylbut-2-enyl) flavanone | -5.66 | 1.026 | 91.129 | Yes | Yes | Yes |
| 32 | Abyssinone III | -6.081 | 1.724 | 93.715 | Yes | Yes | Yes |
| 33 | Abyssinone IV | -5.307 | 0.981 | 90.944 | Yes | Yes | Yes |
| 34 | Abyssinone-IV-4′-O-methyl ether | -5.851 | 1.553 | 93.436 | Yes | Yes | Yes |
| 40 | Erythribyssin G | -4.601 | 1.056 | 93.298 | Yes | Yes | Yes |
| 49 | Abyssinone V | -5.307 | 0.981 | 90.944 | Yes | Yes | Yes |
| 50 | Abyssinone-V-4'-O-methyl ether | -5.144 | 1.039 | 92.151 | Yes | Yes | Yes |
| 51 | 6-Prenylabyssinone V | -4.843 | 1.086 | 89.344 | Yes | Yes | Yes |
| 52 | Iespedezaflavanone B (Euchrestaflavanone A) | -4.71 | 0.949 | 91.198 | Yes | Yes | Yes |
| 53 | 5-Hydroxysophoranone | -4.826 | 1.115 | 89.945 | Yes | Yes | Yes |

| Compound No | Compound | Water solubility | Caco2 permeability | Intestinal absorption (human) | P-glycoprotein substrate | P-glycoprotein I inhibitor | P-glycoprotein II inhibitor |
|---|---|---|---|---|---|---|---|
| 54 | Burttinonedehydrate | -4.816 | 0.627 | 78.576 | Yes | Yes | Yes |
| 55 | Burttinone | -4.886 | 0.551 | 76.712 | Yes | Yes | Yes |
| 56 | Erycaffra D | -4.698 | 0.614 | 70.795 | Yes | Yes | Yes |
| 57 | Erycaffra F | -4.783 | 0.54 | 68.915 | Yes | Yes | Yes |
| 58 | Sigmoidin A | -3.629 | 1.19 | 83.931 | Yes | Yes | No |
| 61 | 4′-O-Methylsigmoidin | -4.11 | 0.545 | 80.286 | Yes | Yes | No |
| 64 | Sigmoidin E | -4.992 | 1.017 | 92.43 | Yes | Yes | Yes |
| 65 | Sigmoidin F | -4.463 | 1.409 | 87.274 | Yes | Yes | No |
| 67 | 2(S)-5,5′,7-Trihydroxy-2′-prenyl- (2″,2″-dimethylpyrano)- (5″,6″:3′,4′) flavanone | -4.478 | 1.247 | 87.406 | Yes | Yes | No |
| 70 | 2(S)-5,7-Dihydroxy-[(5″,6″:3′,4′)- (2″,2″-dimethylpyrano)- (5‴,6‴:5′,6′)]-(2‴,2‴-dimethylpyrano) flavanone | -4.248 | 1.233 | 92.875 | Yes | Yes | No |
| 71 | Erysenegalone (Erythrisenegalone) | -4.804 | 1.14 | 90.369 | Yes | Yes | Yes |
| 73 | Lonchocarpol A (Senegalensein) | -4.818 | 1.028 | 89.393 | Yes | Yes | Yes |
| 74 | Lonchocarpol C | -4.953 | 1.214 | 91.778 | Yes | Yes | Yes |
| 75 | Lonchocarpol D | -4.832 | 1.107 | 89.418 | Yes | Yes | No |
| 76 | Lupinifolin | -5.012 | 1.159 | 91.852 | Yes | Yes | Yes |
| 77 | Fuscaflavanones A1 | -4.996 | 1.237 | 92.417 | Yes | Yes | Yes |
| 78 | Fuscaflavanones A2 | -4.996 | 1.237 | 92.417 | Yes | Yes | Yes |
| 79 | Fuscaflavanones B | -4.982 | 1.193 | 92.025 | Yes | Yes | No |

| Compound No | Compound | Water solubility | Caco2 permeability | Intestinal absorption (human) | P-glycoprotein substrate | P-glycoprotein I inhibitor | P-glycoprotein II inhibitor |
|---|---|---|---|---|---|---|---|
| 82 | Abyssinin III | -3.919 | 0.666 | 83.229 | Yes | No | No |
| 83 | Abyssinoflavanone IV | -4.306 | 1.305 | 84.348 | Yes | Yes | No |
| 85 | Abyssinoflavanone VI | -4.537 | 0.996 | 93.811 | Yes | Yes | No |
| 86 | Abyssinoflavanone VII | -4.03 | 0.756 | 74.367 | Yes | Yes | No |
| 87 | 2(S)-5′-(2-Hydroxy-3-methylbut-3-enyl)licoflavone-4′-O-methyl ether | -5.029 | 0.799 | 78.873 | Yes | Yes | Yes |
| 88 | 2(S)-5,7-Dihydroxy-5′-prenyl- [2″,2″-(3″-hydroxy)-dimethylpyrano]-(5″,6″:3′,4′) flavanone | -4.455 | 1.56 | 83.644 | Yes | Yes | No |
| 92 | 2(S)-5,5′,7-Dihydroxy-6′-prenyl [2″,2″-(3″,4″-dihydroxy)-dimethylpyrano]-(5″,6″:3′,4′) flavanone | -3.863 | 0.491 | 65.684 | Yes | Yes | No |
| 97 | (2S)-5,7-Dihydroxy-5′-prenyl-2″- (4″-hydroxyisopropyl)- 3″-hydroxy-dihydrofurano [1′ ′,3″:3′,4′] flavanone | -4.225 | 1.345 | 78.313 | Yes | Yes | No |
| 99 | (2S)-5,7,5′-Trihydroxy-6′-prenyl-2″-(4″-hydroxyisopropyl)-3″- hydroxy-dihydrofurano [1′ ′,3″:4′,5′] flavanone | -3.856 | 0.521 | 70.676 | Yes | Yes | No |
| 100 | Addisoniaflavanone I | -4.006 | 0.922 | 84.521 | Yes | Yes | No |
| 101 | Addisoniaflavanone II | -3.729 | 0.526 | 66.635 | Yes | Yes | No |
| 117 | Abyssinone VI | -4.331 | 0.985 | 89.902 | Yes | Yes | Yes |
| 118 | Abyssinone-VI-4-O-methyl ether | -4.487 | 1.031 | 92.834 | Yes | Yes | Yes |
| 128 | Eryzerin C | -4.087 | 0.936 | 92.806 | Yes | Yes | Yes |
| 129 | 4′,7-Dihydroxy-2′-methoxy-3′-(3- methylbut-2- | -4.108 | 1.552 | 93.133 | Yes | Yes | No |

| Compound No | Compound | Water solubility | Caco2 permeability | Intestinal absorption (human) | P-glycoprotein substrate | P-glycoprotein I inhibitor | P-glycoprotein II inhibitor |
|---|---|---|---|---|---|---|---|
| | enyl) isoflavan | | | | | | |
| 130 | Eryzerin D | -4.787 | 1.447 | 94.445 | Yes | Yes | Yes |
| 138 | 2′,7-Dihydroxy-3′ -(3-methylbut-2- enyl)-2′′′,2′′′-dimethylpyrano [5′′,6′′:4′,5′] isoflavan | -4.468 | 1.322 | 91.914 | Yes | Yes | Yes |
| 148 | Eriotrichin B (Bidwillon A) | -4.1 | 1.078 | 93.843 | Yes | Yes | No |
| 153 | Orientanol F | -4.269 | 1.041 | 97.095 | Yes | Yes | Yes |
| 154 | 5,2',4'-Trihydroxy-6-prenyl-2′′′,2′′′dimethyldihydropyrano[5′′′,6′′′] isoflavanone | -4.217 | 1.117 | 95.822 | Yes | Yes | Yes |
| 160 | Bidwillon B | -4.58 | 1.157 | 95.253 | Yes | Yes | Yes |
| 163 | Eryzerin A | -4.417 | 1.01 | 92.962 | Yes | Yes | Yes |
| 164 | Eryvarin B | -4.546 | 1.014 | 92.723 | Yes | Yes | Yes |
| 167 | Eryvarin V | -4.349 | 1.299 | 82.085 | Yes | Yes | No |
| 168 | Eryzerin B | -4.378 | 1.074 | 95.494 | Yes | Yes | Yes |
| 171 | Orientanol E | -3.813 | 0.771 | 78.202 | Yes | Yes | Yes |
| 172 | 2,3-Dihydro-2′-hydroxyosajin | -4.548 | 0.939 | 87.038 | Yes | Yes | No |
| 176 | 5,7,3′-Trihydroxy-4′-methoxy-6,5′di(γ,γ-dimethylallyl) isoflavanone | -4.586 | 0.583 | 73.278 | Yes | Yes | Yes |
| 180 | 2,3-Dihydroauriculatin | -4.749 | 1.108 | 87.177 | Yes | Yes | No |
| 181 | 5,4-Dihydroxy-2-methoxy-8-(3,3- dimethylallyl)-2,2-dimethylpyrano [5,6:6,7] isoflavanone | -4.994 | 1.129 | 91.775 | Yes | Yes | Yes |
| 188 | Vogelin D | -5.47 | 0.99 | 92.972 | Yes | Yes | Yes |

| Compound No | Compound | Water solubility | Caco2 permeability | Intestinal absorption (human) | P-glycoprotein substrate | P-glycoprotein I inhibitor | P-glycoprotein II inhibitor |
|---|---|---|---|---|---|---|---|
| 189 | Auriculatin 4’-O-glucoside | -3.231 | 0.194 | 41.73 | Yes | No | No |
| 193 | Erysubin F | -4.015 | 0.591 | 91.824 | Yes | Yes | Yes |
| 194 | Eryvarin S | -4.713 | 0.723 | 93.449 | Yes | Yes | Yes |
| 195 | Erythraddison II | -4.002 | 0.967 | 92.53 | Yes | Yes | Yes |
| 206 | 6,8-Diprenylgenistein | -4.49 | 0.973 | 92.116 | Yes | Yes | Yes |
| 208 | Lupiwighteone (8-Prenylgenistein) | -3.95 | 0.852 | 93.067 | Yes | No | Yes |
| 210 | Isolupabigenin | -3.043 | 0.664 | 77.554 | Yes | No | Yes |
| 211 | 6,8-Diprenylorobol | -3.705 | 0.914 | 83.215 | Yes | Yes | Yes |
| 222 | Vogelin G | -3.999 | 1.032 | 89.982 | Yes | Yes | Yes |
| 242 | Warangalone (Scandenone) | -4.353 | 1.011 | 93.257 | Yes | Yes | Yes |
| 243 | Auriculasin | -4.11 | 0.891 | 92.519 | Yes | No | Yes |
| 244 | Auriculatin | -4.077 | 0.635 | 92.655 | Yes | No | Yes |
| 245 | Warangalone 4′-O-methyl ether | -5.795 | 0.561 | 93.73 | Yes | Yes | Yes |
| 256 | 5,4′-Dihydroxy-2′-methoxy-8-(3,3-dimethylallyl)-2″,2″- dimethylpyrano [5,6:6,7] isoflavone | -4.362 | 0.833 | 91.473 | Yes | No | Yes |
| 257 | 5,7,4′-Trihydroxy-6-(3″,3″-dimethylallyloxiranylmethyl) isoflavone | -4.362 | 0.73 | 86.715 | Yes | No | Yes |
| 259 | 5,4-Dihydroxy-8-(3,3- dimethylallyl)-2-methoxyisopropylfurano [4,5:6,7] isoflavone | -4.499 | 0.909 | 100 | Yes | Yes | Yes |
| 260 | Erymildbraedin B | -4.585 | 0.785 | 98.815 | Yes | Yes | Yes |
| 261 | Erysenegalensein D | -3.345 | 0.261 | 77.997 | Yes | Yes | Yes |

| Compound No | Compound | Water solubility | Caco2 permeability | Intestinal absorption (human) | P-glycoprotein substrate | P-glycoprotein I inhibitor | P-glycoprotein II inhibitor |
|---|---|---|---|---|---|---|---|
| 262 | Erysenegalensein E | -4.001 | 0.685 | 85.088 | Yes | No | Yes |
| 263 | Isoerysenegalensein E (Lysisteisoflavone) | -3.764 | 1.132 | 79.875 | Yes | No | Yes |
| 264 | Erysenegalensein F | -4.586 | 0.992 | 96.808 | Yes | No | Yes |
| 265 | Erysenegalensein G | -4.548 | 1.372 | 100 | Yes | Yes | Yes |
| 266 | Erysenegalensein K | -3.719 | 0.694 | 97.552 | Yes | Yes | Yes |
| 267 | Erysenegalensein L | -4.034 | 1.117 | 87.345 | Yes | No | Yes |
| 268 | Erysenegalensein M | -4.141 | 1.548 | 93.961 | Yes | Yes | Yes |
| 269 | Erysenegalensein N | -3.121 | 1.022 | 72.939 | Yes | No | Yes |
| 273 | Senegalensin | -4.399 | 0.871 | 90.89 | Yes | No | Yes |
| 276 | 8-Prenylerythrinin C (Isosenegalensein) (Euchrenone b10) | -4.588 | 1.22 | 90.779 | Yes | Yes | Yes |
| 277 | Vogelin H | -4.682 | 1.204 | 93.513 | Yes | Yes | Yes |
| 278 | Vogelin I | -3.423 | 1.265 | 86.865 | Yes | Yes | Yes |
| 279 | Eriotriochin | -4.972 | 0.87 | 93.09 | Yes | Yes | Yes |
| 280 | Erythraddison I | -3.89 | 0.784 | 90.771 | Yes | Yes | Yes |
| 285 | 8-Prenylluteone | -3.639 | 0.781 | 83.519 | Yes | Yes | Yes |
| 286 | 4′-Hydroxyisoflavone-7-O-β-ᴅ-glucopyranoside | -3.303 | 0.43 | 52.734 | Yes | No | No |
| 287 | 4′-Hydroxyisoflavone-7-O-α-L-rhamnosyl/ (1 → 6)-β-ᴅ-glucopyranoside | -3.918 | 0.335 | 68.972 | Yes | No | Yes |
| 294 | 1-Methoxyerythrabyssin II | -4.891 | 1.22 | 94.091 | Yes | Yes | Yes |
| 329 | Erysubin D | -4.699 | 0.973 | 94.038 | Yes | Yes | Yes |

| Compound No | Compound | Water solubility | Caco2 permeability | Intestinal absorption (human) | P-glycoprotein substrate | P-glycoprotein I inhibitor | P-glycoprotein II inhibitor |
|---|---|---|---|---|---|---|---|
| 333 | Demethylerystagallin A | -4.279 | 0.985 | 93.66 | Yes | Yes | Yes |
| 334 | Erystagallin B | -4.546 | 1.008 | 94.573 | Yes | Yes | Yes |
| 350 | Eryvarin W | -4.364 | 0.945 | 91.728 | Yes | Yes | Yes |
| 360 | Erysenegalensein J | -4.05 | 1.038 | 70.123 | Yes | No | No |
| 378 | Bis-Sigmodiol | -3.393 | 0.211 | 100 | Yes | Yes | Yes |

Table S4. pkCSM distribution

| Compound No | Compound | VDss (human) | Fraction unbound (human) | BBB permeability | CNS permeability |
|---|---|---|---|---|---|
| 7 | Neocyclomorusin | 0.178 | 0.179 | -1.117 | -2.973 |
| 11 | Vitexin | 0.027 | 0.226 | -1.155 | -3.636 |
| 14 | Apigenin-7-O-rhamnosyl-6-C-glucoside | -0.068 | 0.199 | -1.905 | -5.224 |
| 15 | Vicenin-1 | 0.082 | 0.251 | -2.006 | -5.273 |
| 16 | Vicenin-2 | 0.061 | 0.255 | -2.122 | -5.597 |
| 20 | Kaempferol-3-O-(2′′-O-β-D-glucopyranosyl-6′′-O-α-L-rhamnopyranosyl-β-D-glucopyranoside) | -0.24 | 0.348 | -2.162 | -6.472 |
| 28 | 5′-(2-Hydroxy-3-methylbut-3-enyl) abyssinone II | 0.321 | 0.094 | -0.944 | -2.148 |
| 29 | 7-Hydroxy-4′-methoxy-3′-(3- hydroxy-3-methyl-trans-but-1- enyl)-5′-(3-methylbut-2-enyl) flavanone | -0.219 | 0.113 | -0.307 | -1.987 |
| 32 | Abyssinone III | 0.386 | 0.103 | -0.146 | -1.531 |
| 33 | Abyssinone IV | 0.316 | 0.052 | -0.48 | -1.74 |
| 34 | Abyssinone-IV-4′-O-methyl ether | -0.144 | 0.11 | -0.162 | -1.713 |
| 40 | Erythribyssin G | 0.131 | 0.177 | 0.028 | -1.888 |
| 49 | Abyssinone V | 0.316 | 0.052 | -0.48 | -1.74 |
| 50 | Abyssinone-V-4'-O-methyl ether | -0.542 | 0.078 | 0.163 | -1.938 |
| 51 | 6-Prenylabyssinone V | -0.271 | 0.003 | -0.913 | -1.717 |
| 52 | Iespedezaflavanone B (Euchrestaflavanone A) | -0.173 | 0.113 | -0.889 | -1.874 |
| 53 | 5-Hydroxysophoranone | -0.302 | 0.012 | -0.893 | -1.739 |
| 54 | Burttinonedehydrate | -0.385 | 0.109 | -1.017 | -2.948 |
| 55 | Burttinone | -0.519 | 0.087 | -1.019 | -2.867 |
| 56 | Erycaffra D | -0.316 | 0.115 | -1.143 | -3.195 |
| 57 | Erycaffra F | -0.492 | 0.094 | -1.139 | -3.091 |
| 58 | Sigmoidin A | 0.215 | 0.126 | -1.158 | -2.868 |
| 61 | 4′-O-Methylsigmoidin | -0.087 | 0.135 | -0.948 | -2.972 |

| Compound No | Compound | VDss (human) | Fraction unbound (human) | BBB permeability | CNS permeability |
|---|---|---|---|---|---|
| 64 | Sigmoidin E | 0.1 | 0.091 | 0.195 | -1.756 |
| 65 | Sigmoidin F | 0.215 | 0.143 | -1.058 | -2.78 |
| 67 | 2(S)-5,5′,7-Trihydroxy-2′-prenyl- (2″,2″-dimethylpyrano)- (5″,6″:3′,4′) flavanone | 0.176 | 0.149 | -1.034 | -2.784 |
| 70 | 2(S)-5,7-Dihydroxy-[(5″,6″:3′,4′)- (2″,2″-dimethylpyrano)- (5‴,6‴:5′,6′)]-(2‴,2‴-dimethylpyrano)flavanone | 0.014 | 0.145 | 0.106 | -2.763 |
| 71 | Erysenegalone (Erythrisenegalone) | 0.351 | 0.087 | 0.121 | -1.676 |
| 73 | Lonchocarpol A (Senegalensein) | -0.137 | 0.037 | -0.971 | -1.852 |
| 74 | Lonchocarpol C | 0.026 | 0.071 | 0.176 | -1.713 |
| 75 | Lonchocarpol D | 0.366 | 0.1 | -0.926 | -2.926 |
| 76 | Lupinifolin | 0.219 | 0.011 | -0.136 | -1.737 |
| 77 | Fuscaflavanones A1 | 0.014 | 0.026 | -0.355 | -2.778 |
| 78 | Fuscaflavanones A2 | 0.014 | 0.026 | -0.355 | -2.778 |
| 79 | Fuscaflavanones B | 0.187 | 0.104 | -0.072 | -2.85 |
| 82 | Abyssinin III | 0.064 | 0.109 | -1.127 | -2.976 |
| 83 | Abyssinoflavanone IV | 0.101 | 0.182 | -0.981 | -2.993 |
| 85 | Abyssinoflavanone VI | -0.002 | 0.112 | 0.149 | -2.046 |
| 86 | Abyssinoflavanone VII | 0.291 | 0.104 | -1.108 | -3.009 |
| 87 | 2(S)-5′-(2-Hydroxy-3-methylbut-3-enyl)licoflavone-4′-O-methyl ether | -0.404 | 0.099 | -1.031 | -2.905 |
| 88 | 2(S)-5,7-Dihydroxy-5′-prenyl- [2″,2″-(3″-hydroxy)-dimethylpyrano]-(5″,6″:3′,4′) flavanone | -0.002 | 0.141 | -0.899 | -2.932 |
| 92 | 2(S)-5,5′,7-Dihydroxy-6′-prenyl [2″,2″-(3″,4″-dihydroxy)-dimethylpyrano]-(5″,6″:3′,4′) flavanone | 0.511 | 0.082 | -1.419 | -3.346 |
| 97 | (2S)-5,7-Dihydroxy-5′-prenyl-2″- (4″-hydroxyisopropyl)- 3″-hydroxy-dihydrofurano [1′′,3″:3′,4′] flavanone | 0.135 | 0.178 | -1.157 | -3.17 |
| 99 | (2S)-5,7,5′-Trihydroxy-6′-prenyl-2″-(4″-hydroxyisopropyl)-3″- hydroxy-dihydrofurano [1′ | 0.783 | 0.119 | -1.343 | -3.34 |

| Compound No | Compound | VDss (human) | Fraction unbound (human) | BBB permeability | CNS permeability |
|---|---|---|---|---|---|
| | ′,3″:4′,5′] flavanone | | | | |
| 100 | Addisoniaflavanone I | 0.352 | 0.099 | -0.96 | -2.95 |
| 101 | Addisoniaflavanone II | 0.251 | 0.108 | -1.317 | -3.334 |
| 117 | Abyssinone VI | -0.079 | 0.061 | -0.816 | -1.958 |
| 118 | Abyssinone-VI-4-O-methyl ether | -0.439 | 0.113 | -0.42 | -1.913 |
| 128 | Eryzerin C | 0.013 | 0.039 | -0.823 | -1.873 |
| 129 | 4′,7-Dihydroxy-2′-methoxy-3′-(3- methylbut-2-enyl) isoflavan | 0.12 | 0.08 | -0.753 | -1.985 |
| 130 | Eryzerin D | 0.428 | 0 | -0.138 | -1.715 |
| 138 | 2′,7-Dihydroxy-3′ -(3-methylbut-2- enyl)-2‴,2‴-dimethylpyrano [5″,6″:4′,5′] isoflavan | 0.569 | 0.057 | -0.141 | -1.604 |
| 148 | Eriotrichin B (Bidwillon A) | 0.19 | 0.065 | -0.894 | -2.136 |
| 153 | Orientanol F | -0.219 | 0 | -0.263 | -2.133 |
| 154 | 5,2',4'-Trihydroxy-6-prenyl-2‴,2‴dimethyldihydropyrano[5‴,6‴] isoflavanone | -0.356 | 0.031 | 0.061 | -2.134 |
| 160 | Bidwillon B | 0.171 | 0.008 | -0.164 | -1.862 |
| 163 | Eryzerin A | -0.043 | 0.054 | -0.914 | -1.954 |
| 164 | Eryvarin B | -0.044 | 0.046 | 0.099 | -1.814 |
| 167 | Eryvarin V | 0.277 | 0.012 | -1.026 | -3.008 |
| 168 | Eryzerin B | -0.169 | 0.107 | -0.106 | -2.004 |
| 171 | Orientanol E | -0.009 | 0.117 | -1.109 | -2.81 |
| 172 | 2,3-Dihydro-2′-hydroxyosajin | 0.17 | 0.095 | -0.877 | -2.898 |
| 176 | 5,7,3′-Trihydroxy-4′-methoxy-6,5′di(γ,γ-dimethylallyl) isoflavanone | -0.013 | 0.031 | -1.058 | -2.64 |
| 180 | 2,3-Dihydroauriculatin | 0.058 | 0.089 | -0.94 | -2.918 |
| 181 | 5,4-Dihydroxy-2-methoxy-8-(3,3- dimethylallyl)-2,2-dimethylpyrano [5,6:6,7] isoflavanone | 0.187 | 0.005 | -0.114 | -2.632 |
| 188 | Vogelin D | -0.272 | 0 | -0.025 | -1.916 |
| 189 | Auriculatin 4’-O-glucoside | -0.041 | 0.184 | -1.443 | -4.077 |

| Compound No | Compound | VDss (human) | Fraction unbound (human) | BBB permeability | CNS permeability |
|---|---|---|---|---|---|
| 193 | Erysubin F | 0.001 | 0.087 | 0.222 | -1.601 |
| 194 | Eryvarin S | -0.071 | 0.028 | -0.101 | -1.615 |
| 195 | Erythraddison II | -0.377 | 0.042 | -1.001 | -1.81 |
| 206 | 6,8-Diprenylgenistein | -0.416 | 0.054 | -1.047 | -1.849 |
| 208 | Lupiwighteone (8-Prenylgenistein) | -0.016 | 0.166 | -1.051 | -2.101 |
| 210 | Isolupabigenin | -0.073 | 0.086 | -1.457 | -2.076 |
| 211 | 6,8-Diprenylorobol | -0.271 | 0.051 | -1.311 | -2.069 |
| 222 | Vogelin G | 0.152 | 0.068 | -1.056 | -2.08 |
| 242 | Warangalone (Scandenone) | 0.234 | 0.148 | 0.044 | -1.627 |
| 243 | Auriculasin | 0.234 | 0.06 | -1.15 | -1.866 |
| 244 | Auriculatin | 0.051 | 0.054 | -1.106 | -1.863 |
| 245 | Warangalone 4′-O-methyl ether | 0.37 | 0.009 | -0.322 | -1.611 |
| 256 | 5,4′-Dihydroxy-2′-methoxy-8-(3,3-dimethylallyl)-2″,2″- dimethylpyrano [5,6:6,7] isoflavone | 0.154 | 0.127 | -0.936 | -2.059 |
| 257 | 5,7,4′-Trihydroxy-6-(3″,3″-dimethylallyloxiranylmethyl) isoflavone | 0.081 | 0.069 | -1.11 | -2.022 |
| 259 | 5,4-Dihydroxy-8-(3,3- dimethylallyl)-2-methoxyisopropylfurano [4,5:6,7] isoflavone | -0.044 | 0.174 | -0.081 | -1.746 |
| 260 | Erymildbraedin B | 0.047 | 0.16 | -0.164 | -2.039 |
| 261 | Erysenegalensein D | -0.035 | 0.061 | -1.446 | -3.102 |
| 262 | Erysenegalensein E | -0.084 | 0.05 | -1.242 | -2.27 |
| 263 | Isoerysenegalensein E (Lysisteisoflavone) | 0.223 | 0.161 | -1.375 | -2.367 |
| 264 | Erysenegalensein F | 0.137 | 0.062 | -1.234 | -3.231 |
| 265 | Erysenegalensein G | 0.248 | 0.162 | -0.158 | -2.047 |
| 266 | Erysenegalensein K | -0.219 | 0.166 | -1.189 | -1.893 |
| 267 | Erysenegalensein L | 0.2 | 0.113 | -1.229 | -3.278 |
| 268 | Erysenegalensein M | 0.446 | 0.171 | -1.024 | -2.139 |
| 269 | Erysenegalensein N | 0.307 | 0.217 | -1.592 | -3.361 |

| Compound No | Compound | VDss (human) | Fraction unbound (human) | BBB permeability | CNS permeability |
|---|---|---|---|---|---|
| 273 | Senegalensin | 0.172 | 0.089 | -0.906 | -2.125 |
| 276 | 8-Prenylerythrinin C (Isosenegalensein) (Euchrenone b10) | 0.229 | 0.132 | -0.963 | -2.148 |
| 277 | Vogelin H | 0.291 | 0.129 | -1.026 | -2.166 |
| 278 | Vogelin I | 0.327 | 0.184 | -1.389 | -3.431 |
| 279 | Eriotriochin | 0.087 | 0.144 | -1.006 | -2.303 |
| 280 | Erythraddison I | 0.218 | 0.096 | -1.345 | -3.553 |
| 285 | 8-Prenylluteone | -0.342 | 0.104 | -1.256 | -2.039 |
| 286 | 4′-Hydroxyisoflavone-7-O-β-D-glucopyranoside | -0.641 | 0.08 | -1.239 | -4.092 |
| 287 | 4′-Hydroxyisoflavone-7-O-α-L-rhamnosyl/ (1→6)-β-D-glucopyranoside | -0.526 | 0.106 | -1.485 | -4.023 |
| 294 | 1-Methoxyerythrabyssin II | -0.392 | 0.055 | 0.18 | -1.725 |
| 329 | Erysubin D | 0.175 | 0.166 | -0.105 | -2.211 |
| 333 | Demethylerystagallin A | 0.157 | 0 | -0.691 | -1.882 |
| 334 | Erystagallin B | 0.259 | 0 | -0.904 | -2.684 |
| 350 | Eryvarin W | -0.033 | 0.116 | -0.51 | -1.44 |
| 360 | Erysenegalensein J | 1.082 | 0.039 | -1.005 | -2.93 |
| 378 | Bis-Sigmodiol | -0.992 | 0.347 | -1.578 | -3.059 |

Table S5. pkCSM metabolism

| Compound No | Compound | CYP2D6 substrate | CYP3A4 substrate | CYP1A2 inhibitor | CYP2C19 inhibitor | CYP2C9 inhibitor | CYP2D6 inhibitor | CYP3A4 inhibitor |
|---|---|---|---|---|---|---|---|---|
| 7 | Neocyclomorusin | No | No | Yes | No | Yes | No | Yes |
| 11 | Vitexin | No | No | No | No | No | No | No |
| 14 | Apigenin-7-O-rhamnosyl-6-C-glucoside | No | No | No | No | No | No | No |
| 15 | Vicenin-1 | No | No | No | No | No | No | No |

| Compound No | Compound | CYP2D6 substrate | CYP3A4 substrate | CYP1A2 inhibitor | CYP2C19 inhibitor | CYP2C9 inhibitor | CYP2D6 inhibitor | CYP3A4 inhibitor |
|---|---|---|---|---|---|---|---|---|
| 16 | Vicenin-2 | No | No | No | No | No | No | No |
| 20 | Kaempferol-3-O-(2′′-O-β-D-glucopyranosyl-6′′-O-α-L-rhamnopyranosyl-β-D-glucopyranoside) | No | No | No | No | No | No | No |
| 28 | 5′-(2-Hydroxy-3-methylbut-3-enyl) abyssinone II | No | No | No | Yes | Yes | No | Yes |
| 29 | 7-Hydroxy-4′-methoxy-3′-(3- hydroxy-3-methyl-trans-but-1- enyl)-5′-(3-methylbut-2-enyl) flavanone | No | Yes | No | Yes | Yes | No | Yes |
| 32 | Abyssinone III | No | No | No | Yes | Yes | No | Yes |
| 33 | Abyssinone IV | No | No | No | Yes | Yes | No | Yes |
| 34 | Abyssinone-IV-4′-O-methyl ether | No | Yes | No | Yes | No | No | Yes |
| 40 | Erythribyssin G | No | No | No | Yes | Yes | No | Yes |
| 49 | Abyssinone V | No | No | No | Yes | Yes | No | Yes |
| 50 | Abyssinone-V-4'-O-methyl ether | No | No | No | Yes | Yes | No | Yes |
| 51 | 6-Prenylabyssinone V | No | Yes | No | Yes | Yes | No | No |
| 52 | Iespedezaflavanone B (Euchrestaflavanone A) | No | No | No | Yes | Yes | No | No |
| 53 | 5-Hydroxysophoranone | No | No | No | Yes | Yes | No | No |
| 54 | Burttinonedehydrate | No | No | No | Yes | Yes | No | Yes |
| 55 | Burttinone | No | No | No | Yes | Yes | No | Yes |
| 56 | Erycaffra D | No | No | No | Yes | Yes | No | Yes |
| 57 | Erycaffra F | No | No | No | Yes | Yes | No | Yes |
| 58 | Sigmoidin A | No | No | No | No | No | No | No |

| Compound No | Compound | CYP2D6 substrate | CYP3A4 substrate | CYP1A2 inhibitor | CYP2C19 inhibitor | CYP2C9 inhibitor | CYP2D6 inhibitor | CYP3A4 inhibitor |
|---|---|---|---|---|---|---|---|---|
| 61 | 4′-O-Methylsigmoidin | No | No | Yes | Yes | Yes | No | No |
| 64 | Sigmoidin E | No | No | No | Yes | Yes | No | Yes |
| 65 | Sigmoidin F | No | No | No | Yes | Yes | No | No |
| 67 | 2(S)-5,5′,7-Trihydroxy-2′-prenyl- (2′′,2′′-dimethylpyrano)- (5′′,6′′:3′,4′) flavanone | No | No | No | Yes | Yes | No | No |
| 70 | 2(S)-5.7-Dihydroxy-[(5′′,6′′:3′,4′)- (2′′,2′′-dimethylpyrano)- (5′′′,6′′′:5′.6′)]-(2′′′.2′′′-dimethylpyrano)flavanone | No | No | No | Yes | Yes | No | No |
| 71 | Erysenegalone (Erythrisenegalone) | No | No | No | Yes | Yes | No | Yes |
| 73 | Lonchocarpol A (Senegalensein) | No | No | No | Yes | Yes | No | Yes |
| 74 | Lonchocarpol C | No | Yes | No | Yes | Yes | No | Yes |
| 75 | Lonchocarpol D | No | No | No | Yes | Yes | No | Yes |
| 76 | Lupinifolin | No | No | No | Yes | Yes | No | Yes |
| 77 | Fuscaflavanones A1 | No | No | No | Yes | Yes | No | Yes |
| 78 | Fuscaflavanones A2 | No | No | No | Yes | Yes | No | Yes |
| 79 | Fuscaflavanones B | No | No | No | Yes | Yes | No | Yes |
| 82 | Abyssinin III | No | No | No | No | Yes | No | No |
| 83 | Abyssinoflavanone IV | No | No | Yes | Yes | Yes | No | No |
| 85 | Abyssinoflavanone VI | No | No | Yes | Yes | Yes | No | Yes |
| 86 | Abyssinoflavanone VII | No | No | No | Yes | Yes | No | No |
| 87 | 2(S)-5′-(2-Hydroxy-3-methylbut-3- | No | No | No | Yes | Yes | No | Yes |

| Compound No | Compound | CYP2D6 substrate | CYP3A4 substrate | CYP1A2 inhibitor | CYP2C19 inhibitor | CYP2C9 inhibitor | CYP2D6 inhibitor | CYP3A4 inhibitor |
|---|---|---|---|---|---|---|---|---|
| | enyl)licoflavone-4′-O-methyl ether | | | | | | | |
| 88 | 2(S)-5,7-Dihydroxy-5′-prenyl- [2″,2″-(3″-hydroxy)-dimethylpyrano]-(5″,6″:3′,4′) flavanone | No | No | No | Yes | Yes | No | Yes |
| 92 | 2(S)-5,5′,7-Dihydroxy-6′-prenyl [2″.2″-(3″.4′ ′-dihydroxy)-dimethylpyrano]-(5″,6″:3′,4′) flavanone | No | No | No | No | No | No | No |
| 97 | (2S)-5,7-Dihydroxy-5′-prenyl-2″- (4″-hydroxyisopropyl)- 3″-hydroxy-dihydrofurano [1″,3″:3′,4′] flavanone | No | No | No | No | Yes | No | No |
| 99 | (2S)-5,7,5′-Trihydroxy-6′-prenyl-2″-(4″-hydroxyisopropyl)-3″- hydroxy-dihydrofurano [1″.3″:4′.5′] flavanone | No | No | No | No | No | No | No |
| 100 | Addisoniaflavanone I | No | No | No | Yes | Yes | No | No |
| 101 | Addisoniaflavanone II | No | No | No | No | No | No | No |
| 117 | Abyssinone VI | No | No | No | Yes | Yes | No | Yes |
| 118 | Abyssinone-VI-4-O-methyl ether | No | No | No | Yes | No | No | Yes |
| 128 | Eryzerin C | No | No | Yes | Yes | Yes | No | No |
| 129 | 4′,7-Dihydroxy-2′-methoxy-3′-(3-methylbut-2-enyl) isoflavan | No | No | Yes | Yes | Yes | No | Yes |
| 130 | Eryzerin D | No | Yes | No | Yes | Yes | No | Yes |
| 138 | 2′,7-Dihydroxy-3′ -(3-methylbut-2- enyl)-2‴,2‴-dimethylpyrano [5″.6″:4′.5′] isoflavan | No | No | No | Yes | Yes | No | Yes |
| 148 | Eriotrichin B (Bidwillon A) | No | No | Yes | Yes | Yes | No | Yes |
| 153 | Orientanol F | No | No | Yes | Yes | Yes | No | Yes |

| Compound No | Compound | CYP2D6 substrate | CYP3A4 substrate | CYP1A2 inhibitor | CYP2C19 inhibitor | CYP2C9 inhibitor | CYP2D6 inhibitor | CYP3A4 inhibitor |
|---|---|---|---|---|---|---|---|---|
| 154 | 5,2',4'-Trihydroxy-6-prenyl-2‴,2‴dimethyldihydropyrano[5‴,6‴] isoflavanone | No | No | Yes | Yes | Yes | No | Yes |
| 160 | Bidwillon B | No | No | No | Yes | Yes | No | Yes |
| 163 | Eryzerin A | No | No | No | Yes | Yes | No | No |
| 164 | Eryvarin B | No | Yes | No | Yes | Yes | No | Yes |
| 167 | Eryvarin V | No | No | No | Yes | No | No | No |
| 168 | Eryzerin B | No | No | No | Yes | Yes | No | Yes |
| 171 | Orientanol E | No | No | No | Yes | No | No | No |
| 172 | 2,3-Dihydro-2′-hydroxyosajin | No | No | No | Yes | Yes | No | No |
| 176 | 5,7,3′-Trihydroxy-4′-methoxy-6,5′di(γ.γ-dimethylallyl) isoflavanone | No | No | No | Yes | Yes | No | No |
| 180 | 2,3-Dihydroauriculatin | No | No | No | Yes | Yes | No | No |
| 181 | 5,4-Dihydroxy-2-methoxy-8-(3.3-dimethylallyl)-2,2-dimethylpyrano [5,6:6,7] isoflavanone | No | Yes | No | Yes | Yes | No | Yes |
| 188 | Vogelin D | No | Yes | No | Yes | Yes | No | Yes |
| 189 | Auriculatin 4’-O-glucoside | No | No | No | No | No | No | No |
| 193 | Erysubin F | No | Yes | Yes | Yes | Yes | No | No |
| 194 | Eryvarin S | No | Yes | Yes | Yes | Yes | No | Yes |
| 195 | Erythraddison II | No | No | Yes | Yes | Yes | No | No |
| 206 | 6,8-Diprenylgenistein | No | No | Yes | Yes | Yes | No | No |
| 208 | Lupiwighteone (8-Prenylgenistein) | No | No | Yes | Yes | Yes | No | No |

| Compound No | Compound | CYP2D6 substrate | CYP3A4 substrate | CYP1A2 inhibitor | CYP2C19 inhibitor | CYP2C9 inhibitor | CYP2D6 inhibitor | CYP3A4 inhibitor |
|---|---|---|---|---|---|---|---|---|
| 210 | Isolupabigenin | No | No | Yes | Yes | Yes | No | No |
| 211 | 6,8-Diprenylorobol | No | No | Yes | Yes | Yes | No | No |
| 222 | Vogelin G | No | No | Yes | Yes | Yes | No | Yes |
| 242 | Warangalone (Scandenone) | No | No | Yes | Yes | Yes | No | No |
| 243 | Auriculasin | No | No | No | Yes | Yes | No | No |
| 244 | Auriculatin | No | No | No | Yes | Yes | No | No |
| 245 | Warangalone 4′-O-methyl ether | No | Yes | Yes | Yes | Yes | No | Yes |
| 256 | 5,4′-Dihydroxy-2′-methoxy-8-(3,3-dimethylallyl)-2″,2″- dimethylpyrano [5,6:6,7] isoflavone | No | No | Yes | Yes | Yes | No | No |
| 257 | 5,7,4′-Trihydroxy-6-(3″,3″-dimethylallyloxiranylmethyl) isoflavone | No | No | No | Yes | Yes | No | No |
| 259 | 5,4-Dihydroxy-8-(3,3- dimethylallyl)-2-methoxyisopropylfurano [4,5:6,7] isoflavone | No | No | Yes | Yes | Yes | Yes | Yes |
| 260 | Erymildbraedin B | No | No | Yes | Yes | Yes | No | No |
| 261 | Erysenegalensein D | No | No | No | Yes | Yes | No | No |
| 262 | Erysenegalensein E | No | No | No | Yes | Yes | No | No |
| 263 | Isoerysenegalensein E (Lysisteisoflavone) | No | No | Yes | Yes | Yes | No | No |
| 264 | Erysenegalensein F | No | No | No | Yes | Yes | No | No |
| 265 | Erysenegalensein G | No | No | Yes | Yes | Yes | No | Yes |
| 266 | Erysenegalensein K | No | No | Yes | Yes | Yes | No | Yes |
| 267 | Erysenegalensein L | No | No | No | Yes | Yes | No | No |
| 268 | Erysenegalensein M | No | No | Yes | Yes | Yes | No | No |

| Compound No | Compound | CYP2D6 substrate | CYP3A4 substrate | CYP1A2 inhibitor | CYP2C19 inhibitor | CYP2C9 inhibitor | CYP2D6 inhibitor | CYP3A4 inhibitor |
|---|---|---|---|---|---|---|---|---|
| 269 | Erysenegalensein N | No | No | No | Yes | Yes | No | No |
| 273 | Senegalensin | No | No | No | Yes | Yes | No | No |
| 276 | 8-Prenylerythrinin C (Isosenegalensein) (Euchrenone b10) | No | No | Yes | Yes | Yes | No | Yes |
| 277 | Vogelin H | No | No | No | Yes | Yes | No | Yes |
| 278 | Vogelin I | No | No | No | Yes | Yes | No | No |
| 279 | Eriotriochin | No | No | No | Yes | Yes | No | Yes |
| 280 | Erythraddison I | No | No | No | No | Yes | No | No |
| 285 | 8-Prenylluteone | No | No | Yes | Yes | Yes | No | No |
| 286 | 4′-Hydroxyisoflavone-7-O-β-D-glucopyranoside | No | No | No | No | No | No | No |
| 287 | 4′-Hydroxyisoflavone-7-O-α-L-rhamnosyl/ (1→6)-β-D-glucopyranoside | No | No | No | No | No | No | No |
| 294 | 1-Methoxyerythrabyssin II | No | No | No | Yes | Yes | No | Yes |
| 329 | Erysubin D | No | Yes | No | No | No | No | No |
| 333 | Demethylerystagallin A | No | No | No | Yes | Yes | No | No |
| 334 | Erystagallin B | No | No | No | Yes | Yes | No | No |
| 350 | Eryvarin W | No | Yes | Yes | Yes | Yes | No | No |
| 360 | Erysenegalensein J | No | No | No | No | No | No | No |
| 378 | Bis-Sigmodiol | No | Yes | No | No | Yes | No | Yes |

Table S6. pkCSM excretion

| Compound No | Compound | Total clearance | Renal OCT2 substrate |
|---|---|---|---|
| 7 | Neocyclomorusin | -0.209 | No |
| 14 | Apigenin-7-O-rhamnosyl-6-C-glucoside | 0.132 | No |
| 15 | Vicenin-1 | 0.307 | No |
| 16 | Vicenin-2 | 0.369 | No |
| 20 | Kaempferol-3-O-(2′′-O-β-D-glucopyranosyl-6′′-O-α-L-rhamnopyranosyl-β-D-glucopyranoside) | -0.237 | No |
| 11 | Vitexin | 0.413 | No |
| 28 | 5′-(2-Hydroxy-3-methylbut-3-enyl) abyssinone II | 0.796 | No |
| 29 | 7-Hydroxy-4′-methoxy-3′-(3- hydroxy-3-methyl-trans-but-1- enyl)-5′-(3-methylbut-2-enyl) flavanone | 0.708 | No |
| 32 | Abyssinone III | 0.588 | No |
| 33 | Abyssinone IV | 0.825 | No |
| 34 | Abyssinone-IV-4′-O-methyl ether | 0.98 | No |
| 40 | Erythribyssin G | 0.331 | No |
| 49 | Abyssinone V | 0.825 | No |
| 50 | Abyssinone-V-4'-O-methyl ether | 0.701 | No |
| 51 | 6-Prenylabyssinone V | 0.458 | No |
| 52 | Iespedezaflavanone B (Euchrestaflavanone A) | 0.57 | No |
| 53 | 5-Hydroxysophoranone | 0.463 | No |
| 54 | Burttinonedehydrate | 0.654 | No |
| 55 | Burttinone | 0.416 | No |
| 56 | Erycaffra D | 0.493 | No |
| 57 | Erycaffra F | 0.335 | No |
| 58 | Sigmoidin A | 0.394 | No |

| Compound No | Compound | Total clearance | Renal OCT2 substrate |
|---|---|---|---|
| 61 | 4′-O-Methylsigmoidin | 0.232 | No |
| 64 | Sigmoidin E | 0.308 | No |
| 65 | Sigmoidin F | 0.115 | No |
| 67 | 2(S)-5,5′,7-Trihydroxy-2′-prenyl- (2′′,2′′-dimethylpyrano)- (5′′,6′′:3′,4′) flavanone | 0.103 | No |
| 70 | 2(S)-5,7-Dihydroxy-[(5′′,6′′:3′,4′)- (2′′,2′′-dimethylpyrano)- (5′′′,6′′′:5′,6′)]-(2′′′,2′′′-dimethylpyrano)flavanone | -0.267 | No |
| 71 | Erysenegalone (Erythrisenegalone) | 0.509 | No |
| 73 | Lonchocarpol A (Senegalensein) | 0.617 | No |
| 74 | Lonchocarpol C | 0.451 | No |
| 75 | Lonchocarpol D | 0.344 | No |
| 76 | Lupinifolin | 0.51 | No |
| 77 | Fuscaflavanones A1 | 0.474 | No |
| 78 | Fuscaflavanones A2 | 0.474 | No |
| 79 | Fuscaflavanones B | 0.058 | No |
| 82 | Abyssinin III | 0.316 | No |
| 83 | Abyssinoflavanone IV | 0.412 | No |
| 85 | Abyssinoflavanone VI | 0.198 | No |
| 86 | Abyssinoflavanone VII | 0.518 | No |
| 87 | 2(S)-5′-(2-Hydroxy-3-methylbut-3- enyl) licoflavone-4′-O-methyl ether | 0.705 | No |
| 88 | 2(S)-5,7-Dihydroxy-5′-prenyl- [2′′,2′′-(3′′-hydroxy)-dimethylpyrano]-(5′′,6′′:3′,4′) flavanone | 0.313 | No |
| 92 | 2(S)-5,5′,7-Dihydroxy-6′-prenyl [2′′,2′′-(3′′,4′′-dihydroxy)-dimethylpyrano]-(5′′,6′′:3′,4′) flavanone | 0.132 | No |
| 97 | (2S)-5,7-Dihydroxy-5′-prenyl-2′′- (4′′-hydroxyisopropyl)- 3′′-hydroxy-dihydrofurano [1′′,3′′:3′,4′] flavanone | 0.226 | No |
| 99 | (2S)-5,7,5′-Trihydroxy-6′-prenyl-2′′-(4′′- | 0.114 | No |

| Compound No | Compound | Total clearance | Renal OCT2 substrate |
|---|---|---|---|
| | hydroxyisopropyl)-3″- hydroxy-dihydrofurano [1″,3″:4′,5′] flavanone | | |
| 100 | Addisoniaflavanone I | 0.193 | No |
| 101 | Addisoniaflavanone II | 0.432 | No |
| 117 | Abyssinone VI | 0.306 | No |
| 118 | Abyssinone-VI-4-O-methyl ether | 0.39 | No |
| 128 | Eryzerin C | 0.6 | No |
| 129 | 4′,7-Dihydroxy-2′-methoxy-3′-(3-methylbut-2-enyl) isoflavan | 0.421 | No |
| 130 | Eryzerin D | 0.315 | No |
| 138 | 2′,7-Dihydroxy-3′ -(3-methylbut-2- enyl)-2‴,2‴-dimethylpyrano [5″,6″:4′,5′] isoflavan | 0.362 | No |
| 148 | Eriotrichin B (Bidwillon A) | 0.268 | No |
| 153 | Orientanol F | 0.126 | No |
| 154 | 5,2',4'-Trihydroxy-6-prenyl-2‴,2‴dimethyldihydropyrano[5‴,6‴] isoflavanone | 0.288 | No |
| 160 | Bidwillon B | 0.343 | No |
| 163 | Eryzerin A | 0.59 | No |
| 164 | Eryvarin B | 0.812 | No |
| 167 | Eryvarin V | 0.195 | No |
| 168 | Eryzerin B | 0.5 | No |
| 171 | Orientanol E | 0.435 | No |
| 172 | 2,3-Dihydro-2′-hydroxyosajin | 0.155 | No |
| 176 | 5,7,3′-Trihydroxy-4′-methoxy-6,5′di(γ.γ-dimethylallyl) isoflavanone | 0.47 | No |
| 180 | 2,3-Dihydroauriculatin | 0.163 | No |
| 181 | 5,4-Dihydroxy-2-methoxy-8-(3,3-dimethylallyl)-2,2-dimethylpyrano [5,6:6,7] isoflavanone | 0.245 | No |

| Compound No | Compound | Total clearance | Renal OCT2 substrate |
|---|---|---|---|
| 188 | Vogelin D | 0.704 | No |
| 189 | Auriculatin 4’-O-glucoside | -0.038 | No |
| 193 | Erysubin F | 0.312 | No |
| 194 | Eryvarin S | 0.306 | No |
| 195 | Erythraddison II | 0.446 | No |
| 206 | 6,8-Diprenylgenistein | 0.407 | No |
| 208 | Lupiwighteone (8-Prenylgenistein) | 0.401 | No |
| 210 | Isolupabigenin | 0.243 | No |
| 211 | 6,8-Diprenylorobol | 0.378 | No |
| 222 | Vogelin G | 0.127 | No |
| 242 | Warangalone (Scandenone) | 0.223 | No |
| 243 | Auriculasin | 0.155 | No |
| 244 | Auriculatin | 0.312 | No |
| 245 | Warangalone 4′-O-methyl ether | 0.23 | No |
| 256 | 5,4′-Dihydroxy-2′-methoxy-8-(3,3-dimethylallyl)-2″,2″- dimethylpyrano [5,6:6,7] isoflavone | 0.243 | No |
| 257 | 5,7,4′-Trihydroxy-6-(3″,3″-dimethylallyloxiranylmethyl) isoflavone | 0.112 | No |
| 259 | 5,4-Dihydroxy-8-(3.3- dimethylallyl)-2-methoxyisopropylfurano [4,5:6,7] isoflavone | 0.5 | No |
| 260 | Erymildbraedin B | 0.192 | No |
| 261 | Erysenegalensein D | 0.588 | No |
| 262 | Erysenegalensein E | 0.493 | No |
| 263 | Isoerysenegalensein E (Lysisteisoflavone) | 0.558 | No |
| 264 | Erysenegalensein F | -0.215 | No |
| 265 | Erysenegalensein G | -0.022 | No |
| 266 | Erysenegalensein K | 0.475 | No |
| 267 | Erysenegalensein L | 0.489 | No |

| Compound No | Compound | Total clearance | Renal OCT2 substrate |
|---|---|---|---|
| 268 | Erysenegalensein M | 0.376 | No |
| 269 | Erysenegalensein N | 0.686 | No |
| 273 | Senegalensin | 0.148 | No |
| 276 | 8-Prenylerythrinin C (Isosenegalensein) (Euchrenone b10) | 0.175 | No |
| 277 | Vogelin H | 0.23 | No |
| 278 | Vogelin I | 0.137 | No |
| 279 | Eriotriochin | 0.296 | No |
| 280 | Erythraddison I | 0.096 | No |
| 285 | 8-Prenylluteone | 0.549 | No |
| 286 | 4′-Hydroxyisoflavone-7-O-β-D-glucopyranoside | 0.217 | No |
| 287 | 4′-Hydroxyisoflavone-7-O-α-L-rhamnosyl/ (1 →6)-β-D-glucopyranoside | 2.607 | No |
| 294 | 1-Methoxyerythrabyssin II | 0.434 | No |
| 329 | Erysubin D | 0.431 | Yes |
| 333 | Demethylerystagallin A | 0.369 | No |
| 334 | Erystagallin B | 0.325 | No |
| 350 | Eryvarin W | 0.407 | No |
| 360 | Erysenegalensein J | -0.156 | No |
| 378 | Bis-Sigmodiol | -0.573 | No |

Table S7. pkCSM toxicity

| Compound No | Compound | AMES toxicity | hERG I inhibitor | hERG II inhibitor | Hepatotoxicity |
|---|---|---|---|---|---|
| 7 | Neocyclomorusin | No | No | Yes | Yes |
| 11 | Vitexin | No | No | No | No |
| 14 | Apigenin-7-O-rhamnosyl-6-C-glucoside | No | No | Yes | No |
| 15 | Vicenin-1 | Yes | No | Yes | No |
| 16 | Vicenin-2 | Yes | No | Yes | No |
| 20 | Kaempferol-3-O-(2′′-O-β-D-glucopyranosyl-6′′-O-α-L-rhamnopyranosyl-β-D-glucopyranoside) | No | No | Yes | No |
| 28 | 5′-(2-Hydroxy-3-methylbut-3-enyl) abyssinone II | No | No | Yes | No |
| 29 | 7-Hydroxy-4′-methoxy-3′-(3-hydroxy-3-methyl-trans-but-1-enyl)-5′-(3-methylbut-2-enyl) flavanone | No | No | Yes | No |
| 32 | Abyssinone III | No | No | Yes | No |
| 33 | Abyssinone IV | No | No | Yes | No |
| 34 | Abyssinone-IV-4′-O-methyl ether | No | No | Yes | No |
| 40 | Erythribyssin G | No | No | Yes | No |
| 49 | Abyssinone V | No | No | Yes | No |
| 50 | Abyssinone-V-4'-O-methyl ether | No | No | Yes | No |
| 51 | 6-Prenylabyssinone V | No | No | Yes | No |
| 52 | Iespedezaflavanone B (Euchrestaflavanone A) | No | No | No | No |
| 53 | 5-Hydroxysophoranone | No | No | Yes | No |
| 54 | Burttinonedehydrate | No | No | No | No |
| 55 | Burttinone | No | No | Yes | No |
| 56 | Erycaffra D | No | No | No | No |

| Compound No | Compound | AMES toxicity | hERG I inhibitor | hERG II inhibitor | Hepatotoxicity |
|---|---|---|---|---|---|
| 57 | Erycaffra F | No | No | No | No |
| 58 | Sigmoidin A | No | No | No | No |
| 61 | 4′-O-Methylsigmoidin | No | No | No | No |
| 64 | Sigmoidin E | No | No | No | No |
| 65 | Sigmoidin F | No | No | No | No |
| 67 | 2(S)-5.5′.7-Trihydroxy-2′-prenyl-(2′′,2′′-dimethylpyrano)- (5′′,6′′:3′,4′) flavanone | No | No | No | No |
| 70 | 2(S)-5,7-Dihydroxy-[(5′′,6′′:3′,4′)-(2′′,2′′-dimethylpyrano)- (5′′′,6′′′:5′,6′)]-(2′′′,2′′′-dimethylpyrano)flavanone | No | No | No | No |
| 71 | Erysenegalone (Erythrisenegalone) | Yes | No | No | No |
| 73 | Lonchocarpol A (Senegalensein) | No | No | No | No |
| 74 | Lonchocarpol C | No | No | No | No |
| 75 | Lonchocarpol D | No | No | No | No |
| 76 | Lupinifolin | No | No | No | No |
| 77 | Fuscaflavanones A1 | No | No | No | No |
| 78 | Fuscaflavanones A2 | No | No | No | No |
| 79 | Fuscaflavanones B | No | No | No | No |
| 82 | Abyssinin III | No | No | Yes | No |
| 83 | Abyssinoflavanone IV | No | No | No | No |
| 85 | Abyssinoflavanone VI | No | No | No | No |
| 86 | Abyssinoflavanone VII | No | No | Yes | No |
| 87 | 2(S)-5′-(2-Hydroxy-3-methylbut-3-enyl)licoflavone-4′-O-methyl ether | No | No | No | No |
| 88 | 2(S)-5.7-Dihydroxy-5′-prenyl- [2′′,2′′-(3′′-hydroxy)-dimethylpyrano]-(5′′,6′′:3′,4′) flavanone | No | No | No | No |
| 92 | 2(S)-5.5′.7-Dihydroxy-6′-prenyl [2′′,2′′-(3′′,4′′-dihydroxy)- | Yes | No | No | No |

| Compound No | Compound | AMES toxicity | hERG I inhibitor | hERG II inhibitor | Hepatotoxicity |
|---|---|---|---|---|---|
| | dimethylpyrano]-(5″,6″:3′,4′) flavanone | | | | |
| 97 | (2S)-5,7-Dihydroxy-5′-prenyl-2″- (4′ ′-hydroxyisopropyl)- 3″-hydroxy-dihydrofurano [1″,3″:3′,4′] flavanone | Yes | No | No | No |
| 99 | (2S)-5,7,5′-Trihydroxy-6′-prenyl-2″-(4″-hydroxyisopropyl)-3″- hydroxy-dihydrofurano [1″,3″:4′,5′] flavanone | Yes | No | No | No |
| 100 | Addisoniaflavanone I | No | No | No | No |
| 101 | Addisoniaflavanone II | No | No | No | No |
| 117 | Abyssinone VI | No | No | Yes | No |
| 118 | Abyssinone-VI-4-O-methyl ether | No | No | Yes | Yes |
| 128 | Eryzerin C | No | No | Yes | No |
| 129 | 4′,7-Dihydroxy-2′-methoxy-3′-(3-methylbut-2-enyl) isoflavan | No | No | Yes | No |
| 130 | Eryzerin D | No | No | Yes | No |
| 138 | 2′,7-Dihydroxy-3′ -(3-methylbut-2-enyl)-2‴,2‴-dimethylpyrano [5″,6″:4′,5′] isoflavan | No | No | Yes | No |
| 148 | Eriotrichin B (Bidwillon A) | No | No | No | No |
| 153 | Orientanol F | No | No | Yes | No |
| 154 | 5,2',4'-Trihydroxy-6-prenyl-2‴,2‴dimethyldihydropyrano[5‴,6‴ ] isoflavanone | No | No | No | No |
| 160 | Bidwillon B | No | No | Yes | No |
| 163 | Eryzerin A | No | No | Yes | No |
| 164 | Eryvarin B | No | No | Yes | No |
| 167 | Eryvarin V | No | No | No | No |
| 168 | Eryzerin B | No | No | Yes | No |
| 171 | Orientanol E | No | No | No | No |
| 172 | 2,3-Dihydro-2′-hydroxyosajin | No | No | No | No |
| 176 | 5,7,3′-Trihydroxy-4′-methoxy- | No | No | Yes | No |

| Compound No | Compound | AMES toxicity | hERG I inhibitor | hERG II inhibitor | Hepatotoxicity |
|---|---|---|---|---|---|
| | 6,5′di(γ.γ-dimethylallyl) isoflavanone | | | | |
| 180 | 2.3-Dihydroauriculatin | No | No | No | No |
| 181 | 5,4-Dihydroxy-2-methoxy-8-(3,3-dimethylallyl)-2,2-dimethylpyrano [5,6:6,7] isoflavanone | No | No | No | No |
| 188 | Vogelin D | No | No | Yes | No |
| 189 | Auriculatin 4'-O-glucoside | Yes | No | No | No |
| 193 | Erysubin F | No | No | Yes | Yes |
| 194 | Eryvarin S | Yes | No | Yes | No |
| 195 | Erythraddison II | No | No | Yes | No |
| 206 | 6,8-Diprenylgenistein | No | No | Yes | No |
| 208 | Lupiwighteone (8-Prenylgenistein) | No | No | Yes | Yes |
| 210 | Isolupabigenin | No | No | Yes | No |
| 211 | 6.8-Diprenylorobol | No | No | Yes | No |
| 222 | Vogelin G | No | No | Yes | Yes |
| 242 | Warangalone (Scandenone) | No | No | Yes | No |
| 243 | Auriculasin | No | No | Yes | No |
| 244 | Auriculatin | No | No | Yes | No |
| 245 | Warangalone 4′-O-methyl ether | No | No | Yes | No |
| 256 | 5,4′-Dihydroxy-2′-methoxy-8-(3,3-dimethylallyl)-2″,2″-dimethylpyrano [5,6:6,7] isoflavone | No | No | Yes | No |
| 257 | 5,7,4′-Trihydroxy-6-(3″,3″-dimethylallyloxiranylmethyl) isoflavone | No | No | Yes | No |
| 259 | 5,4-Dihydroxy-8-(3,3-dimethylallyl)-2-methoxyisopropylfurano [4,5:6,7] isoflavone | No | No | Yes | Yes |
| 260 | Erymildbraedin B | No | No | Yes | No |

| Compound No | Compound | AMES toxicity | hERG I inhibitor | hERG II inhibitor | Hepatotoxicity |
|---|---|---|---|---|---|
| 261 | Erysenegalensein D | No | No | Yes | No |
| 262 | Erysenegalensein E | No | No | Yes | No |
| 263 | Isoerysenegalensein E (Lysisteisoflavone) | No | No | Yes | Yes |
| 264 | Erysenegalensein F | No | No | Yes | No |
| 265 | Erysenegalensein G | No | No | Yes | Yes |
| 266 | Erysenegalensein K | Yes | No | Yes | No |
| 267 | Erysenegalensein L | No | No | Yes | No |
| 268 | Erysenegalensein M | No | No | Yes | Yes |
| 269 | Erysenegalensein N | No | No | Yes | No |
| 273 | Senegalensin | No | No | Yes | No |
| 276 | 8-Prenylerythrinin C (Isosenegalensein) (Euchrenone b10) | No | No | Yes | No |
| 277 | Vogelin H | No | No | Yes | Yes |
| 278 | Vogelin I | Yes | No | Yes | Yes |
| 279 | Eriotriochin | No | No | Yes | Yes |
| 280 | Erythraddison I | No | No | Yes | Yes |
| 285 | 8-Prenylluteone | No | No | Yes | No |
| 286 | 4′-Hydroxyisoflavone-7-O-β-D-glucopyranoside | No | No | Yes | Yes |
| 287 | 4′-Hydroxyisoflavone-7-O-α-L-rhamnosyl/ (1 → 6)-β-D-glucopyranoside | No | No | Yes | Yes |
| 294 | 1-Methoxyerythrabyssin II | No | No | Yes | No |
| 329 | Erysubin D | No | No | No | No |
| 333 | Demethylerystagallin A | No | No | Yes | No |
| 334 | Erystagallin B | No | No | Yes | No |
| 350 | Eryvarin W | No | No | Yes | No |
| 360 | Erysenegalensein J | No | No | No | No |
| 378 | Bis-Sigmodiol | No | No | Yes | No |

Table S8. Non-bonded interactions of orientanol E (**171**)

| Category | Type | % | Occurrence | Poses | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 |
| Electrostatic | Pi-Anion | 12.2 | 5 | | | | | | | | | | | | | | | HIS41 | HIS41 | HIS41 | HIS41 | | HIS41 |
| Electrostatic | Salt Bridge;Attractive Charge | 48.78 | 20 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 |
| Hydrogen Bond | Carbon Hydrogen Bond | 17.07 | 7 | | | ALA191 | ALA191 | ALA191 | | | | ALA191 | | | | | ALA191 | ALA191 | ALA191 | | | | |
| Hydrogen Bond | Carbon Hydrogen Bond | 0 | 0 | | | | | | | | | | | | | | | | | | | | |
| Hydrogen Bond | Carbon Hydrogen Bond | 0 | 0 | | | | | | | | | | | | | | | | | | | | |
| Hydrogen Bond | Carbon Hydrogen Bond | 9.76 | 4 | | | | LEU167 | | | | | LEU167 | | | | | | LEU167 | LEU167 | | | | |
| Hydrogen Bond | Carbon Hydrogen Bond | 2.44 | 1 | | | | | | PRO168 | | | | | | | | | | | | | | |
| Hydrogen Bond | Conventional Hydrogen Bond | 36.59 | 15 | CYS145 | CYS145 | CYS145 | CYS145 | | | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | | CYS145 | CYS145 | | CYS145 | | CYS145 | CYS145 | CYS145 |
| Hydrogen Bond | Conventional Hydrogen Bond | 24.39 | 10 | GLN192 | GLN192 | GLN192 | GLN192 | GLN192 | GLN192 | | | GLN192 | | | | | GLN192 | GLN192 | GLN192 | | | | |
| Hydrogen Bond | Conventional Hydrogen Bond | 2.44 | 1 | | | | | | GLU166 | | | | | | | | | | | | | | |
| Hydrogen Bond | Conventional Hydrogen Bond | 17.07 | 7 | | | MET165 | MET165 | MET165 | | | | MET165 | | | | | MET165 | MET165 | MET165 | | | | |
| Hydrogen Bond | Conventional Hydrogen Bond | 31.71 | 13 | THR190 | THR190 | | | | THR190 | THR190 | THR190 | | THR190 | THR190 | THR190 | THR190 | | | | THR190 | THR190 | THR190 | THR190 |
| Hydrophobic | Alkyl | 7.32 | 3 | | | | | | | | | | ARG188 | | | | | | | | | ARG188 | ARG188 |
| Hydrophobic | Alkyl | 43.9 | 18 | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 |
| Hydrophobic | Alkyl | 34.15 | 14 | | | CYS44 | CYS44 | CYS44 | | CYS44 | CYS44 | CYS44 | | CYS44 | CYS44 | CYS44 | CYS44 | CYS44 | CYS44 | CYS44 | CYS44 | | |
| Hydrophobic | Alkyl | 48.78 | 20 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 |
| Hydrophobic | Alkyl | 12.2 | 5 | | | PRO52 | PRO52 | | | | | | PRO52 | PRO52 | PRO52 | | | | | | | | |
| Hydrophobic | Alkyl | 29.27 | 12 | | | | | | | PRO52 | PRO52 | PRO52 | | | | PRO52 | PRO52 | PRO52 | PRO52 | PRO52 | PRO52 | PRO52 | PRO52 |
| Hydrophobic | Amide-Pi Stacked | 2.44 | 1 | | | | | | | | | | | | | | | | | | | GLN189 | |
| Hydrophobic | Pi-Alkyl | 48.78 | 20 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 |
| Hydrophobic | Pi-Alkyl | 0 | 0 | | | | | | | | | | | | | | | | | | | | |
| Hydrophobic | Pi-Alkyl | 2.44 | 1 | | | | | | HIS172 | | | | | | | | | | | | | | |
| Hydrophobic | Pi-Alkyl | 2.44 | 1 | | | | | | HIS41 | | | | | | | | | | | | | | |
| Hydrophobic | Pi-Alkyl | 39.02 | 16 | | | MET165 | MET165 | MET165 | | MET165 | | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 |
| Hydrophobic | Pi-Alkyl | 48.78 | 20 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 |
| Hydrophobic | Pi-Alkyl | 31.71 | 13 | | | TYR54 | | TYR54 | | TYR54 | TYR54 | TYR54 | | TYR54 | TYR54 | TYR54 | TYR54 | TYR54 | TYR54 | TYR54 | TYR54 | | |
| Hydrophobic | Pi-Pi T-shaped | 46.34 | 19 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 |
| Hydrophobic | Pi-Sigma | 43.9 | 18 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | |
| Other | Pi-Lone Pair | 0 | 0 | | | | | | | | | | | | | | | | | | | | |
| Other | Pi-Sulfur | 39.02 | 16 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | | | MET165 | MET165 | | |
| Unfavorable | | 12.2 | 5 | GLU166 | GLU166 | | | | GLU166 | | | | | | | | | | | GLU166 | | | GLU166 |
| Unfavorable | | 34.15 | 14 | | | ARG188 | | ARG188 | | ARG188 | ARG188 | ARG188 | ARG188 | ARG188 | ARG188 | ARG188 | ARG188 | ARG188 | ARG188 | | ARG188 | ARG188 | |
| Unfavorable | | 19.51 | 8 | | | | | | | GLN192 | GLN192 | | GLN192 | GLN192 | GLN192 | GLN192 | | | | | GLN192 | GLN192 | |

Table S8. Continued non-bonded interactions of orientanol E (**171**)

| Category | Type | % | Occurrence | Poses | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 | 41 |
| Electrostatic | Pi-Anion | 36.59 | 15 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | | | | | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | | | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 |
| Electrostatic | Salt Bridge;Attractive Charge | 51.22 | 21 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 |
| Hydrogen Bond | Carbon Hydrogen Bond | 21.95 | 9 | | | | | | | | ALA191 | | ALA191 | ALA191 | | ALA191 | ALA191 | ALA191 | | ALA191 | ALA191 | | | ALA191 |
| Hydrogen Bond | Carbon Hydrogen Bond | 17.07 | 7 | | | | | | | | ARG188 | | | ARG188 | | ARG188 | ARG188 | | | ARG188 | ARG188 | | | ARG188 |
| Hydrogen Bond | Carbon Hydrogen Bond | 2.44 | 1 | | | | | | | | | | GLN189 | | | | | | | | | | | |
| Hydrogen Bond | Carbon Hydrogen Bond | 4.88 | 2 | | | | | | | | | | LEU167 | | | | | | | | | | | LEU167 |
| Hydrogen Bond | Carbon Hydrogen Bond | 0 | 0 | | | | | | | | | | | | | | | | | | | | | |
| Hydrogen Bond | Conventional Hydrogen Bond | 41.46 | 17 | CYS145 | CYS145 | CYS145 | | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | | CYS145 | CYS145 | CYS145 | | CYS145 | CYS145 | CYS145 | | CYS145 |
| Hydrogen Bond | Conventional Hydrogen Bond | 17.07 | 7 | | | | | | | | GLN192 | GLN192 | | | | GLN192 | | GLN192 | GLN192 | | GLN192 | | GLN192 | |
| Hydrogen Bond | Conventional Hydrogen Bond | 7.32 | 3 | | | GLU166 | | | GLU166 | GLU166 | | | | | | | | | | | | | | |
| Hydrogen Bond | Conventional Hydrogen Bond | 19.51 | 8 | | | | | | | | MET165 | MET165 | | MET165 | | MET165 | | MET165 | MET165 | MET165 | MET165 | | | |
| Hydrogen Bond | Conventional Hydrogen Bond | 26.83 | 11 | THR190 | THR190 | THR190 | THR190 | THR190 | THR190 | THR190 | | | | | THR190 | THR190 | | | | | | THR190 | THR190 | |
| Hydrophobic | Alkyl | 12.2 | 5 | | | | | | | | | | | ARG188 | | ARG188 | ARG188 | | | ARG188 | | ARG188 | | |
| Hydrophobic | Alkyl | 46.34 | 19 | CYS145 | CYS145 | | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 |
| Hydrophobic | Alkyl | 12.2 | 5 | CYS44 | | | CYS44 | CYS44 | | | | | | | CYS44 | | | | | | | | CYS44 | |
| Hydrophobic | Alkyl | 46.34 | 19 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | MET49 | | MET49 | | MET49 | MET49 | MET49 |
| Hydrophobic | Alkyl | 0 | 0 | | | | | | | | | | | | | | | | | | | | | |
| Hydrophobic | Alkyl | 31.71 | 13 | PRO52 | PRO52 | PRO52 | PRO52 | PRO52 | | | | | PRO52 | PRO52 | PRO52 | PRO52 | PRO52 | | | PRO52 | | PRO52 | | PRO52 |
| Hydrophobic | Amide-Pi Stacked | 17.07 | 7 | GLN189 | | | | GLN189 | | | GLN189 | | GLN189 | | | | | GLN189 | GLN189 | | GLN189 | | | |
| Hydrophobic | Pi-Alkyl | 43.9 | 18 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | | | HIS163 | HIS163 | HIS163 | HIS163 | | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 |
| Hydrophobic | Pi-Alkyl | 2.44 | 1 | | | | | | | | | | | | | | | | | | HIS164 | | | |
| Hydrophobic | Pi-Alkyl | 9.76 | 4 | | | | | | | | HIS172 | HIS172 | | | | | | | HIS172 | | HIS172 | | | |
| Hydrophobic | Pi-Alkyl | 26.83 | 11 | | | HIS41 | | | HIS41 | HIS41 | HIS41 | HIS41 | | | | HIS41 | HIS41 | HIS41 | HIS41 | | HIS41 | | HIS41 | |
| Hydrophobic | Pi-Alkyl | 41.46 | 17 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | | | | MET165 | MET165 | MET165 | MET165 | MET165 | | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 |
| Hydrophobic | Pi-Alkyl | 51.22 | 21 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 |
| Hydrophobic | Pi-Alkyl | 7.32 | 3 | | TYR54 | | TYR54 | | | | | | | | TYR54 | | | | | | | | | |
| Hydrophobic | Pi-Pi T-shaped | 34.15 | 14 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | | | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | | | HIS41 | | HIS41 | | |
| Hydrophobic | Pi-Sigma | 24.39 | 10 | HIS41 | HIS41 | | HIS41 | HIS41 | | | | | HIS41 | HIS41 | HIS41 | | | | | HIS41 | | HIS41 | | HIS41 |
| Other | Pi-Lone Pair | 12.2 | 5 | | | | | | | | | | | | | | THR190 | | | THR190 | | THR190 | THR190 | THR190 |
| Other | Pi-Sulfur | 29.27 | 12 | | | MET165 | MET165 | MET165 | | MET165 | MET165 | | | MET165 | MET165 | MET165 | | | | MET165 | MET165 | MET165 | MET165 | |
| Unfavorable | | 14.63 | 6 | | | | | | | | GLU166 | GLU166 | | GLU166 | | | | | GLU166 | | GLU166 | | GLU166 | |
| Unfavorable | | 17.07 | 7 | ARG188 | ARG188 | ARG188 | ARG188 | ARG188 | | | | | ARG188 | | ARG188 | | | | | | | | | |
| Unfavorable | | 17.07 | 7 | GLN192 | GLN192 | GLN192 | GLN192 | GLN192 | | | | | | | GLN192 | | | | | | | GLN192 | | |

Table S9. Non-bonded interactions of erycaffra F (**57**)

Table S9. Continued non-bonded interactions of erycaffra F (**57**)

| Category | Type | % | Occurrence | Poses | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 |
| Hydrogen Bond | Carbon Hydrogen Bond | 38.89 | 7 | LEU167 | | LEU167 | | | LEU167 | | LEU167 | LEU167 | LEU167 | | LEU167 | | | | | | |
| Hydrogen Bond | Carbon Hydrogen Bond | 44.44 | 8 | PRO168 | PRO168 | | PRO168 | PRO168 | | | | | | PRO168 | PRO168 | PRO168 | | PRO168 | | | |
| Hydrogen Bond | Carbon Hydrogen Bond | 16.67 | 3 | | | | ALA191 | | | | | | | ALA191 | | | | ALA191 | | | |
| Hydrogen Bond | Carbon Hydrogen Bond | 33.33 | 6 | | HIS172 | HIS172 | | HIS172 | HIS172 | HIS172 | | | | | | HIS172 | | | | | |
| Hydrogen Bond | Carbon Hydrogen Bond | 16.67 | 3 | | | | GLU166 | | | | | | | GLU166 | | | | | GLU166 | | |
| Hydrogen Bond | Carbon Hydrogen Bond | 11.11 | 2 | | | | | | | | | | ARG188 | | ARG188 | | | | | | |
| Hydrogen Bond | Pi-Donor Hydrogen Bond | 27.78 | 5 | GLU166 | GLU166 | | | | | | | | | GLU166 | GLU166 | | | | | GLU166 | |
| Hydrogen Bond | Pi-Donor Hydrogen Bond | 38.89 | 7 | HIS41 | | | HIS41 | | HIS41 | | | HIS41 | | HIS41 | | | HIS41 | | | HIS41 | |
| Hydrogen Bond | Conventional Hydrogen | 11.11 | 2 | | | | | | | | | | SER144 | | | | SER144 | | | | |
| Hydrogen Bond | Conventional Hydrogen | 38.89 | 7 | | | TYR54 | | TYR54 | | TYR54 | TYR54 | | | | | | | | TYR54 | TYR54 | TYR54 |
| Hydrogen Bond | Conventional Hydrogen | 61.11 | 11 | CYS145 | | CYS145 | | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | | CYS145 | | | | CYS145 | CYS145 | |
| Hydrogen Bond | Conventional Hydrogen | 100.00 | 18 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 |
| Hydrogen Bond | Conventional Hydrogen | 22.22 | 4 | | | | GLN192 | | | | | | | GLN192 | | GLN192 | | | GLN192 | | |
| Hydrogen Bond | Conventional Hydrogen | 5.56 | 1 | | | | | | | | | | GLN189 | | | | | | | | |
| Hydrogen Bond | Conventional Hydrogen | 100.00 | 18 | GLN192 | GLN192 | GLN192 | GLN192 | GLN192 | GLN192 | GLN192 | GLN192 | GLN192 | GLN192 | GLN192 | GLN192 | GLN192 | GLN192 | GLN192 | GLN192 | GLN192 | GLN192 |
| Hydrogen Bond | Conventional Hydrogen | 5.56 | 1 | | | | | | | | | | | | | GLN192 | | | | | |
| Hydrogen Bond | Conventional Hydrogen | 11.11 | 2 | | | | | | | | | | MET49 | | MET49 | | | | | | |
| Hydrogen Bond | Conventional Hydrogen | 44.44 | 8 | | | ASP187 | | ASP187 | | ASP187 | ASP187 | | ASP187 | | ASP187 | | | ASP187 | | | ASP187 |
| Hydrogen Bond | Conventional Hydrogen | 5.56 | 1 | | | | | | | | | | | | | | | | THR190 | | |
| Hydrogen Bond | Conventional Hydrogen | 44.44 | 8 | | | | | | | | LEU141 | LEU141 | LEU141 | | LEU141 | | LEU141 | | LEU141 | LEU141 | LEU141 |
| Hydrophobic | Alkyl | 72.22 | 13 | | | MET49 | MET49 | MET49 | | MET49 | MET49 | | MET49 | MET49 | MET49 | MET49 | | MET49 | MET49 | MET49 | MET49 |
| Hydrophobic | Alkyl | 11.11 | 2 | | | | PRO52 | PRO52 | | | | | | | | | | | | | |
| Hydrophobic | Alkyl | 5.56 | 1 | | | | | CYS44 | | | | | | | | | | | | | |
| Hydrophobic | Alkyl | 72.22 | 13 | MET49 | MET49 | MET49 | | MET49 | MET49 | MET49 | MET49 | MET49 | | | | MET49 | MET49 | | MET49 | MET49 | MET49 |
| Hydrophobic | Alkyl | 77.78 | 14 | ARG188 | ARG188 | ARG188 | ARG188 | ARG188 | ARG188 | ARG188 | ARG188 | ARG188 | | | | ARG188 | ARG188 | | ARG188 | ARG188 | ARG188 |
| Hydrophobic | Alkyl | 94.44 | 17 | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 | CYS145 |
| Hydrophobic | Alkyl | 0.00 | 0 | | | | | | | | | | | | | | | | | | |
| Hydrophobic | Alkyl | 11.11 | 2 | | | | CYS145 | | | | | | | | | | | CYS145 | | | |
| Hydrophobic | Amide Pi-Stacked | 72.22 | 13 | GLN189 | GLN189 | GLN189 | | GLN189 | GLN189 | GLN189 | GLN189 | GLN189 | GLN189 | | GLN189 | GLN189 | | GLN189 | | | GLN189 |
| Hydrophobic | Pi-Alkyl | 88.89 | 16 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | | HIS41 |
| Hydrophobic | Pi-Alkyl | 72.22 | 13 | | | HIS41 | HIS41 | | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | | HIS41 | HIS41 | HIS41 | HIS41 | HIS41 | | HIS41 |
| Hydrophobic | Pi-Alkyl | 5.56 | 1 | | | | | | | | | | | | | TYR54 | | | | | |
| Hydrophobic | Pi-Alkyl | 11.11 | 2 | | | | | | | | | | HIS41 | | HIS41 | | | | | | |
| Hydrophobic | Pi-Alkyl | 94.44 | 17 | | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 | HIS163 |
| Hydrophobic | Pi-Alkyl | 50.00 | 9 | HIS172 | | | | | | | HIS172 | HIS172 | HIS172 | | HIS172 | | HIS172 | | HIS172 | HIS172 | HIS172 |
| Hydrophobic | Pi-Alkyl | 100.00 | 18 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 | MET165 |
| Hydrophobic | Pi-Alkyl | 94.44 | 17 | PRO168 | PRO168 | PRO168 | PRO168 | | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 | PRO168 |
| Hydrophobic | Pi-Sigma | 33.33 | 6 | HIS41 | HIS41 | | | HIS41 | | | | | | HIS41 | | | | HIS41 | | HIS41 | |
| Other | Pi-Sulfur | 5.56 | 1 | | | | | Cys145 | | | | | | | | | | | | | |

Table S10. Binding energy values and amino acid residues interactions of $3CL^{pro}$ with orientanol E (**171**) and erycaffra (**57**)

| Components | Molecular Docking | | Molecular Dynamics Simulations | |
|---|---|---|---|---|
| | **Binding Energy** | **Amino Acid Residues** | **Binding Energy** | **Amino Acid Residues** |
| N3 | -10.14 kcal/mol | Met49, Gly143, Tyr118, Thr26, Leu27, Ser46, Asn14, Thr25, Thr45, Cys145, His41, Cys44, Asn142, Gln189, Glu166, Thr190, Ala191, Pro168, His164, Asp187, Tyr54, Arg188, Leu167, and Gln192 | -58.11 kcal/mol | Met49, Tyr118, Gly143, Ser46, Thr26, Leu27, Cys145, Thr25, Asn142, Gln189, Thr45, His41, His164, Asp187, Tyr54, Arg188, Leu167, Gln192, Pro168, Glu166, Met65, Cys44, Thr190, and Ala191 |
| GC376 | -7.83 kcal/mol | Met165, His164, Cys145, Asp187, His41, Met49, Arg188, Pro168, Gln189, Leu27, Thr25, Gly170, Leu167, and Glu166 | -20.25 kcal/mol | Met165, Leu167, Glu166, His164, Cys145, Asp187, His41, Met49, Arg188, Gly170, Pro168, Gln189, Leu27, and Thr25 |
| Orientanol E (**171**) | -12.04 kcal/mol | His41, Ala191, Arg188, Gln189, Leu167, Pro168, Cys145, Gln192, Glu166, Met165, Thr190, Cys44, Met49, Pro52, His163, His172, His164, and Tyr54 | -35.47 kcal/mol | His41, Met49, Cys44, His164, Cys145, Gly143, Asn142, Met65, Glu166, Pro168, Leu167, Gln192, Ala191, Thr190, Gln189, Asp187, Val186, and Arg188 |
| Erycaffra (**57**) | -11.93 kcal/mol | Leu167, Pro168, Ala191, His172, Glu166, Arg188, His41, Ser144, Tyr54, Cys145, His163, Gln192, Met49, Asp187, Thr190, Leu141, Pro52, Cys44, Gln189, and Met165 | -20.06 kcal/mol | Gln189, Met165, Phe181, Glu166, Gln192, Thr190, Ala191, Ala193, Met49, Leu167, Phe185, Val186, Arg188, His41, Pro52, Tyr54, Asp187, Cys44, Arg40, His164, and Pro39 |

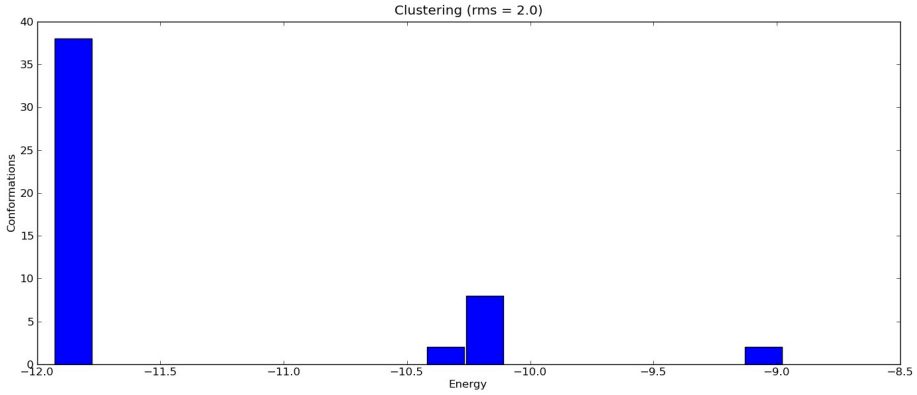


Figure S1. All cluster of erycaffra F (**57**)

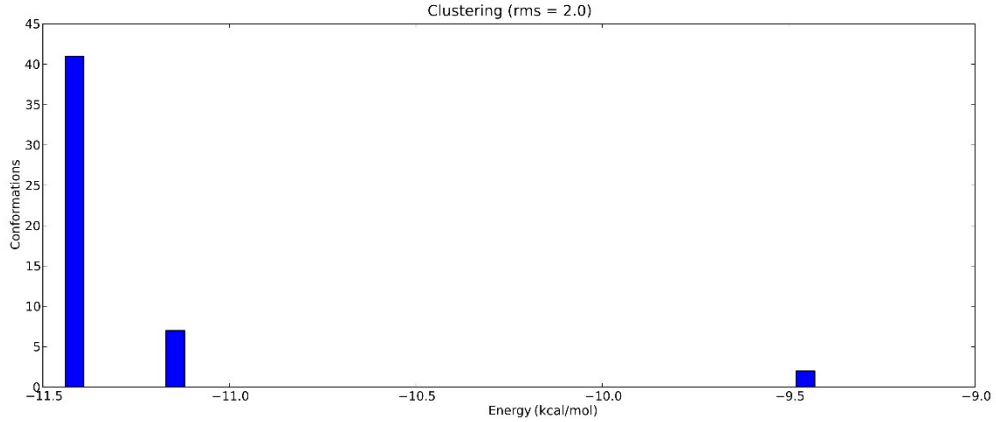


Figure S2. All cluster of orientanol E **(171)**