Supplementary Material

Diagram

Description automatically generated

B)

A)

Figure S1: Chemical structures of a TAS2R39 agonist theaflavin-3,3’-digallate (A) and TAS2R39 antagonist 6,3'-dimethoxyflavone (B). In the structure of 6,3'-dimethoxyflavone, commonly applied ring-nomenclature for flavonoids (A-, B-, and C-ring) is shown. Adapted from Chem Space (https://chem-space.com/)

Table S: All known ligands that activate TAS2R39

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Ligand** | **Effective concentration on hTAS2R39 (μM)** | **EC50 on TAS2R39 (μM)** | **Specific for TAS2R:** | **Source:** |
| AGONISTS | | | | |
| (-)- Epicatechin (EC) | 1000 | 417.1 | 4, 5, 39 | (1), (2) |
| (-)- Epicatechin gallate (ECg) | 32 | 151 | 14, 39 | (1), (2) |
| (-)- Epigallocatechin (EGC) | nd | 395.5 | 39 | (1), (2) |
| (+)- Taxifolin | 125 | nd | 14, 39 | (1) |
| (+/-) Equol | 32 | 55.8 | 14, 39 | (3) |
| 2,2’,4’-trihydroxychalcone | 2 | nd | 14, 39 | (1) |
| 3-(2-hydroxyethyl)-indole | 300 | nd | 4, 39 | (4) |
| 3,2’-dihydroxychalcone | 8 | 53.6 | 14, 39 | (1) |
| 3,6,3’,4’-tetrahydroxyflavone | 2 | nd | 14, 39 | (1) |
| 3,7,4’-trihydroxyflavone | 0.5 | nd | 14, 39 | (1) |
| 4,2’,5’-trihydroxychalcone | 2 | nd | 14, 39 | (1) |
| 4'-hydroxy-7-methoxyflavone | 250 | nd | 14, 39 | (1) |
| 4'-hydroxyflavone | 500 | nd | 39 | (1) |
| 5,2'-dihydroxyflavone | 500 | nd | 39 | (1) |
| 5,4'-dihydroxyflavone | 500 | nd | 14, 39 | (1) |
| 5,7,2'-trihydroxyflavone | 4 | 35.3 | 14, 39 | (1) |
| 5,7'-dimethoxyflavone | 32 | nd | 14, 39 | (1) |
| 5-hydroxyflavone | 500 | nd | 39 | (1) |
| 6,4'-dihydroxyflavone | 500 | nd | 14, 39 | (1) |
| 6,7,4’-trihydroxyisoflavone | 250 | nd | 14, 39 | (3) |
| 6-methoxyluteolin | 8 | 22.9 | 14, 39 | (1) |
| 7,3',4'-trihydroxyflavone | 16 | 141 | 14, 39 | (1) |
| 7,3’,4’-trihydroxyisoflavone | 250 | nd | 14, 39 | (3) |
| 7,4-'dihydroxyflavone | 125 | nd | 14, 39 | (1) |
| 7,8,4’-trihydroxyisoflavone | 63 | 184 | 14, 39 | (3) |
| 7-hydroxyisoflavone | 250 | 315 | 14, 39 | (3) |
| Acetaminophen | 3000 | nd | 39 | (5) |
| Acetylgenistin | 125 | nd | 39 | (3) |
| Amarogentin | 300 | nd | 1, 4, 39, 43, 46, 47, 50 | (5) |
| Apigenin | 1 | nd | 14, 39 | (1) |
| Azathioprine | 1000 | nd | 4, 10, 39, 46 | (5) |
| Biochanin A | 500 | nd | 14, 39 | (3) |
| Butein | 125 | nd | 14, 39 | (1) |
| Chloramphenicol | 1000 | nd | 1, 8, 10, 39, 41, 43, 46 | (5) |
| Chloroquine | 100 | nd | 3, 7, 10, 14, 39 | (5) |
| Chlorpheniramine | 100 | nd | 4, 7, 10, 14, 38, 39, 40, 46 | (5) |
| Chrysin | 16 | nd | 14, 39 | (1) |
| Colchicine | 3000 | nd | 4, 39, 46 | (5) |
| Coumestrol | 250 | nd | 14, 39 | (3) |
| Cyanidin Chloride | 32 | 187 | 14, 39 | (1) |
| Daidzein | 500 | nd | 14, 39 | (3) |
| Datiscetin | 16 | 41.6 | 14, 39 | (1) |
| Denatonium benzoate | 100 | nd | 4, 8, 10, 13, 39, 43, 46, 47 | (5) |
| Denatonium saccharide | nd | nd | 5, 39, 40, 43 | (6) |
| Diphenidol | 100 | nd | 1, 4, 7, 10, 13, 14, 16, 38, 39, 40, 43, 44, 46, 47, 49 | (5) |
| D-tryptophan | 217000 | nd | 4, 39 | (4) |
| Epigallocatechin gallate (EGCg) | 32 | 161 | 39, 43; 14 | (1), (2) |
| Eriodictyol | 16 | 62 | 14, 39 | (1) |
| Eriodictyolchalcone | 16 | 55.5 | 14, 39 | (1) |
| Fisetin | 1 | nd | 39 | (1) |
| Flavone | 8 | 45.9 | 14, 39 | (1) |
| Formomonetin | 500 | nd | 14, 39 | (1) |
| Formononetin | 500 | nd | 14, 39 | (3) |
| Fustin | 250 | nd | 14, 39 | (1) |
| Genistein | 8 | 49.4 | 14, 39 | (3) |
| Genistin | 500 | nd | 39 | (3) |
| Genkwanin | 500 | nd | 39 | (1) |
| Glycitein | 500 | nd | 14, 39 | (3) |
| Glycitin | 500 | nd | 39 | (3) |
| Gossypetin | 250 | 388 | 39 | (1) |
| Herbacetin | 125 | nd | 14, 39 | (1) |
| Hesperitin | 8 | nd | 14, 39 | (1) |
| Homoeriodictyol | 32 | 84.9 | 14, 39 | (1) |
| Isoliquiritigenin | 16 | nd | 14, 39 | (1) |
| Isorhamnetin | 0.12 | nd | 14, 39 | (1) |
| Kaempferol | 14 | nd | 14, 39 | (1) |
| Leu-Trp | 3000 | nd | 1, 4, 39 | (4) |
| Leu-Val-Tyr-Pro-Phe-Pro-Gly-Pro-Ile-His-Asn | 1000 | nd | 1, 39 | (4) |
| Liquiritigenin | 16 | 64.5 | 14, 39 | (1) |
| Luteolin | 0.5 | 7.3 | 14, 39 | (1) |
| Malonylgenistin | nd | 500 | 39 | (3) |
| Morin | 2 | nd | 14, 39 | (1) |
| Myricetin | 1 | nd | 14, 39 | (1) |
| Naringenin | 8 | 32.9 | 14, 39 | (1) |
| Pelargoninidin Chloride | 32 | nd | 14, 39 | (1) |
| Pentagalloylglucose | 3 | 6.6 | 5, 39 | (7) |
| Phe-Phe-Pro-Arg | nd | nd | 8, 39 | (8) |
| Phloretin | 8 | 41.3 | 14, 39 | (1) |
| Pinocembrin | 4 | 48.9 | 14, 39 | (1) |
| Pro-Arg (Prolylarginine) | 10000 | nd | 39 | (8) |
| Pyrocatechin | nd | nd | 1, 14, 39 | (6) |
| Quercetagetin | 2 | nd | 14, 39 | (1) |
| Quinine | 10 | nd | 4, 7, 10, 14, 39,40, 43, 44, 46 | (5) |
| Resveratrol | 63 | 109 | 14, 39 | (1) |
| Scutellarein | 8 | 40.3 | 14, 39 | (1) |
| Silibinin | 8 | 99.2 | 14, 39 | (1) |
| Sucralose | nd | nd | 1, 4, 5, 7, 8, 10, 39, 41, 46 | (6) |
| Sulfuretin | 16 | 48 | 14, 39 | (1) |
| Tenofovir Alafenamide (TAF) | nd | 0.87 | 1,8, 14, 39 | (9) |
| Theaflavin | nd | 2.79 | 39 | (10) |
| Theaflavin-3,3'-O-digallate | nd | 1.55 | 39 | (10) |
| Theaflavin-3'-O-gallate | nd | 0.67 | 3, 14, 39 | (10) |
| Thiamine | 1000 | nd | 1, 39 | (5) |
| Tricetin | 250 | nd | 39 | (1) |
| Trp-Trp | 1000 | 660 | 1, 4, 39 | (4) |
| Trp-Trp | 10000 | nd | 1, 4, 39 | (4) |
| Trp-Trp-Trp | 100 | nd | 1, 4, 14, 39, 46 | (4) |
| Tyr-Pro-Phe-Pro-Gly-Pro-Ile-His-Asn-Ser | 1000 | nd | 1, 39 | (4) |
| Vanilin | nd | 0.87 | 14, 29, 39 | (11) |
| Xanthone | 500 | nd | 14, 39 | (1) |
| ANTAGONISTS | | | | |
| 4'-fluoro-6-methoxyflavanone | nd | 102 | 14, 39 | (12) |
| 6,3'-dimethoxyflavanone | nd | 407 | 14, 39 | (12) |
| 6-methoxyflavanone | nd | 479 | 39 | (12) |
| 6-Methylflavone | nd | 4.9 | 39 | (9) |

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