**Supplementary material**

***In Silico* Approach for designing Novel SARS-CoV-2 Inhibitors from Medicinal Plants**

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**Table S1.**Structures of the studied compounds with best docking score and their binding energy (kcal/mol)

|  |  |  |  |
| --- | --- | --- | --- |
| Plants | Phytochemical structure + Phytochemical name | Binding energy | |
|  |  | 6lu7 | 6m0j |
| *Millettia griffoniana* | Griffonianones A (**28**) | -7.8 | -8.3 |
|  | Griffonianones B (**29**) | -8.7 | -8.0 |
|  | Griffonianone B methylether (5-methoxydurmillone) (**30**) | -7.8 | -7.6 |
|  | Griffonianones C (**31**) | -7.6 | -7.1 |
|  | Maximaisoflavone G (**30**) | -7.5 | -6.8 |
|  | 7-Hydroxy-6-methoxy-3',4'-methylenedioxyisoflavone (**29**) | -7.0 | -7.1 |
|  | Maximaisoflavone G acetate (**30**) | -7.3 | -7.2 |
|  | 7-Acetoxy-6-methoxy-3',4'-methylenedioxyisoflavone (**35**) | -7.4 | -7.3 |
|  | 7-O-geranylformononetin (**36**) | -7.1 | -7.7 |
|  | 3',4'-dihydroxy-7-O-[(E)-3,7-dimethyl-2,6-octadienyl]isoflavone (**37**) | -7.2 | -8.0 |
|  | Griffonianone D (**38**) | -6.9 | -7.2 |
|  | Griffonianone E (**39**) | -8.0 | -7.4 |
|  | 4'-O-geranylisoliquiritigenin (**40**) | -7.5 | -8.1 |
|  | 3',4'-methylenedioxy-7-O-[(E)-3,7-dimethyl-2,6-octadienyl] isoflavone (**41**) | -7.2 | -8.0 |
|  | Calapogonium isoflavone B (**42**) | -7.9 | -8.0 |
|  | 7-2'-dimethoxy-4',5'-methylenedioxy isoflavone (**43**) | -7.1 | -6.8 |
|  | Jamaicin (**44**) | -8.2 | -7.5 |
|  | Durmillone (**45**) | -7.8 | -7.4 |
|  | 4'-Methoxy-7-O[(E)-3-methyl-7-hydroxymethyl-2,6-octadienyl]isoflavone (**47**) | -7.1 | -7.2 |
|  | 4-Hydroxy-5,6,7-trimethoxy-3-(3',4'-methylenedioxy)phenylcoumarin (**48**) | -6.7 | -7.5 |
| *Rauwolfa vomitoria* | Normacusine B (**58**) | -7.7 | -7.7 |
|  | Peraksine (vomifoline) (**61**) | -7.5 | -8.0 |
|  | Geissoschizine (**62**) | -7.5 | -6.6 |
|  | Tetrahydroalstonine (**63**) | -6.8 | -7.2 |
|  | Urs-12-en-28-ol (**89**) | -7.7 | -7.9 |
|  | Neonorreserpine (**92**) | -8.6 | -7.3 |
| *Eucalyptus globulus* | Sesamin (**99**) | -8.4 | -8.3 |
|  | 3β,11α-Dihydroxyurs-12-en-28-oic acid (**100**) | -7.1 | -7.0 |
|  | Cypellocarpa C (**102**) | -9.0 | -7.6 |
|  | Aromadendrenea (**105**) | -7.3 | -6.7 |
| *Acanthus montanus* | Acanmontanoside (**117**) | -8.3 | -7.1 |
|  | Decaffeoylverbascoside (**118**) | -7.7 | -6.8 |
|  | Isoverbascoside (**120**) | -7.7 | -6.5 |
|  | Leucosceptoside A (**121**) | -7.9 | -6.8 |
|  | Verbascoside (**124**) | -7.9 | -7.4 |

**Table 2.** Drug-like properties of phytochemicals (The phytochemicals marked in **bold** satisfy the bioavailability rules).

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **n-ROTB** | **MW**  **(Da)** | **TPSA (Å)** | **n-OHNH donors** | **n-OHNH acceptors** | **Drug likeness** | | | | **MlogP** | **Solubility** | **Synthetic accessibility** |
| **Lipinski** | **Ghose** | **Veber** | **Egan** |
| **28** | 8 | 496.55 | 103.68 | 2 | 8 | 2 | 0 | 0 | 0 | 1.29 | Moderately | 5.12 |
| **29** | 2 | 378.37 | 67.13 | 0 | 2 | 0 | 0 | 0 | 0 | 1.94 | Moderately | 4.01 |
| **30** | 2 | 392.40 | 67.13 | 0 | 2 | 0 | 0 | 0 | 0 | 2.15 | Moderately | 4.13 |
| 31 | 6 | 448.51 | 74.97 | 0 | 6 | 0 | 0 | 0 | 1 | 2.14 | Moderately | 4.50 |
| **32** | 2 | 312.27 | 78.13 | 1 | 2 | 0 | 0 | 0 | 0 | 0.87 | Soluble | 3.29 |
| **33** | 2 | 312.27 | 78.13 | 1 | 2 | 0 | 0 | 0 | 0 | 0.87 | Soluble | 3.27 |
| **34** | 4 | 354.31 | 84.20 | 0 | 4 | 0 | 0 | 0 | 0 | 1.28 | Soluble | 3.49 |
| **35** | 4 | 354.31 | 84.20 | 0 | 4 | 0 | 0 | 0 | 0 | 1.28 | Soluble | 3.47 |
| 36 | 8 | 404.50 | 48.67 | 0 | 8 | 1 | 0 | 1 | 1 | 3.40 | Poorly soluble | 3.93 |
| **37** | 9 | 438.51 | 89.13 | 2 | 9 | 0 | 0 | 0 | 0 | 1.83 | Moderately | 4.53 |
| **38** | 9 | 438.51 | 89.13 | 2 | 9 | 0 | 0 | 0 | 0 | 1.83 | Moderately | 4.53 |
| 39 | 7 | 390.47 | 59.67 | 1 | 7 | 1 | 0 | 1 | 1 | 3.20 | Poorly soluble | 3.86 |
| **40** | 8 | 452.50 | 98.36 | 2 | 8 | 0 | 0 | 0 | 0 | 1.71 | Moderately | 4.66 |
| 41 | 7 | 418.48 | 57.90 | 0 | 7 | 1 | 0 | 1 | 1 | 3.25 | Poorly soluble | 4.07 |
| **42** | 1 | 348.35 | 57.90 | 0 | 1 | 0 | 0 | 0 | 0 | 2.26 | Moderately | 3.83 |
| **43** | 3 | 326.30 | 67.13 | 0 | 3 | 0 | 0 | 0 | 0 | 1.11 | Moderately | 3.42 |
| **44** | 2 | 378.37 | 67.13 | 0 | 2 | 0 | 0 | 0 | 0 | 1.94 | Moderately | 4.01 |
| **45** | 2 | 378.37 | 67.13 | 0 | 2 | 0 | 0 | 0 | 0 | 1.94 | Moderately | 4.03 |
| 47 | 9 | 420.50 | 68.90 | 1 | 9 | 0 | 0 | 0 | 1 | 2.58 | Moderately | 3.96 |
| **48** | 4 | 372.33 | 96.59 | 1 | 4 | 0 | 0 | 0 | 0 | 1.10 | Soluble | 3.66 |
| **58** | 1 | 322.44 | 39.26 | 2 | 2 | 0 | 0 | 0 | 0 | 3.08 | Soluble | 4.71 |
| **61** | 0 | 324.42 | 48.49 | 2 | 3 | 0 | 0 | 0 | 0 | 3.08 | Soluble | 4.71 |
| **62** | 3 | 366.45 | 65.56 | 2 | 4 | 0 | 0 | 0 | 0 | 2.27 | Moderately | 4.20 |
| **63** | 2 | 394.51 | 54.56 | 1 | 4 | 0 | 0 | 0 | 0 | 2.77 | Moderately | 4.91 |
| 89 | 1 | 426.72 | 20.23 | 1 | 1 | 1 | 3 | 0 | 1 | 6.92 | Poorly soluble | 6.18 |
| 91 | 9 | 594.65 | 128.78 | 2 | 10 | 2 | 3 | 0 | 0 | 1.57 | Moderately | 5.76 |
| **93** | 2 | 382.41 | 55.38 | 0 | 6 | 0 | 0 | 0 | 0 | 2.42 | Moderately | 4.36 |
| **94** | 1 | 472.70 | 77.76 | 3 | 4 | 1 | 3 | 0 | 1 | 4.97 | Poorly soluble | 6.42 |
| **96** | 7 | 520.53 | 176.12 | 5 | 11 | 2 | 2 | 1 | 1 | -0.70 | Soluble | 5.94 |
| **99** | 0 | 204.35 | 0.00 | 0 | 0 | 1 | 0 | 0 | 0 | 5.65 | Moderately | 3.70 |
| **117** | 16 | 804.74 | 290.05 | 9 | 19 | 3 | 2 | 1 | 5 | -2.04 | Moderately | 7.30 |
| **118** | 7 | 462.45 | 198.76 | 8 | 12 | 1 | 1 | 1 | 3 | -2.95 | Very soluble | 5.42 |
| **120** | 11 | 624.59 | 245.29 | 9 | 15 | 4 | 2 | 1 | 4 | -2.37 | Soluble | 6.37 |
| **121** | 12 | 638.61 | 234.29 | 8 | 15 | 4 | 2 | 1 | 4 | -2.18 | Soluble | 6.46 |
| **124** | 11 | 624.59 | 245.29 | 9 | 15 | 4 | 2 | 1 | 4 | -2.37 | Soluble | 6.37 |