**Supplementary material**

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

Romuald Tematio Fouedjou (a), Ossama Daoui (b), Hassan Nour (c), Monisa Ayoub (d), Hervet Paulain Dongmo Fogang (e), Farhan Siddique (d), Souad Elkhattabi (b), Mohamed Bakhouch (f), Salah Belaidi (g), Samir Chtita (c, \*)

 (a) Research Unit of Environmental and Applied Chemistry, Department of Chemistry, Faculty of Science, University of Dschang, Box 67, Dschang, Cameroon.

 (b) Laboratory of Engineering, Systems and Applications, National School of Applied Sciences, Sidi Mohamed Ben Abdellah-Fez University, BP Box 72, Fez, Morocco.

(c) Laboratory of Analytical and Molecular Chemistry, Faculty of Sciences Ben M’Sik, Hassan II University of Casablanca, B.P 7955, Casablanca, Morocco.

(d) Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Bahauddian Zakariya University, Multan 60800 Pakistan.

(e) Department of Physiological Sciences and Biochemistry, Faculty of Medicine and Biomedical Sciences of Garoua, University of Garoua, Garoua, Cameroon.

(f) Laboratory of Bioorganic Chemistry, Department of Chemistry, Faculty of Sciences, Chouaïb Doukkali University, P.O. Box 24, 24000 El Jadida, Morocco.

(g) Group of Computational and Medicinal Chemistry, LMCE Laboratory, University of Biskra, Biskra, Algeria

(\*) Corresponding author: E-mail: samirchtita@gmail.com; Tel: +212 660005554

**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 |