**Potential of terpenes from African herbs as inhibitors of DPP-4 and PTP1B targets in diabetes: molecular and quantum mechanics calculations**

Oludare M. Ogunyemi1\*, Gideon A. Gyebi2, Femi Olawale3, Ibrahim M. Ibrahim4, Opeyemi Iwaloye5, Modupe M. Fabusiwa1, Stephen Omowaye6, Charles O. Olaiya1

Table S1: Top docking terpenes against DPP4 and PTP1B

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  |  | DPP4 | PTP1B |
| S1 | Alogliptin |  |  | -7.7 |  |
| S2 | Isothiazolidinone |  |  |  | -10.0 |
| 1 | **3- Benzoylhosloppone**  | Abietane diterpenes  | Hoslundia opposita (Lamiaceae) | -10.0 | -8.0 |
| 2 | **20-*Epi*-isoiguesterinol (101)** | Bisnorterpenes  | Bisnorterpenes  | -9.9 | -7.1 |
| 3 | **Cucurbitacin B (169)** | Pentacyclic triterpenes  | Cogniauxia podolaena (Cucurbitaceae) | -9.9 | -6.4 |
| 4 | **Isoiguesterin (100)** | Bisnorterpenes  | Bisnorterpenes  | -9.7 | -7.6 |
| 5 | **Cryptobeilic acid C (151)** | Beilshmiedic acid derivatives  | Beilschmiedia cryptocaryoides(Lauraceae)  | -9.5 | -8.6 |
| 6 | **Ent-18-*E*-Caffeoyloxy-7 -hydroxy-3-cleroden-15-oic acid (67)** | Clerodane and labdanediterpenoids  | Nuxia sphaerocephala (Loganiaceae)  | -9.4 | -8.0 |
| 7 | **6-Oxoisoiguesterin (103)** | Bisnorterpenes  | Bisnorterpenes  | -9.3 | -7.5 |
| 8 | **Liriodenine (106)** | Acyclic triterpenes  | Ekebergia capensis (Zingiberaceae)  | -9.2 | -7.7 |
| 9 | **Isoiguesterinol (102** | Bisnorterpenes  | Bisnorterpenes  | -9.0 | -7.1 |
| 10 | **1-Deacetylkhivorin (92)** | Limonoids  | Khaya grandifoliola (Meliaceae)  | -8.9 | -5.6 |
| 11 | **Cucurbitacin D (170)** | Pentacyclic triterpenes  | Cogniauxia podolaena (Cucurbitaceae) | -8.9 | -7.0 |
| 12 | **Ent-18-*E*-Caffeoyloxy-8(17)-labden-15-oic acid (69)** | Clerodane and labdanediterpenoids  | Nuxia sphaerocephala (Loganiaceae)  | -8.8 | -7.0 |
| 13 | **7-Deacetylkhivorin (91):** | Limonoids  | Khaya grandifoliola (Meliaceae)  | -8.8 | -5.4 |
| 14 | **Gedunin (90)** | Limonoids  | Khaya grandifoliola (Meliaceae)  | -8.7 | -6.0 |
| 15 | **Tsangibeilin B (153)** | Beilshmiedic acid derivatives  | Beilschmiedia cryptocaryoides(Lauraceae)  | -8.6 | -8.5 |
| 16 | **Oleanolic acid (160)** | Pentacyclic triterpenes  | Nuxia sphaerocephala (Loganiaceae)  | -8.6 | -6.1 |
| 17 | **(13*S*)-Ent-18-*E*-Coumaroyloxy-8(17)-labden-15-oic acid (68)** | Clerodane and labdanediterpenoids  | Nuxia sphaerocephala (Loganiaceae)  | -8.5 | -7.4 |
| 18 | **Ekeberin C1 (97)** | Limonoids  | Ekebergia capensis (Zingiberaceae)  | -8.5 | -6.2 |
| 19 | **24-Methylene cycloartenol (164)** | Pentacyclic triterpenes  | Entandrophragma angolense(Meliaceae)  | -8.5 | -7.1 |
| 20 | **3-Friedelanone (166)** | Pentacyclic triterpenes  | Hypericum lanceolatum (Hypericaceae) | -8.5 | -6.6 |
| 21 | **Lupeol (161** | Pentacyclic triterpenes  | Hymenocardia acida (Phyllanthaceae)  | -8.3 | -5.2 |
| 22 | **3-Oxolupenal (3-oxolup-20(29)-en-30-al) (156)** | Pentacyclic triterpenes  | Nuxia sphaerocephala (Loganiaceae)  | -8.2 | -7.0 |
| 23 | **3-Oxolupenol (30-hydroxylup-20(29)-en-3-one) (158)** | Pentacyclic triterpenes  | Nuxia sphaerocephala (Loganiaceae)  | -8.2 | -6.2 |
| 24 | **Hydroxyvernolide (124)** | Sesquiterpenes andsesquiterpene lactones  | Vernonia amygdalina (Asteraceae)  | -8.1 | -5.5 |
| 25 | **Pristimerin (155)** | Pentacyclic triterpenes  | Maytenus senegalensis (Celastraceae) | -8.1 | -7.5 |
| 26 | 3 -Hydroxylupenal (3 -hydroxylup-20(29)-en-30-al) (**157**) | Pentacyclic triterpenes  | Nuxia sphaerocephala (Loganiaceae)  | -8.1 | -7.0 |
| 27 | Vernolide (**123**) | Sesquiterpenes andsesquiterpene lactones  | Vernonia amygdalina (Asteraceae)  | -8.0 | -5.5 |
| 28 | 3-*O*-betulinic acid *p*-coumarate (**167**) | Pentacyclic triterpenes  | Baillonella toxisperma (Sapotaceae) | -8.0 | -5.2 |
| 29 | 2 ,3 ,19 -Trihydroxy-urs-12-20-en-28-oic acid (**168**) | Pentacyclic triterpenes  | Kigelia africana (Bignoniaceae) | -8.0 | -5.4 |
| 30 | Ferruginol (**118**) | Abietane diterpenes  | Fuerstia africana (Lamiaceae) | -7.9 | -7.6 |
| 31 | Betulinic acid (**165** | Pentacyclic triterpenes  | Entandrophragma angolense(Meliaceae)  | -7.9 | -5.6 |
| 32 | Galanolactone (**85**) | Clerodane and labdanediterpenoids  | Aframomum arundinaceum(Zingiberaceae)  | -7.8 | -6.5 |
| 33 | Artemisinin (**137**) | Sesquiterpenes andsesquiterpene lactones  | Artemisia annua (Asteraceae) | -7.8 | -5.9 |
| 34 | Cryptobeilic acid A (**149**) | Beilshmiedic acid derivatives  | Beilschmiedia cryptocaryoides(Lauraceae)  | -7.8 | -6.7 |
|  | Alogliptin |  |  | -7.7 |  |
| 35 | Caesaldekarin C (110) | Cassane furanoditerpenes  | Caesalpinia volkensii (Leguminosae)  | -7.7 | -5.5 |
| 36 | Tagitinin C (**139**) | Sesquiterpenes andsesquiterpene lactones  | Tithonia diversifolia (Asteraceae) | -7.7 | -5.9 |
| 37 | Cryptobeilic acid D(**152**) | Beilshmiedic acid derivatives  | Beilschmiedia cryptocaryoides(Lauraceae)  | -7.7 | -7.0 |

Table S2: Post-docking MMGBSA scores of top terpenes against DPP-4 and PTP1B

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| S/N | Compounds | MMGBSA Bind  | Bind Coulomb |  Covalent |  Hbond |  Bind Lipo |  Bind Packing | Bind Solv GB | Bind vdW |
| DPP-4 |
| S1 | Alogliptin | -37.02 | -8.32 | 1.758 | -2.305 | -14.135 | -2.882 | 28.224 | -39.358 |
| T1 | Cucurbitacin B (169) | **-47.80** | -35.29 | 11.264 | -3.363 | -19.397 | 0 | 57.773 | -58.782 |
| T2 | 20-*Epi*-isoiguesterinol (101) | -29.78 | -19.15 | 0.991 | -2.029 | -23.209 | -0.795 | 54.704 | -40.289 |
| T3 | Isoiguesterin (100) | -28.75 | -10.864 | 1.379 | -0.883 | -23.836 | -0.785 | 46.43 | -40.191 |
| T4 | 6-Oxoisoiguesterin (103) | -32.90 | -17.498 | 0.971 | -1.881 | -22.559 | -0.867 | 46.477 | -37.532 |
| T5 | Liriodenine (106) | **-39.11** | -7.721 | 1.263 | -0.708 | -17.902 | -5.46 | 23.842 | -32.426 |
| T6 | Isoiguesterinol (102 | -29.36 | -16.714 | 2.695 | -1.903 | -21.807 | -0.776 | 50.067 | -40.923 |
| T7 | 1-Deacetylkhivorin (92) | -19.72 | -15.43 | 5.832 | -2.132 | -15.078 | -1.142 | 44.856 | -36.626 |
| T8 | 7-Deacetylkhivorin (91): | -25.71 | 2.965 | 2.832 | -1.306 | -14.321 | -2.303 | 34.239 | -47.818 |
| PTP1B |
| S2 | ISOTHIAZOLIDINONE | -85.23 | -99.344 | 4.973 | -6.852 | -20.154 | -3.171 | 92.36 | -53.038 |
| T9 | Tsangibeilin B (153) | -42.32 | -26.194 | 1.513 | -2.345 | -28.259 | -1.313 | 51.722 | -37.444 |
| T10 | Cryptobeilic acid C (151) | -44.09 | -33.452 | 0.954 | -2.304 | -27.212 | -1.285 | 57.253 | -38.042 |
| T5 | Liriodenine (106) | -34.39 | -1.887 | 0.367 | -0.871 | -20.387 | -6.538 | 28.248 | -33.322 |
| T3 | Isoiguesterin (100) | -42.07 | -21.819 | 5.568 | -2.717 | -22.009 | -2.469 | 31.443 | -30.066 |
| T4 | 6-Oxoisoiguesterin (103) | -41.11 | -17.819 | 5.163 | -2.82 | -20.149 | -2.49 | 28.487 | -31.482 |
| T6 | Isoiguesterinol (102 | -45.82 | -31.997 | 6.987 | -3.171 | -21.847 | -2.484 | 35.587 | -28.891 |
| T11 | Galanolactone (85) | -43.56 | -38.903 | 4.492 | -2.116 | -19.293 | 0 | 40.361 | -28.1 |
| T2 | 20-*Epi*-isoiguesterinol (101) | -29.06 | -22.418 | 4.903 | -2.383 | -16.142 | -2.405 | 36.822 | -27.439 |