Supplementary Information

Molecular docking, MD simulations and ADME studies of phytoconstituents of *Plumeria alba* as potential antidiabetics

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Table-I: Literature known compounds from *Plumeria alba*

S. No.	Compound
1)	β-sitosterol (L1)
2)	β-sitosterol glucoside (L2)
3)	β-amyrin (L3) and β-amyrin acetate (L3a/PA-2)
4)	α-amyrin (L4)
5)	Geraniol (L5)
6)	Eugenol (L6)
7)	Rutin (L7)
8)	Plumieride acid (L8) and Plumieride (L8a/PA-10)
9)	Hyperin (L9)
10)	Plumericin (L10)

Characterization of compound PA-1

Compound PA-1 was obtained as a white low melting solid on crystallisation with methanol. It gave a positive Libermann Burchard test and a violet colouration with 5% sulphuric acid followed by heating on TLC (Rf = 0.68 in petroleum ether/chloroform, 80:20) and was thought to be a triterpenoid.

IR ν_{max} (KBr): 2921, 2852, 1730, 1245, 1215, 1174, 981, 757 cm^{-1}.

^{1}H NMR (δ, $CDCl_3$, 300 MHz): 4.68 and 4.56 (2s, 1H each, >C=CH_2), 4.46 (m, 1H, H-3), 2.38 (m, 1H, H-19), 2.31 (m, 2H, CH_2-CO), 1.68 (s, 3H, vinylic-CH_3), 1.93 & 1.38 (2m, H, -CH_2 & -CH-), 1.02 (s, 3H, 27-CH_3), 0.94 (s, 3H, 26-CH_3), 0.85 (s, 3H, 25-CH_3), 0.83 (s, 6H, 23-CH_3 & 28-CH_3), 0.78 (s, 3H, 24-CH_3).

Mass spectral data, EIMS *m/z* (%): 524 (M^+, 6), 465 (10), 451 (8), 437 (12), 423 (10), 408 (40), 396 (20), 367 (14), 339 (8), 297 (18), 273 (21), 218 (24), 203 (38), 189 (100), 175 (44), 161 (48), 147 (42), 135 (70), 121 (68), 109 (68), 95 (90).

PA-1 was identified as hexyl ester of lupeol and characterized as **lup-20(29)-ene-3-yl-hexanoate**.

Characterization of compound PA-2

Compound **PA-2** was obtained by preparative TLC as a white solid having m.p. 238-9 ºC. It gave an intense violet coloured spot on TLC plate (R_f = 0.62 in chloroform/petroleum ether, 50:50) with 5% sulphuric acid solution on heating indicating it to be a triterpene. This was however confirmed by a positive Libermann Burchard test for triterpene.

IR ν_{max} (KBr): 2924, 2854, 1734, 1245, 1024, 1003, 985, 968, 722 cm^{-1}.

^{1}H NMR (δ, $CDCl_3$, 300 MHz): 5.13 (m, 1H, H-12), 4.50 (m, 1H, H-3α), 2.84 (m, 1H, H-18), 2.04 (s, 3H, CH_3CO-), 1.93 (m, 2H, H-11), 1.29 & 1.60 (3m, 20H, -CH_2- & -CH-), 1.06 (s, 3H, 27-CH_3), 0.98 (s, 3H, 25-CH_3), 0.87 & 0.86 (2s, 9H, 23-CH_3, 29-CH_3 & 30-CH_3), 0.83 (s, 3H, 26-CH_3), 0.78 (s, 3H, 28-CH_3).

^{13}C NMR (δ, $CDCl_3$, 75.5 MHz): 171.8 (>C=O), 140.4, 128.1, 81.7, 56.1, 52.2, 48.5, 48.0, 47.6, 42.9, 42.3, 40.4, 39.3, 38.5, 37.9, 35.5, 34.9, 33.7, 31.5, 27.4, 26.3, 25.7, 24.4, 22.2, 22.1, 19.0, 18.3, 17.7, 17.5, 16.5, 14.9.

Mass spectral data, EIMS *m/z* (%): 468 (M^+, 12), 452 (6), 408 (7), 393 (5), 257 (10), 218 (100), 203 (32), 189 (30), 161 (16), 135 (24), 121 (16), 109 (22).

Matching the melting point with that reported in literature (241°C), compound **PA-2** was identified as **3β-O-acetyl-olean-12-ene** commonly known as **β-amyrin acetate**.

Characterization of PA-3

Compound **PA-3** was obtained as white solid on crystallization from acetone, m.p. 210-12 ºC. It gave a positive Libermann Burchard test and a brick red colour with 5% sulphuric acid followed by heating on TLC (R_f = 0.61 in chloroform/petroleum ether, 50:50) and thus could be a triterpene or steroid.

IR ν_{max} (KBr): 2938, 2856, 1736, 1662, 1511, 1247, 1214, 1195, 950 cm^{-1}.

^{1}H NMR (δ, $CDCl_3$, 300 MHz): 4.68 and 4.57 (2s, 1H each, C=CH_2), 4.45 (m, 1H, H-3), 2.35 (m, 1H, H-19), 2.04 (s, 3H, CH_3CO-), 1.68 (s, 3H, vinylic-CH_3), 1.24-1.64 (m, 24H, -CH_2- & -CH-), 1.02 (s, 3H, 27-CH_3), 0.93 (s, 3H, 26-CH_3), 0.85 (s, 3H, 25-CH_3), 0.84 (s, 3H, 23-CH_3), 0.83 (s, 3H, 28-CH_3), 0.78 (s, 3H, 24-CH_3).

^{13}C NMR (δ, $CDCl_3$, 75.5 MHz): 172.8 (>C=O), 152.7, 111.1 (C=**C**H_2), 82.8 (C-3), 57.2, 52.2, 50.1, 49.8, 44.8, 44.6, 42.7, 41.8, 40.2, 39.9, 39.6, 37.4, 36.9, 36.0, 31.7, 29.7, 29.2, 26.9, 25.5, 23.4, 22.8, 21.1, 20.0, 19.8, 18.3, 18.0, 17.8, 16.3.

DEPT (δ, $CDCl_3$, 75.5 MHz): 172.8 (q), 152.7 (q), 111.1 (CH_2), 82.8 (CH), 57.2 (CH), 52.2 (CH), 50.1 (CH), 49.8 (CH), 44.8 (q), 44.6 (q), 42.7 (q), 41.8 (CH_2), 40.2 (CH_2), 39.9 (CH), 39.6 (q), 37.4 (CH_2), 36.9 (q), 36.0 (CH_2), 31.7 (CH_2), 29.7 (CH_3), 29.2 (CH_2), 26.9 (CH_2), 25.5 (CH_2), 23.4 (CH_3), 22.8 (CH_2), 21.1 (CH_3), 20.0 (CH_2), 19.8 (CH_3), 18.3 (CH_3), 18.0 (CH_3), 17.8 (CH_3), 16.3 (CH_3).

Mass spectral data, EIMS *m/z* (%): 468 (M^+, 34), 453 (8), 411 (12), 408 (14), 396 (60), 393 (14), 382 (18), 357 (8), 296 (10), 276 (16), 218 (42), 205 (22), 203 (34), 189 (96), 175 (28), 161 (40), 147 (54), 135 (74), 121 (70), 109 (82), 95 (92).

The observed melting point matched with that reported in literature, compound **PA-3** was identified as **3β-O-acetyllup-20(29)-ene**.

This is the first report of the isolation of this compound from the species *Plumeria alba*.

Characterization of PA-4

Compound **PA-4** was obtained as white crystalline solid on crystallization from acetone, m.p. 212-13 ºC. It gave a positive Liebermann-Burchard test and a violet colour by spraying TLC with 5% sulphuric acid and subsequent heating (R_f = 0.53 in petroleum ether/ethylacetate, 95:5).

IR ν_{max} (KBr): 3310, 2927, 2846, 1641, 1591, 1451, 1380, 1227, 1037, 880 (C=CH_2), 668 cm^{-1}.

^{1}H NMR (δ, $CDCl_3$, 300 MHz): 4.69 and 4.56 (2s, 1H each, C=CH_2), 3.21 (m, 1H, H-3α), 2.37 (m, 1H, H-19), 1.68 (s, 3H, vinylic-CH_3), 1.90 & 1.25-1.64 (2m, 24H, -CH_2- & -CH-), 1.03 (s, 3H, 27-CH_3), 0.96 (s, 3H, 26-CH_3), 0.94 (s, 3H, 25-CH_3), 0.83 (s, 3H, 28-CH_3), 0.78 (s, 3H, 24-CH_3), 0.76 (s, 3H, 23-CH_3).

^{13}C NMR (δ, $CDCl_3$, 75.5 MHz): 151.3 (C=**C**H_2), 109.7 (**C**=CH_2), 79.4 (C-3), 55.7, 50.8, 48.7, 48.3, 43.2, 41.9, 41.2, 40.4, 39.1, 38.4, 37.5, 35.9, 34.7, 33.3, 30.2, 30.0, 28.3, 27.8, 25.5, 23.7, 21.3, 19.7, 18.7, 18.3, 16.5, 16.3, 15.7, 14.9.

DEPT (δ, $CDCl_3$, 75.5 MHz): 151.3 (q), 109.7 (CH_2), 79.4 (CH), 55.7 (CH), 50.8 (CH), 48.7 (CH), 48.3 (CH), 43.2 (q), 41.9 (q), 41.2 (q), 40.4 (CH_2), 39.1 (CH_2), 38.4 (CH), 37.5 (q), 35.9 (CH_2), 34.7 (CH_2), 33.3 (q), 30.2 (CH_2), 30.0 (CH_2), 28.3 (CH), 27.8 (CH_2), 25.5 (CH_2), 23.7, 21.3 (CH_2), 19.7 (CH_3), 18.7 (CH_2), 18.3 (CH_3), 16.5 (CH_3), 16.3 (CH_3), 15.7 (CH_3), 14.9 (CH_3).

Mass spectral data, EIMS *m/z* (%): 426 (M^+, 20), 411 (15), 408 (12), 393 (7), 383 (6), 315 (11), 272 (5), 234 (9), 218 (89), 205 (32), 203 (57), 189 (100), 175 (35), 135 (95), 109 (89), 95 (97).

Thus, it was thought to be a triterpene and using spectral data and comparison of the observed melting point with that reported in literature, compound **PA-4** was identified as **lup-20(29)-en-3β-ol**. Further, it was confirmed by the preparation of its acetate using acetic anhydride and N,N-dimethylpyridine. The melting point, R_f and spectral data of the resulting compound matched with that of **PA-3** earlier identified as lupeol acetate.

This is the first report of isolation of compound lup-20(29)-en-3β-ol from *Plumeria alba*.

Characterization of PA-5

Compound **PA-5** was isolated as white solid crystallized from chloroform/methanol, m.p. 163-64 °C. It's spot on the developed TLC plate (R_f = 0.33 using petroleumether/ethyl acetate, 95:5, as the developing solvent) gave an intense violet colour on spraying with 5% sulphuric acid solution followed by heating. It also gave the positive Libermann Burchard test for triterpenes.

IR ν_{max} (KBr): 3420, 2926, 2853, 1626, 1253, 665 cm^{-1}.

^{1}H NMR (δ, $CDCl_3$, 300 MHz): 5.35 (m, 1H, H-7), 5.12 (m, 1H, H-28), 3.51 (m, 1H, H-3α), 2.74 (m, 1H, H-25), 2.28 (m, 2H, H-23), 1.48 (d, 3H, *J* = 6.4 Hz, 29-CH_3), 2.00, 1.84 & 1.44-1.12 (3m, 22H, -CH_2- & -CH-), 1.01 (s, 3H, 19-CH_3), 0.93 (d, 3H, *J* = 6.2 Hz, 4-CH_3), 0.83 (d, 3H, 27-CH_3), 0.82 (s, 3H, 21-CH_3), 0.80 (d, 3H, 26-CH_3), 0.68 (s, 3H, 18-CH_3).

^{13}C NMR (δ,$CDCl_3$, 75.47 MHz): 142.2, 139.2, 130.0, 123.4, 73.6, 53.1, 51.8, 43.9, 43.3, 41.7, 38.7, 36.9, 35.4, 32.6, 32.2, 32.0, 31.4, 31.2, 30.3, 28.4, 27.8, 27.2, 25.4, 22.9, 22.8, 21.0,20.7, 19.7, 13.4, 12.1.

Mass spectral data, EIMS *m/z* (%):.426 (M^+, 30), 411 (18), 393 (12), 380 (10), 366 (8), 286 (22), 261 (14), 247 (20), 191 (30), 161 (50), 81 (100).

These types of steroids, known as 4α-methylsterols are reported in the literature[69] and thus by comparison of above mentioned spectral data and melting point, **PA-5** was confirmed as **4α-methyl-5α-stigmast-7,24(28)-dien-3β-ol (α-sitosterol)**.

This is the first report of isolation of α-sitosterol from the genus *Plumeria*.

Characterization of PA-6

Compound **PA-6** was crystallized as light brown crystals from chloroform/methanol, having m.p. 206-8 ºC. It showed a single spot on TLC (R_f = 0.17 in chloroform/methanol, 95:5) as developing solvent and was $FeCl_3$ active indicating the presence of a phenolic group in the compound. It also gave effervescence with saturated $NaHCO_3$ solution showing indicating it to be an acid.

IR ν_{max} (KBr): 3395, 2925, 2859, 1674, 1621, 1510, 1449, 1319, 1244, 1210, 831 cm^{-1}.

^{1}H NMR (δ, CD_3COCD_3, 300 MHz): 7.61 (d, 1H, *J* = 16.0 Hz, H-3), 7.56 (dd, 2H, *J* = 6.6 & 2.0 Hz, H-2′ & H-6′), 6.89 (dd, 2H, *J* = 6.6 & 2.0 Hz, H-3′ & H-5′), 6.35 (d, 1H, *J* = 16.0 Hz, H-2).

^{13}C NMR (δ, CD_3COCD_3, 75.47 MHz): 164.2, 161.2, 145.2, 130.6, 126.8, 116.4, 115.5.

Mass spectral data, EIMS *m/z* (%): 164 (M^+, 100), 147 (46), 119 (28), 107 (62), 91 (88), 71 (100).

Finally, the melting point comparison of **PA-6** with that reported in literature confirmed it to be p-hydroxy cinnamic acid.

This is the first report of the isolation of p-hydroxycinnamic acid from *Plumeria alba*.

Characterization of PA-7

Compound **PA-7** was crystallized as a white solid from chloroform/methanol (90:10) fraction of the cold extract, m.p. 256-8 ºC. It gave an intense violet colour on TLC spraying with 5% sulphuric acid solution followed by heating (R_f = 0.45, chloroform/methanol, 90:10). Compound **PA-7** gave a positive Liebermann-Burchard test for triterpenes, a pale yellow colour with tetranitromethane indicating unsaturation and a positive Molisch test of carbohydrates.

IR ν_{max} (KBr): 3351, 2924, 2853, 1625, 1073, 1023, 720 cm^{-1}.

^{1}H NMR (δ, DMSO-d_6, 300 MHz): 5.40 (m, 1H, H-7), 5.10 (m, 1H, H-28), 5.01 (m, 1H, H-1′), 4.39-3.61 (m, 11H, H-glu), 3.57 (m, 1H, H-3α), 2.39 (m, 1H, H-23), 2.26-1.83 & 1.25 (m, -CH_2- & -CH-), 1.48 (d, 3H, vinylic-29-CH_3), 1.00 (s, 3H, 19-CH_3), 0.90 (d, *J* = 7.2 Hz, 4-CH_3), 0.84 (d, 6H, 27-CH_3 & 26-CH_3), 0.82 (s, 3H, 21-CH_3), 0.67 (s, 3H, 18-CH_3).

Mass spectral data, EIMS *m/z* (%): 425 (M^+- glu, 8), 411 (14), 396 (26), 382 (14), 357 (8), 329 (6), 286 (12), 161, (24), 118 (44), 97 (60), 81 (100).

Acetylatin of PA-7

Compound **PA-7** (5 mg) was acetylated using acetic anhydride (1ml) and in the presence of catalytic amount of N,N-dimethyl aminopyridine. The acetyl derivative was crystallized as a white solid using acetone.

IR ν_{max} (KBr): 2924, 2855, 1739, 1629, 1220, 1169, 903 cm^{-1}.

^{1}H NMR (δ, $CDCl_3$, 300 MHz): 5.41 (m, 1H, H-7), 5.11 (m, 1H, H-28), 5.05 (m, 1H, H-1′), 4.32-3.73 (m, 7H, H-glu), 3.64 (m, 1H, H-3α), 2.38 (m, 1H, H-23), 2.30-1.83 & 1.25 (m, -CH_2- & -CH-), 2.07, 2.04, 2.02 & 2.00 (4s, 12H, 4x$COCH_3$), 1.48 (d, 3H, vinylic-29-CH_3), 1.00 (s, 3H, 19-CH_3), 0.90 (d, *J* = 7.2 Hz, 4-CH_3), 0.84 (d, 6H, 27-CH_3 & 26-CH_3), 0.82 (s, 3H, 21-CH_3), 0.67 (s, 3H, 18-CH_3).

Hydrolysis of PA-7

Compound **PA-7** (10 mg) was refluxed with 7% ethanolic hydrochloric acid (4 ml) in an oil bath at 100-110°C for 4-5 hours. The reaction mixture was kept overnight. The solvent was then removed under pressure and the contents were added to ice-water with vigrous swirling and extracted with diethylether. The organic layer was dried & solvent was removed to recover the aglycone. The aglycone was crystallized from methanol/chloroform as white solid. It showed a single spot on TLC using petroleum ether/ethylacetate (95:5) as developing solvent, R_f = 0.33. The Co-TLC & Co-IR was checked with the authentic sample of α-sitosterol.

Mass spectral data, EIMS *m/z* (%): 426 (M^+, 6), 411 (8), 393 (76), 380 (26), 329 (20), 286 (18), 261 (40), 213, (40), 191 (14), 161 (40), 147 (48), 119 (38), 81 (100).

The aqueous part was neutralized with barium carbonate and the sugar obtained was identified as glucose by comparing authentic sample on paper chromatography using butanol:ethanol:water (5:3:2) and by HPLC using carbohydrate column.

The structure of the compound **PA-7** was finally confirmed by acid hydrolysis that yielded an aglycone of molecular weight m/z 426, corresponding to the molecular formula $C_{30}H_{50}O$ and characterized as α-sitosterol (**PA-5**) on the basis of a single spot on Co-TLC and a superimposable IR spectrum. The sugar part was identified as glucose on its comparison with authentic sample on paper chromatography.

On the basis of above spectral data compound **PA-7** was characterized as 4α-methyl-5α-stigmast-7,24(28)-dien-3β-O-glucoside.

This is the first report of isolation of 4α-methyl-5α-stigmast-7,24(28)-dien-3β-O-glucoside from the genus *Plumeria*.

Characterization of PA-8

PA-8 was obtained as a white solid from extract A, m.p. 169-71 °C and gave a positive Liebermann Burchard test for triterpene. It gave a single spot on TLC with R_f = 0.48 in chloroform/petroleum ether, 50:50 as developing solvent and turned violet on spraying with 5% sulphuric acid and subsequent heating.

IR ν_{max} (KBr): 2924, 2854, 1707, 1639, 1109, 882, 665 cm^{-1}.

^{1}H NMR (δ, $CDCl_3$, 300 MHz): 4.69 & 4.57 (2s, 1H each, C=C**H_2**), 2.31 (m, 3H, H-19 & H-2), 1.68 (s, 3H, vinylic-CH_3), 1.93 & 1.64-1.25 (2m, 22H, -CH_2- & -CH-), 1.09 (s, 3H, 23-

CH_3), 1.02 (s, 3H, 26-CH_3), 0.95, 0.93 & 0.87 (3s, 9H, 24-, 25- & 27-CH_3), 0.79 (s, 3H, H-28).

Mass spectral data, EIMS *m/z* (%): 424 (M^+, 22), 409 (18), 368 (6), 313 (12), 271 (8), 245 (18), 218 (86), 205 (58), 203 (48), 189 (90), 175 (24), 149 (84), 135 (60), 121 (64), 121 (60), 109 (82), 95 (100).

The comparison of the observed melting point with that reported in literature, compound **PA-8** was identified as lup-20(29)-3-one commonly known as lupenone. This was also confirmed by its direct comparison with the oxidation product of lupeol (**PA-4**) using PCC (pyridinium chlorochromate) in dichloromethane.

Oxidation of PA-4

Compound **PA-4** was oxidized by stirring it with PCC (Pyridinium chlorochromate) in dichloromethane for few hours at room temperature. The contents were then passed through a small column of silica gel so as to remove the chromium salt and get a white solid which appeared at the same R_f value as **PA-8** by Co-TLC. Its melting point was comparable and it has superimposable Co-IR.

IR ν_{max} (film): 3391, 2918, 2850, 1697, 1465, 1261, 1095, 1038, 801, 722, 686 cm^{-1}.

^{1}H NMR (δ, $CDCl_3$, 300 MHz): 2.35 (t, 2H, -CH_2CO), 1.63 (m, 2H, -**CH_2**CH_2CO), 1.25 (brs, 38H, 19x-CH_2), 0.88 (t, 3H, -CH_3).

Mass spectral data, EIMS *m/z* (%): 354 (M^+, 12), 309 (8), 295 (10), 281 (12), 253 (16), 225 (22), 155 (28), 97 (50), 71 (100).

On this comparison with the oxidation product of lupeol, compound **PA-8** was identified as lup-20(29)-en-3-one, also known as lupenone.

This is the first report of isolation of lupenone from the genus *Plumeria*.

Characterization of PA-9

Compound **PA-9** was obtained as low melting solid. It showed a single spot on TLC using chloroform as dev

Characterization of PA-10

Compound **PA-10** was obtained as a white crystalline solid from extract E, m.p. 222-23 ºC. It gave a single spot on TLC (R_f = 0.23, in chloroform/methanol, 90:10) which showed up as a yellowish green fluorescent colour on heating the plate sprayed with 5% sulphuric acid. This coloration indicated that it may be an iridoid.

IR ν_{max} (KBr): 3568, 3377, 2918, 2854, 1757, 1695, 1633, 1437, 1374, 1289, 1181, 1076, 1037, 1003, 865, 748, 638 cm^{-1}.

^{1}H NMR (δ, $CDCl_3$, 300 MHz): 7.54 (d, 1H, *J* = 1.8 Hz, H-3), 7.47 (d, 1H, *J* = 1.4 Hz, H-10), 6.50 (dd, 1H, *J* = 2.4 & 5.5 Hz, H-6), 5.60 (dd, 1H, *J* = 2.2 & 5.5 Hz, H-7), 5.32 (d, 1H, *J* = 5.2 Hz, H-1), 4.80 (d, 1H, *J* = 7.7 Hz, H-1′), 4.62 (dq, 1H, *J* = 5.2 & 1.1 Hz, H-13), 3.98-3.83 (m, 6H, H-5, 5x-OH), 3.80 (s, 3H, -CO_2CH_3), 3.50 & 3.29 (2m, 6H, H-2′, H-3′, H-4′, H-5′ & H-6′), 2.82 (m, 1H, H-9), 1.45 (d, 3H, *J* = 6.4 Hz, H-14).

^{13}C NMR (δ, $CDCl_3$, 75.47 MHz): 178.4, 174.1, 158.8, 156.2, 147.6, 145.3, 137.0, 117.0, 106.4, 103.7, 100.2, 85.1, 84.5, 80.9, 77.6, 69.4, 68.9, 59.1, 56.7, 46.7, 30.2.

Mass spectral data, EIMS *m/z* (%): 307 (M^+-glu, 14), 291 (40), 273 (38), 262 (82), 242 (18), 230 (88), 213 (14), 202 (44), 184 (18), 160 (100), 139 (24), 115 (16), 97 (24), 85 (68).

It was identified as plumeria iridoid, plumieride, and its structure was further confirmed on the basis of comparison of spectral data of **PA-10** and its acetate with reported data and melting points of plumieride and its penta acetate.

Acetylation of PA-10

PA-10 was acetylated using acetic anhydride and N,N-dimethylaminopyridine. The compound was obtained as white solid; R_f = 0.47 in chloroform as a developing solvent.

IR ν_{max} (KBr): 2923, 2853, 1755, 1694, 1638, 1224, 1287, 1224, 1062, 1037 cm^{-1}.

^{1}H NMR (δ, $CDCl_3$, 300 MHz): 7.38 (s, 1H, H-3), 6.94 (s, 1H, H-10), 6.43 (s, 1H, H-6), 5.65 (d, 1H, *J* = 6.2 Hz, H-13), 5.44 (d, 1H, *J* = 4.6 Hz, H-7), 5.19 (d, 1H, *J* = 9.3 Hz, H-1′), 5.08 (m, 1H, H-1), 5.12 & 4.83 (2m, 4H, H-2′, H-3′, H-4′ & H-5′), 4.30 & 4.11 (2dd, 2H, *J* = 11.9 & 4.0 Hz each, H-6′), 3.76 (s, 3H, -CO_2**CH_3**), 3.48 (s, 1H, H-5), 3.13(d, 1H, *J* = 7.5 Hz, H-9), 2.09, 2.08, 2.02, 2.00 & 1.92 (5s, 15H, 5x**CH_3**CO-), 1.51 (d, 3H, *J* = 6.2 Hz, H-14).

Characterization of PA-11

Compound **PA-11** was obtained as yellowish green solid from extract D, m.p. 202-3 ºC. It gave a positive $FeCl_3$ test on TLC (R_f = 0.31 in chloroform/methanol (97:3)) thus showing the presence of phenolic group.

IR ν_{max} (KBr): 3396, 2921, 2851, 1707, 1608, 1565, 1510, 1435, 1291, 1263, 1141, 1020, 922, 860, 820, 745 cm^{-1}.

^{1}H NMR (δ, $CDCl_3$, 300 MHz): 7.59 (d, 1H, *J* = 9.4 Hz, H-4), 6.91 (s, 1H, -OH & D_2O exchangeable), 6.84 (s, 1H, H-5), 6.26 (d, 1H, *J* = 9.4 Hz, H-3), 6.14 (s, 1H, H-8), 3.95 (s,

3H, -OCH_3).

^{13}C NMR (δ, $CDCl_3$, 75.47 MHz): 165.1 (C-2), 150.1, 143.6, 128.1, 123.9, 124.5, 113.8, 107.9, 103.6, 56.8 (OCH_3).

Mass spectral data, EIMS *m/z* (%): 192 (M^+).

PA-11 was characterized as 7-hydroxy-6-methoxy-1*H*-benzopyran-2-one, commonly known as scopoletin.

Characterization of PA-12

Compound **PA-12** was crystallized as colourless needles from extract D, m.p. 288-90 ºC. It gave positive Libermann Burchard test and violet colouration with 5% sulphuric acid on TLC (R_f = 0.51, in chloroform/methanol, 95:5), on heating. The presence of double bond was indicated by yellow colour with tetranitromethane solution.

IR ν_{max} (KBr): 3417, 2923, 2853, 1689 1458, 1026, 729 cm^{-1}.

^{1}H NMR (δ, $CDCl_3$, 300 MHz): 5.25 (m, 1H, H-12), 3.29 (m, 1H, H-3α), 2.20 (d, 1H, *J* = 10.2 Hz, H-18), 1.71-1.25 (m, -CH_2- & -CH-), 1.08 (s, 3H, 27-CH_3), 0.98 (s, 3H, 25-CH_3), 0.93 (s, 3H, 26-CH_3), 0.86 (d, 6H, *J* = 6.6 Hz, 29-CH_3 & 30-CH_3), 0.77 (s, 6H, 23-CH_3 & 24-CH_3).

^{13}C NMR (δ, $CDCl_3$, 75.47 MHz): 179.1, 139.8, 126.0, 78.4, 57.1, 54.0, 48.2, 48.0, 41.8, 40.2, 40.1, 39.8, 39.4, 37.9, 37.2, 34.1, 32.0, 30.4, 29.3, 29.6, 28.3, 25.5, 24.8, 24.4, 22.6, 19.7, 18.6, 18.5, 17.4, 16.8.

Mass spectral data, EIMS *m/z* (%): 456 (M^+, 12), 441 (12), 411 (38), 392 (8), 377 (6), 300 (8), 248 (100), 233 (10), 218 (12), 207 (16), 203 (62), 189 (18), 175 (14), 147 (18), 135 (15), 119 (20).

PA-12 was identified as 3β-hydroxy-12-ursen-28-oic acid commonly known as ursolic acid.

In Silico Antidiabetic study

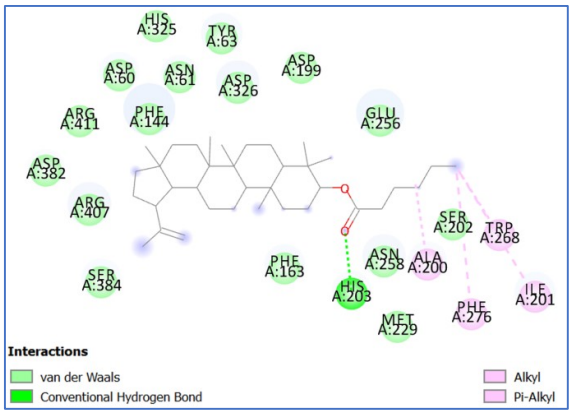
Table S1. Docking interactions and free energy of binding of screened compounds against GH 13 α glucosidase (PDB ID: 2ZE0)

Compound	Free Energy of binding kcal/mol	Inhibition constant Ki	Interaction type	Interactions
PA-1	-9.80	65.27 nM	Van der Waals Pi Alkyl Alkyl Conventional Hydrogen Bond	Asp 382, Arg 411, Asp 60, His 325, Tyr 63, Asp 326, Asp 199, Phe 144, Arg 407, Ser 384, Phe 163, Asn 258, Met 229, Ser 202 Trp 268, Phe 276 Ala 200 His 203
PA-2	-8.95	274.19 nM	Pi Alkyl Alkyl Van der Waal	Phe 144, Phe 163 Ile 143, Ala 200 Asp 382, Ser 384, Val 383, Met 229, Phe 225, His 203, Asn 258, Glu 256, Asp 326, Gln 167, Tyr 63, Asn 61, Arg 407, Arg 411, Asp 60
PA-3	-8.89	302.21 nM	Van der Waal Conventional H bond	Asp 382, Arg 411, Asp 60, His 325, Asn 61, Asp 326, Tyr 63, Asp 199, Glu 256, Asp 382, Arg 407, Ser 384, Ile 143, Phe 163, Ser 202, Met 229 Ala 200, His 203
PA-4	-8.68	437.36 nM	Van der Waals Alkyl, Pi alkyl Pi sigma Conventional H Bonding	Leu 285, Asn 324, Arg 407, Phe 144, Tyr 63, His 103, Ala 200, Asn 258, Glu 256 Leu 327, Phe 282 Phe 163 Gln 167, Asp 60
PA-5	-9.54	101.55 nM	Van der Waals Pi Alkyl Conventional H Bonding	Asn 61, Gln 167, His 103, Ala 200, Asp 199, Trp 49, Arg 197, Asn 324, Phe 282, Glu 256, Asp 60 Phe 163, Phe 144, Tyr 63, His 325 Asp 326
PA-6	-4.55	459.08 uM	Van der Waal Pi-Pi stacked Conventional H Bonding	Phe 163, His 103, Asp 326, Arg 407, Phe 144, Asn 61, Asp 164 Tyr 63 Gln 167, Asp 382, Arg 411
PA-7	-9.54	101.93 nM	Van der Waals Pi Sigma Alkyl Pi alkyl Conventional H Bonding Carbon Hydrogen bond	Asn 258, Arg 197, Trp 49, Glu 256, Asp 199, Val 100, His 103, Gln 167, Ala 59, Asp 60, Phe 144, Asn 61, Arg 411, Val 383 Tyr 63 Ala 200 Phe 282, Phe 163, His 325 Arg 407, Asp 382 Ser 384

PA-8	-9.24	170.07 nM	Van der Waals Alkyl Pi alkyl	Asp 199, Glu 256, Val 100, His 103, Asn 61, Phe 144, Asp 60, Ala 59, Gln 167, Val 383, Asp 382, Ser 384, Arg 407, Phe 163, Asp 326, His 325 Ala 200 Tyr 63
PA-9	+6.58	-	-	No interactions
PA-10	-7.33	4.21 uM	Van der Waals Pi sigma Alkyl Conventional H Bonding	Phe 163, Phe 225, Ile 143, Arg 197, Asn 258, Asp 199, Leu 285, Leu 327 Tyr 63, Phe 282 Ala 200 His 325, Asp 326, Asn 324, His 203, Glu 256
PA-11	-5.71	65.73 uM	Van der Waals Pi-Pi stacked and pi alkyl Conventional H Bonding	Asp 60, Phe 144, Gln 167, Asn 61, His 325, Asp 382, Arg 407 Tyr 63 Arg 411, Asp 326
PA-12	-9.03	239.03 nM	Van der Waals Conventional H Bonding	Arg 197, Asn 258, Asp 326, Arg 407, Ser 384, Phe 144, Asn 61, Asp 60, Tyr 63, His 325, Asp 199, Ala 200, His 103 Glu 256, Asp 382, Arg 411
L1	-9.72	74.87 nM	Van der Waals Pi alkyl Alkyl Conventional H Bonding	Asp 98, Glu 256, Asp 199, Trp 49, Arg 197, Phe 282, His 325, Asp 326, Asn 324, Arg 411, Arg 407, Asn 61, Ser 384, Asp 60, Asn 61, Phe 144, Asp 60, Gln 167, His 103 Tyr 63 Ala 200 Asp 382
L2	-7.12	6.03 uM	Pi-Alkyl Alkyl Conventional H Bonding	Tyr63, Phe144, Phe163 Ile143, Ala200 Asn258, Gly259
L3	-9.22	173.99 nM	Van der Waals Pi sigma	Asp 382, Arg 411, Ser 384, Arg 407, Asp 326, Tyr 63, Ala 200, Glu 256, Asp 199, Val 100, His 103, Gln 167, Phe 144, Asn 61, Asp 60 Phe 163
L4	-8.77	370.33 nM	Van der Waal Conventional Hydrogen Bond Pi sigma	Phe 225, Met 229, Asn 258, His 203, Ala 200, His 103, Val 100, Asp 199, Glu 256, Ser 202, Glu 256, Asp 199, Ile 143, Phe 163, Phe 144, Asp 60 Tyr 63, Gln 67 Tyr 63
L5	-4.39	609.39 uM	Van der Waals Pi alkyl Alkyl Conventional H Bonding	Asp 60, Gln 167, His 325, His 103, Val 100, Glu 256, Asp 199 Phe 1441, Phe 163, Tyr 63 Ala 200 Asp 326
L6	-4.48	520.96 uM	Van der Waals Pi alkyl Pi Pi stacked Conventional H Bonding	Arg 197, Glu 256, Asp 60, Asp 164, His 103, Phe 163, Asp 199 Phe 144, Ala 200 Tyr 63 Gln 167
L7	-6.40	20.51 uM	Conventional H Bonding Pi cation/Pi anion Pi Pi stacked/Pi Pi T-shaped	Gln 167, His 325, Asp 326, Asn 324, Arg 411 Arg 197, Glu 256, Asp326 Phe 163, Phe 282
L8	-5.85	51.35 uM	Van der Waal	Met 229, Asp 199, Leu 285, Leu 327, Arg 197, Asn 258, Ile 143, Phe 225, Phe 163

			Conventional Hydrogen Bond Pi sigma Pi alkyl Alkyl	His 203, His 325, Asp 326, Asn 324, Glu 256 Phe 282 Tyr 63 Ala 200
L9	-6.25	26.02 uM	Van der Waal Carbon Hydrogen Bond Conventional Hydrogen Bond Pi Pi stacked Pi alkyl	Arg 407, Phe 144, Asn 324, Asp 98, Trp 49, Val 100, Asp 164, Asp 60 His 103, Glu 256 Gln 167, Ala 200, Glu 256, Tyr 63, His 325, Asp 326 Phe 163 Ala 200
L10	-7.20	5.27 uM	Conventional Hydrogen Bond Alkyl Pi alkyl Pi sigma	Gln 13, Arg 197 Ala 200 Tyr 63, His 325 Phe 280
Acarbose	-4.34	662.70 uM	Van der Waals Pi sigma Pi lone pair Conventional H Bonding	Leu 327, Leu 285, Phe 282, Asn 324, Arg 187, Ala 200, Phe 144, Ala 59, Arg 411, Ile143, His 103 Tyr 63 Phe 163 Asp 326, Glu 256, Asp 60, Asn 61, Gln 167, His 325, Asn 258

PA-1



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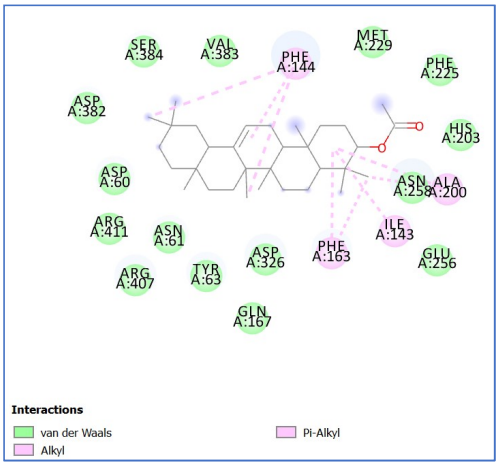

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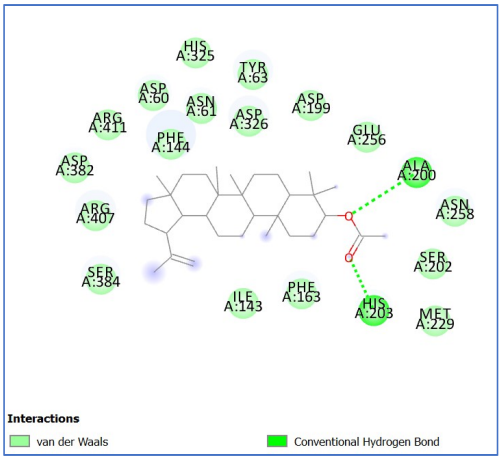

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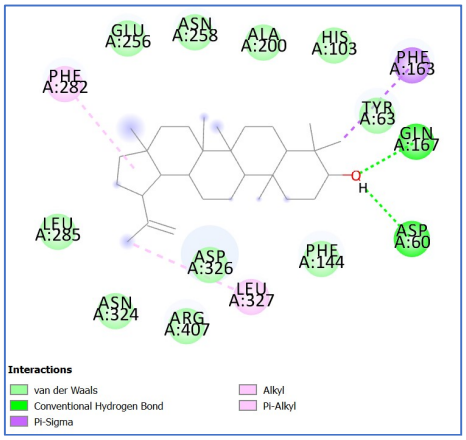

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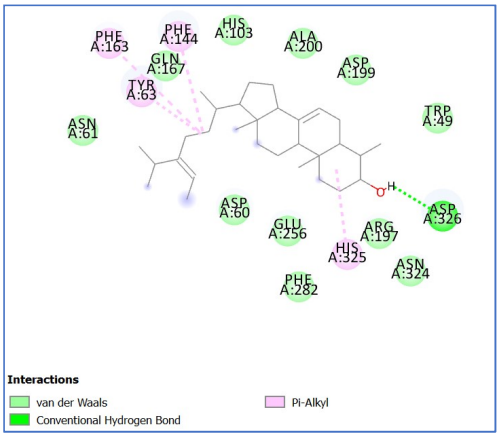
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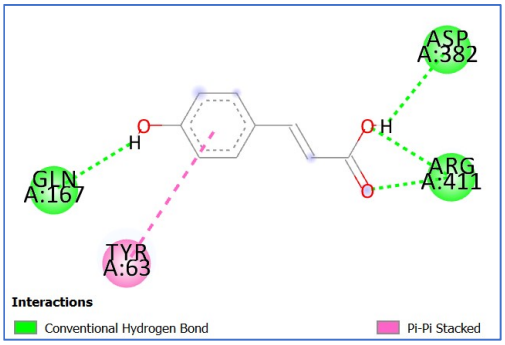
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Alkyl

PA-6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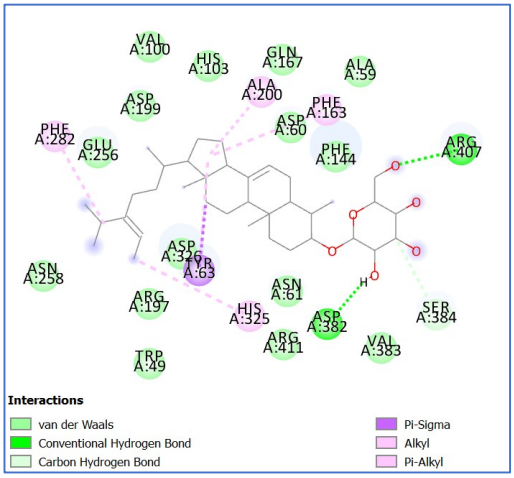
Conventional Hydrogen Bond
Pi-Pi Stacked

PA-7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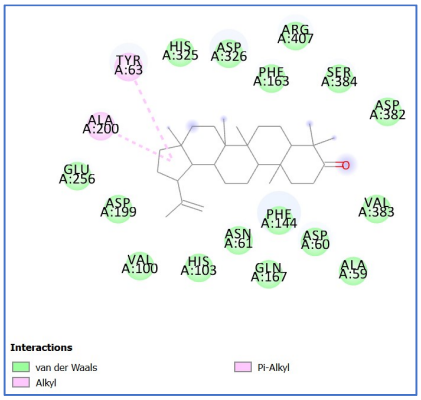
Carbon Hydrogen Bond
Pi-Sigma
Alkyl
Pi-Alkyl

PA-8



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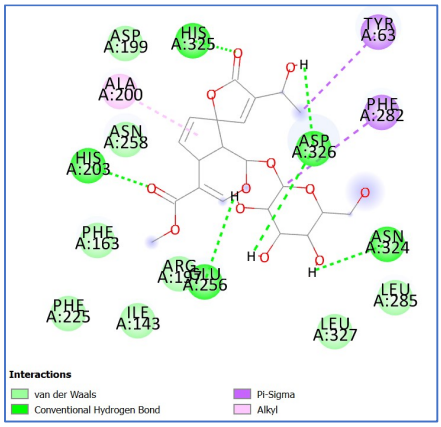

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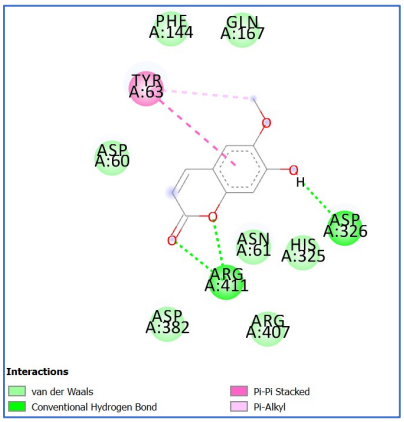

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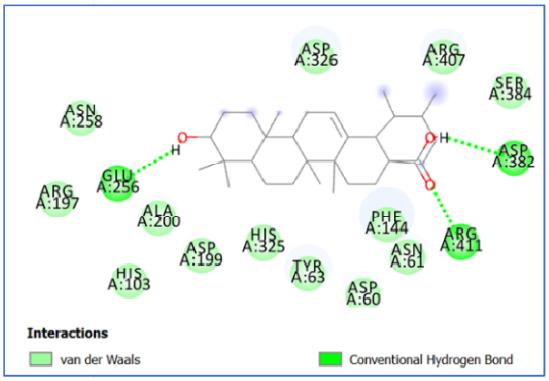
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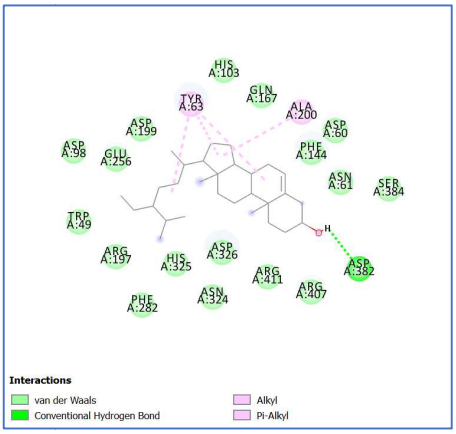
Interactions
van der Waals
Conventional Hydrogen Bond

L1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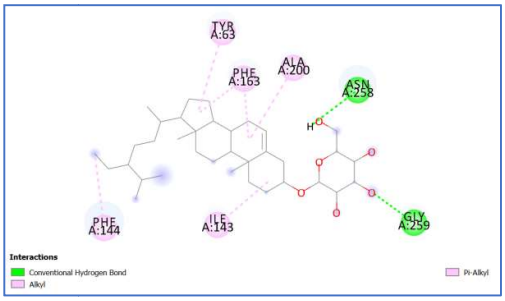
Interactions
van der Waals
Conventional Hydrogen Bond
Alkyl
Pi-Alkyl

L2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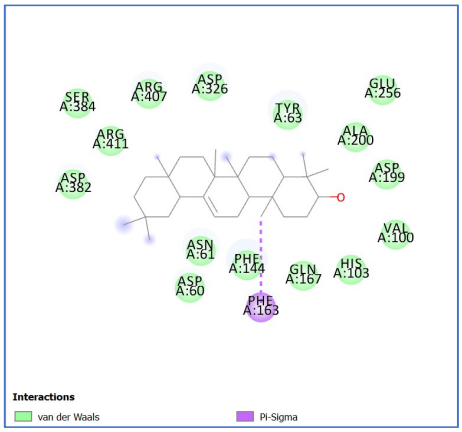
Interactions
Conventional Hydrogen Bond
Alkyl
Pi-Alkyl

L3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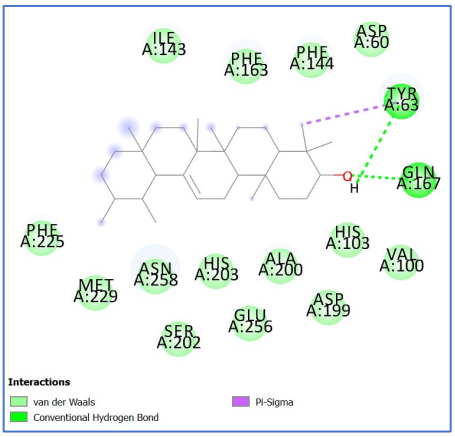
Interactions
van der Waals
Pi-Sigma

L4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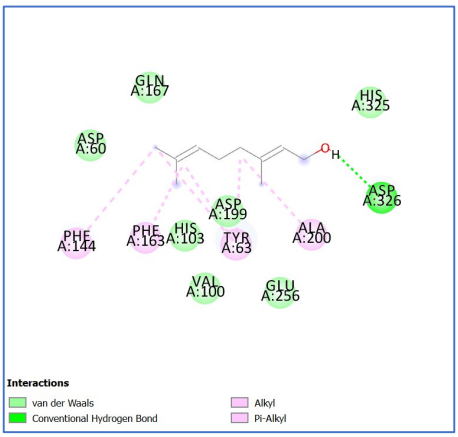
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Sigma

L5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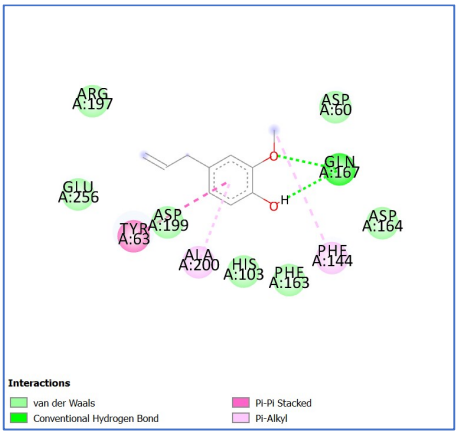
Interactions
van der Waals
Conventional Hydrogen Bond
Alkyl
Pi-Alkyl

L6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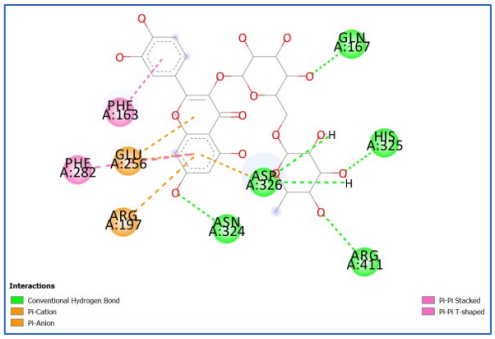
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Pi Stacked
Pi-Alkyl

L7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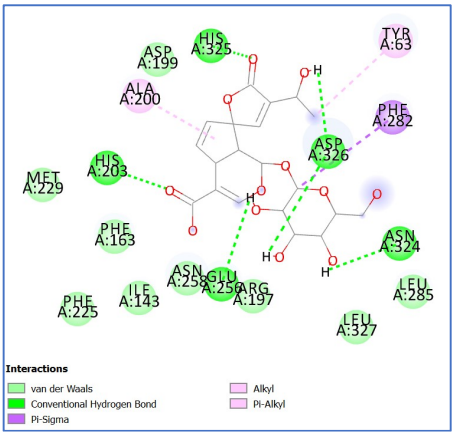
Interactions
Conventional Hydrogen Bond
Pi-Cation
Pi-Anion
Pi-Pi Stacked
Pi-Pi T-shaped

L8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Interactions
van der Waals
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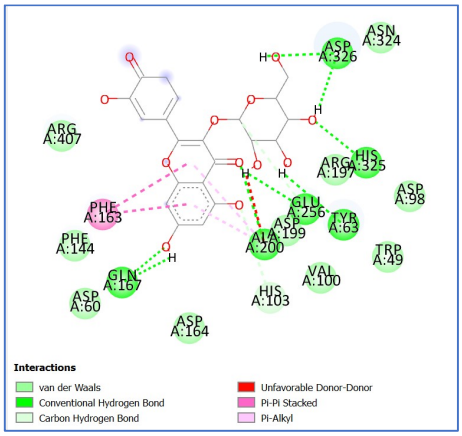
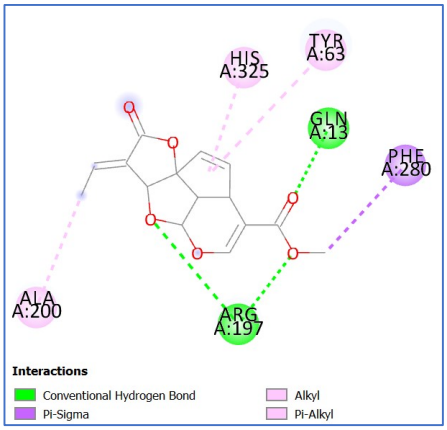
Alkyl
Pi-Alkyl

L9



L10



Acarbose complex 5