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# Twenty-Eight Selected Phytoconstituents Of *Neptunia Oleracea* (Water Mimosa) As Antioxidant, Antidiabetic And Antimalarial Activities: An *In-Silico* Study

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Running title: *28 selected phytoconstituents of Water Mimosa as antioxidant, antidiabetic and antimalarial activities: An in silico study*
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***Abstract***
*Neptunia oleracea (Water Mimosa) has been known to demonstrate numerous pharmacological activities. In the current investigation, we aimed to assess twenty-eight chosen phytoconstituents of N. oleracea (Water Mimosa) as excellent inhibitory agents of human prolidase (hPEPD), human protein tyrosine phosphatase 1B (hPTP 1B) and Anopheles gambiae glutathione-S-transferase delta-class (agGSTd1-6) using molecular docking method.*
*The twenty-eight selected constituents of N. oleracea (Water Mimosa) were studied on the docking behaviour of hPEPD, hPTP 1B and agGSTd1-6 by utilizing the Swiss dock approach. The docking analysis showed that quercetin-3-O-rutinoside, narcissoside and quercetin-3, 7-di-O-glucoside of N. oleracea (Water Mimosa) has exhibited the maximum binding energy (-9.27, -9.02 and -9.95 kcal/mol) with the hPEPD, hPTP 1B and agGSTd1-6 respectively. Thus, the current result provides a new insight regarding the twenty-eight chosen ligands of N. oleracea (Water Mimosa) as excellent inhibitory agents of human prolidase (hPEPD), human protein tyrosine phosphatase 1B (hPTP 1B) and Anopheles gambiae glutathione-S-transferase delta-class (agGSTd1-6), which thereby will aid in managing wounds, diabetes mellitus and malaria.*
***Keywords***: *Neptunia oleracea, Water Mimosa, Prolidase, Protein tyrosine phosphatase 1B, Anopheles gambiae glutathione-S-transferase, narcissoside*

## INTRODUCTION

*Neptunia oleracea* (Water Mimosa) belongs to Fabaceae (Pea) family and which is native to Africa, Asia and South America [1]. Genus *Neptunia* has been reported to comprise twenty two species (namely *Neptunia amplexicaulis, Neptunia dimorphantha, Neptunia gracilis, Neptunia heliophila*, *Neptunia hispida*, *Neptunia insignis*, *Neptunia javanica, Neptunia longipila, Neptunia major, Neptunia monosperma, Neptunia oleracea, Neptunia paucijuga, Neptunia plena, Neptunia proxima, Neptunia scutata, Neptunia tactilis, Neptunia valida, Neptunia xanthonema)* and which are distributed in the regions like Africa, Asia, Australia, Malesia, North and South America [2]. Among above said *Neptunia* species, *Neptunia oleracea* (Water Mimosa) is one the most cultivated species particularly for the purpose of human consumption and application [3]. The vernacular names for *Neptunia oleracea* (Water Mimosa) are "Pani najak" in Bengali (India), "Kanhchhnaet" in Cambodia, 'Neptunie potegere" in France, "Lajjalu" in Hindi (India), "Kemon" in Indonesia, "Nidrayam" in Kannada, "Neer thottavadi" in Malayalam (India), "Kemon air" in Malaysia, "Eshing ekaithabi" in Manipuri (India), "Juqueri manso" in Portugal, "Alambusha" in Sanskrit (India), "Sundaikeerai" in Tamil (India), "Niru thalavapu" in Telugu (India), "Phakkrachet" in Thailand, "Garden

puff" in United States [4, 5]. Different plant parts of *Neptunia oleracea* (Water Mimosa) are traditional used as follows: i) flowers are used to cure earache and syphilis, ii) leaves are used to cure dysentery, earache, intestinal infection and syphilis, iii) leaves, shoot and stem are used to cure uterine infections and discharge, iv) roots are used to treat dysentery, hard palate and necrosis of the nose, v) whole plant is used to cure guinea worm infection and yellow fever [5].

*Neptunia oleracea* (Water Mimosa) has been reported to exhibit various biological activities such as a) analgesic, b) anti-bacterial, c) anti-cancer, d) anti-inflammatory, e) antimicrobial, f) antioxidant, g) antitumor, h) antiulcer, i) antiviral, j) hepato-protective, k) glucosidase inhibition and l) 5-alpha reductase inhibition [1, 5, 6]. The previous studies prompted us to execute the current study on twenty eight selected *Neptunia oleracea* (Water Mimosa) constituents which includes quercetin-3,7-di-O-glucoside, quercetin-3-O-rutinoside, isoquercetin, quercetin-3-O-xyloside, narcissoside, quercetin-3-O-arabinoside, myricetin, quercetin, vitexin 2"-O-rhamnoside. vitexin, apigenin, salvianolic acid, hydroxytyrosol, leucenine, orientin, kaempferol 7-O-glucoside, kaempferol-3-O-arabinoside, kaempferol-3-O-rhamnoside, kaempferol, catechin, methylgallate, rutin, malic acid, syringic acid, digalloylglucose, caffeic acid, gallic acid and 3,4-O-dimethylgallic acid. These above said *Neptunia oleracea* (Water Mimosa) phytoconstituents were aimed to investigate on the docking analysis of human prolidase (hPEPD), human protein tyrosine phosphatase 1B (hPTP 1B) and *Anopheles gambiae* glutathione-S-transferase delta-class (agGSTd1-6) by utilizing the swissdock method.

## METHODOLOGY

### Ligand preparation

The chemical structures of twenty eight (Water Mimosa) ligands namely i) quercetin-3,7-di-O-glucoside (CID 13345441); ii) quercetin-3-O-rutinoside (CID 5280805); iii) isoquercetin (CID 5280804); iv) quercetin-3-O-xyloside (CID 5878729); v) narcissoside (CID 5481663); vi) quercetin-3-O-arabinoside (CID 12309865); vii) myricetin (CID 5281672); viii) quercetin (CID 5280343); ix) vitexin 2"-O-rhamnoside (CID 5282151); x) vitexin (CID 5280441); xi) apigenin (CID 5280443); xii) salvianolic acid (CID 5281793); xiii) hydroxytyrosol (CID 82755); xiv) leucenine (CID 440473); xv) orientin (CID 5281675); xvi) kaempferol 7-O-glucoside (CID 10095180); xvii) kaempferol-3-O-arabinoside (CID 5481882); xviii) kaempferol-3-O-rhamnoside (CID 5835713); xix) kaempferol (CID 5280863); xx) catechin (CID 9064); xxi) methylgallate (CID 7428); xxii) rutin (CID 5280805); xxiii) malic acid (CID 525); xxiv) syringic acid (CID 10742); xxv) digalloylglucose (CID 129628549); xxvi) caffeic acid (CID 689043); xxvii) gallic acid (CID 370) and xxviii) 3,4-O-dimethylgallic acid (CID 74709) were downloded from PubChem (https://pubchem.ncbi.nlm.nih.gov/) compound database. The Water Mimosa ligands were prepared by utilizing ChemDraw 2D and 3D (CambridgeSoft, Cambridge, USA) software tools [7]. Thus, these prepared 3-dimensional structures were utilized for further investigations (swissdock).

### Preparation of target enzymes

The 3-dimensional structure of human prolidase [hPEPD] (PDB$^{\diamond}$ ID: 2IW2 with a resolution of 1.82 A$^{o}$), human protein tyrosine phosphatase 1B [hPTP 1B] (PDB$^{\diamond}$ ID: 2QBS with a resolution of 2.10 A$^{o}$) and *Anopheles gambiae* glutathione-S-transferase delta-class [agGSTd1-6] (PDB$^{\diamond}$ ID: 1PN9 with a resolution of 2.00 A$^{o}$) was retrieved from $^{\diamond}$Protein Data Bank (PDB). "A" chain of these enzymes were prepared individually by deleting other chains, ligands, and even the crystallographically observed "water" ($H_2O$) molecules by adopting UCSF Chimera (Regents, University of California, San Francisco, USA) software tool [8].

### Docking study

A docking analysis was carried out for twenty-eight chosen phytoconstituents of *Neptunia oleracea* (Water Mimosa) with three target enzymes (hPEPD, hPTP 1B and agGSTd1-6) using the Swissdock (http://old.swissdock.ch/) free web server [9]. Finally, PyMOL (Molecular Graphics System, Version 2.4.1, Schrödinger, New York, USA) software was used to analysis the binding site of best-docked pose for each ligand [10, 11].

**RESULTS**

The current Swissdock analysis showed that quercetin-3-O-rutinoside has shown the maximum binding energy [MBE] (-9.27 kcal per mol) with the human prolidase (hPEPD) enzyme. On the other hand, malic acid has exhibited the lowest binding energy (-6.33 kcal per mol) with the hPEPD enzyme (as shown in Table 1).

In the present investigation ten ligands (myricetin, quercetin, apigenin, salvianolic acid, methylgallate, malic acid, syringic acid, digalloylglucose, caffeic acid and 3,4-O-dimethylgallic acid) have shown interactions with Cys284 amino acid residue of human prolidase (hPEPD) enzyme (as shown in Table 1). Similarly, six ligands (quercetin-3-O-arabinoside, kaempferol 7-O- glucoside, kaempferol-3-O-arabinoside, kaempferol-3-O-rhamnoside, kaempferol and catechin) have shown interactions with Lys111 amino acid residue of hPEPD enzyme.

The current Swissdock analysis showed that narcissoside has exhibited the maximum binding energy [MBE] (-9.02 kcal per mol) with the human protein tyrosine phosphatase 1B (hPTP 1B) enzyme. On the other hand, methylgallate has exhibited the lowest binding energy (-6.14 kcal per mol) with the hPTP 1B second target enzyme (as shown in Table 2).

In the current investigation six ligands (quercetin-3-O-rutinoside, narcissoside, myricetin, kaempferol 7-O-glucoside, kaempferol-3-O-rhamnoside and rutin) have shown interaction with Gln262 amino acid residue of human protein tyrosine phosphatase 1B (hPTP 1B) enzyme (as shown in Table 2). Similarly, five ligands (quercetin-3-O-rutinoside, narcissoside, kaempferol 7-O-glucoside, kaempferol-3-O-rhamnoside and rutin) have shown interaction with Asp48 amino acid residue of hPTP 1B enzyme.

The docking analysis showed that quercetin-3, 7-di-O-glucoside has shown the highest binding energy [HBE] (-9.95 kcal/mol) with the *Anopheles gambiae* glutathione -S-transferase delta-class (agGSTd1-6) enzyme. On the other hand, hydroxytyrosol has exhibited the lowest binding energy (-6.17 kcal per mol) with the agGSTd1-6 enzyme (as shown in Table 3).

In the present investigation eight ligands (quercetin-3-O-rutinoside, quercetin-3-O-xyloside, narcissoside, quercetin-3-O-arabinoside, vitexin, orientin, malic acid and digalloylglucose) have shown interaction with Ile52 amino acid residue of *Anopheles gambiae* glutathione -S-transferase delta-class (agGSTd1-6) enzyme (as shown in Table 3). Similarly, ten ligands (quercetin-3-O-rutinoside, quercetin-3-O-arabinoside, myricetin, vitexin, apigenin, leucenine, kaempferol, catechin, syringic acid and caffeic acid) have shown interaction with Tyr113 amino acid residue of agGSTd1-6 enzyme.

Discussion

The Water Mimosa (*Neptunia oleracea*) is an edible herb which is cultivated as vegetable in Southeast Asia. And moreover *N. oleracea* (Water Mimosa) has been known to exhibit both anti-oxidant and antidiabetic activities [6]. Furthermore *N. oleracea* (Water Mimosa) has been demonstrated to inhibit enzymes (alpha glucosidase and 5-alpha reductase) activities [12, 13]. Prolidase is a hydrolase enzyme which belongs to matrix metalloproteinase (MMP) family that cleaves both 'imidopeptides and imidotripeptides' with carboxyl (C) terminal proline (Pro) and hydroxyproline (Hyp) [14]. Prolidase activity has been reported to found in several tissues like amniotic fluid, brain, heart, kidney, liver, pancreas and stomach [15]. Prolidase enzyme activity has been reported to elevate during pathological conditions like i) bipolar disorder, ii) breast cancer, iii) endometrial cancer, iv) erectile dysfunction, v) *Helicobacter pylori* infection, vi) hypertension, vii) keloid scar formation, viii) liver disease, ix) lung cancer, x) melanoma and xi) thalassaemia [16]. Recently, serum prolidase activity has been reported to elevate due to more oxidative stress along with reduced anti-oxidant levels in prostate cancer [17]. Hence prolidase has been chosen as the first target enzyme for the present study. In the present investigation chosen *Neptunia oleracea* (Water Mimosa) ligands have shown interaction with Ser241, Asp376 and Val377 amino acid residues of human prolidase (hPEPD) enzyme. This result showed good agreement with earlier report [18].

In the current investigation one ligand (methylgallate) has shown interaction with Arg45 amino acid residue (AAR) of human protein tyrosine phosphatase 1B (hPTP 1B) enzyme. This result was on par with

previous report, where dodecanoic acid methyl ester has shown interaction with Arg45 amino acid residue of hPTP 1B enzyme [19]. Similarly, chosen *Neptunia oleracea* (Water Mimosa) ligands have shown interaction with Arg24, Tyr46, Asp48 and Gln262 amino acid residues of hPTP 1B enzyme. This result showed good agreement with earlier report [20].

In the current investigation, four ligands (isoquercetin, quercetin-3-O-xyloside, vitexin and orientin) have shown interaction with Ser9 amino acid residue (AAR) of *Anopheles gambiae* glutathione -S-transferase delta-class (agGSTd1-6) enzyme. This result showed good agreement with earlier reports [21, 22, 23, 24].

The findings of the present investigation purely based on *in silico* (molecular docking) method which gives new insight regarding the twenty eight chosen *Neptunia oleracea* (Water Mimosa) constituents and their interactions with three target enzymes namely human prolidase (hPEPD), human protein tyrosine phosphatase 1B (hPTP 1B) and *Anopheles gambiae* glutathione -S-transferase delta-class (agGSTd1-6) However, further *in vitro* biochemical assay, insecticidal potential and detoxifying enzyme inhibition studies are needed to confirm their enzyme inhibition, larvicidal and mosquito repellent activities of chosen phytoconstituents.

## CONCLUSION

In the current investigation, the twenty-eight chosen *Neptunia oleracea* (Water Mimosa) phytoconstituents have shown the potential to dock with two targeted human enzymes (hPEPD and hPTP 1B) and one *An. Gambiae* GST target enzyme (agGSTd1-6) respectively. However, five ligands (quercetin, hydroxytyrosol, kaempferol-3-O-arabinoside, kaempferol-3-O-rhamnoside and 3,4-O-dimethylgallic acid) does not show any interaction with amino acid residues of *An. Gambiae* GST (agGSTd1-6) enzyme. Thus, the current results give a new information about the twenty-eight chosen ligands of *N. oleracea* (Water Mimosa) as potent inhibitory agents of hPEPD, hPTP 1B and *Anopheles gambiae* GST (agGSTd1-6), which thereby will help in managing wounds, diabetes mellitus and malaria.

Conflicts of Interest: The authors declare that they have no conflicts of interest.

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Table 1 The Swissdock binding energy (SDBE) analysis of 28 selected *Neptunia oleracea* (Water Mimosa) ligands with the human prolidase (hPEPD) enzyme using Swissdock method

| S.no | Ligand name | SDBE▫ (-kcal per mol) | Interactions of (AAR) amino acids residues | BD▪ (A°) |
|---|---|---|---|---|
| 1 | Quercetin-3,7-di-O-glucoside | 9.19 | Glu53 | 2.0 and 3.2 |
| | | | Arg67 | 3.3 |
| | | | Glu228 | 3.0 |
| | | | His239 | 3.0 |
| | | | Thr243 | 2.9 and 3.4 |
| | | | Glu281 | 1.8 |
| | | | Val377 | 3.3 |
| 2 | Quercetin-3-O-rutinoside | 9.27 | Glu53 | 2.8 |

| | | | | |
|---|---|---|---|---|
| | | | Thr55 | 3.4 |
| | | | Leu65 | 2.0 |
| | | | Glu69 | 1.9 |
| | | | Ser70 | 3.4 |
| | | | Asn152 | 3.3 |
| | | | Asp376 | 2.5 and 2.6 |
| 3 | Isoquercetin | 8.10 | Glu54 | 2.2 and 3.0 |
| 4 | Quercetin-3-O-xyloside | 8.44 | Glu54 | 2.1, 2.2 and 2.8 |
| | | | Lys111 | 2.2 |
| 5 | Narcissoside | 9.18 | Thr55 | 3.4 |
| | | | Leu65 | 3.2 |
| | | | Arg67 | 3.2 |
| | | | Glu228 | 1.9 |
| | | | Ser240 | 3.1 and 3.4 |
| | | | Asp376 | 2.0 |
| 6 | Quercetin-3-O-arabinoside | 8.46 | Glu54 | 2.1, 2.2 and 2.8 |
| | | | Lys111 | 2.2 |
| 7 | Myricetin | 7.26 | Tyr232 | 3.2 |
| | | | Arg238 | 3.3 |
| | | | Glu281 | 2.3 and 2.5 |
| | | | Cys284 | 3.2 |
| 8 | Quercetin | 7.20 | Thr79 | 2.2 |
| | | | Gly236 | 2.3 |
| | | | Arg238 | 3.5 |
| | | | Cys284 | 3.3 |
| 9 | Vitexin 2"-O-rhamnoside | 7.11 | Arg67 | 2.6 |
| | | | Glu69 | 1.8 |
| | | | Ser240 | 2.2 |
| 10 | Vitexin | 8.03 | Leu65 | 2.4 and 3.0 |
| | | | Arg67 | 3.1 |
| | | | Ser70 | 3.2 and 3.3 |
| | | | Ser241 | 1.9 |
| | | | Glu281 | 1.9, 2.2 and 2.5 |
| 11 | Apigenin | 7.00 | Gln68<br>Arg238 | 3.4<br>3.3 |
| | | | Cys284 | 3.2 |
| 12 | Salvianolic acid | 8.12 | Thr79 | 3.3 |
| | | | Gly236 | 2.8 |
| | | | Arg238 | 3.5 and 3.5 |
| | | | Glu281 | 2.7 |
| | | | Tyr283 | 3.0 |
| | | | Cys284 | 3.1 |
| 13 | Hydroxytyrosol | 7.17 | Gln68 | 3.4 |
| | | | Thr79 | 2.6 |

| | | | | |
|---|---|---|---|---|
| | | | Arg238 | 3.5 |
| | | | Glu281 | 2.1 |
| | | | Tyr283 | 3.4 |
| 14 | Leucenine | 6.89 | Phe66 | 2.7 |
| | | | Gln68 | 3.0 |
| | | | Thr79 | 2.5 |
| | | | Gly236 | 2.5 and 3.1 |
| | | | Arg238 | 3.4 |
| | | | Glu281 | 3.2 |
| | | | Tyr283 | 3.2 |
| 15 | Orientin | 8.43 | Leu65 | 2.3 and 3.1 |
| | | | Arg67 | 3.1 |
| | | | Glu228 | 1.8 and 1.9 |
| | | | Ser240 | 3.5 |
| | | | Ser241 | 2.7 |
| | | | Glu281 | 1.9, 2.1 and 2.7 |
| 16 | Kaempferol 7-O-glucoside | 9.12 | Glu54 | 2.3 and 2.9 |
| | | | Gln68 | 3.0 |
| | | | Lys111 | 2.1 |
| | | | Arg238 | 3.1 |
| 17 | Kaempferol-3-O-arabinoside | 8.40 | Glu54 | 2.1, 2.2 and 2.8 |
| | | | Lys111 | 2.2 |
| 18 | Kaempferol-3-O-rhamnoside | 8.60 | Glu54 | 2.4 and 2.9 |
| | | | Lys111 | 2.3 |
| 19 | Kaempferol | 7.21 | Glu54 | 1.8 |
| | | | Thr79 | 3.3 |
| | | | Lys111 | 1.9 |
| 20 | Catechin | 7.38 | Glu54 | 2.0 |
| | | | Lys111 | 2.0 |
| 21 | Methylgallate | 6.92 | Gly236 | 2.5 |
| | | | Arg238 | 3.2 |
| | | | Glu281<br>Thr283 | 2.3 and 2.4<br>3.5 |
| | | | Cys284 | 3.2 |
| 22 | Rutin | 8.42 | Glu53 | 2.3 |
| | | | Arg67 | 3.5 |
| | | | Ser241 | 2.7 |
| | | | Glu281 | 2.3 |
| 23 | Malic acid | 6.33 | Gly236 | 1.9 and 3.5 |
| | | | Arg238 | 3.3 |
| | | | Glu281 | 2.2 |
| | | | Tyr283 | 3.0 |
| | | | Cys284 | 3.2 |

| | | | | |
|---|---|---|---|---|
| 24 | Syringic acid | 6.99 | Gln68 | 3.0 |
| | | | Thr79 | 2.6 |
| | | | Tyr283 | 3.5 |
| | | | Cys284 | 3.2 |
| 25 | Digalloylglucose | 8.30 | Thr79 | 3.2 |
| | | | Tyr232 | 3.0 |
| | | | Gly236 | 2.1 |
| | | | Arg238 | 3.0, 3.1 and 3.3 |
| | | | Tyr283 | 3.2 and 3.4 |
| | | | Cys284 | 3.2 |
| 26 | Caffeic acid | 7.05 | Phe66 | 3.2 |
| | | | Gln68 | 3.0 |
| | | | Thr79 | 2.4 and 2.9 |
| | | | Arg238 | 3.3 |
| | | | Glu281 | 2.2 and 2.3 |
| | | | Tyr283 | 3.4 |
| | | | Cys284 | 3.5 |
| 27 | Gallic acid | 6.63 | Gly236 | 2.1 |
| | | | Arg238 | 3.3 |
| | | | Glu281 | 2.2 and 2.3 |
| | | | Tyr283 | 3.5 |
| 28 | 3,4-O-dimethylgallic acid | 6.93 | Thr79 | 2.6 |
| | | | Glu281 | 2.0 |
| | | | Tyr283 | 3.1 |
| | | | Cys284 | 3.4 |

Note: SDBE▫ - Swissdock binding energy analysis, BD▪- Bond distance.

Table 2 The Swissdock binding energy (SDBE) analysis of 28 chosen *Neptunia oleracea* (Water Mimosa) ligands with the human protein tyrosine phosphatase 1B (hPTP 1B) enzyme using Swissdock method

| S.no | Ligand name | SDBE▫ (-kcal per mol) | Interactions of (AAR) amino acids residues | BD▪ (A°) |
|---|---|---|---|---|
| 1 | Quercetin-3,7-di-O-glucoside | 8.62 | Lys73 | 3.0 and 3.6 |
| | | | Gln78 | 2.6 |
| | | | Ser80 | 3.2 |
| | | | Gln102 | 1.8 |
| 2 | Quercetin-3-O-rutinoside | 8.88 | Arg24 | 3.2 |
| | | | Tyr46 | 3.3 |
| | | | Asp48 | 2.5 |
| | | | Ser118 | 3.4 |
| | | | Gln262 | 3.3 and 3.4 |
| 3 | Isoquercetin | 7.96 | Gln78 | 3.2 and 3.4 |

| | | | | |
|---|---|---|---|---|
| | | | His208 | 2.0 |
| 4 | Quercetin-3-O-xyloside | 7.75 | Leu204 | 1.8 |
| | | | Pro206 | 2.2 |
| 5 | Narcissoside | 9.02 | Arg24 | 3.1 and 3.3 |
| | | | Thr46 | 3.3 |
| | | | Asp48 | 3.3 |
| | | | Gln262 | 3.2 and 3.3 |
| 6 | Quercetin-3-O-arabinoside | 7.79 | Leu204 | 1.8 |
| | | | Pro206 | 2.1 |
| 7 | Myricetin | 7.08 | Arg24 | 3.5 |
| | | | Tyr46 | 3.4 |
| | | | Gln262 | 3.4 and 3.5 |
| 8 | Quercetin | 6.91 | Leu204 | 1.9 |
| 9 | Vitexin 2"-O-rhamnoside | 8.09 | Arg47 | 2.9, 3.2 and 3.3 |
| 10 | Vitexin | 7.63 | Leu204 | 2.1 |
| | | | Pro206 | 1.9 |
| 11 | Apigenin | 6.83 | No interactions | - |
| 12 | Salvianolic acid | 7.74 | Gln78 | 3.0 |
| | | | Arg79 | 3.0 and 3.1 |
| | | | Ser80 | 3.0 |
| | | | Leu204 | 2.6 |
| 13 | Hydroxytyrosol | 6.26 | Leu204 | 2.0 |
| | | | Pro206 | 2.7 |
| | | | Gly209 | 2.5 |
| 14 | Leucenine | 6.45 | Asp29 | 1.9 and 3.2 |
| | | | Arg254 | 3.2 and 3.3 |
| 15 | Orientin | 8.09 | Leu204 | 2.2 |
| | | | Glu207 | 2.3 |
| | | | Gly209 | 2.5 |
| 16 | Kaempferol 7-O-glucoside | 7.99 | Arg24 | 3.3 |
| | | | Tyr46 | 3.4 |
| | | | Asp48 | 2.2 |
| | | | Lys120 | 3.1 |
| | | | Gln262 | 3.3 |
| 17 | Kaempferol-3-O-arabinoside | 7.46 | Gln78 | 3.3 |
| | | | Pro206 | 2.0 |
| 18 | Kaempferol-3-O-rhamnoside | 7.15 | Arg47 | 3.2 |
| | | | Asp48 | 3.0 |
| | | | Gln262 | 2.3 |
| 19 | Kaempferol | 6.77 | Gln78 | 3.3 |
| | | | Ser80 | 2.9 |
| | | | Leu204 | 2.4 |
| 20 | Catechin | 7.55 | Gln102 | 2.1 |
| | | | Leu204 | 2.3 |

| | | | | |
|---|---|---|---|---|
| | | | Pro206 | 2.3 |
| | | | Gly209 | 2.4 |
| 21 | Methylgallate | 6.14 | Arg45 | 3.1 and 3.2 |
| | | | Leu119 | 3.4 |
| 22 | Rutin | 8.70 | Arg24 | 3.2 and 3.6 |
| | | | Tyr46 | 3.4 |
| | | | Arg47 | 3.1 |
| | | | Asp48 | 3.1 |
| | | | Gln262 | 3.2 and 3.3 |
| 23 | Malic acid | 6.48 | Ser28 | 1.9 |
| | | | Arg254 | 3.1 and 3.3 |
| | | | Gly259 | 3.1 |
| 24 | Syringic acid | 6.57 | Glu2 | 1.8 and 3.4 |
| 25 | Digalloylglucose | 7.63 | Gln78 | 2.0 and 3.3 |
| | | | Ser80 | 3.0 |
| | | | Ser205 | 2.7 |
| | | | His208 | 2.2 |
| 26 | Caffeic acid | 6.36 | Leu204 | 2.1 |
| | | | Gly209 | 2.5 |
| 27 | Gallic acid | 6.30 | Pro89 | 1.9 |
| | | | Glu136 | 3.4 |
| | | | Asp137 | 2.0 and 3.4 |
| 28 | 3,4-O-dimethylgallic acid | 6.56 | Glu2 | 1.8 and 3.4 |

Note: SDBE▫ - Swissdock binding energy analysis, BD▪- Bond distance.

Table 3 The Swissdock binding energy (SDBE) analysis of 28 chosen *Neptunia oleracea* (Water Mimosa) ligands with the *Anopheles gambiae* glutathione -S-transferase delta-class (agGSTd1-6) enzyme using Swissdock method

| S.no | Ligand name | SDBE▫ (-kcal per mol) | Interactions of (AAR) amino acids residues | BD▪ (A°) |
|---|---|---|---|---|
| 1 | Quercetin-3,7-di-O-glucoside | 9.95 | Glu64 | 1.9 |
| | | | Ser65 | 2.9 and 3.2 |
| | | | Asp110 | 1.8 |
| 2 | Quercetin-3-O-rutinoside | 9.11 | Gly8 | 2.0 |
| | | | His38 | 3.4 |
| | | | Ile52 | 2.8 and 3.2 |
| | | | Tyr113 | 3.1 |
| 3 | Isoquercetin | 8.33 | Ser9 | 3.1 |
| | | | Glu64 | 1.9 |
| | | | Gln106 | 3.2 |
| 4 | Quercetin-3-O-xyloside | 8.08 | Ser9 | 3.3 |
| | | | Ile52 | 1.9 and 3.2 |
| 5 | Narcissoside | 8.93 | Gly8 | 2.4 |
| | | | Ile52 | 2.4 |

| | | | | |
|---|---|---|---|---|
| | | | Gln106 | 3.5 |
| 6 | Quercetin-3-O-arabinoside | 7.81 | Gly8 | 2.7 |
| | | | Ile52 | 2.0 |
| | | | Tyr113 | 3.3 |
| 7 | Myricetin | 7.05 | Gly8 | 2.3 |
| | | | Tyr113 | 3.5 |
| 8 | Quercetin | 7.05 | No interactions | - |
| 9 | Vitexin 2"-O-rhamnoside | 8.59 | Glu64 | 3.4 |
| 10 | Vitexin | 8.14 | Ser9 | 3.3 and 3.5 |
| | | | Ile52 | 2.6 |
| | | | Tyr105 | 2.9 |
| | | | Tyr113 | 3.3 |
| 11 | Apigenin | 6.85 | Tyr113 | 3.2 |
| 12 | Salvianolic acid | 8.60 | Asp110 | 1.9 |
| 13 | Hydroxytyrosol | 6.17 | No interactions | - |
| 14 | Leucenine | 6.38 | Gly8 | 2.2 |
| | | | Tyr105 | 3.3 |
| | | | Tyr113 | 3.4 |
| 15 | Orientin | 6.56 | Ser9 | 3.1 and 3.4 |
| | | | Gln49 | 3.3 |
| | | | Ile52 | 1.9 |
| | | | Pro53 | 2.6 |
| | | | Glu64 | 2.2 and 3.0 |
| | | | Ser65 | 3.0 and 3.1 |
| | | | Arg66 | 3.4 |
| 16 | Kaempferol 7-O-glucoside | 9.05 | Glu64 | 1.9, 2.0 and 2.5 |
| | | | Arg66 | 3.2 |
| 17 | Kaempferol-3-O-arabinoside | 7.71 | No interactions | - |
| 18 | Kaempferol-3-O-rhamnoside | 8.01 | No interactions | - |
| 19 | Kaempferol | 7.07 | Tyr113 | 3.2 |
| 20 | Catechin | 6.89 | Gly8 | 2.3 |
| | | | Tyr113 | 3.5 |
| 21 | Methylgallate | 6.18 | Gly8 | 2.5 |
| 22 | Rutin | 9.06 | Glu64 | 2.5 |
| | | | Ser65 | 3.2 and 3.3 |
| | | | Tyr105 | 3.2 and 3.5 |
| 23 | Malic acid | 6.54 | Ile52 | 2.6 |
| | | | Glu64 | 1.8 |
| | | | Ser65 | 3.1 and 3.4 |
| | | | Arg66 | 3.3, 3.3 and 3.5 |
| 24 | Syringic acid | 6.26 | Tyr105 | 3.1 and 3.1 |
| | | | Tyr113 | 3.5 |
| 25 | Digalloylglucose | 8.18 | Ser9 | 3.2 and 3.5 |
| | | | Ile52 | 3.0 |

| | | | | |
|---|---|---|---|---|
| | | | Glu64 | 2.4 |
| | | | Ser65 | 3.5 |
| | | | Tyr105 | 3.0 and 3.2 |
| 26 | Caffeic acid | 6.18 | Tyr113 | 3.5 |
| 27 | Gallic acid | 6.47 | Glu64 | 1.8 |
| 28 | 3,4-O-dimethylgallic acid | 6.30 | No interactions | - |

Note: SDBE▫ - Swissdock binding energy analysis, BD▪- Bond distance.