*Article*

# Exploring the Potential of Plant Bioactive Compounds Against Male Infertility: An In Silico and In Vivo Study

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## *Supporting information*

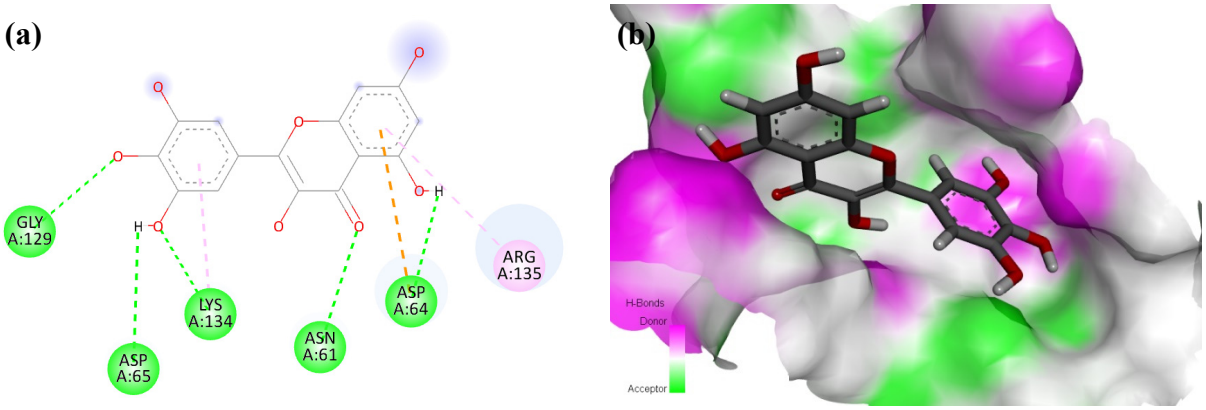


Figure S1. Interaction (a) and binding pattern (b) of myricetin with sex hormone-binding globulin as the receptor.

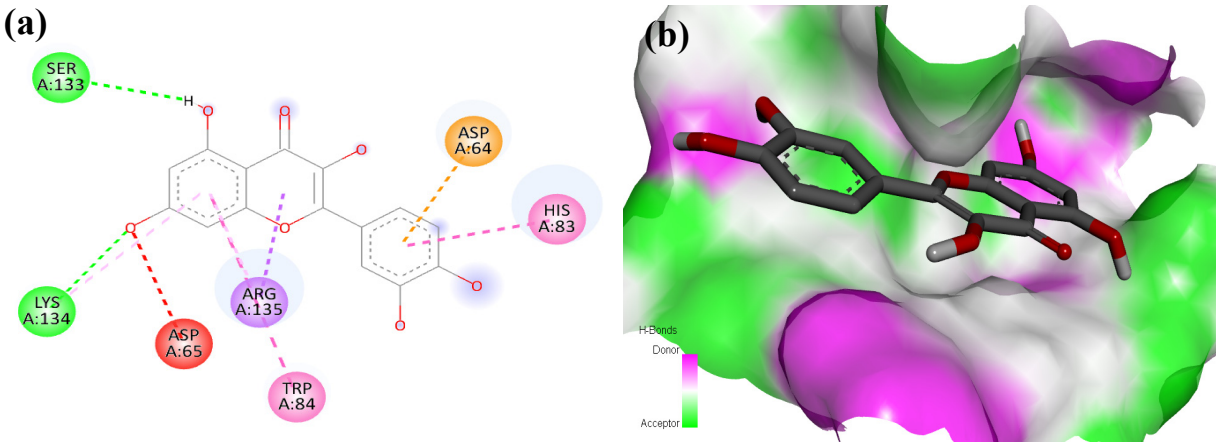


Figure S2. Interactions (a) and binding patterns (b) of quercetin with SHBG as a receptor protein.

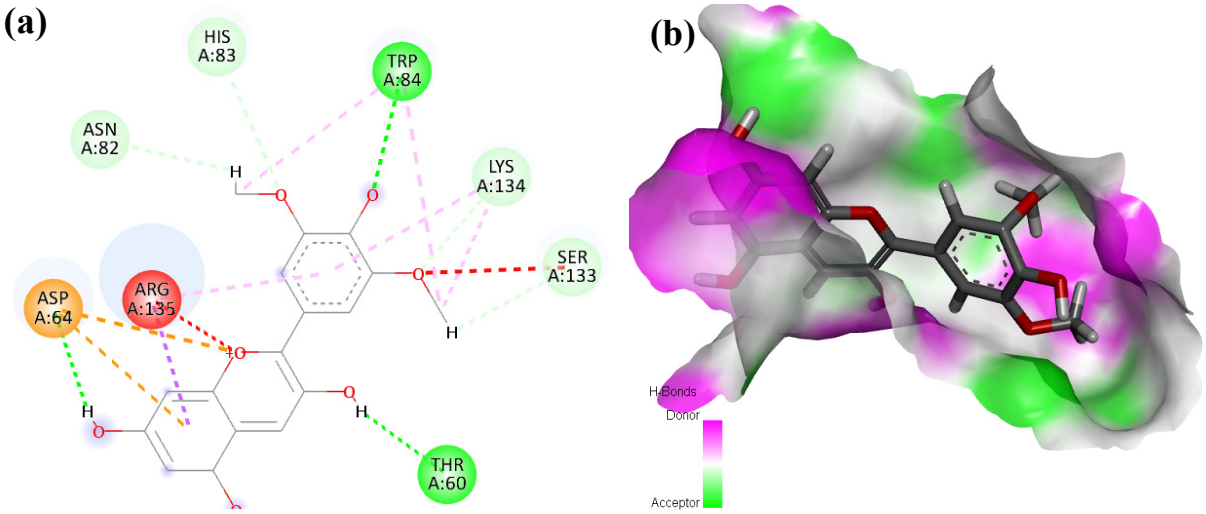


Figure S3. Interactions (a) and binding patterns (b) of malvidin with SHBG as a receptor protein.

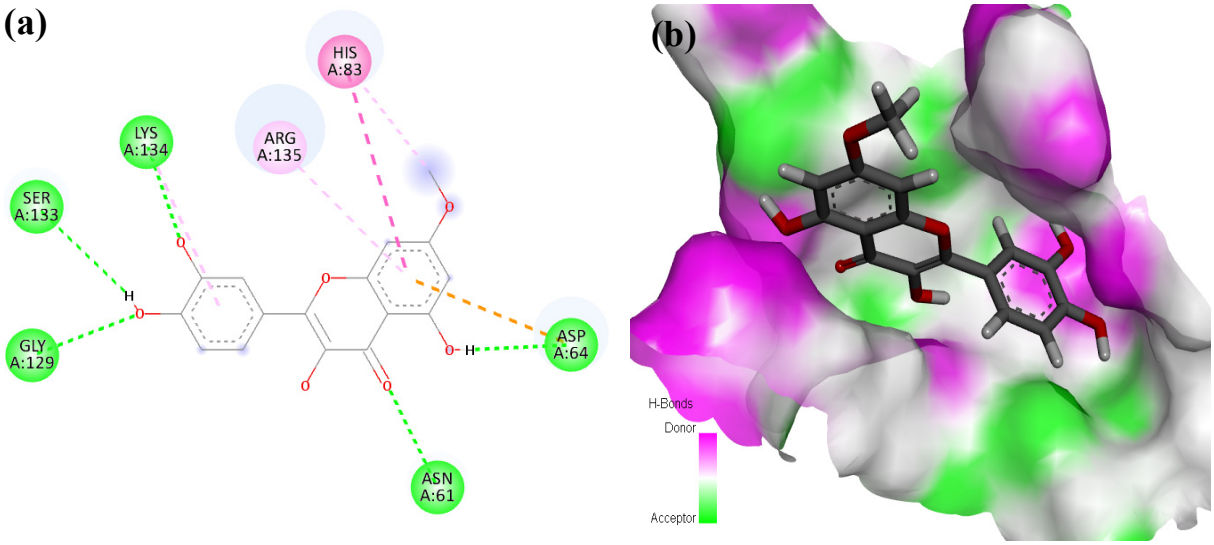


Figure S4. Interactions (a) and binding patterns (b) of rhamnetin with SHBG as a receptor protein.

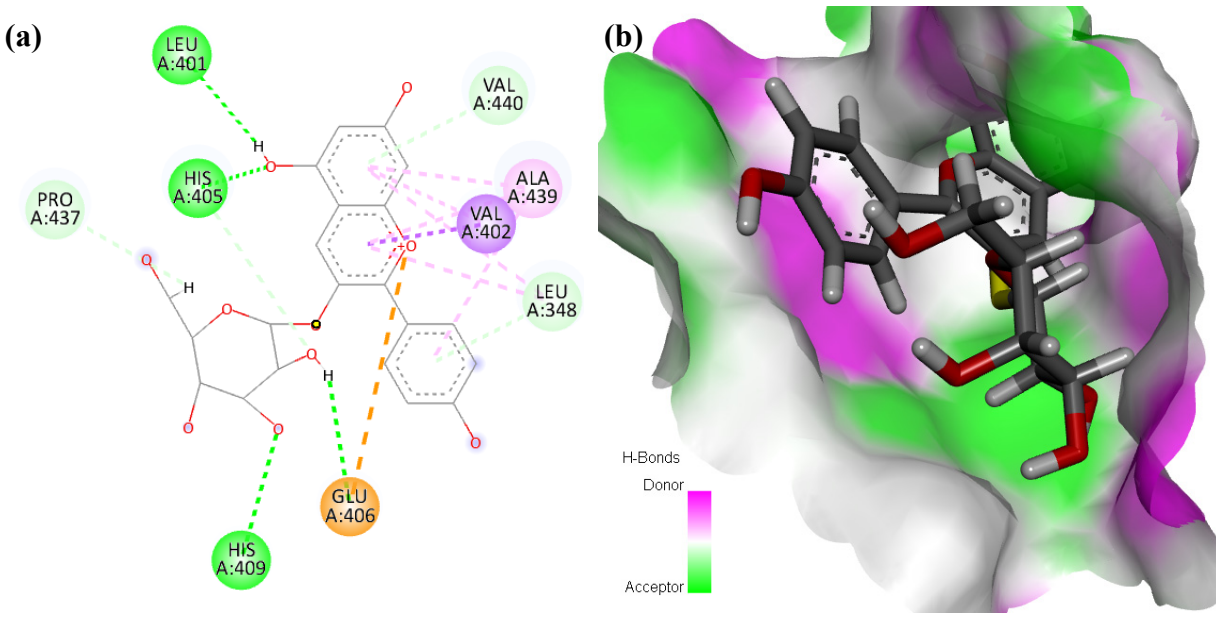


Figure S5. Interaction (a) and binding pattern (b) of callistephin with disintegrin and metalloproteinase 17 (ADAM17) as the receptor.

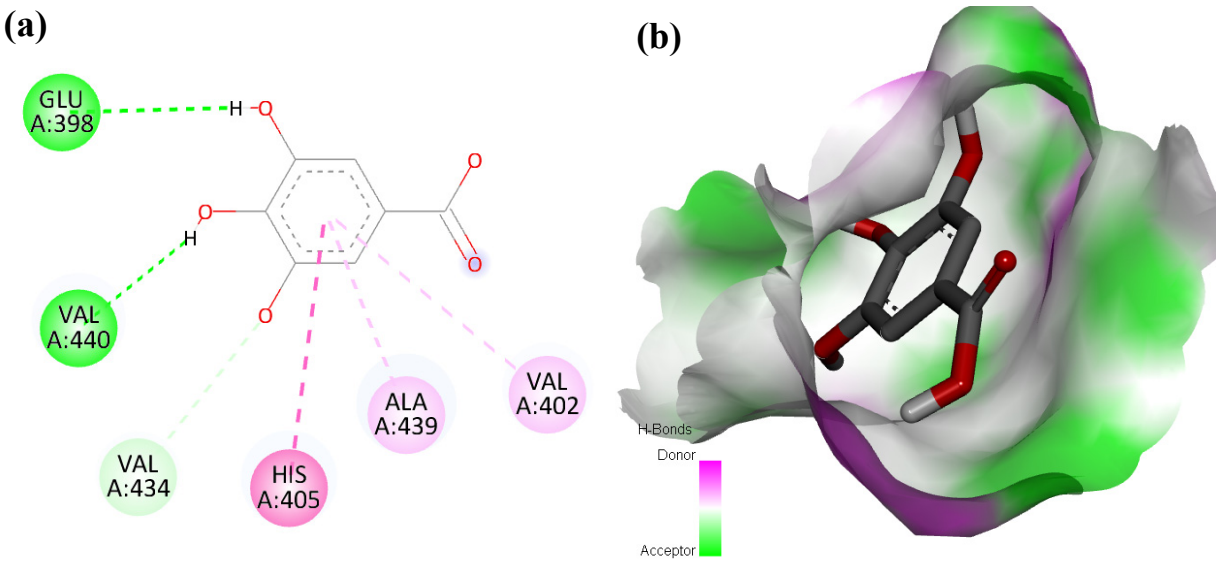


Figure S6. Interactions (a) and binding patterns (b) of gallic acid with ADAM17 as a receptor protein.

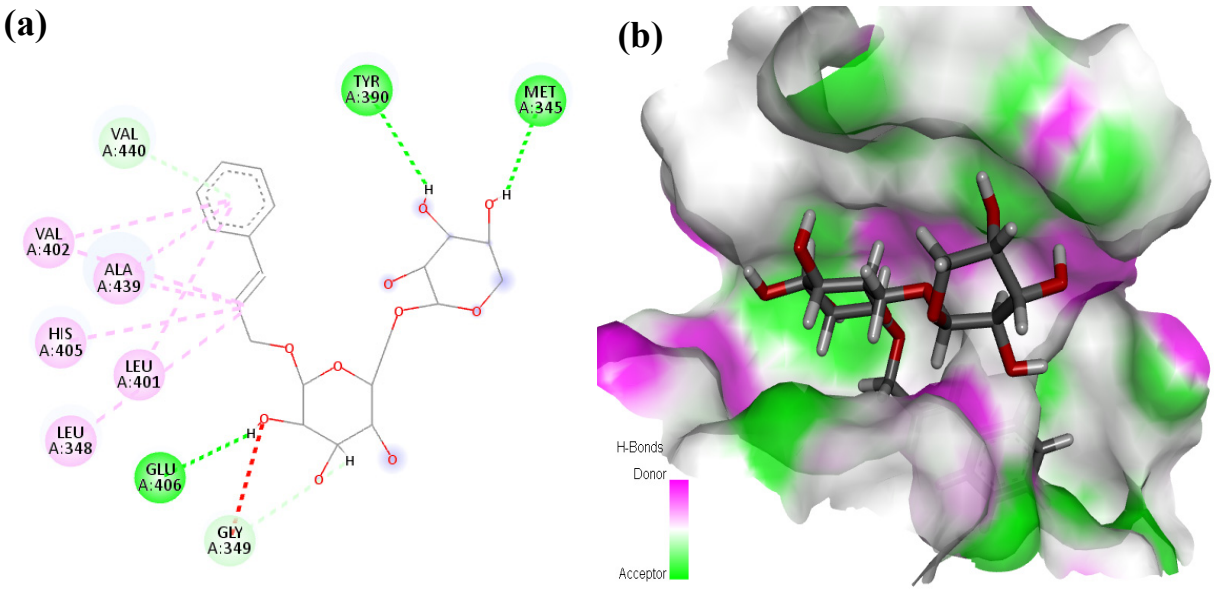


Figure S7. Interactions (a) and binding patterns (b) of rosavin with ADAM17 as a receptor protein.

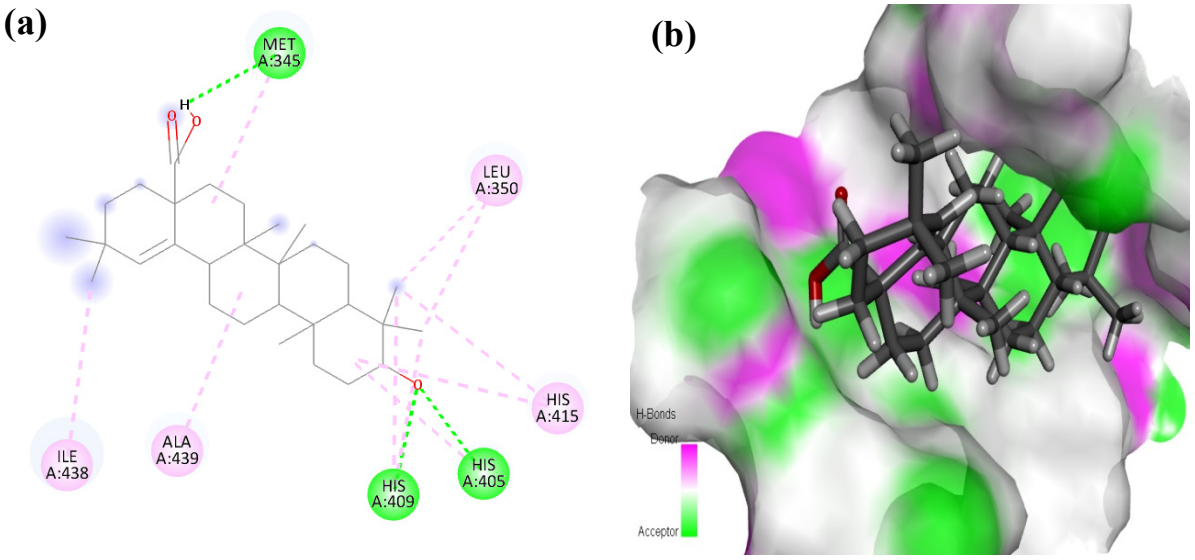


Figure S8. Interactions (a) and binding patterns (b) of moronic acid with ADAM17 as a receptor protein.

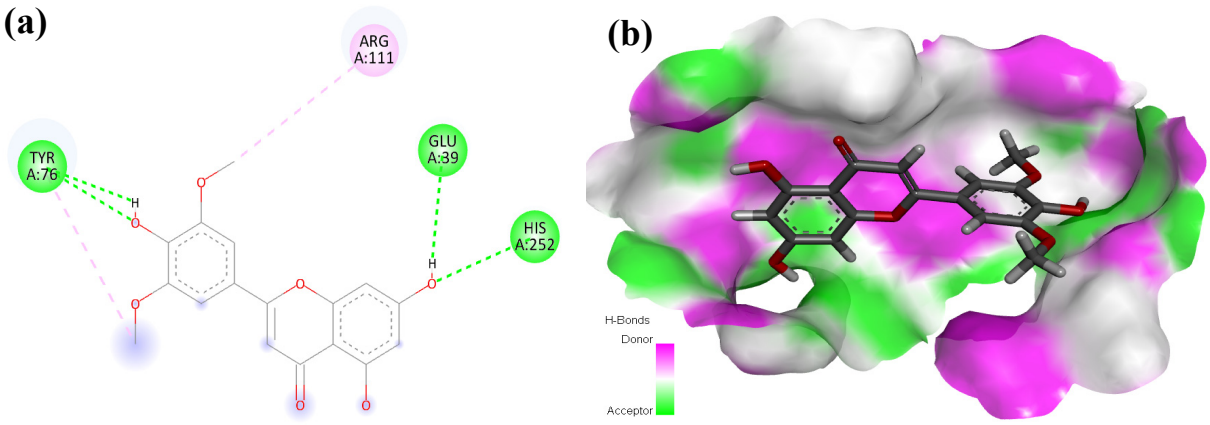


Figure S9. Interactions (a) and binding patterns (b) of tricin with DNaseI as a receptor protein.

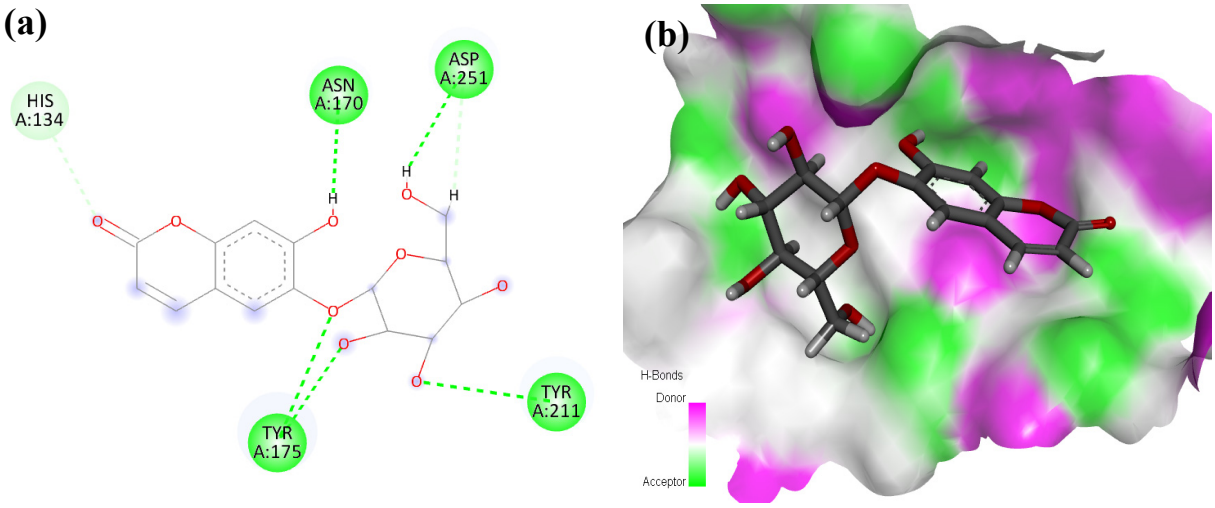


Figure S10. Interactions (a) and binding patterns (b) of esculin with DNaseI as a receptor protein.

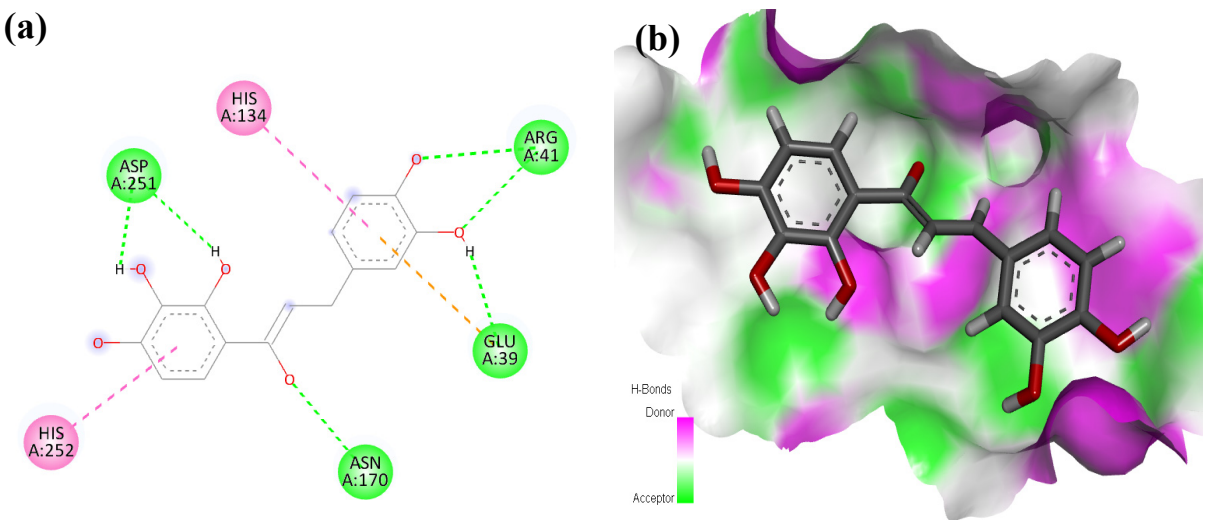


Figure S11. Interactions (a) and binding patterns (b) of okanin with DNaseI as a receptor protein.

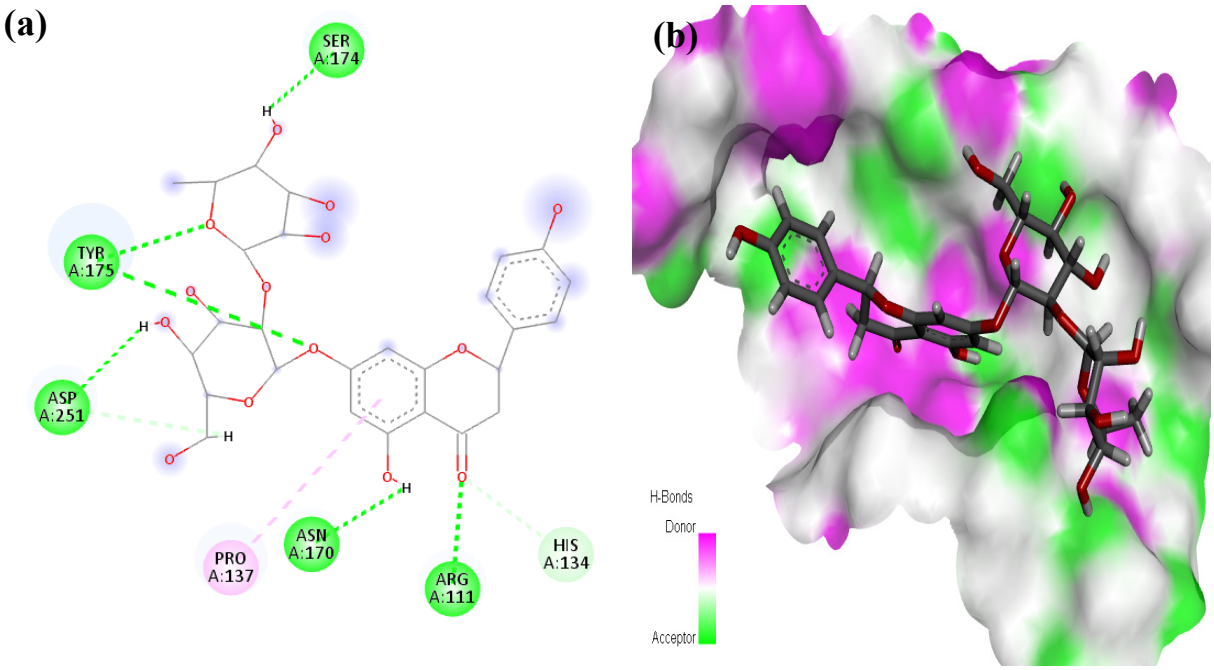


Figure S12. Interactions (a) and binding patterns (b) of naringin with DNaseI as a receptor protein.

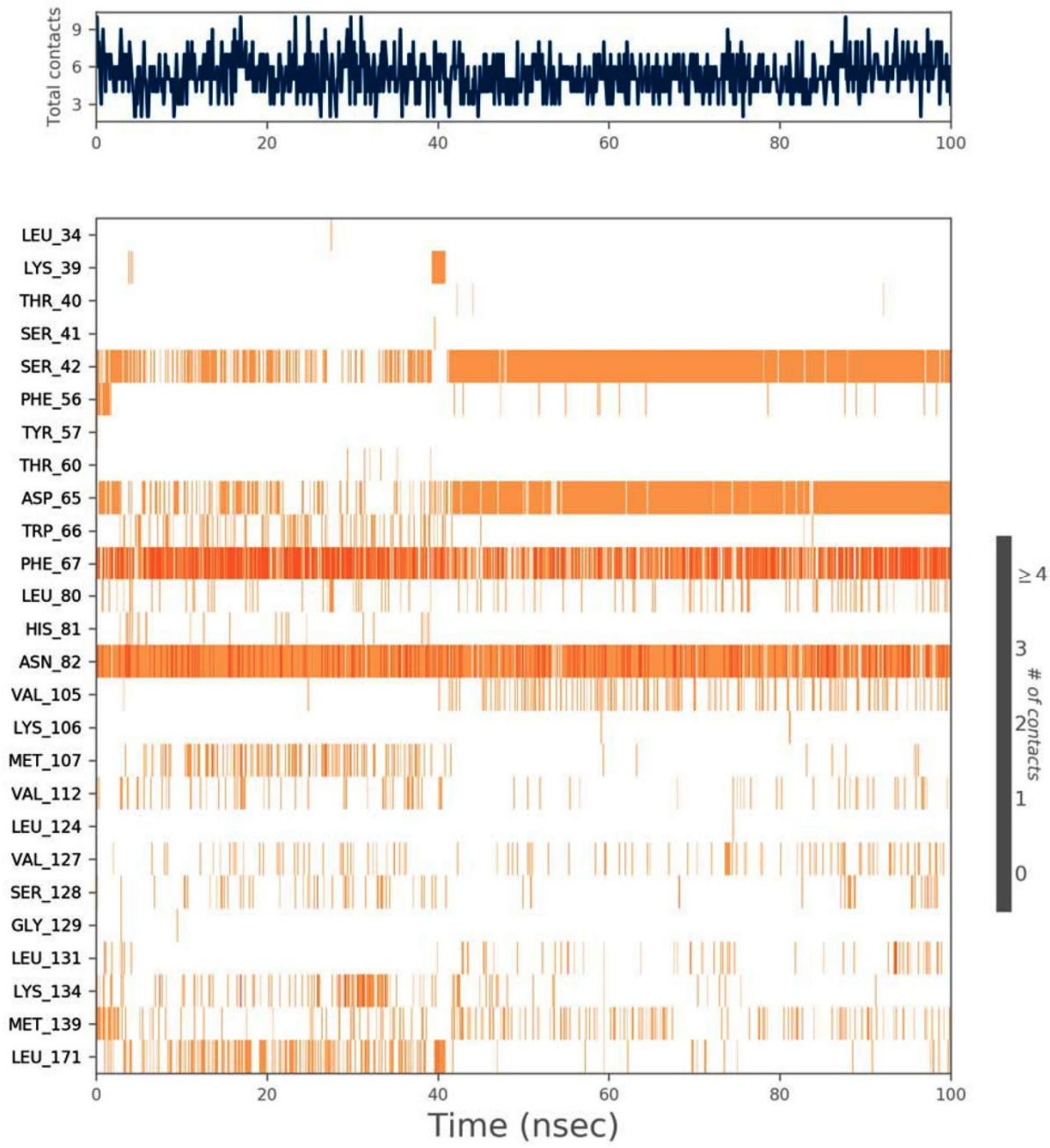


Figure S13. Hydrogen bond interaction stability (consistency) of key residues of SHBG protein with tricin.

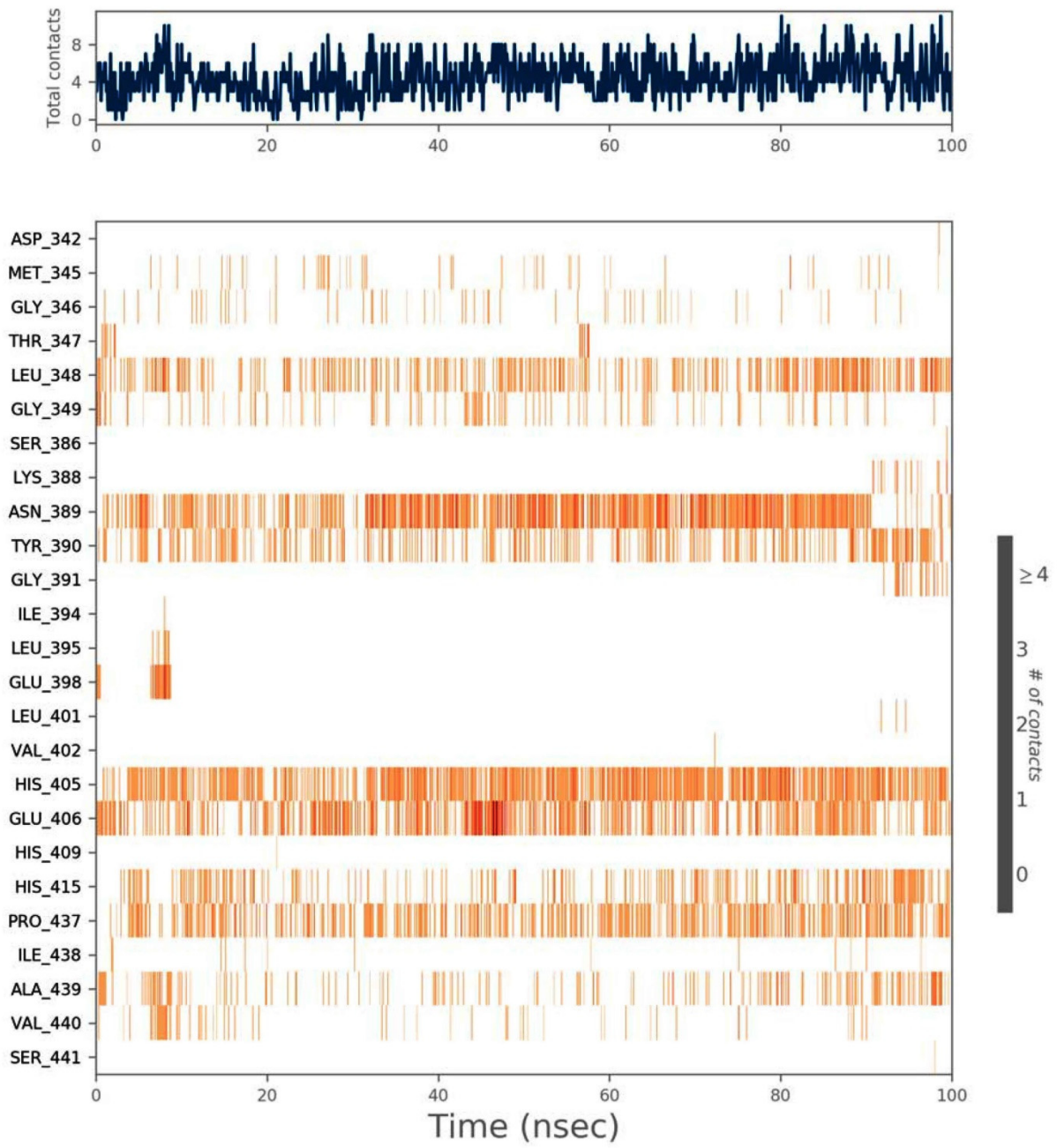


Figure S14. Hydrogen bond interaction stability (consistency) of key residues of the ADAM17 protein with tricin.

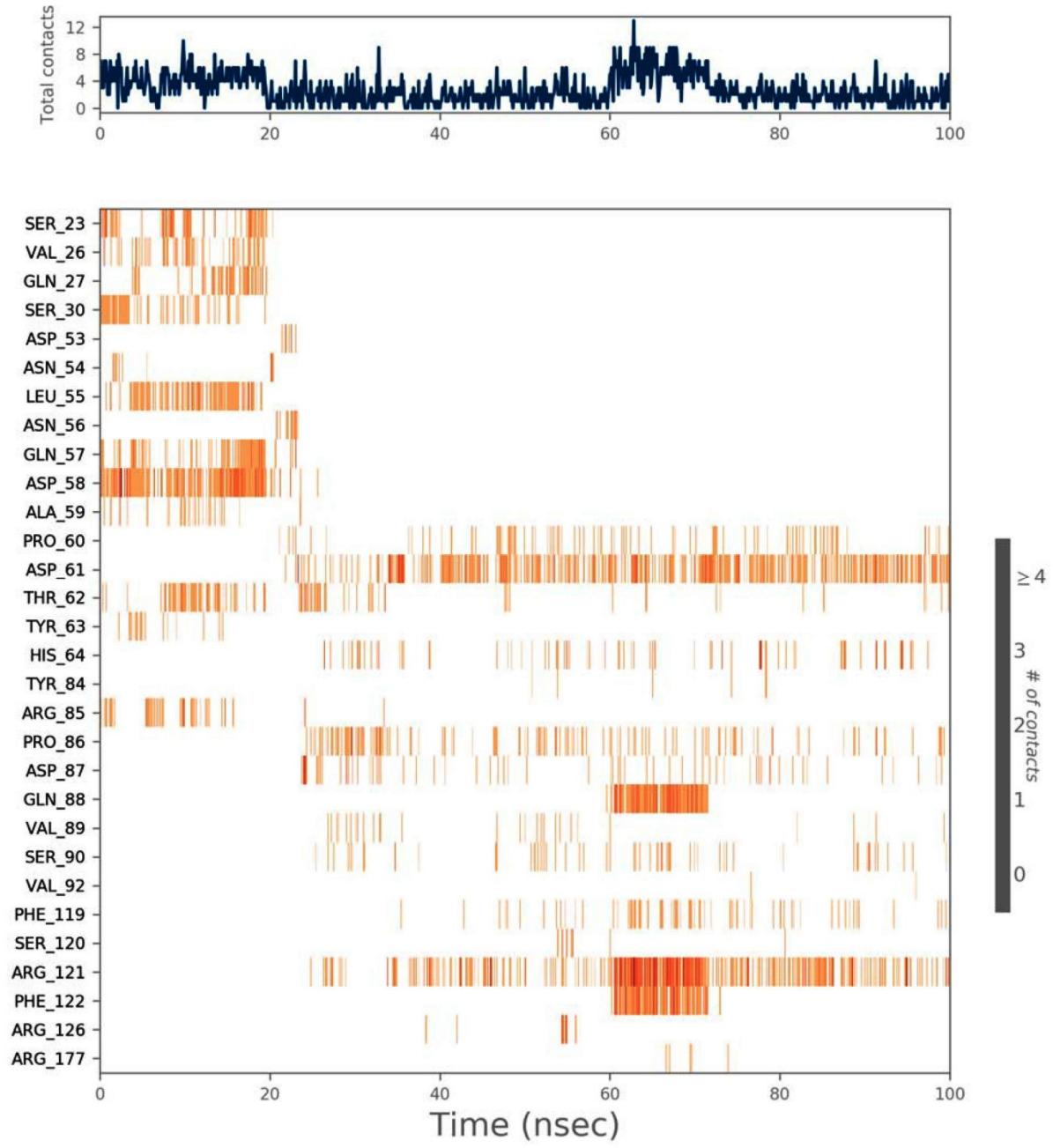


Figure S15. Hydrogen bond interaction stability (consistency) of key residues of the DNaseI protein with tricin.

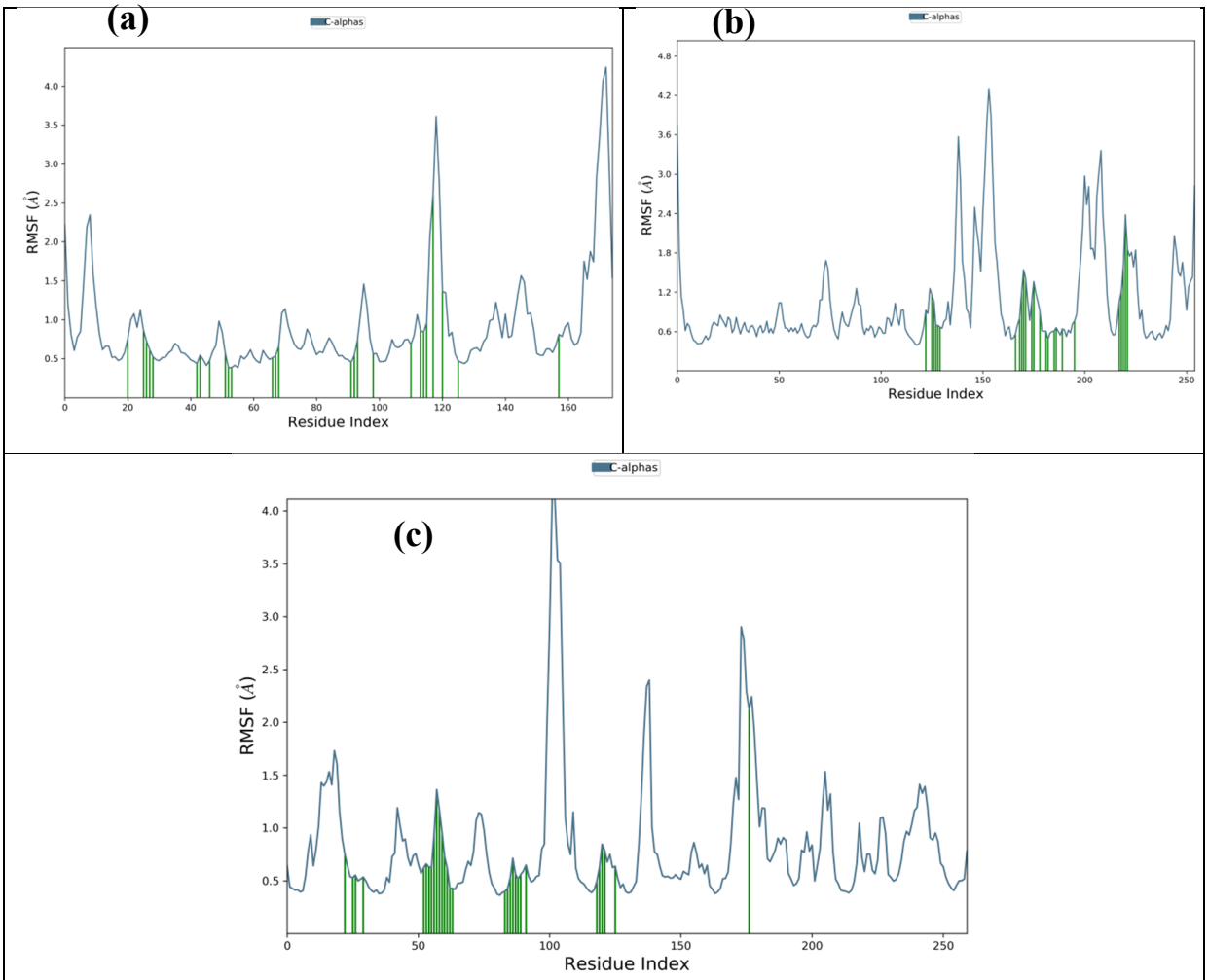


Figure S16. Residue-wise Root Mean Square Fluctuation (RMSF) of protein–ligand complexes during 100 ns. (a) Tricin-SHBG protein; (b) tricin-ADAM17 protein; (c) tricin-DNase I protein. The RMSF of docked protein showed no fluctuation of interacting residues, where green vertical lines represent interacting residues.

Table S1. ADMET screening through pkCSM.

| | Myricetin | Malvidin | Rhamnetin | Quercetin | Isorhamnetin | Okanin | Callistephin | kaempferol | Gallic Acid | Rosavin | Esculin | Robinetin | Tricin |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| GI absorption | Low | High | High | High | High | High | Low | High | High | Low | Low | High | High |
| BBB | No | No | No | No | No | No | No | No | No | No | No | No | No |
| Caco-2 Permeability | 0.095cm/s | -0.381 | -0.361 | -0.229 | -0.003 | | 0.345 | 0.032 | -0.081 | 0.269 | 0.277 | -0.563 | 0.12 |
| PGS | yes | yes | No | | Yes | No | Yes | Yes | No | Yes | Yes | Yes | Yes |
| PGI | No | No | No | | No | No | No | No | No | No | No | No | No |
| CYP2D6 substrate | No | No | No | No | No | No | No | No | No | No | No | No | No |
| CYP3A4 substrate | No | No | No | No | No | No | No | No | No | No | No | No | No |
| CYP1A2 inhibitor | Yes | Yes | Yes | Yes | Yes | No | No | Yes | No | No | No | Yes | Yes |
| CYP2C19 inhibitor | No | No | No | No | No | No | No | No | No | No | No | No | Yes |
| CYP2C9 inhibitor | No | No | No | No | No | No | No | No | No | No | No | No | No |
| CYP2D6 inhibitor | No | No | No | No | No | No | No | No | No | No | No | No | No |
| CYP3A4 inhibitor | No | No | No | No | No | No | No | No | No | No | No | No | No |
| AMES Toxicity | No | No | No | No | No | No | No | No | No | No | No | No | No |
| Skin Sensitization | No | No | No | No | No | No | No | No | No | No | No | No | No |
| Hepatotoxicity | No | No | No | No | No | No | No | No | No | No | No | No | No |

Table S2. Medical biochemistry of drugs.

| Sr. No. | | SA score (<6 easy to synthesize) | Lipinski Rule | Pfizer Rule | GSK Rule | Golden Triangle |
|---|---|---|---|---|---|---|
| 1 | Myricetin | 2.733 | Accepted | Accepted | Accepted | Accepted |
| 2 | Malvidin | 2.944 | Accepted | Accepted | Accepted | Accepted |
| 3 | Rhamnetin | 2.456 | Accepted | Accepted | Accepted | Accepted |
| 4 | Quercetin | 2.545 | Accepted | Accepted | Accepted | Accepted |
| 5 | Isorhamnetin | 2.453 | Accepted | Accepted | Accepted | Accepted |
| 7 | Okanin | 2.392 | Accepted | Accepted | Accepted | Accepted |
| 11 | Callistephin | 4.139 | Accepted | Accepted | Rejected | Accepted |
| 12 | Kaempferol | 2.375 | Accepted | Accepted | Accepted | Accepted |
| 13 | Gallic Acid | 2.095 | Accepted | Accepted | Accepted | Accepted |
| 14 | Moronic acid | 4.653 | Accepted | Rejected | Rejected | Rejected |
| 15 | Rosavin | 4.291 | Accepted | Accepted | Rejected | Accepted |
| 16 | Esculin | 3.732 | Accepted | Accepted | Accepted | Accepted |
| 17 | Robinetin | 2.558 | Accepted | Accepted | Accepted | Accepted |
| 18 | Tricin | 2.430 | Accepted | Accepted | Accepted | Accepted |