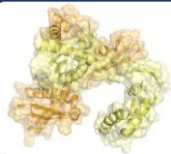
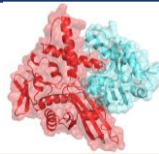
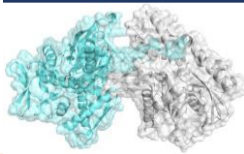


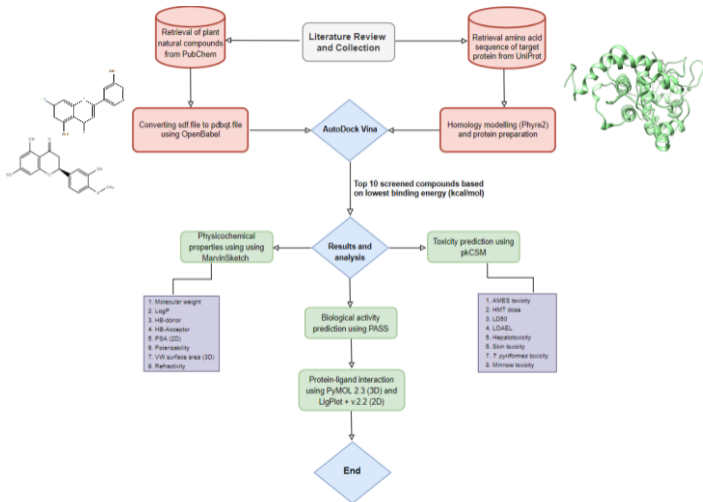
Virtual screening of plant natural compounds targeting hydrolytic and lignin-degrading enzymes of *Ganoderma boninense*

Hadiatullah Hadiatullah

Young Scientists flash presentations; 25 May, 2022



In silico based screening



Top 10 selected compounds

Lignin-degrading enzymes

| Laccase | | MnP | | LiP | |
|-------------------------------|--------------------------------|---------------------------------|--------------------------------|--------------------------------|-------------------------------|
| | Azadirachtin -10.7 kcal/mol | | Quinine -10.2 kcal/mol | | Hydrastine -10.1 kcal/mol |
| Oleanane -10.4 kcal/mol | Solasodine -10.1 kcal/mol | (+)-Coccoline -10.1 kcal/mol | Azadirachtin -10.0 kcal/mol | (+)-Coccoline -9.7 kcal/mol | Azadirachtin -9.5 kcal/mol |
| Clausenol -9.9 kcal/mol | (+)-Coccoline -9.9 kcal/mol | Guaiazulene -9.9 kcal/mol | Tylophorine -9.9 kcal/mol | Naringenin -9.0 kcal/mol | Oleanane -8.9 kcal/mol |
| Abietic acid -9.7 kcal/mol | Kaempferol -9.3 kcal/mol | Vetivazulene -9.6 kcal/mol | Jatrorrhizine -9.6 kcal/mol | Apigenin -8.8 kcal/mol | Hesperetin -8.8 kcal/mol |
| Daidzein -9.3 kcal/mol | Apigenin -9.2 kcal/mol | Waltherione -9.6 kcal/mol | Luteolin -9.5 kcal/mol | Strychnine -8.8 kcal/mol | Sanguinarine -8.8 kcal/mol |
| Berberine -9.2 kcal/mol | Methfuroxam -8.0 kcal/mol | Daidzein -9.5 kcal/mol | Methfuroxam -8.0 kcal/mol | Quercetin -8.7 kcal/mol | Methfuroxam -8.6 kcal/mol |

Hydrolytic enzymes

| Cellulase | | Amylase | | Xylanase | |
|--------------------------------|--------------------------------|-------------------------------|--------------------------------|--------------------------------|--------------------------------|
| | Azadirachtin -12.9 kcal/mol | | Azadirachtin -10.6 kcal/mol | | Azadirachtin -11.0 kcal/mol |
| Sanguinarine -12.4 kcal/mol | Oleanane -11.5 kcal/mol | Rotenone -10.1 kcal/mol | (+)-Coccoline -9.9 kcal/mol | (+)-Coccoline -9.4 kcal/mol | Rotenone -8.7 kcal/mol |
| Solasodine -11.5 kcal/mol | Berberine -11.0 kcal/mol | Solasodine -9.7 kcal/mol | Strychnine -9.6 kcal/mol | Oleanane -8.6 kcal/mol | Lobeline -8.6 kcal/mol |
| Dicentrine -10.3 kcal/mol | Hesperetin -10.0 kcal/mol | Vetivazulene -9.3 kcal/mol | Oleanane -9.3 kcal/mol | Strychnine -8.5 kcal/mol | Cucurbitacin -8.3 kcal/mol |
| Luteolin -10.0 kcal/mol | Jatrorrhizine -9.9 kcal/mol | Lobeline -9.2 kcal/mol | Apigenin -9.1 kcal/mol | Senecionine -8.3 kcal/mol | Luteolin -8.1 kcal/mol |
| Strychnine -9.8 kcal/mol | Methfuroxam -6.7 kcal/mol | Luteolin -9.1 kcal/mol | Methfuroxam -8.8 kcal/mol | Quercetin -8.1 kcal/mol | Methfuroxam -6.6 kcal/mol |

Physico-chemical characterization of selected compounds

| No | Compounds | Molecular weight (<100 Dalton) | Hydrophilicity (logP) (<1) | H bond donor (<10) | H bond acceptor (<10) | Polar surface area (PSA) (<60 Å) | Polarizability | Van der Waals' surface area (SA) (<100 Å) | Refractivity (40-100) |
|----------------|----------------------|--------------------------------|----------------------------|--------------------|-----------------------|----------------------------------|----------------|---|-----------------------|
| Lactase | | | | | | | | | |
| 1 | Azadirachtin | 720.721 | -0.13 | 3 | 12 | 215 | 67.69 | 978 | 166.27 |
| 2 | Oleanane | 412.746 | 0.04 | 0 | 0 | 52.44 | 796 | 129.54 | |
| 3 | Solizodine | 413.645 | 4.61 | 2 | 3 | 41.49 | 48.69 | 693.87 | 121.95 |
| 4 | Oleanolone | 408.81 | 8.68 | 1 | 1 | 20.23 | 58.82 | 872.2 | 167.31 |
| 5 | (+)-Coccoline | 548.638 | 5.79 | 2 | 4 | 72.42 | 60.82 | 766.2 | 157.59 |
| 6 | Asiatic acid | 302.458 | 4.95 | 1 | 2 | 37.5 | 35.1 | 502.8 | 96.21 |
| 7 | Kampferol | 286.238 | 2.46 | 4 | 6 | 107.22 | 27.75 | 331.71 | 74.89 |
| 8 | Daidzin | 270.24 | 3.08 | 3 | 5 | 86.99 | 27.11 | 322.67 | 72.91 |
| 9 | Apigenin | 270.24 | 2.71 | 3 | 5 | 86.99 | 27.11 | 322.67 | 72.91 |
| 10 | Berberine | 336.365 | -4.38 | 0 | 4 | 40.8 | 38.45 | 424.22 | 90.82 |
| MtP | | | | | | | | | |
| 1 | Quinine | 326.424 | 2.51 | 1 | 4 | 45.59 | 38.35 | 477.31 | 94.69 |
| 2 | (+)-Coccoline | 548.638 | 5.79 | 2 | 4 | 72.42 | 60.82 | 766.2 | 157.59 |
| 3 | Azadirachtin | 720.721 | -0.13 | 3 | 12 | 215 | 67.69 | 978 | 166.27 |
| 4 | Galactulose | 198.209 | 5.23 | 0 | 0 | 27.02 | 353.83 | 66.78 | |
| 5 | Tylophosine | 201.482 | 3.77 | 0 | 5 | 40.16 | 46.49 | 601.19 | 113.87 |
| 6 | Verticilline | 198.209 | 5.23 | 0 | 0 | 27.02 | 353.83 | 66.78 | |
| 7 | Jatrophanine | 338.382 | -1.37 | 1 | 4 | 51.8 | 39.12 | 493.45 | 96.2 |
| 8 | Walterin | 291.439 | 2.89 | 2 | 6 | 77.02 | 41.61 | 538.99 | 111.69 |
| 9 | Luteolin | 286.239 | 2.4 | 4 | 6 | 107.22 | 27.75 | 331.71 | 74.89 |
| 10 | Daidzin | 270.24 | 3.08 | 3 | 5 | 86.99 | 27.11 | 322.67 | 72.91 |
| LP | | | | | | | | | |
| 1 | Hydroxine | 383.4 | 2.74 | 0 | 6 | 64.46 | 39.23 | 535.23 | 106.1 |
| 2 | (+)-Coccoline | 548.638 | 5.79 | 2 | 4 | 72.42 | 60.82 | 766.2 | 157.59 |
| 3 | Azadirachtin | 720.721 | -0.13 | 3 | 12 | 215 | 67.69 | 978 | 166.27 |
| 4 | Naringenin | 272.256 | 2.84 | 3 | 5 | 86.99 | 27.29 | 348.54 | 71.29 |
| 5 | Oleanane | 412.746 | 0.04 | 0 | 0 | 52.44 | 796 | 129.54 | |
| 6 | Apigenin | 270.24 | 2.71 | 3 | 5 | 86.99 | 27.11 | 322.67 | 72.91 |
| 7 | Hypericin | 302.282 | 2.68 | 3 | 6 | 96.22 | 29.84 | 396.24 | 77.75 |
| 8 | Strychnine | 334.429 | 0.93 | 0 | 3 | 32.78 | 36.75 | 449.13 | 94.51 |
| 9 | Sanguinarine | 332.334 | -0.94 | 0 | 4 | 40.8 | 38.96 | 424.22 | 90.82 |
| 10 | Quercetin | 302.238 | 2.16 | 5 | 7 | 127.45 | 28.42 | 342.28 | 76.46 |

| No | Compounds | Molecular weight (>100 Dalton) | Hydrophilicity (logP) (>1) | H bond donor (>10) | H bond acceptor (>10) | Polar surface area (PSA) (>60 Å) | Polarizability | Van der Waals' surface area (SA) (>100 Å) | Refractivity |
|------------------|----------------------|--------------------------------|----------------------------|--------------------|-----------------------|----------------------------------|----------------|---|--------------|
| Cellulase | | | | | | | | | |
| 1 | Azadirachtin | 720.721 | -0.13 | 3 | 12 | 215 | 67.69 | 978 | 166.27 |
| 2 | Sanguinarine | 332.334 | -0.94 | 0 | 4 | 40.8 | 38.96 | 424.22 | 90.82 |
| 3 | Oleanane | 412.746 | 0.04 | 0 | 0 | 52.44 | 796 | 129.54 | |
| 4 | Solizodine | 413.645 | 4.61 | 2 | 3 | 41.49 | 48.69 | 693.87 | 121.95 |
| 5 | Berberine | 336.365 | -1.38 | 0 | 4 | 40.8 | 38.45 | 472.50 | 39.52 |
| 6 | Oleanone | 339.341 | 3.01 | 0 | 5 | 40.16 | 27.89 | 495.97 | 94.72 |
| 7 | Hypericin | 302.282 | 2.68 | 3 | 6 | 96.22 | 29.84 | 396.24 | 77.75 |
| 8 | Luteolin | 286.239 | 2.4 | 4 | 6 | 107.22 | 27.75 | 331.71 | 74.89 |
| 9 | Jatrophanine | 338.382 | -1.37 | 1 | 4 | 51.8 | 39.12 | 493.45 | 96.2 |
| 10 | Strychnine | 334.429 | 0.93 | 0 | 3 | 32.78 | 36.75 | 449.13 | 94.51 |
| Amylase | | | | | | | | | |
| 1 | Azadirachtin | 720.721 | -0.13 | 3 | 12 | 215 | 67.69 | 978 | 166.27 |
| 2 | Rotenone | 294.423 | 3.32 | 0 | 6 | 62.22 | 41.12 | 542.79 | 105.71 |
| 3 | (+)-Coccoline | 548.638 | 5.79 | 2 | 4 | 72.42 | 60.82 | 766.2 | 157.59 |
| 4 | Solizodine | 413.645 | 4.61 | 2 | 3 | 41.49 | 48.69 | 693.87 | 121.95 |
| 5 | Strychnine | 334.429 | 0.93 | 0 | 3 | 32.78 | 36.75 | 449.13 | 94.51 |
| 6 | Verticilline | 198.209 | 5.23 | 0 | 0 | 27.02 | 354.91 | 66.78 | |
| 7 | Oleanane | 412.746 | 0.04 | 0 | 0 | 52.44 | 796 | 129.54 | |
| 8 | Lobeline | 337.463 | 3.78 | 1 | 3 | 40.54 | 39.83 | 537.03 | 101.51 |
| 9 | Apigenin | 270.24 | 2.71 | 3 | 5 | 86.99 | 27.11 | 322.67 | 72.91 |
| 10 | Luteolin | 286.239 | 2.4 | 4 | 6 | 107.22 | 27.75 | 331.71 | 74.89 |
| Nyctase | | | | | | | | | |
| 1 | Azadirachtin | 720.721 | -0.13 | 3 | 12 | 215 | 67.69 | 978 | 166.27 |
| 2 | (+)-Coccoline | 548.638 | 5.79 | 2 | 4 | 72.42 | 60.82 | 766.2 | 157.59 |
| 3 | Rotenone | 294.423 | 3.32 | 0 | 6 | 62.22 | 41.12 | 542.79 | 105.71 |
| 4 | Oleanane | 412.746 | 0.04 | 0 | 0 | 52.44 | 796 | 129.54 | |
| 5 | Lobeline | 337.463 | 3.78 | 1 | 3 | 40.54 | 39.83 | 537.03 | 101.51 |
| 6 | Strychnine | 334.429 | 0.93 | 0 | 3 | 32.78 | 36.75 | 449.13 | 94.51 |
| 7 | Cucubitalcin | 558.712 | 3.13 | 3 | 7 | 138.2 | 58.15 | 863.27 | 151.04 |
| 8 | Senecianolone | 335.4 | 1.64 | 1 | 4 | 76.07 | 34.92 | 495.17 | 89.41 |
| 9 | Luteolin | 286.239 | 2.4 | 4 | 6 | 107.22 | 27.75 | 331.71 | 74.89 |
| 10 | Quercetin | 302.238 | 2.16 | 5 | 7 | 127.45 | 28.42 | 342.28 | 76.46 |

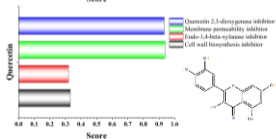
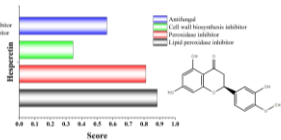
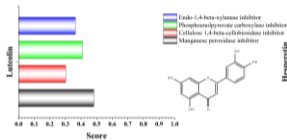
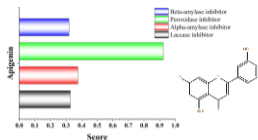
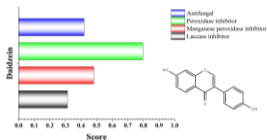
Toxicity prediction

| No | Compounds | AMES toxicity | Max. tolerated dose (human) (log mg/kg/day) | Oral Rat Acute Toxicity (LD50) (mol/kg) | Oral Rat Chronic Toxicity (LOAEL) (log mg/kg_bw/day) | Hepatotoxicity | Skin Sensitisation | T.Pyiformis toxicity (log ug/L) | Minnow toxicity (log mM) |
|-------------------|----------------------|---------------|---|---|--|----------------|--------------------|---------------------------------|--------------------------|
| Gb-Laccase | | | | | | | | | |
| 1 | Solasodine | No | -0.375 | 2.489 | 1.332 | Yes | No | 0.311 | 0.381 |
| 2 | Abietic acid | No | 0.134 | 1.803 | 2.284 | Yes | No | 0.377 | -0.41 |
| 3 | Kaempferol | No | 0.531 | 2.449 | 2.505 | Yes | No | 0.312 | 2.885 |
| 4 | Daidzein | No | 0.187 | 2.164 | 1.187 | No | No | 0.893 | 1.035 |
| 5 | Apigenin | No | 0.328 | 2.45 | 2.298 | No | No | 0.38 | 2.432 |
| 6 | Berberine | Yes | 0.144 | 2.571 | 1.89 | Yes | No | 0.354 | -0.277 |
| Gb-MnP | | | | | | | | | |
| 1 | Quinine | Yes | -0.418 | 2.728 | 0.635 | Yes | No | 0.488 | -0.204 |
| 2 | Tylophorine | Yes | -0.027 | 3.116 | 1.686 | Yes | No | 0.31 | -0.646 |
| 3 | Jatrorrhizine | No | 0.175 | 2.445 | 1.356 | Yes | No | 0.385 | 0.177 |
| 4 | Waltherione | No | 0.231 | 2.305 | 1.394 | Yes | No | 0.34 | 1.168 |
| 5 | Luteolin | No | 0.499 | 2.455 | 2.409 | No | No | 0.326 | 3.169 |
| 6 | Daidzein | No | 0.187 | 2.164 | 1.187 | No | No | 0.893 | 1.035 |
| Gb-LIP | | | | | | | | | |
| 1 | Hydrastine | No | -0.1 | 2.893 | 2.319 | No | No | 0.423 | 1.219 |
| 2 | Naringenin | No | -0.178 | 1.791 | 1.944 | No | No | 0.369 | 2.136 |
| 3 | Apigenin | No | 0.328 | 2.45 | 2.298 | No | No | 0.38 | 2.432 |
| 4 | Hesperetin | No | 0.25 | 2.042 | 2.605 | No | No | 0.39 | 2.305 |
| 5 | Strychnine | No | -0.535 | 2.798 | 1.693 | No | No | 0.349 | 0.529 |
| 6 | Sanguinarine | Yes | 0.172 | 2.588 | 1.729 | No | No | 0.308 | -0.718 |
| 7 | Quercetin | No | 0.499 | 2.471 | 2.612 | No | No | 0.288 | 3.721 |

Toxicity prediction

| No | Compounds | AMES toxicity | Max. tolerated dose (human) (log mg/kg/day) | Oral Rat Acute Toxicity (LD50) (mol/kg) | Oral Rat Chronic Toxicity (LOAEL) (log mg/kg_bw/day) | Hepatotoxicity | Skin Sensitisation | T.Pyiformis toxicity (log ug/L) | Minnow toxicity (log mM) |
|---------------------|----------------------|---------------|---|---|--|----------------|--------------------|---------------------------------|--------------------------|
| Gb-Cellulase | | | | | | | | | |
| 1 | Sanguinarine | Yes | 0.172 | 2.588 | 1.729 | No | No | 0.308 | -0.718 |
| 2 | Solasodine | No | -0.375 | 2.489 | 1.332 | Yes | No | 0.311 | 0.381 |
| 3 | Berberine | Yes | 0.144 | 2.571 | 1.89 | Yes | No | 0.354 | -0.277 |
| 4 | Dicentrine | Yes | -0.512 | 2.953 | 1.307 | Yes | No | 0.903 | 0.878 |
| 5 | Hesperetin | No | 0.25 | 2.042 | 2.605 | No | No | 0.39 | 2.305 |
| 6 | Luteolin | No | 0.499 | 2.455 | 2.409 | No | No | 0.326 | 3.169 |
| 7 | Jatrorrhizine | No | 0.175 | 2.445 | 1.356 | Yes | No | 0.385 | 0.177 |
| 8 | Strychnine | No | -0.535 | 2.798 | 1.693 | No | No | 0.349 | 0.529 |
| Gb-Amylase | | | | | | | | | |
| 1 | Rotenone | No | 0.483 | 2.64 | 1.575 | Yes | No | 0.346 | 0.736 |
| 2 | Solasodine | No | -0.375 | 2.489 | 1.332 | Yes | No | 0.311 | 0.381 |
| 3 | Strychnine | No | -0.535 | 2.798 | 1.693 | No | No | 0.349 | 0.529 |
| 4 | Lobeline | No | -0.33 | 2.53 | 1.444 | Yes | No | 1.377 | 0.35 |
| 5 | Apigenin | No | 0.328 | 2.45 | 2.298 | No | No | 0.38 | 2.432 |
| 6 | Luteolin | No | 0.499 | 2.455 | 2.409 | No | No | 0.326 | 3.169 |
| Gb-Xylanase | | | | | | | | | |
| 1 | Rotenone | No | 0.483 | 2.64 | 1.575 | Yes | No | 0.346 | 0.736 |
| 2 | Lobeline | No | -0.33 | 2.53 | 1.444 | Yes | No | 1.377 | 0.35 |
| 3 | Strychnine | No | -0.535 | 2.798 | 1.693 | No | No | 0.349 | 0.529 |
| 4 | Senecionine | Yes | -0.01 | 2.664 | 1.821 | Yes | No | 0.325 | 2.747 |
| 5 | Luteolin | No | 0.499 | 2.455 | 2.409 | No | No | 0.326 | 3.169 |
| 6 | Quercetin | No | 0.499 | 2.471 | 2.612 | No | No | 0.288 | 3.721 |

Biological activity probability



Conclusion

1. Several compounds, **Apigenin, daidzein, luteolin, and hesperetin**, exhibited **anti-lignin degrading enzyme** with low binding energy
2. Several compounds, **Hesperetin, apigenin, daidzein, and quercetin** revealed **anti-hydrolytic enzymes** with high binding affinity
3. ***in vitro and in vivo*** validation (e.g., structure elucidation) of these findings await for further confirmation

thank you

