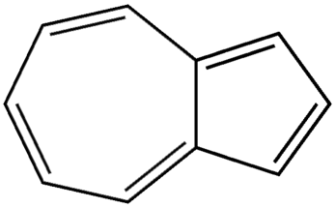
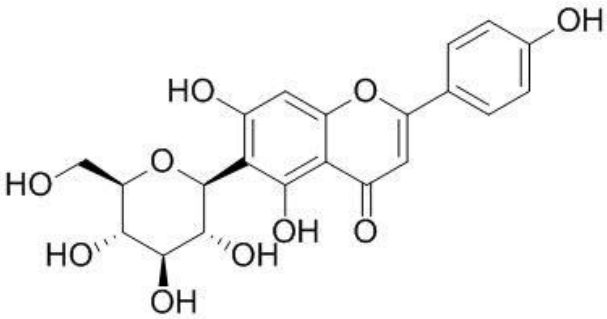
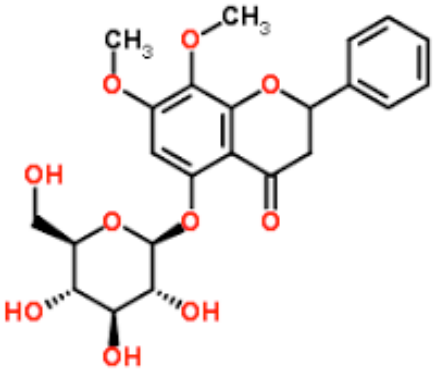
**Supplementary Material**



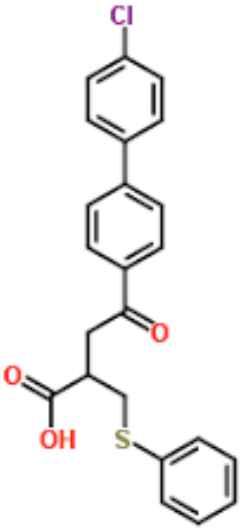
**Azulene**




**Isovitexin**




**Andrographidine A**




**Tanomastat**

**Fig. S1:** Chemical structures of the lead compounds and Tanomastat (the standard drug).

**Table S1** List and docking scores of *Spondias mombin* phytochemicals, docked into MMP-2 catalytic site and arranged in order of decreasing docking score.

| Phytochemicals | Docking scores | Phytochemicals | Docking scores |
|---|---|---|---|
| Quercetin | -8.7 | Protocatechuic acid | -6.5 |
| Hyperoside | -8.6 | Cinnamylalcohol | -6.4 |
| Chlorogenicacid | -8.4 | Terpinenol | -6.4 |
| Isoquercitrin | -8.4 | Caryophylleneoxide | -6.3 |
| Avicularin | -8.2 | Linalyl acetate | -6.3 |
| Epicatechin | -8.2 | Transalphabergamotene | -6.3 |
| Betulinicacid | -8.1 | Bcaryophellene | -6.3 |
| Lupeol | -8.1 | Elemicin | -6.2 |
| Reynoutrin | -8.1 | Ethyl benzoate | -6.2 |
| Ellagic acid | -7.8 | Eugenol | -6.2 |
| Gamma-Muurolene | -7.8 | Geraniol | -6.2 |
| Kaempferol | -7.8 | Nerol | -6.2 |
| Beta-Selinene | -7.7 | Alphathujene | -6.1 |
| Benzothiazole | -7.6 | Geranial | -6.1 |
| Betasesquiphellandrene | -7.6 | Xanthine | -6.1 |
| Betacadinene | -7.5 | Cisaconiticacid | -6 |
| Torreyol | -7.4 | Gamma-cadinene | -6 |
| Alphaselinene | -7.3 | Neral | -6 |
| Alpha-bisabolene | -7.2 | Tetradecanoic acid | -6 |
| Betabisabolene | -7.2 | Linalool | -5.9 |
| Guavanoic acid | -7.2 | Γcadinene | -5.9 |
| Alpha-copane | -7.1 | Epicedrol | -5.8 |
| Isocedranol acetate | -7.1 | Transaconitic acid | -5.8 |
| Cadinene | -7 | Alphapinene | -5.7 |
| Acetyl eugenol | -6.9 | Alphaterpineol | -5.7 |
| Bicyclogermacrene | -6.9 | Fenchone | -5.7 |
| Alpha-gurjunene | -6.8 | Hexadecanoic acid | -5.7 |
| Betaelemene | -6.7 | Alpha-Humulene | -5.6 |
| Ethyl cinnamate | -6.7 | E3Hexenyl acetate | -5.3 |
| Thymyl methyl ether | -6.7 | 3-Mercaptohexyl acetate | -5 |
| Alpha-muurolene | -6.6 | Citric acid | -5 |
| Betacaryophyllene | -6.6 | Maleic acid | -5 |
| Protocatechuic acid | -6.5 | Borneol | -4.8 |
| Cinnamylalcohol | -6.4 | Prenol | -4.6 |
| Terpinenol | -6.4 | Dimethyl disulfide | -2.3 |
| Caryophylleneoxide | -6.3 | Elemicin | -6.2 |
| Linalyl acetate | -6.3 | Ethyl benzoate | -6.2 |
| Transalphabergamotene | -6.3 | Eugenol | -6.2 |
| Bcaryophellene | -6.3 | Geraniol | -6.2 |
| Nerol | -6.2 | Elemicin | -6.2 |
| Alphathujene | -6.1 | Cisaconiticacid | -6 |
| Geranial | -6.1 | Gamma-cadinene | -6 |
| Xanthine | -6.1 | Neral | -6 |
| Tetradecanoic acid | -6 | Hexadecanoic acid | -5.7 |
| Linalool | -5.9 | Alpha-Humulene | -5.6 |
| Γcadinene | -5.9 | E3Hexenyl acetate | -5.3 |
| Epicedrol | -5.8 | 3-Mercaptohexyl acetate | -5 |
| Transaconitic acid | -5.8 | Citric acid | -5 |
| Alphapinene | -5.7 | Maleic acid | -5 |
| Alphaterpineol | -5.7 | Borneol | -4.8 |
| Fenchone | -5.7 | Dimethyl disulfide | -2.3 |
| Prenol | -4.6 | | |

**Table S2** List and docking scores of *Curcuma longa* phytochemicals docked into the MMP-2 catalytic site and arranged in order of decreasing docking score.

| Phytochemicals | Docking scores | Phytochemicals | Docking scores |
|---|---|---|---|
| 1-Dehydro-10-gingerdione | -8.8 | Dehydrozingerone | -7.1 |
| 4-gingerol | -8.8 | Diterpenoid | -7.1 |
| 4-shogaol | -8.7 | Galanal A | -7.1 |
| 6 gingersulfonic acid | -8.6 | Galanal B | -7 |
| 6-dihydroparadols | -8.1 | Galanolactone | -6.9 |
| 6-gingerdione | -8.1 | Gelanolactone | -6.9 |
| 6-gingerol | -8 | Geranial | -6.9 |
| 6-isohogaol | -7.8 | Geraniol | -6.7 |
| 6 shogaol | -7.8 | Gingerdiol | -6.6 |
| 7-gingerol | 7.7 | Gingerol | -6.5 |
| 8-gingerol | -7.7 | Linalool | -6.5 |
| 8-paradol | -7.6 | Nicotinic acid | -6.3 |
| 8-shogaol | -7.6 | Paradol | -6.2 |
| 10-gingerol | -7.5 | Phenol | -6.2 |
| 10-shagaol | -7.5 | Pyridoxine | -6.1 |
| 12-shogaol | -7.5 | Riboflavin | -6.1 |
| Alpha phellandrene | -7.5 | Sequiterpene | -6.1 |
| Alpha farnesene | -7.5 | Terpineol | -6.1 |
| Beta sesquiphellandrene | -7.4 | Thiamine | -5.9 |
| Beta bisabolene | -7.4 | Vitamin A | -5.8 |
| Beta phellandrene | -7.4 | Vitamin C | -5.8 |
| Beta sesquiphellandrene | -7.4 | Vitamin E | -5.7 |
| Bisabolene | -7.3 | Yakuchinone-A | -5.3 |
| Borneol | -7.2 | Zerumbone | -5.3 |
| Camphene | -7.2 | Zingerone | -5.3 |
| Camphor | -7.2 | Zingiber | -4.6 |
| Cineole | -7.2 | Zingiberene | -4.5 |
| Citral | -7.1 | | |

**Table S3** Showing the Docking scores of *Andrographis paniculata* phytochemicals docked into the MMP-2 catalytic site and arranged in order of decreasing docking score.

| Phytochemicals | Docking scores | Phytochemicals | Docking scores |
|---|---|---|---|
| Andrographidine A | -9.2 | Skullcapflavone | -7.8 |
| Alpha sisosterol | -9 | 14 deoxy 11 oxo andrographolide | -7.7 |
| Andrograpanin | -9 | Andrographolide | -7.7 |
| Eugenol | -8.7 | Chlorogenic acid | -7.7 |
| Dicaffeoylquinic acid | -8.6 | Beta sisosterol | -7.3 |
| Caffeic acid | -8.4 | Andropanoside | -7.2 |
| Paniculide A | -8.3 | Daucosterol | -7.1 |
| Wogonin | -8.3 | Apigenin 7,4 dimethyl ether | -6.9 |
| Andrographidine C | -8.2 | Oroxylina | -6.8 |
| Paniculide B | -8.2 | Trans cinnamic acid | -6.7 |
| Myristic acid | -8.1 | 2 methoxycinnamaldehde | -6.3 |
| 7,8 tetramethoxyflavone | -8 | Hentriacontane | -6.2 |
| Andrographiside | -8 | 5hydroxy 7,8 dimethoxyflavone | -5.9 |
| Panuiculoside | -7.9 | Lupeol | -5.8 |
| Paniculide C | -7.8 | Oleanolic acid | -5.7 |

**Table S4** List and docking scores of *Ocimum graticimum* phytochemicals docked into the MMP-2 catalytic site and arranged in order of decreasing docking score.

| Phytochemicals | Docking scores | Phytochemicals | Docking scores |
|---|---|---|---|
| Isovitexin | -10.2 | P-cymene | -6.5 |
| Nepetoidin A | -8.8 | Methyl eugenol | -6.4 |
| Basilimoside | -8.7 | Eugenol | -6.3 |
| Apigenin | -8.5 | Methyl chavical | -6.3 |
| Luteolin | -8.5 | Sinapic acid | -6.3 |
| Rosmarinic acid | -8.4 | Geraniol | -6.2 |
| Salvigenin | -8.4 | Palmitic acid | -6.2 |
| Apigenin 7,4'-dimethyl ether | -8.3 | Citral | -6.1 |
| Bisaboline | -8.1 | Geraniol | -6.1 |
| Nevadensin | -7.8 | Limonene | -6.1 |
| Vitexin | -7.6 | Trans-carypohyllene | -6 |
| Xanthomicrol | -7.5 | Beta-caryophyllene | -5.9 |
| Cubenene | -7.3 | Linalool | -5.9 |
| L-bisabolene | -7.3 | T-cadinol | -5.9 |
| Alpha-copaene, | -7.1 | Trans-ocimene | -5.9 |
| Farnesene | -7.1 | Trans sabiene hydrate | -5.8 |
| Gamma-eudesmol | -7 | Alpha-pinene | -5.7 |
| Hymenoxin | -7 | Alpha-terpineol | -5.7 |
| Beta-bisoboline | -6.9 | Cis-ocimene | -5.7 |
| Beta-elemene | -6.9 | Fenchone | -5.7 |
| Germacrene- D | -6.8 | Pinene | -5.7 |
| Oleanolic acid | -6.8 | 1, 8-cineole | -5.6 |
| Thymol | -6.8 | Alpha-humelene | -5.6 |
| Ethyl cinnamate | -6.7 | Myrcene | -5.6 |
| Methyl isoeugeneol | -6.7 | Camphene | -5.3 |
| Terpinolene | -6.7 | Camphor | -4.6 |
| Bisabolol | -6.6 | | |

**Table S5** The docking scores of *Zingiber officinale* phytochemicals docked with MMP-2 protein, arranged in order of decreasing docking score.

| Phytochemicals | Docking score | Phytochemicals | Docking score |
|---|---|---|---|
| 1-Dehydro-10-gingerdione | -8.8 | Dehydrozingerone | -7.1 |
| 4-gingerol | -8.8 | Diterpenoid | -7.1 |
| 4-shogaol | -8.7 | Galanal A | -7.1 |
| 6 gingersulfonic acid | -8.6 | Galanal B | -7 |
| 6-dihydroparadols | -8.1 | Galanolactone | -6.9 |
| 6-gingerdione | -8.1 | Gelanolactone | -6.9 |
| 6-gingerol | -8 | Geranial | -6.9 |
| 6-isohogaol | -7.8 | Geraniol | -6.7 |
| 6 shogaol | -7.8 | Gingerdiol | -6.6 |
| 7-gingerol | -7.7 | Gingerol | -6.5 |
| 8-gingerol | -7.7 | Linalool | -6.5 |
| 8-paradol | -7.6 | Nicotinic acid | -6.3 |
| 8-shogaol | -7.6 | Paradol | -6.2 |
| 10-gingerol | -7.5 | Phenol | -6.2 |
| 10-shagaol | -7.5 | Pyridoxine | -6.1 |
| 12-shogaol | -7.5 | Riboflavin | -6.1 |
| Alpha phellandrene | -7.5 | Sequiterpene | -6.1 |
| Alpha farnesene | -7.5 | Terpineol | -6.1 |
| Beta sesquiphellandrene | -7.4 | Thiamine | -5.9 |
| Beta bisabolene | -7.4 | Vitamin A | -5.8 |
| Beta phellandrene | -7.4 | Vitamin C | -5.8 |
| Beta sesquiphellandrene | -7.4 | Vitamin E | -5.7 |
| Bisabolene | -7.3 | Yakuchinone-A | -5.3 |
| Borneol | -7.2 | Zerumbone | -5.3 |
| Camphene | -7.2 | Zingerone | -5.3 |
| Camphor | -7.2 | Zingiber | -4.6 |
| Cineole | -7.2 | Zingiberene | -4.5 |
| Citral | -7.1 | | |

**Table S6** Model summary showing R, R-square, adjusted R square, Standard error of the estimate and Durbin-Watson values.

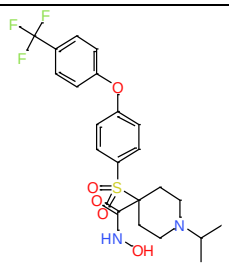
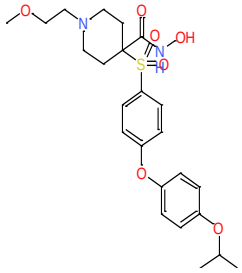
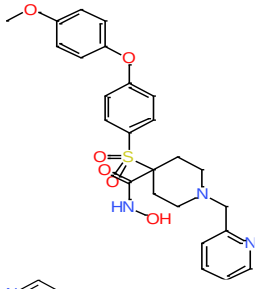
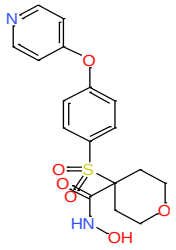
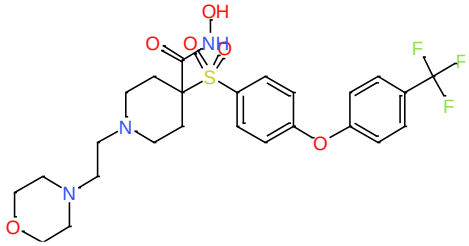
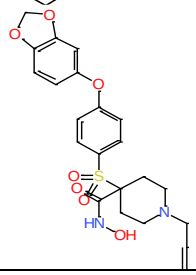
| Model | R | R square | Adjusted R square | Durbin-Watson | F |
|---|---|---|---|---|---|
| 1 | 0.976 | 0.952 | 0.908 | 1.311 | 21.776 |

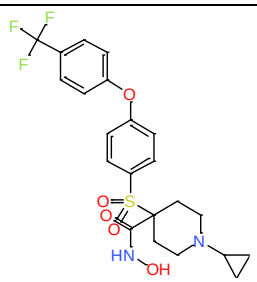
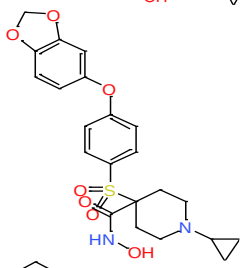
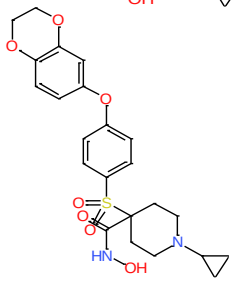
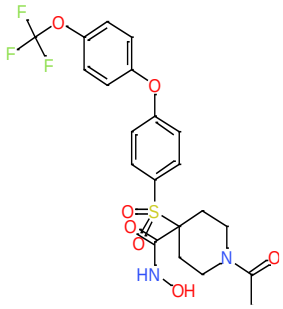
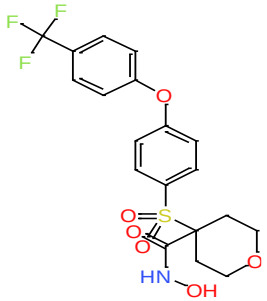
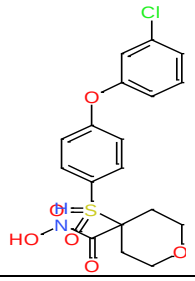
**Table S7** The ANOVA table.

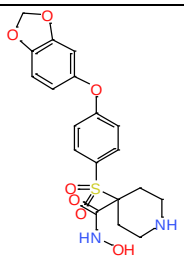
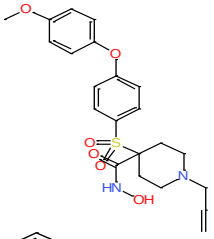
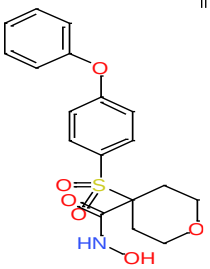
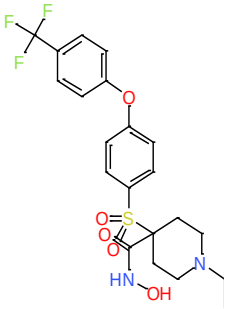
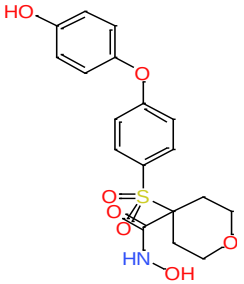
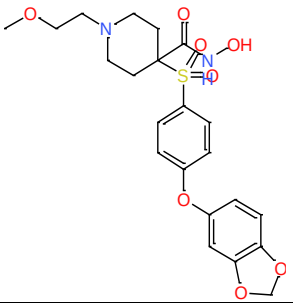
| Model | Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|
| Regression | 1.535 | 10 | .154 | 21.776 | .000 |
| Residual | .078 | 11 | .007 | | |
| Total | 1.613 | 21 | | | |

Predictors: (Constant), MOMI-Z, BCUTw-1l, nSmallRings, 0tomLAC, khs.sCH3, ATSc2, MOMI-YZ, DPSA-3, MOMI-XY, Wlambda2.unity

**Table S8** The CHEMBL-Identification number, structure, observed pIC50, predicted pIC50, and residual of some of the compounds in the training data set.

| CHEMBL-ID | Structures | Observed pIC50 | Predicted pIC50 | Residual |
|---|---|---|---|---|
| CHEMBL1801426 |  | 9.52 | 9.46255 | -.01173 |
| CHEMBL1801416 |  | 9.52 | 9.46830 | .06295 |
| CHEMBL1801057 |  | 9.7 | 9.64786 | -.01166 |
| CHEMBL1801055 |  | 9.3 | 9.30865 | .01343 |
| CHEMBL1800089 |  | 9.52 | 9.51968 | -.05480 |
| CHEMBL1801420 |  | 9.7 | 9.66396 | .04201 |

| | | | | |
|---|---|---|---|---|
| CHEMBL1801424 |  | 10 | 9.93815 | .04108 |
| CHEMBL1801422 |  | 9.3 | 9.29132 | -.03237 |
| CHEMBL1801423 |  | 9.7 | 9.66891 | .07169 |
| CHEMBL1801396 |  | 10 | 9.99936 | -.02463 |
| CHEMBL1229868 |  | 10 | 10.01941 | .00917 |
| CHEMBL1801045 |  | 9.52 | 9.50720 | -.01760 |

| | | | | |
|---|---|---|---|---|
| CHEMBL1801419 |  | 9.4 | 9.47167 | -.10560 |
| CHEMBL1801056 |  | 9.4 | 9.53830 | -.28207 |
| CHEMBL1801044 |  | 10 | 9.92722 | -.04213 |
| CHEMBL1801427 |  | 9.7 | 9.66286 | .17180 |
| CHEMBL1801048 |  | 9.7 | 9.70227 | .10560 |
| CHEMBL1801421 |  | 9.6 | 9.54160 | .12493 |

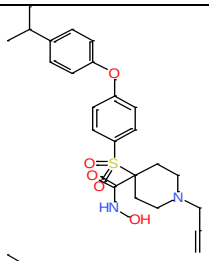
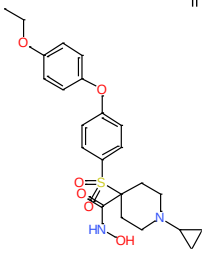
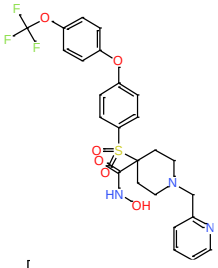
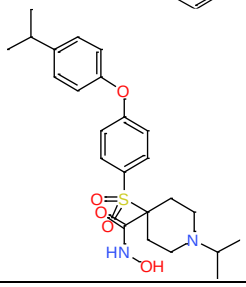
| | | | | |
|---|---|---|---|---|
| CHEMBL1801413 |  | 10 | 9.97136 | .15134 |
| CHEMBL1801412 |  | 10 | 10.12625 | -.05916 |
| CHEMBL1801431 |  | 9.7 | 9.79037 | -.05542 |
| CHEMBL1801415 |  | 9.0 | 9.05276 | -.09682 |

**Table S9** The $pIC_{50}$ of the lead phytochemicals and standard drug.

| **Phytochemicals** | **$pIC_{50}$** |
|---|---|
| Andrographidine A | 9.597692 |
| Azulene | 8.704469 |
| Isovitexin | 10.52391 |
| Tanomastat (Standard Drug) | 11.43615 |