



# Supplementary Materials: In Silico Screening of Potential Phytocompounds from Several Herbs against SARS-CoV-2 Indian Delta Variant B.1.617.2 to Inhibit the Spike Glycoprotein Trimer

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A)

## STAMP Sequence Alignment

 Identical Residues  
 Similar Residues

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WT-NTD  QCVNLTTRTQLPPA Y TNSFTRGVYYP DKVFRSSVL HS TQDLFLPFFS NVTWFHAI HVT KR
MT-NTD  QCVNLTTRTQLPPA Y TNSFTRGVYYP DKVFRSSVL HS TQDLFLPFFS NVTWFHAI HVT KR

WT-NTD  FDNPVLPFNDGVYF A STEKS NI I RGWI FGTTLDS K TQSL LI VNNATNVVI KVCEFQFC ND
MT-NTD  FDNPVLPFNDGVYF A STEKS NI I RGWI FGTTLDS K TQSL LI VNNATNVVI KVCEFQFC ND

WT-NTD  PFLGVYYHKNNKS WMESEFRVYSS AN N CTFEYVS Q PFLMDLEGKQGNFKNL REFVFKN I D
MT-NTD  PFLGVYYHKNNKS WMESEFRVYSS AN Q CTFEYVS Q PFLMDLEGKQGNFKNL REFVFKN I D

WT-NTD  GYFKI YSKHTPI NL VRDLPQGFSALE PLVDLP I GI N TRFQTLLALHRS YL TPGDSSS GW
MT-NTD  GYFKI YSKHTPI NL VRDLPQGFSALE PLVDLP I GI Q TRFQTLLALHRS YL TPGDSSS GW

WT-NTD  TAGAAAYYVGYLQP RTFLLKYNENGT I TDAVDCAL DPLS ETKCTLKS FTVE KGI YQTS NF
MT-NTD  TAGAAAYYVGYLQP RTFLLKYNENGT I TDAVDCAL DPLS ETKCTLKS FTVE KGI YQTS NF

WT-NTD  RVQPTESI VRFPNI T NLCPFGEVFNA TRFAS VYAWNRRKRI SNCVADYS VLYNSASFST FK
MT-NTD  RVQPTESI VRFPNI T NLCPFGEVFNA TRFAS VYAWNRRKRI SNCVADYS VLYNSASFST FK

WT-NTD  CYGVS PTKLNDLCF T NVYADS FVI RGDEV RQI APG QTGKI ADYNYKL PDDF TGCVI AWNS
MT-NTD  CYGVS PTKLNDLCF T NVYADS FVI RGDEV RQI APG QTGKI ADYNYKL PDDF TGCVI AWNS

WT-NTD  NNLDS KVGGNYNYL Y RLFKRKS NLKPF ERDI STEI Y QAGS TPCNGVEGFNCY FPLQSYGFQ
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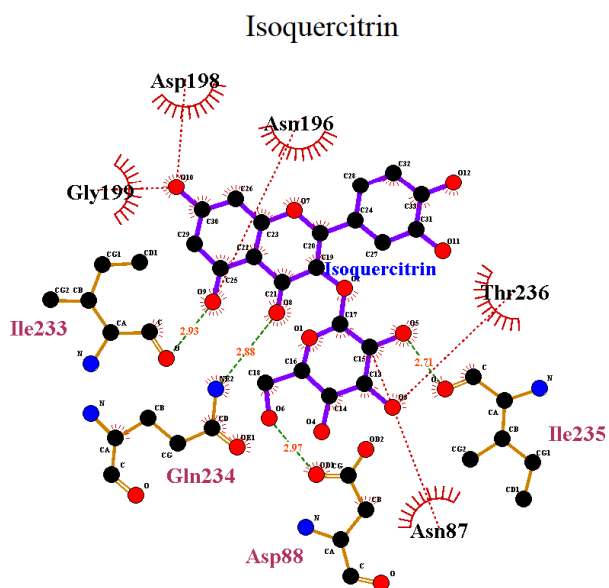
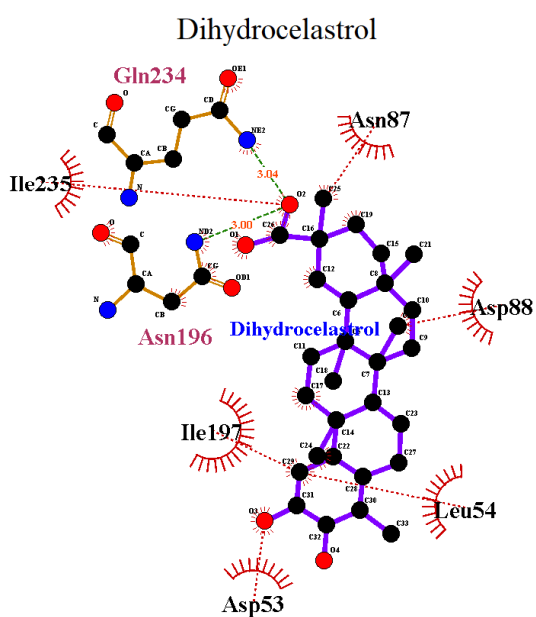
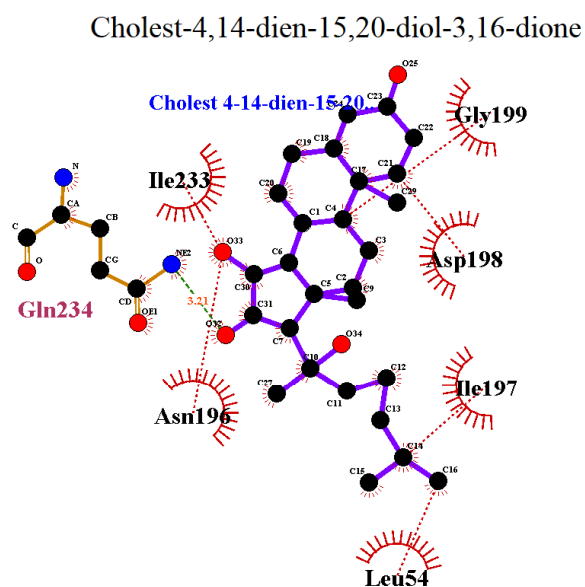
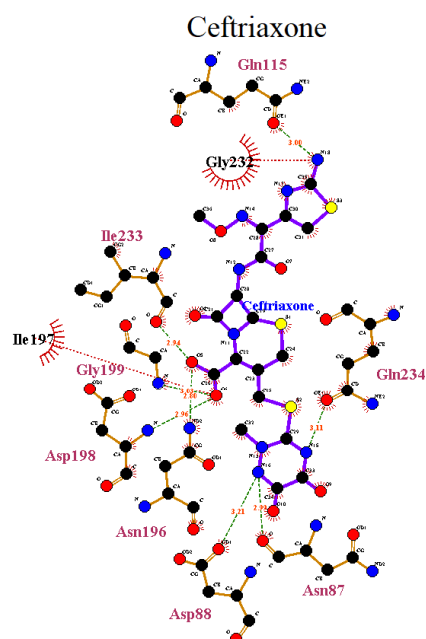
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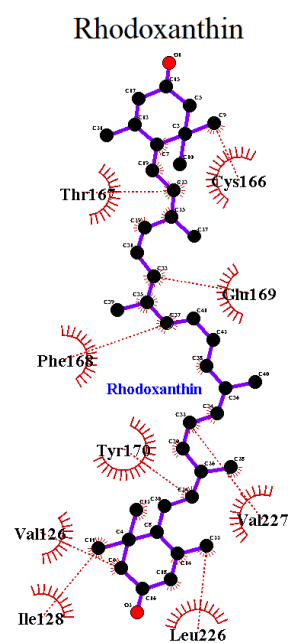
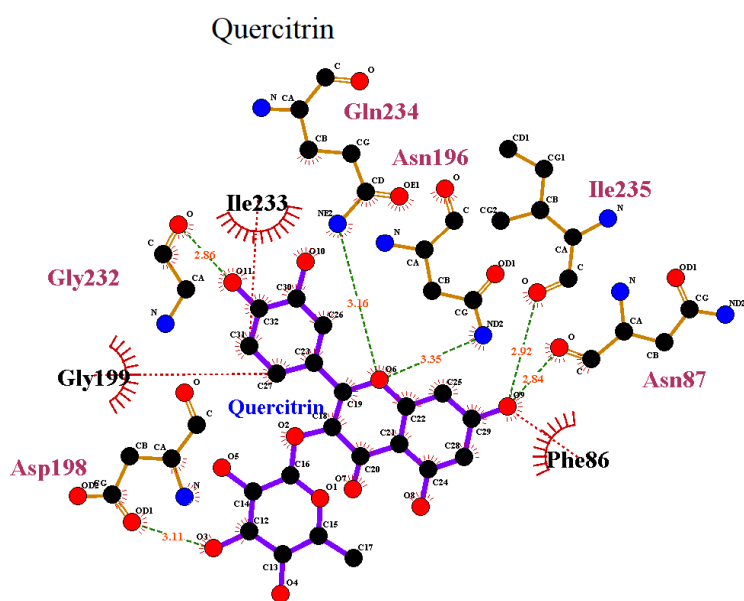
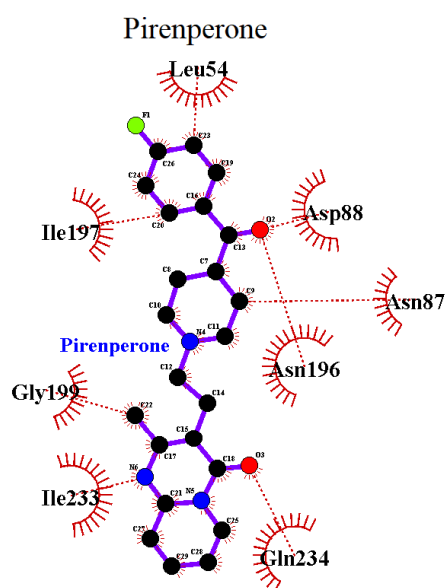
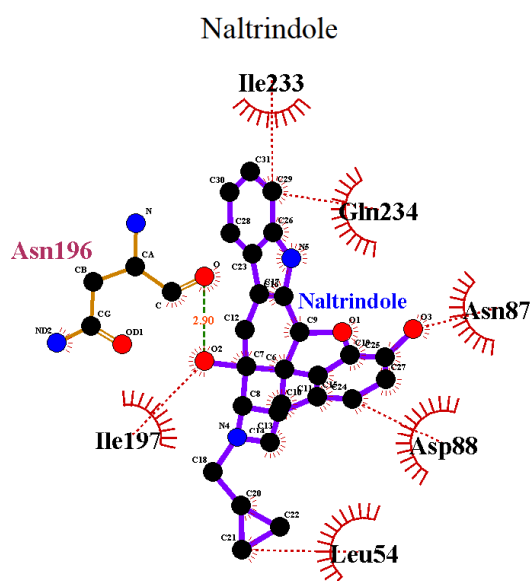
WT-NTD  FLPFQQFGRDI ADT T DAVRDPQTLEI LDI TPCSFSG GVS VI TPGTNTS NQVA VLYQDVN CW
MT-NTD  FLPFQQFGRDI ADT T DAVRDPQTLEI LDI TPCSFSG GVS VI TPGTNTS NQVA VLYQDVN CW

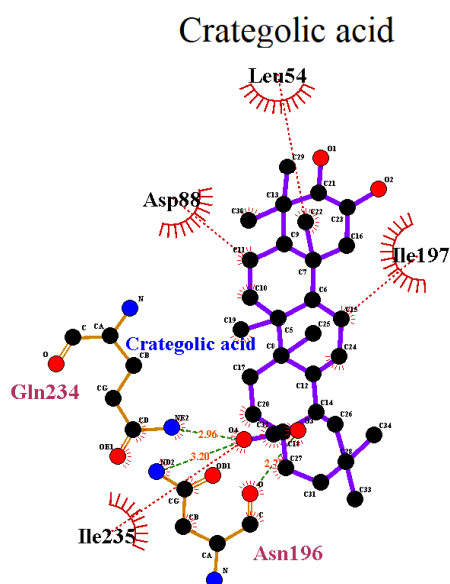
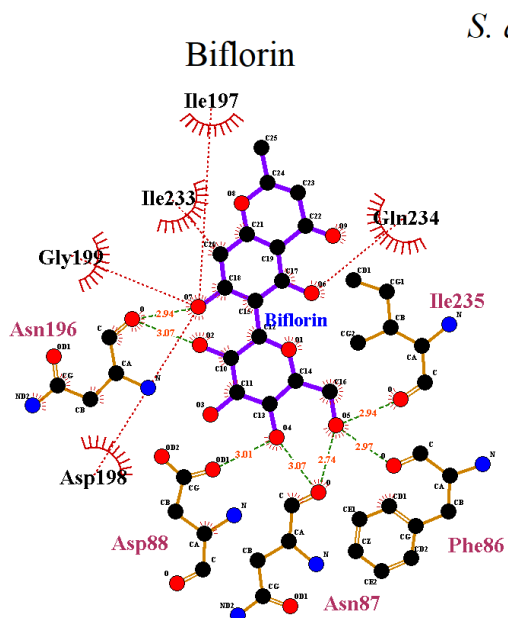
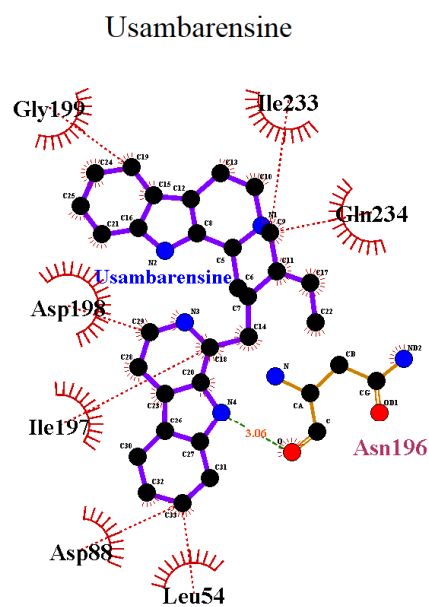
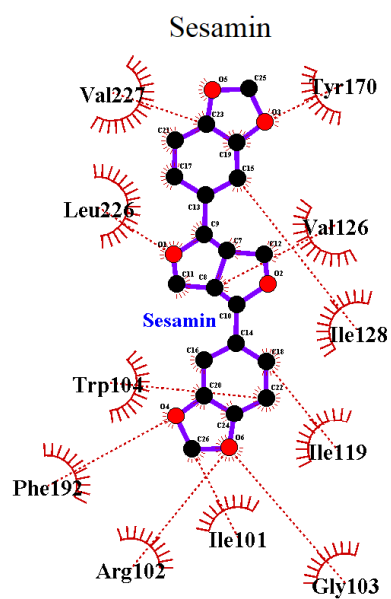
WT-NTD  RVYS TGSNVFQTRA G CLI GAHVNNNS YECD
MT-NTD  RVYS TGSNVFQTRA G CLI GAHVNNNS YECD
    
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**Figure S1.** The sequence alignment for the wild and mutated type NTD in S-Protein.

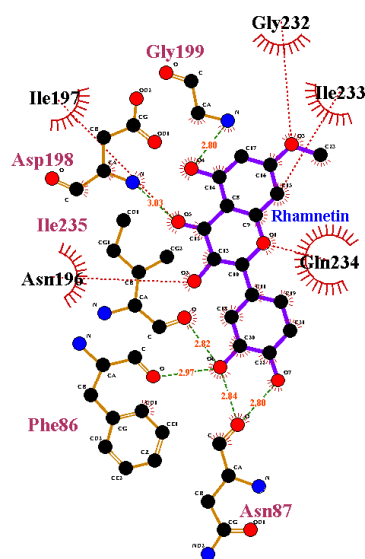
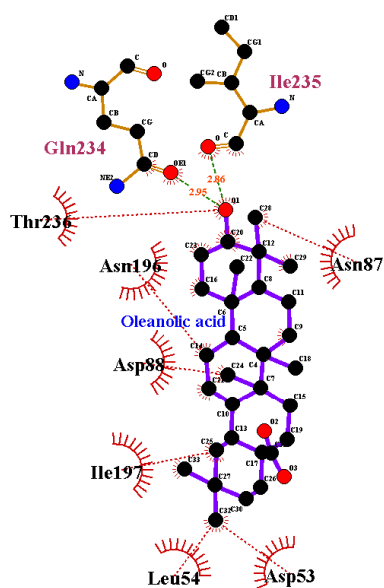
## S-Protein-N-Domain (Mutated) and Ligands





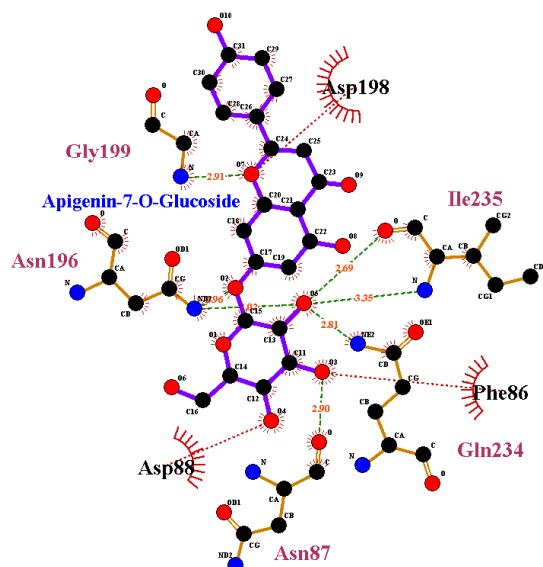
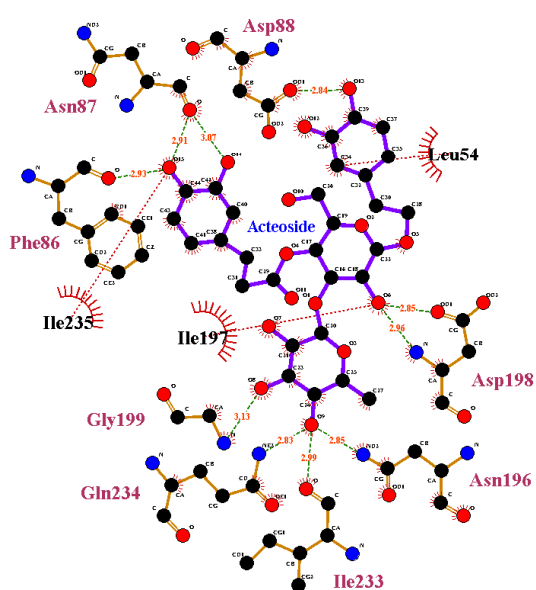


## Rhamnetin

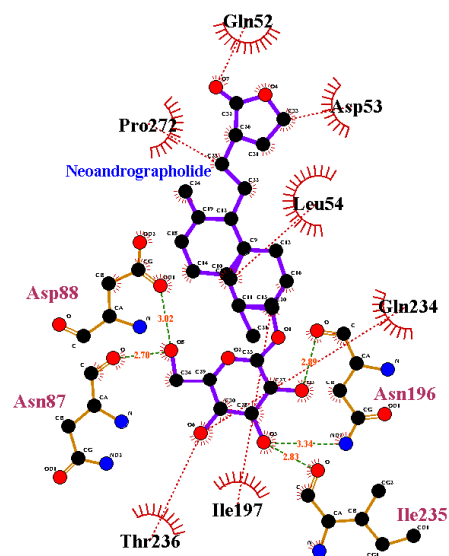
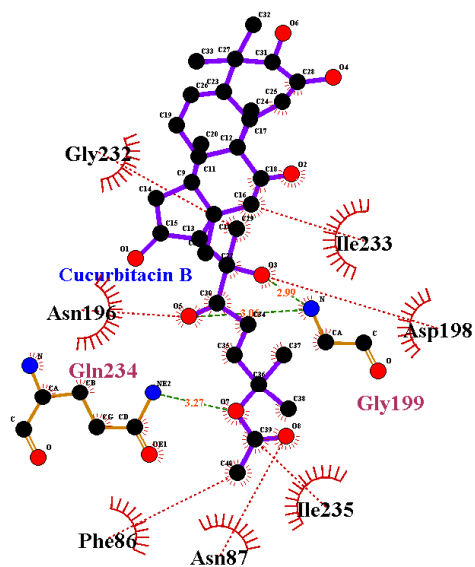


## Kabasura kudineer

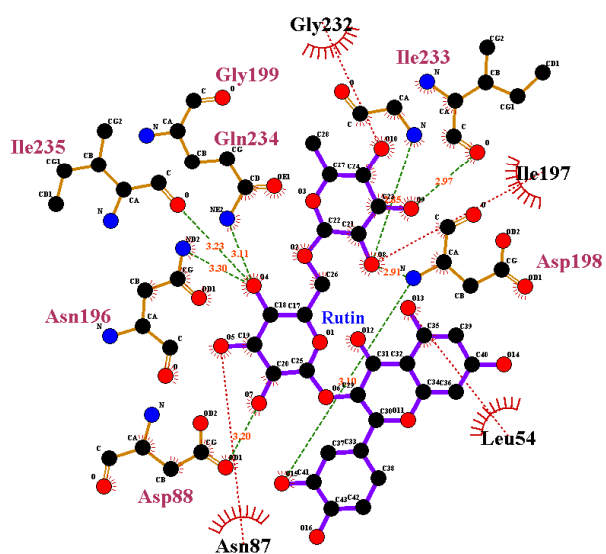
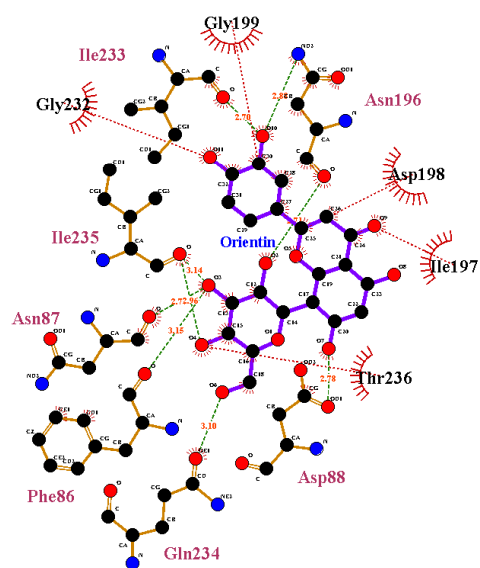
Apigenin 7-O-glucoside



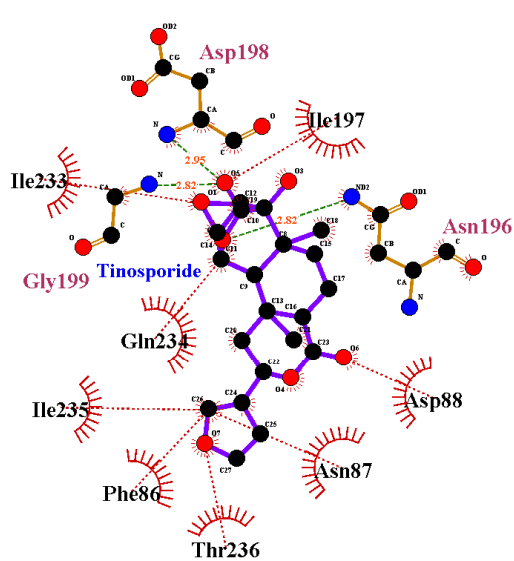
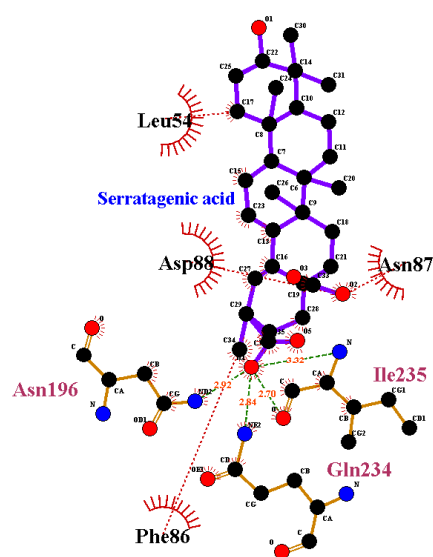
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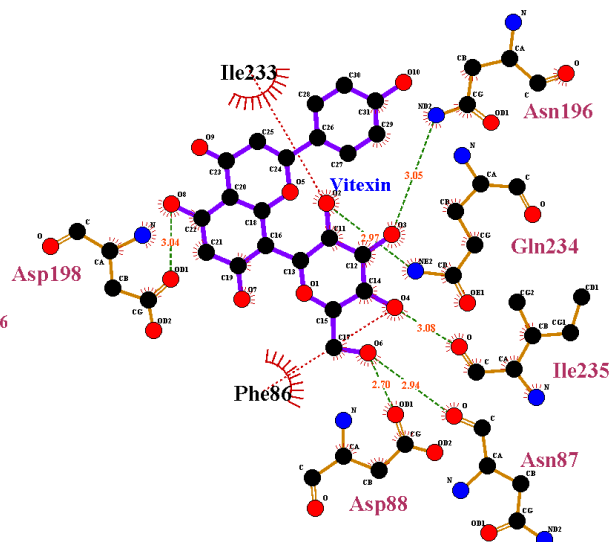
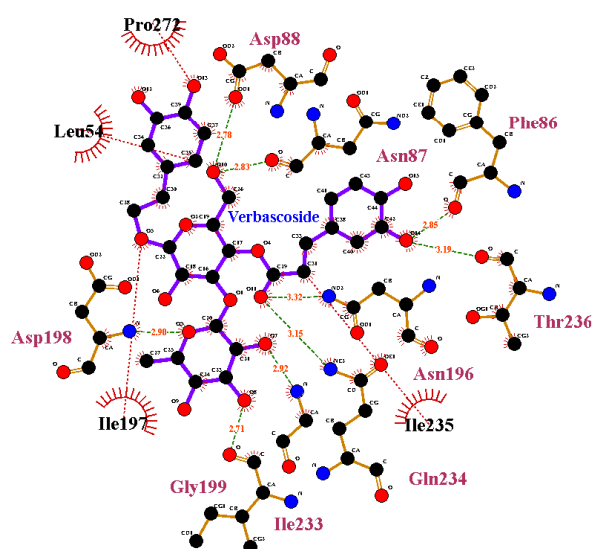
## Rutin



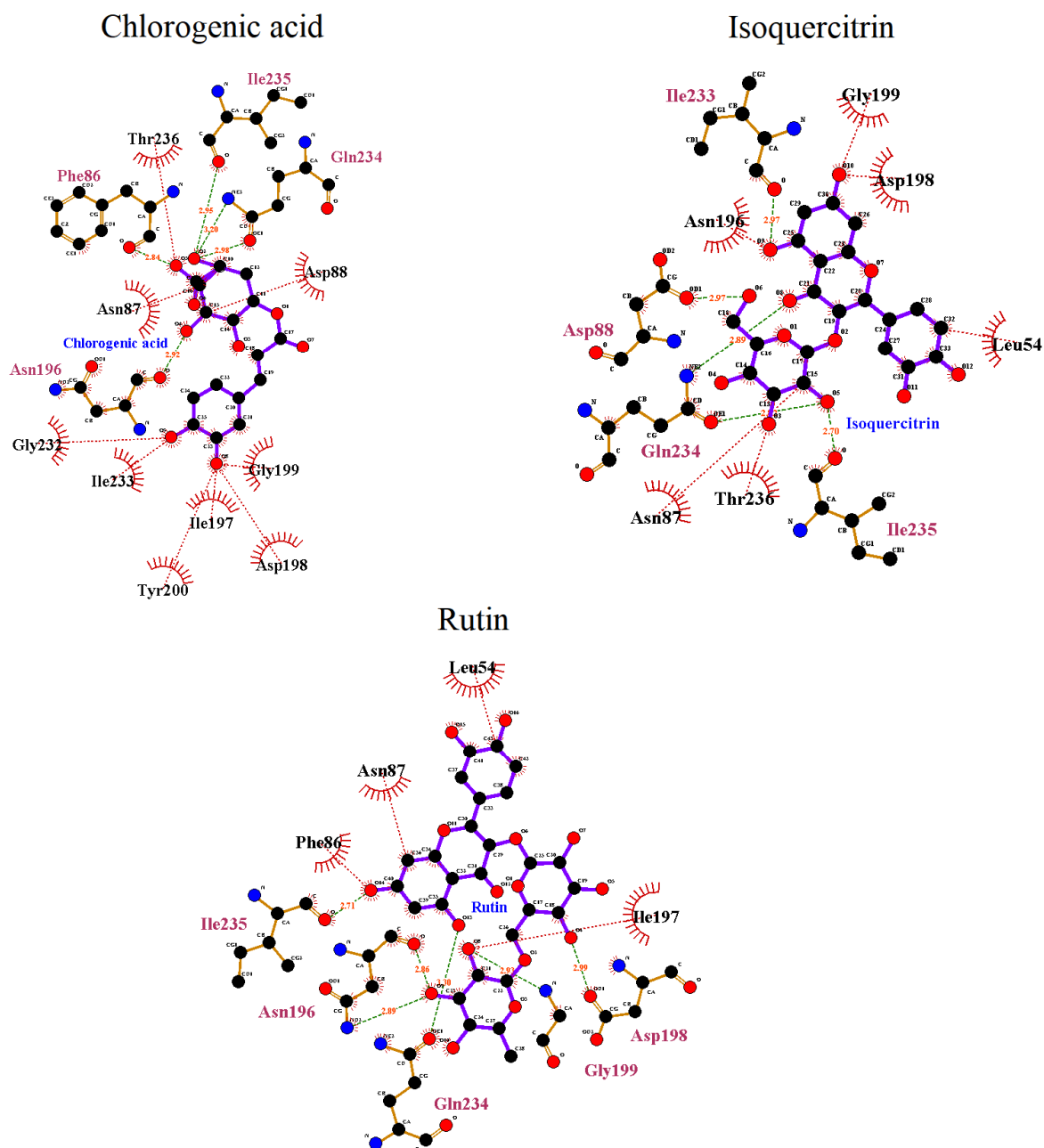
## Tinosporide



## Vitexin



*M. speciosa* (Korth) Haveli

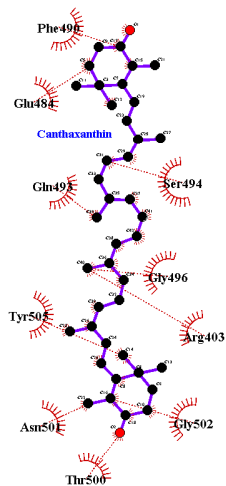


**Figure S2.** The Ligplot interaction for the mutated NTD domain and the screened phytocompounds based on the binding affinity -6.0 kcal/mol.

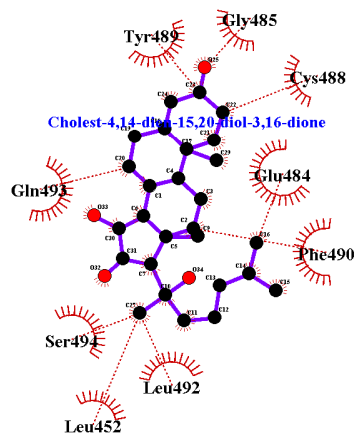
## S-Protein-RBD Domain and Ligands

*H. cordata*

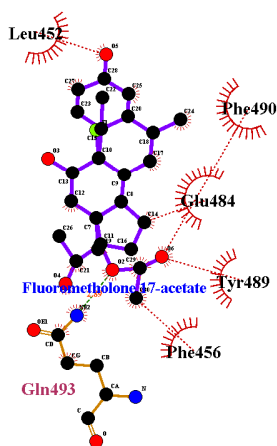
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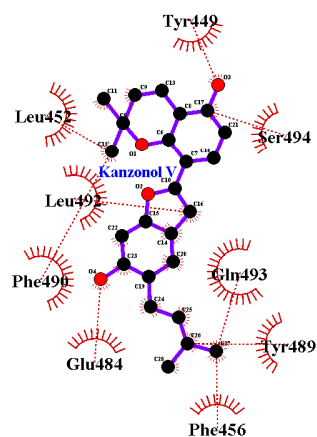
Cholest-4,14-dien-15,20-diol-3,16-dione



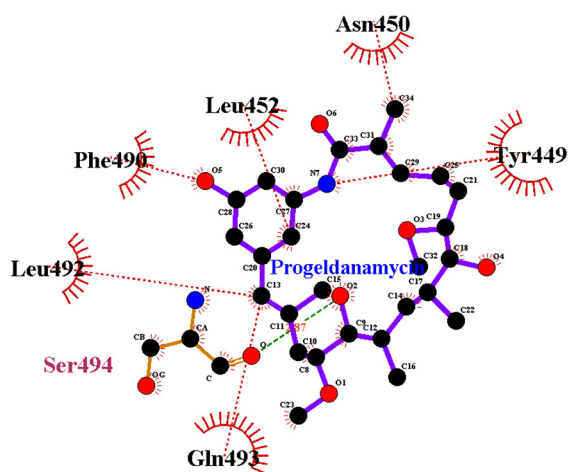
Fluorometholone 17-acetate



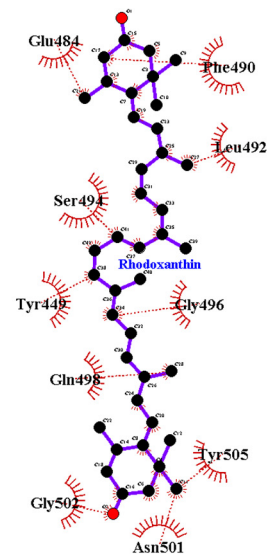
Kanzonol V



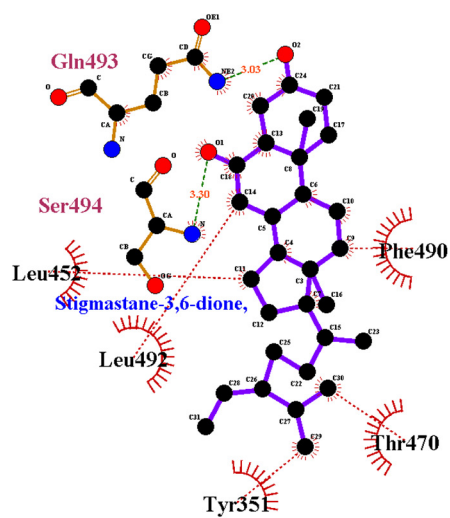
## Progeldanamycin



## Rhodoxanthin

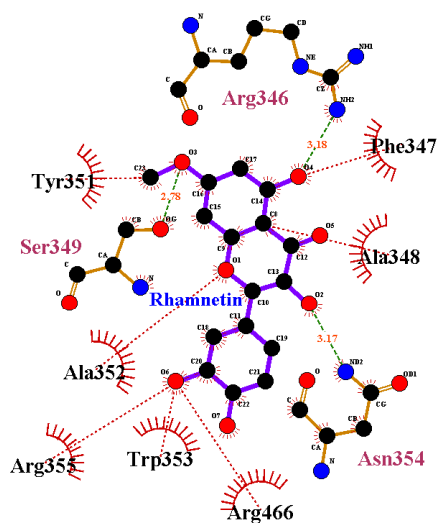


## Stigmastane-3,6-dione, (5.alpha.)



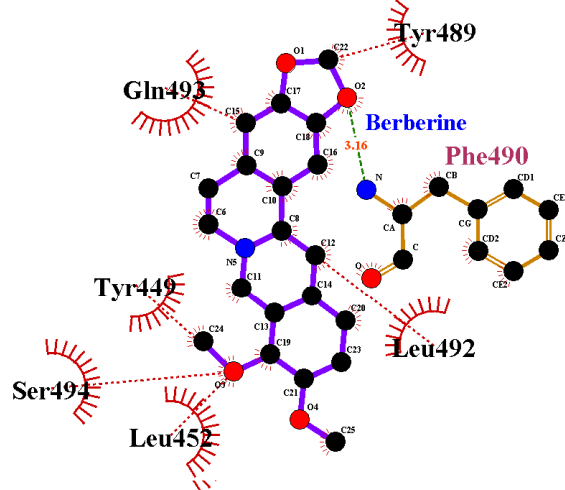
*S. aromaticum*

## Rhamnetin

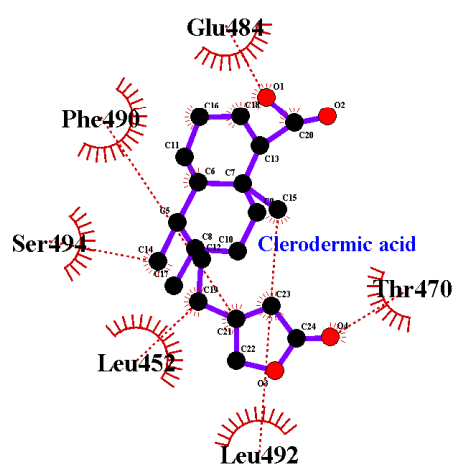


## Kabasura kudineer

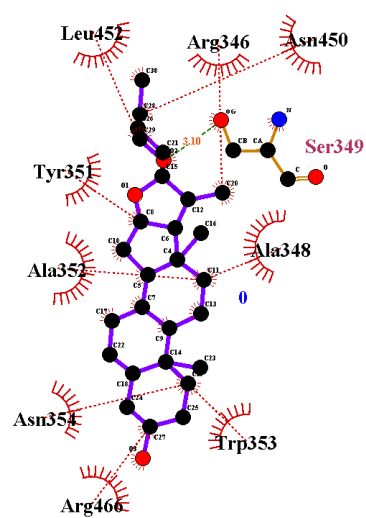
## Berberine

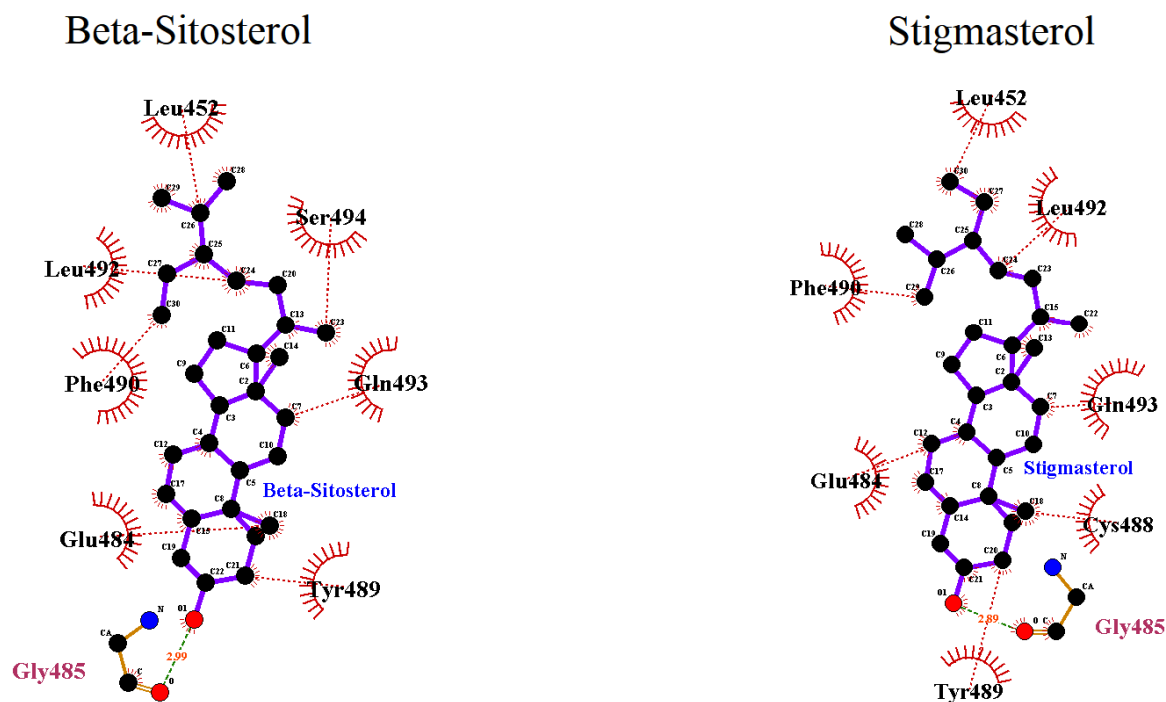


## Clerodermic acid



## Diosgenin



*M. speciosa (Korth) Haveli*

**Figure S3.** The Ligplot interaction for the RBD domain and the screened phytocompounds based on the binding affinity -6.0 kcal/mol.

**Table S1.** The molecular properties of screened phytocompounds with the  $\leq -6.0$  kcal/mol binding energy against mutated NTD Domain.

Plant Name	Compound Name	Molecular Formula	Mol. Weight (g/mol)	PubChem ID
<b>B.1.617.2. S-Protein – NTD Mutated</b>				
<i>H. cordata</i>	Ceftriaxone	C <sub>18</sub> H <sub>18</sub> N <sub>8</sub> O <sub>7</sub> S <sub>3</sub>	554.6	5479530
	Cefuroxime	C <sub>16</sub> H <sub>16</sub> N <sub>4</sub> O <sub>8</sub> S	424.4	5479529
	6alpha,9-Difluoro-11beta-hydroxypregn-4-ene-3,20-dione	C <sub>21</sub> H <sub>28</sub> F <sub>2</sub> O <sub>3</sub>	366.4	255970
	Cholest-4,14-dien-15,20-diol-3,16-dione	C <sub>27</sub> H <sub>40</sub> O <sub>4</sub>	428.6	52931329
	Dihydrocelastrol	C <sub>29</sub> H <sub>40</sub> O <sub>4</sub>	452.6	10411574
	Diosgenin	C <sub>27</sub> H <sub>42</sub> O <sub>3</sub>	414.6	99474
	Isoquercitrin	C <sub>21</sub> H <sub>20</sub> O <sub>12</sub>	464.4	5280804
	Kanzonol	C <sub>25</sub> H <sub>30</sub> O <sub>5</sub>	410.5	85088559
	Murrayenol	C <sub>30</sub> H <sub>46</sub> O <sub>4</sub>	470.7	73086673
	Naltrindole	C <sub>26</sub> H <sub>26</sub> N <sub>2</sub> O <sub>3</sub>	414.5	5497186
	Pirenperone	C <sub>23</sub> H <sub>24</sub> FN <sub>3</sub> O <sub>2</sub>	393.5	4847
	Quercitrin	C <sub>15</sub> H <sub>10</sub> O <sub>7</sub>	302.23	5280343
	Rhodoxanthin	C <sub>40</sub> H <sub>50</sub> O <sub>2</sub>	562.8	5281251
	Sesamin	C <sub>20</sub> H <sub>18</sub> O <sub>6</sub>	354.4	72307

<i>S. aromaticum</i>	Usambarensine	C <sub>29</sub> H <sub>28</sub> N <sub>4</sub>	432.6	5281413
	Biflorin	C <sub>16</sub> H <sub>18</sub> O <sub>9</sub>	354.31	441959
	Crategolic acid	C <sub>30</sub> H <sub>48</sub> O <sub>4</sub>	472.7	73659
	Myricetin	C <sub>15</sub> H <sub>10</sub> O <sub>8</sub>	318.23	5281672
	Oleanolic acid	C <sub>30</sub> H <sub>48</sub> O <sub>3</sub>	456.7	10494
	Rhamnetin	C <sub>16</sub> H <sub>12</sub> O <sub>7</sub>	316.26	5281691
<i>Citrus spp.</i>	Stigmasterol	C <sub>29</sub> H <sub>48</sub> O	412.7	5280794
	Hesperidin	C <sub>28</sub> H <sub>34</sub> O <sub>15</sub>	610.6	10621
	Naringin	C <sub>27</sub> H <sub>32</sub> O <sub>14</sub>	580.5	442428
<i>N. sativa</i>	β-sitosterol	C <sub>31</sub> H <sub>52</sub> O <sub>2</sub>	456.7	521199
	Cycloartenol	C <sub>30</sub> H <sub>50</sub> O	426.7	92110
<i>O. basilicum</i>	Chicoric acid	C <sub>22</sub> H <sub>18</sub> O <sub>12</sub>	474.4	5281764
<i>P. nigrum</i> Linn	Piperettine	C <sub>19</sub> H <sub>21</sub> NO <sub>3</sub>	311.4	101878852
	2-Phenylquinoline-4-carboxylic acid	C <sub>16</sub> H <sub>11</sub> NO <sub>2</sub>	249.26	8593
	3-Methyl-3H-cyclonona[def]biphenylene	C <sub>18</sub> H <sub>14</sub>	230.3	5376621
	5-beta-Cholest-24-en-12-one	C <sub>27</sub> H <sub>44</sub> O	384.6	22212498
	Beta-Sitosterol	C <sub>29</sub> H <sub>50</sub> O	414.7	222284
	Campesterol	C <sub>28</sub> H <sub>48</sub> O	400.7	173183
<i>M. speciosa korthi</i>	Chlorogenic acid	C <sub>16</sub> H <sub>18</sub> O <sub>9</sub>	354.31	1794427
	Cholest-24-en-12-one	C <sub>27</sub> H <sub>44</sub> O	384.6	22212498
	Dibenzo[a,h]cyclotetradecene	C <sub>30</sub> H <sub>52</sub>	412.7	634348
	Gamma-Sitosterol	C <sub>29</sub> H <sub>50</sub> O	414.7	457801
	Isoquercitrin	C <sub>21</sub> H <sub>20</sub> O <sub>12</sub>	464.4	5280804
	Rutin	C <sub>27</sub> H <sub>30</sub> O <sub>16</sub>	610.5	5280805
	Stigmasterol	C <sub>29</sub> H <sub>48</sub> O	412.7	5280794
<b>Kabasura kudineer</b>				
<i>C. serratum</i>	Acteoside	C <sub>29</sub> H <sub>36</sub> O <sub>15</sub>	624.6	5281800
	Serratagenic acid	C <sub>30</sub> H <sub>46</sub> O <sub>5</sub>	486.7	21594175
	Verbascoside	C <sub>29</sub> H <sub>36</sub> O <sub>15</sub>	624.6	5281800
	Campesterol	C <sub>28</sub> H <sub>48</sub> O	400.7	173183
<i>H. schumach</i>	Apigenin 7-O-glucoside	C <sub>21</sub> H <sub>18</sub> O <sub>11</sub>	446.4	5319484
<i>T. cucumerina</i>	Cucurbitacin B	C <sub>32</sub> H <sub>46</sub> O <sub>8</sub>	558.7	5281316
<i>A. paniculate</i>	Neoandrographolide	C <sub>26</sub> H <sub>40</sub> O <sub>8</sub>	480.6	9848024
	Orientin	C <sub>21</sub> H <sub>20</sub> O <sub>11</sub>	448.4	5281675
<i>M. cerviana</i>	Vitexin	C <sub>21</sub> H <sub>20</sub> O <sub>10</sub>	432.4	5280441
<i>T. involucrate</i>	Rutin	C <sub>27</sub> H <sub>30</sub> O <sub>16</sub>	610.5	5280805
<i>T. cordifolia</i>	Tinosporide	C <sub>20</sub> H <sub>22</sub> O <sub>7</sub>	374.4	167631

**Table S2.** The molecular properties of screened phytochemicals with the  $\leq -6.0$  kcal/mol binding energy against RBD Domain.

Plant Name	Compound Name	Molecular Formula	Mol. Weight (g/mol)	PubChem ID
<b>B.1.617.2. S-Protein - RBD-Domain</b>				
<i>H. cordata</i>	3-Benzoyloxy-6-oxo-12-ursen-28-oic acid	C <sub>37</sub> H <sub>50</sub> O <sub>5</sub>	574.8	131751331
	26,26,26-trifluoro-25-hydroxy-27-norvitamin D3	C <sub>26</sub> H <sub>39</sub> F <sub>3</sub> O <sub>2</sub>	440.6	9547284
	Canthaxanthin	C <sub>40</sub> H <sub>52</sub> O <sub>2</sub>	564.8	5281227
	Cholest-4,14-dien-15,20-diol-3,16-dione	C <sub>27</sub> H <sub>42</sub> O	382.6	11280
	Fluorometholone 17-acetate	C <sub>24</sub> H <sub>31</sub> FO <sub>5</sub>	418.5	240767
	Kanzonol V	C <sub>24</sub> H <sub>24</sub> O <sub>4</sub>	376.4	102444980
	Murrayenol	C <sub>30</sub> H <sub>46</sub> O <sub>4</sub>	470.7	73086673
	Progeldanamycin	C <sub>27</sub> H <sub>41</sub> NO <sub>6</sub>	475.6	49787025
	Quercetin	C <sub>15</sub> H <sub>10</sub> O <sub>7</sub>	302.23	5280343
	Rhamnetin	C <sub>16</sub> H <sub>12</sub> O <sub>7</sub>	316.26	5281691
	Rhodoxanthin	C <sub>40</sub> H <sub>50</sub> O <sub>2</sub>	562.8	5281251
	Sesamin	C <sub>20</sub> H <sub>18</sub> O <sub>6</sub>	354.4	72307
	Stigmastane-3,6-dione, (5.alpha.)	C <sub>29</sub> H <sub>48</sub> O <sub>2</sub>	428.7	13992092
	Usambarensine	C <sub>29</sub> H <sub>28</sub> N <sub>4</sub>	432.6	5281413
<i>S. aromaticum</i>	Kaempferol	C <sub>15</sub> H <sub>10</sub> O <sub>6</sub>	286.24	5280863
	Myricetin	C <sub>15</sub> H <sub>10</sub> O <sub>8</sub>	318.23	5281672
	Oleanolic acid	C <sub>30</sub> H <sub>48</sub> O <sub>3</sub>	456.7	10494
	Rhamnetin	C <sub>16</sub> H <sub>12</sub> O <sub>7</sub>	316.26	5281691
<i>Citrus spp.</i>	Apigenin	C <sub>15</sub> H <sub>10</sub> O <sub>5</sub>	270.24	5280443
	Diosmetin	C <sub>16</sub> H <sub>12</sub> O <sub>6</sub>	300.26	5281612
	Hesperidin	C <sub>28</sub> H <sub>34</sub> O <sub>15</sub>	610.6	10621
	Luteolin	C <sub>15</sub> H <sub>10</sub> O <sub>6</sub>	286.24	5280445
	Naringenin	C <sub>15</sub> H <sub>12</sub> O <sub>5</sub>	272.25	932
	Naringin	C <sub>27</sub> H <sub>32</sub> O <sub>14</sub>	580.5	442428
	Rutin	C <sub>27</sub> H <sub>30</sub> O <sub>16</sub>	610.5	5280805
<i>N. sativa</i>	Nigellidine	C <sub>18</sub> H <sub>18</sub> N <sub>2</sub> O <sub>2</sub>	294.3	136828302
<i>O. basilicum</i>	Chicoric acid	C <sub>22</sub> H <sub>18</sub> O <sub>12</sub>	474.4	5281764
<i>P. nigrum</i>	3-Heptadecen-5-yne, (Z)	C <sub>17</sub> H <sub>30</sub>	234.4	5367448
	Benzo[c] cinnolin-2-amine	C <sub>12</sub> H <sub>9</sub> N <sub>3</sub>	195.22	606883
	Copaene	C <sub>15</sub> H <sub>24</sub>	204.35	12303902
	Dodec-5-yn-6-one	C <sub>12</sub> H <sub>20</sub> O	180.29	572843
	Guineensine	C <sub>24</sub> H <sub>33</sub> NO <sub>3</sub>	383.5	6442405
	Piperine	C <sub>17</sub> H <sub>19</sub> NO <sub>3</sub>	285.34	638024
	Piperolein	C <sub>19</sub> H <sub>25</sub> NO <sub>3</sub>	315.4	11141599
	Sarmentine	C <sub>14</sub> H <sub>23</sub> NO	221.34	6440616

<i>M. speciosa</i> Korthi	2-Phenylquinoline-4-carboxylic acid	C <sub>16</sub> H <sub>11</sub> NO <sub>2</sub>	249.26	8593
	3-Methyl-3H-cyclonona[def]biphenylene	C <sub>18</sub> H <sub>14</sub>	230.3	5376621
	Beta-Sitosterol	C <sub>29</sub> H <sub>50</sub> O	414.7	222284
	Chlorogenic acid	C <sub>16</sub> H <sub>18</sub> O <sub>9</sub>	354.31	1794427
	Corynantheidine	C <sub>22</sub> H <sub>28</sub> N <sub>2</sub> O <sub>3</sub>	368.5	3000341
	Gamma-Sitosterol	C <sub>29</sub> H <sub>50</sub> O	414.7	457801
	Isoquercitrin	C <sub>21</sub> H <sub>20</sub> O <sub>12</sub>	464.4	5280804
	Quercetin 3-galactoside	C <sub>21</sub> H <sub>20</sub> O <sub>12</sub>	464.4	5281643
	Rutin	C <sub>27</sub> H <sub>30</sub> O <sub>16</sub>	610.5	5280805
	Stigmasterol	C <sub>29</sub> H <sub>48</sub> O	412.7	5280794
<b>Kabasura kudineer</b>				
<i>H. auriculata</i>	Apigenin-7-O-glucuronide	C <sub>21</sub> H <sub>18</sub> O <sub>11</sub>	446.4	5319484
	Apigenin-7-O-glucoside	C <sub>21</sub> H <sub>20</sub> O <sub>10</sub>	432.4	44257792
<i>C. serratum</i>	Apigenin	C <sub>15</sub> H <sub>10</sub> O <sub>5</sub>	270.24	5280443
	Clerodermic acid	C <sub>20</sub> H <sub>28</sub> O <sub>4</sub>	332.4	16745295
	Scutellarein	C <sub>15</sub> H <sub>10</sub> O <sub>6</sub>	286.24	5281697
<i>T. chebula</i>	Arjungenin	C <sub>30</sub> H <sub>48</sub> O <sub>6</sub>	504.7	12444386
	Ellagic acid	C <sub>14</sub> H <sub>6</sub> O <sub>8</sub>	302.19	5281855
<i>T. cordifolia</i>	Berberine	C <sub>20</sub> H <sub>18</sub> NO <sub>4</sub> <sup>+</sup>	336.4	2353
<i>P. nigrum</i>	Chavicine	C <sub>17</sub> H <sub>19</sub> NO <sub>3</sub>	285.34	1548912
<i>C. aromaticus</i>	Chlorogenic acid	C <sub>16</sub> H <sub>18</sub> O <sub>9</sub>	354.31	1794427
<i>Benth</i>				
<i>C. speciosus</i> Sm	Diosgenin	C <sub>27</sub> H <sub>42</sub> O <sub>3</sub>	414.6	99474
	Eremanthin	C <sub>15</sub> H <sub>18</sub> O <sub>2</sub>	230.3	100572
	Hispidulin	C <sub>16</sub> H <sub>12</sub> O <sub>6</sub>	300.26	5281628
	Lupeol	C <sub>30</sub> H <sub>50</sub> O	426.7	259846
<i>C. rotundus</i>	Luteolin	C <sub>15</sub> H <sub>10</sub> O <sub>6</sub>	286.24	5280445
<i>A. paniculate</i>	Neoandrographolide	C <sub>26</sub> H <sub>40</sub> O <sub>8</sub>	480.6	9848024
<i>P. nigrum</i>	Piperine	C <sub>17</sub> H <sub>19</sub> NO <sub>3</sub>	285.34	638024
<i>C. aromaticus</i>	Rosmarinic acid	C <sub>18</sub> H <sub>16</sub> O <sub>8</sub>	360.3	5281792
<i>Justicia adhatoda</i>	Vasicinolone	C <sub>11</sub> H <sub>10</sub> N <sub>2</sub> O <sub>3</sub>	218.21	13970119
	Vasicoline	C <sub>19</sub> H <sub>21</sub> N <sub>3</sub>	291.4	626005

**Table S3.** Binding affinity, interacting residues and bond length for the screened phytochemicals against mutated NTD in S-Protein.

Plant	Phytochemicals	Binding Affinity	H/C-H Interaction	Bond	Bond length	Hydrophobic interaction	Alkyl interaction	Pi-Sigma /CationStacked Interaction
<b>B.1.617.2. S-Protein – NTD Mutant Type</b>								
Standard Drug	Cefuroxime	-6.1	ARG102, GLY103*, TYR170, SER172*	2.35		ILE101, TRP104, ILE119, VAL120, ASN121, VAL126, ILE128, MET177, PHE192	LEU226,	ARG190
<i>H. cordata</i>	6alpha,9-Difluoro-11beta-hydroxypregn-4-ene-3,20-dione	-8.3	GLY103*	-		ILE101, TRP104, ASN121, VAL126, ILE128, PHE192, LEU226, VAL227	ARG102, ILE119, ARG190,	-
	Diosgenin	-7.5	ASN121	4.64		GLY103, MET177, ARG190	VAL126, ILE101, TRP104, PHE175, PHE192	-
	Kanzonol	-8.0	ASN121*	-		SER172, MET177, VAL227	LEU176, PHE194, PHE192, LEU226	PHE175, ILE128, ILE203,
	Murrayenol	-6.6	PHE157*			ASN122, THR124, GLU154, VAL159	ALA123, MET153,	TYR160

S. <i>aromaticum</i>	Myricetin	-6.0	TYR28, SER60*, TYR269, GLN271,	5.40, 4.46, 4.40, 4.73, 5.90	LEU56, ASN61, - VAL62, THR63, PHE65, LEU84		TYR269
	Stigmasterol	-6.3	-	-	ASN122, THR124, ALA123 TRP152, MET153, GLU154, TYR160, LEU176, LEU179		PHE157
Citrus spp.	Hesperidin	-7.1	GLU154*, VAL159, TYR160, TYR160*, ALA163	5.20, 4.51, 2.92	GLN14, CYS15, ASN122, VAL127, LYS129, SER155, ARG158, SER161, SER162, PHE133		PHE157, GLU156, PHE157, TYR160
	Naringenin	-6.8	ILE101	3.58	GLU96, ARG102, VAL126, LEU226 GLY103, ILE119, ASN121, ILE128, TYR170, SER172, ARG190, ILE203, VAL227, LEU229		TRP104, PHE192
N. sativa	β-sitosterol	-6.0	GLN14	3.26	LEU118, VAL120, VAL127, PHE157, ASN122, LYS129, TYR160 ARG158, VAL15, SER161, VAL171		PHE157, TYR160
	Cycloartenol	-8.6	GLU96	5.80	ILE101, ARG102, VAL126 GLY103, TRP104, ILE119, ASN121,		-

						ILE128, TYR170, SER172, PHE175, PHE192, ILE203, LEU226, VAL227				
<i>O. basilicum</i>	Chicoric acid	-6.6	ASN122, ALA123, 5.02, TYR160 3.56, 5.22			VAL127, LYS129, LEU179 ALA123 TRP152, MET153, PHE157 SER155, GLU156, PHE175, MET177, ASP178				
<i>P. nigrum</i>	Piperettine	-8.0	ARG190, ASN121	4.46, 4.54		GLU96, ILE101, TRP104, ILE119, - ARG102, GLY10, TYR170, PHE192, VAL126, ILE128, LEU226, VAL227 ILE203				
Kabasura kudineer	(3R,8S,9S,10R,13R,14R,17R)-17- [(2R,5S)	-6.8	-	-		ASN121, ILE128, VAL126, PHE175, - TYR170, SER172, LEU226, VAL227 LEU176, MET177, ILE203, LEU229				
	Campesterol	-7.2	ARG190	4.20		ILE119, ASN121, AL126, PHE192, ILE128, TYR170, ILE203, LEU226, SER172, GLN173 VAL227				
<i>Mitragyna speciosa Korthi</i>	2-Phenylquinoline-4-carboxylic acid	-6.8	-			ILE119, ILE128, VAL126, VAL227, TYR170, PHE168, ILE203, TYR170 LEU226 LEU229				
	3-Methyl-3H- cyclonona[def]biphenylene	-6.6	-	-		ILE128, PHE168, TYR170, VAL227 - LEU229				
	5-beta-Cholest-24-en-12-one	-6.4	-	-		ILE128, PHE168, VAL126, TYR170, - SER172, LEU226, VAL227				

				ASP228, LEU229, PRO230				
Beta-Sitosterol	-6.4			ILE119, ILE128, VAL126, LEU226 TYR170 PHE168, PHE192, ILE203, VAL227, LEU229				
Campesterol	-6.7			ILE119, ILE128, VAL126, LEU226 TYR170 PHE168, PHE192, VAL227, LEU229				
Cholest-24-en-12-one	-7.2	-	-	VAL126, ILE128, TRP104, ILE119, - TYR170, LEU229 PHE192, PHE194, ILE203, LEU226, VAL227				
Dibenzo[a,h]cycloetradecene	-6.1	-	-	PHE168, TYR200, ILE128, TYR170, - ASP228, LEU229 VAL227, PRO230				
Gamma-Sitosterol	-6.4	-	-	PHE168, LEU229 ILE119, VAL126, TYR170 ILE128, ILE203, LEU226, VAL227				
Stigmasterol	-7.3	-	-	VAL126, ILE128, TYR170, TYR200, - PHE168, ASP228, LEU226, VAL227, LEU229 PRO230				

**Table S4.** Binding affinity, interacting residues and bond length for the screened phytochemicals against RBD in S-Protein.

Plant	Compound	Binding Affinity	H/C-H Interaction	Bond	Bond length	Hydrophobic interaction	Alkyl interaction	Pi-Sigma /CationStacked Interaction
<b>B.1.617.2. S-Protein - RBD-Domain</b>								
<i>H. cordata</i>	3-Benzoyloxy-6-oxo-12-ursen-28-oic acid	-6.1	ARG408, GLN409		6.01, 5.09	ARG403, GLU406, GLY416, TYR505	ASP405, THR415, ASP420,	LYS417
	26,26,26-trifluoro-25-hydroxy-27-norvitamin D3	-6.1	SER469		2.85	ARG454, ARG457, GLU471, TYR473, THR478, CYC480	PHE456, THR470, ILE472, SER477, PRO479,	LYS458, PRO491
	Murrayenol		GLY482			ARG454, ARG457, ASP467, GLU471, TYR473, CYS480, PRO491	PHE456, LYS458, SER469, ILE472, GLN474, ASN481,	
	Quercetin	-6.6	ARG454, PHE456			ASP467, ILE472, CYS480, PRO491	GU471, ARG457	LYS458, TYR473



								ILE472, TYR473, CYS480, PRO491	
	Luteolin	-7.1	ARG454, SER469	3.53, 5.82				PHE456, ASP467, ARG457 THR470, ILE472, TYR473, GLN474, CYS480, PRO491	LYS458
	Naringenin		GLN474, ASP467	4.76, 4.49				ARG454, PHE456, ARG457, SER469, GLU471, LYS458 ILE472, TYR473, CYS480, PRO491	
	Naringin	-7.7	ARG457, GLU465, ARG466*, ASP467	5.66, 5.27, 7.39*, 2.96				ARG454, PHE456, SER459, ILE468, SER469, GLU471, ILE472, TYR473, GLN474, CYS480, PRO491	LYS458
	Rutin	-7.0	ARG454, ARG457, LYS458, SER459, ASP467, SER469, GLU471, ILE472	4.83, 5.48, 5.20, 4.13, 3.08, 4.02, 4.13				PHE456, TYR473, CYS480, GLY482, PRO491	GLU471
<i>N. sativa</i>	Nigellidine	-6.4	ARG454, PHE456, TYR473*, GLN474	4.32, 5.75, 4.02*, 5.23				SER469, GLU471, ARG457 ILE472, PRO491	LYS458
<i>O. basilicum</i>	Chicoric_acid	-6.7	ARG454, LYS458, ASP467, SER469*, GLU471, ILE472	2.96, 6.55, 5.98, 4.89, 4.75 6.36				THR470, GLN474, ARG457 PRO479, PRO491	
<i>P. nigrum</i> Linn.	3-Heptadecen-5-yne, (Z)-	-7.5	-	-				VAL524 PHE342, PHE338,	-

						ALA363, TYR365, LEU368, TYR369, PHE374, PHE377, LEU387, PHE392, VAL395, ILE434, LEU513, PHE515	
Benzo[c] cinnolin-2-amine	-7.0	ALA372, PHE374	3.66, 5.32	TYR365, SER373		LEU368, ALA372	PHE377, PHE374
Copaene	-8.6	-	-	PHE342, PHE377, ILE434	PHE374, LEU368,	PHE338, ALA363, LEU387, PHE392, CYS432, LEU513, PHE515	TYR365
Dodec-5-yn-6-one	-6.3	-	-	PHE342, PHE392, LEU513, PHE515	LEU387, ILE434,	CYS336, PRO337, PHE338, VAL341, ILE358, ALA363,	-

							TYR365, VAL395, VAL524	
Guineensine	-7.6	-	-		PHE338, ALA372, PHE515, VAL524	ALA363, SER373, VAL524	TYR365, LEU368, TYR369, PHE374, PHE377, PRO384, LEU387, ILE434, LEU513	CYS432, PHE392
Piperine	-6.2	GLU340*, ARG346, ALA352*, SER399	4.67, 4.64		VAL341, SER349, ASN354, LYS356	PHE347, TYR351,	ALA348, ALA352	-
Piperolein	-9.4	-			PHE338, LEU368, SER373, VAL524	PHE342, ALA372, LEU387,	ALA363, TYR365, PHE392, VAL395, ILE434, PHE515, LEU513,	TYR369, PHE374, PHE377
Sarmentine	-7.2	-	-		PHE338, SER373, PHE392	LEU368,	TYR365, PHE377, LEU387, TYR369, ALA372,	-

								PHE374, CYS432, ILE434 LEU513, PHE515	
Kabasura kudineer	Apigenin-7-O-glucuronide	-7.2	ARG454, GLN474	ASP467,		PHE456 GLU471, TYR473	SER469, ILE472,		LYS458
	Apigenin	-6.0	VAL341		3.72	GLU340, SER349, LYS356	ARG346, ASN354,	ALA344, ALA348	PHE347, ALA348
	Apigenin7-O-glucoside	-7.1	ALA352, SER399*		3,52, 6.29	GLU340, ALA348, ASN354, ALA397	VAL341, TRP353, LYS356,	ALA344	PHE347
	Arjungenin	-6.5	SER349, TYR351		2.92, 5.24, 3.48	ARG346, ALA348, ASN354, TYR451, LEU452	PHE347, ALA352, ASN450,	-	-
	Chavicine	-6.1				ARG454, ARG457, GLU471, TYR473, PRO491	PHE456, SER469, ILE472, GLN474,		LYS458
	Chlorogenic acid	-6.5	ASP467, ILE472	GLU471,	5.03, 3.94, 3.96	ARG454, SER469,	PHE456, TYR473,	ARG457, LYS458	-

						GLN474, CYS480, GLY482, PRO491			
Ellagic acid	-6.8	SER469, TYR473, 4.32, 3.87, ARG454, PHE456, - LYS458, GLN474 4.61 ARG457, THR470, GLU471 ILE472, PRO491							
Eremanthin	-	-	-			ARG454, PHE456, ARG457, - ASP467, SER469, LYS458, GLU471, ILE472, TYR473 GLN474, PRO491			
Hispidulin	-6.6	LYS458, GLN474	4.35, 4.89			ARG454, ASP467, ARG457, LYS458 SER469, GLU471, PRO491 ILE472, TYR473			
Lupeol	-	-	-			TYR449, LEU452, PHE490 - GLU484, CYS488, TYR489, LEU492, GLN493, SER494			
Luteolin	-6.9	ARG454, LYS458, 6.11, 3.95, SER469, THR470, ARG457, ARG457, SER459, GLU471 4.37, 3.24, ILE472, TYR473, LYS458 ASP467 4.78 PRO491							
Neoandrographolide	-6.9	ARG454, LYS458, 5.18, 4.28, PHE456, ARG457, - - ASP467, GLU471, 4.27, 4.56, SER469, ILE472, GLN474, CYS480 5.32, 5.18, TYR473, PRO479 4.29							
Piperine	-6.2	GLN474, GLN474*, 4.19, 4.69, ARG454, ARG457, - LYS458 SER469 4.40 GLU471, ILE472, TYR473, GLY476, SER477, PRO491							

	Rosmarinic acid	-6.8	ASP467, GLN474	4.13, 5.07	PHE456, TYR473, ASN481, VAL483	GLU471, CYS480, GLY482,	ARG457	LYS458
	Scutellarein	-6.9	ARG454, PHE456, GLN474	4.30, 6.13, 4.03	ASP467, ILE472	GLU471, ARG457, PRO491		TYR473, LYS458
	Vasicinolone	-6.3	SER469, ILE472	4.65, 5.67	ARG454, ASP467, GLN474	PHE456, TYR473, PRO491	ARG457,	LYS458, GLU471
	Vasicoline	-6.1	-	-	PHE456, SER469, ILE472, GLN474, GLY482	ARG457, GLU471, TYR473, CYS480,	PRO491	LYS458
<i>Mitragyna speciosa</i> <i>Korthi</i>	2-Phenylquinoline-4-carboxylic acid	-6.6	-	-	ARG454, GLU471, GLN474, PRO491	PHE456, ILE472,	ARG457, LYS458	LYS458, TYR473
	3-Methyl-3H-cyclonona[def]biphenylene	-6.6	-	-	ARG454, ASP467, GLU471, ILE472	PHE456, SER469,	ARG457, LYS458, TYR473, PRO491	-
	Chlorogenic acid	-6.6	ARG454, PHE456, GLU471, CYS480*	ARG454*, SER469, GLN474, 5.80, 4.52*, 5.69, 3.45, 3.55, 378, 5.13, 3.87	ARG457, ILE472, PRO479, GLY482	THR470, TYR473,	LYS458, PRO491	-
	Corynantheidine	-6.1	-	-	ARG454, ASP467,	PHE456, SER469,	ARG457, CYS480	LYS458

						ILE472, TYR473, GLN474, GLY482			
Gamma-Sitosterol	-6.3	ARG454		4.60		ARG457, ASP467, LYS458 SER469, GLU471, ILE472, TYR473, GLN474, PRO479, CYS480, ASN481		-	
Isoquercitrin	-6.8	ARG454, PHE456, 4.66, 5.75, LYS458, SER469, 5.69, 4.29, TYR473*, GLN474 3.92*, 3.82				ASP467, ILE472, LYS458 PRO491		LYS458, GLN474	
Quercetin 3-galactoside	-6.7	ARG454, ARG457, 5.65, 5.72, SER469, GLU471*, 2.84, 4.16 CYS480				PHE456, ASP467, PRO491 THR470, GLU471, ILE472, TYR473, GLY482		-	
Rutin	-7.0	ARG454, PHE456, 4.57, 6.48, LYS458*, ASP467, 6.83*, 4.82, SER469, GLU471, 4.63, 4.44, GLN474, CYS480* 4.29, 4.04*				THR470, ILE472, - TYR473, ASN481, GLY482		-	