Supplementary Information

Targeting Ebola Virus VP30 with Quercetin Derivatives: An Integrated Molecular Docking, MD Simulation, ADMET, and DFT Study

Haroon ur Rashid,[a] Shehla Khan,[b] Nasir Ahmad,*,[c] Khalid Khan,[c] Mara Rubia C. Couri,[a] Umar F. Khattak,*,[d] Muhammad Zahoor[e] and Amal Alotaibi[f]

[a]Departamento de Química, Universidade Federal de Juiz de Fora, 36036-900 Juiz de Fora-MG, Brazil

[b]Institute of Chemical Sciences, University of Peshawar, 25120 Peshawar, KP, Pakistan

[c]Department of Chemistry, Islamia College University, 25120 Peshawar, KP, Pakistan

[d]Faculty of Artificial Intelligence and Frontier Technologies, UNITAR International University, 47301 Selangor, Malaysia

[e]Department of Biochemistry, University of Malakand, 18800 Dir Lower, KP, Pakistan

[f]Department of Basic Science, College of Medicine, Princess Nourah bint Abdulrahman University, 11671 Riyadh, Saudi Arabia

*e-mail: nasirdft@gmail.com; umar.farooq@unitar.my

Editor handled this article: Paulo Augusto Netz (Associate)

Haroon ur Rashid: https://orcid.org/0000-0003-3335-7957

Shehla Khan: https://orcid.org/0009-0007-4494-4643

Nasir Ahmad: https://orcid.org/0000-0003-1035-3822

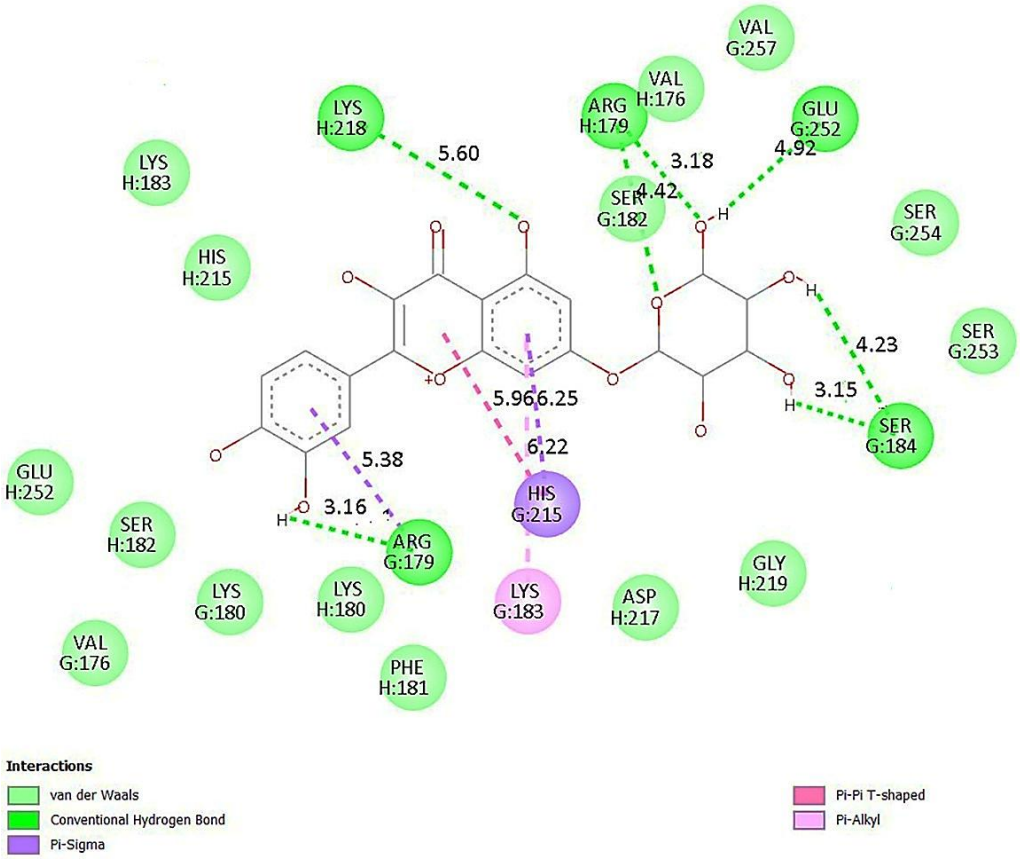
Khalid Khan: https://orcid.org/0000-0002-2135-6976

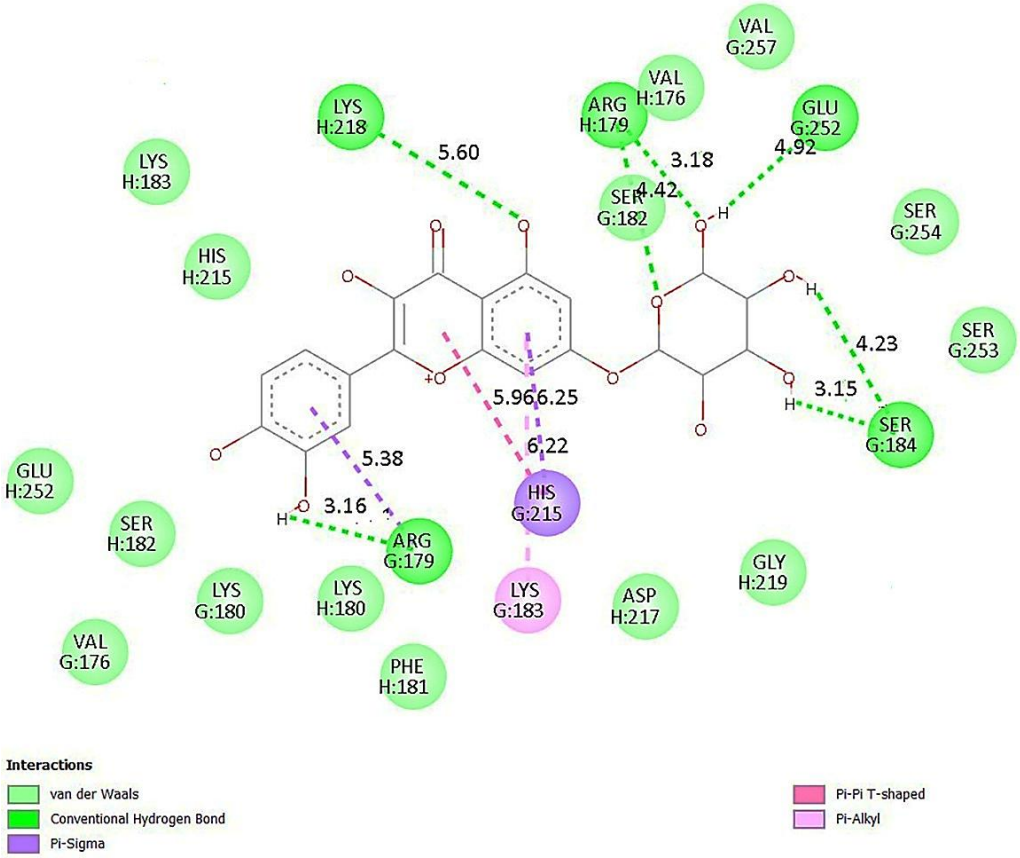
Mara Rubia Costa Couri: https://orcid.org/0000-0002-9482-3862

Umar Farooq Khattak: https://orcid.org/0000-0002-5171-5116

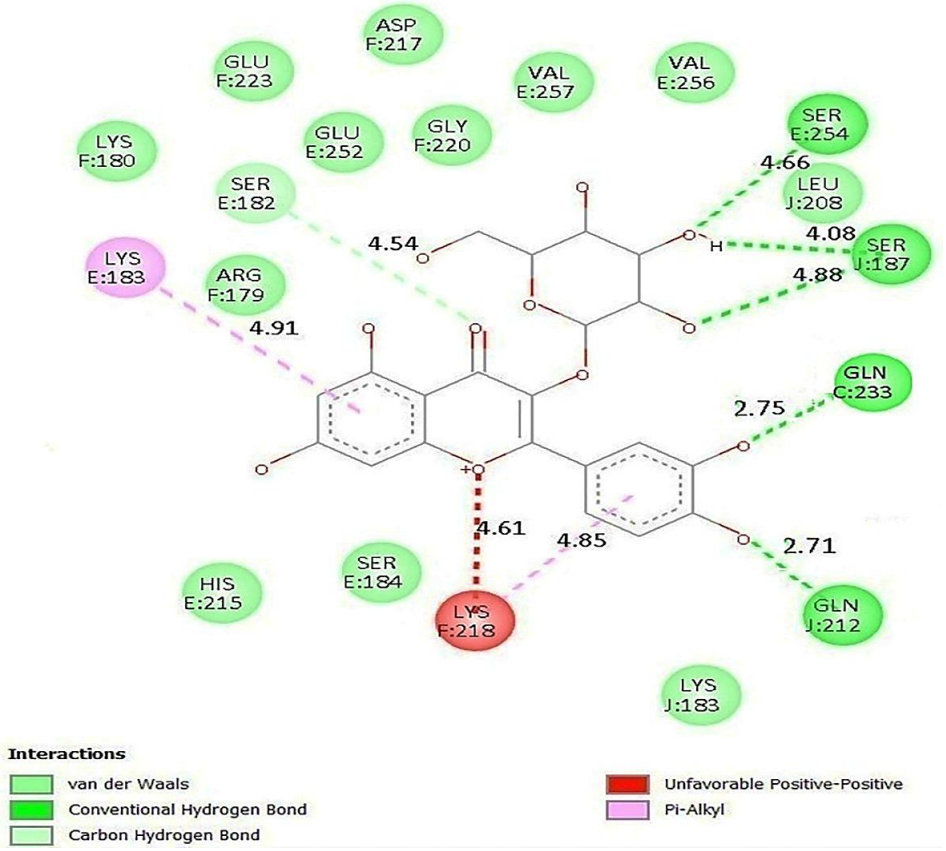
Muhammad Zahoor: https://orcid.org/0000-0002-4528-8517

Amal Alotaibi: https://orcid.org/0009-0005-1900-6124

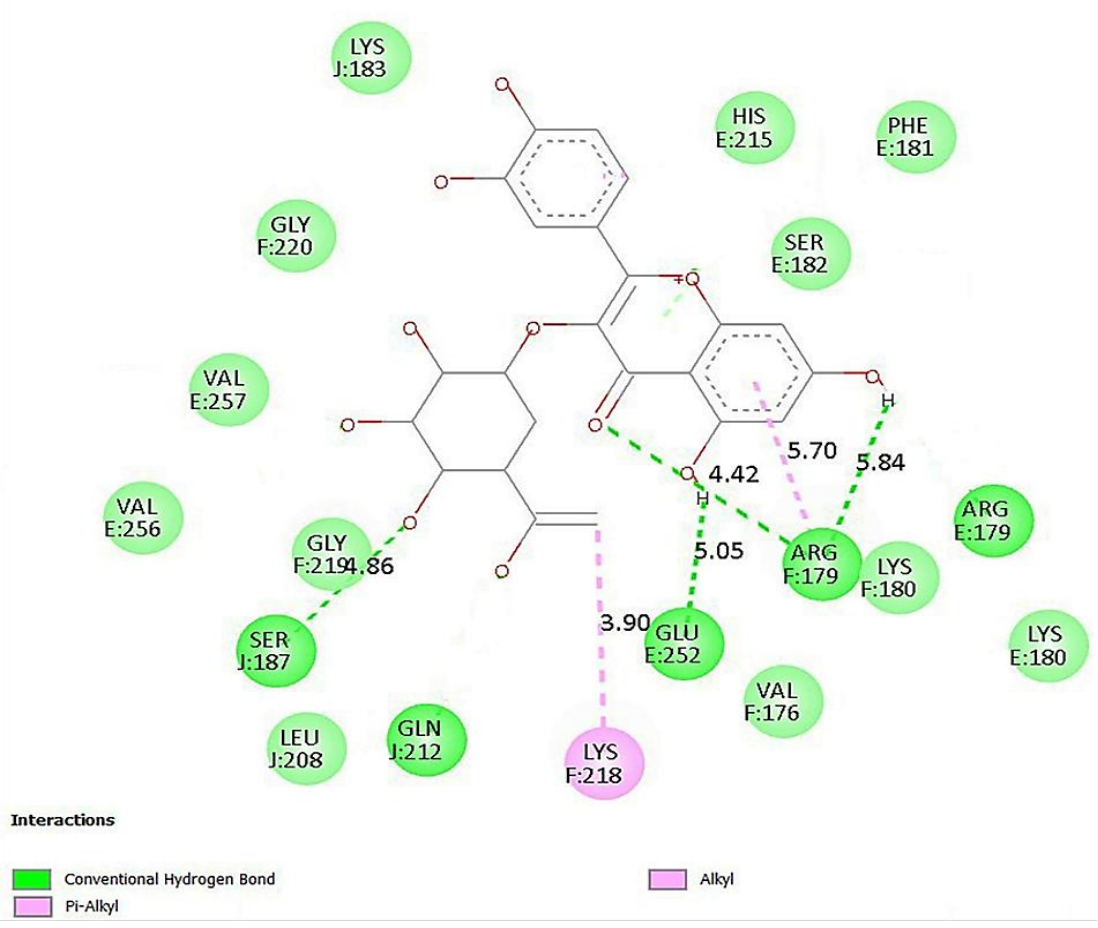

VAL G:257
VAL H:176
LYS H:218
ARG H:179
GLU G:252
LYS H:183
5.60
3.18
4.92
4.42
SER G:182
SER G:254
HIS H:215
4.23
SER G:253
5.96
6.25
3.15
SER G:184
6.22
5.38
GLU H:252
HIS G:215
3.16
SER H:182
ARG G:179
GLY H:219
LYS G:180
LYS H:180
LYS G:183
ASP H:217
VAL G:176
PHE H:181
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Sigma
Pi-Pi T-shaped
Pi-Alkyl


VAL G:257
VAL H:176
LYS H:218
ARG H:179
GLU G:252
LYS H:183
5.60
3.18
4.92
4.42
SER G:182
SER G:254
HIS H:215
4.23
SER G:253
5.96
6.25
3.15
SER G:184
6.22
5.38
GLU H:252
HIS G:215
3.16
SER H:182
ARG G:179
GLY H:219
LYS G:180
LYS H:180
LYS G:183
ASP H:217
VAL G:176
PHE H:181
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Sigma
Pi-Pi T-shaped
Pi-Alkyl

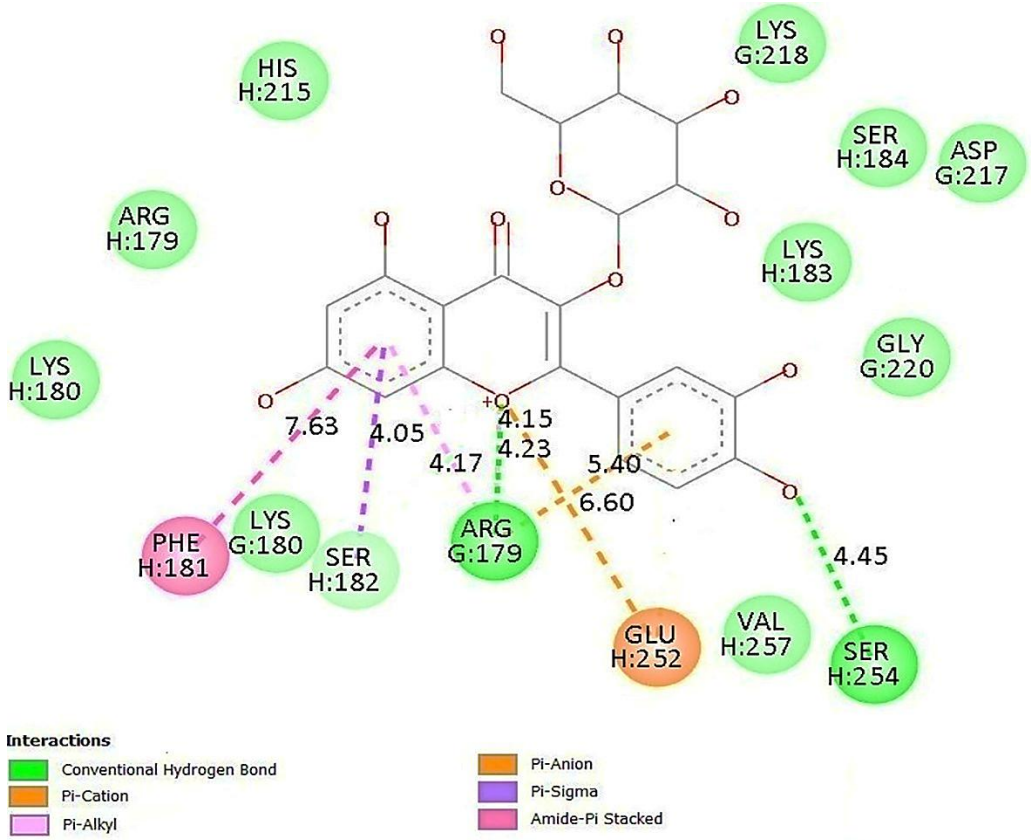
D1


ASP F:217
GLU F:223
VAL E:257
VAL E:256
SER E:254
LYS F:180
GLU E:252
GLY F:220
4.66
LEU J:208
SER E:182
4.08
SER J:187
4.54
LYS E:183
ARG F:179
4.88
4.91
GLN C:233
2.75
4.61
4.85
2.71
SER E:184
HIS E:215
LYS F:218
GLN J:212
LYS J:183
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Unfavorable Positive-Positive
Pi-Alkyl

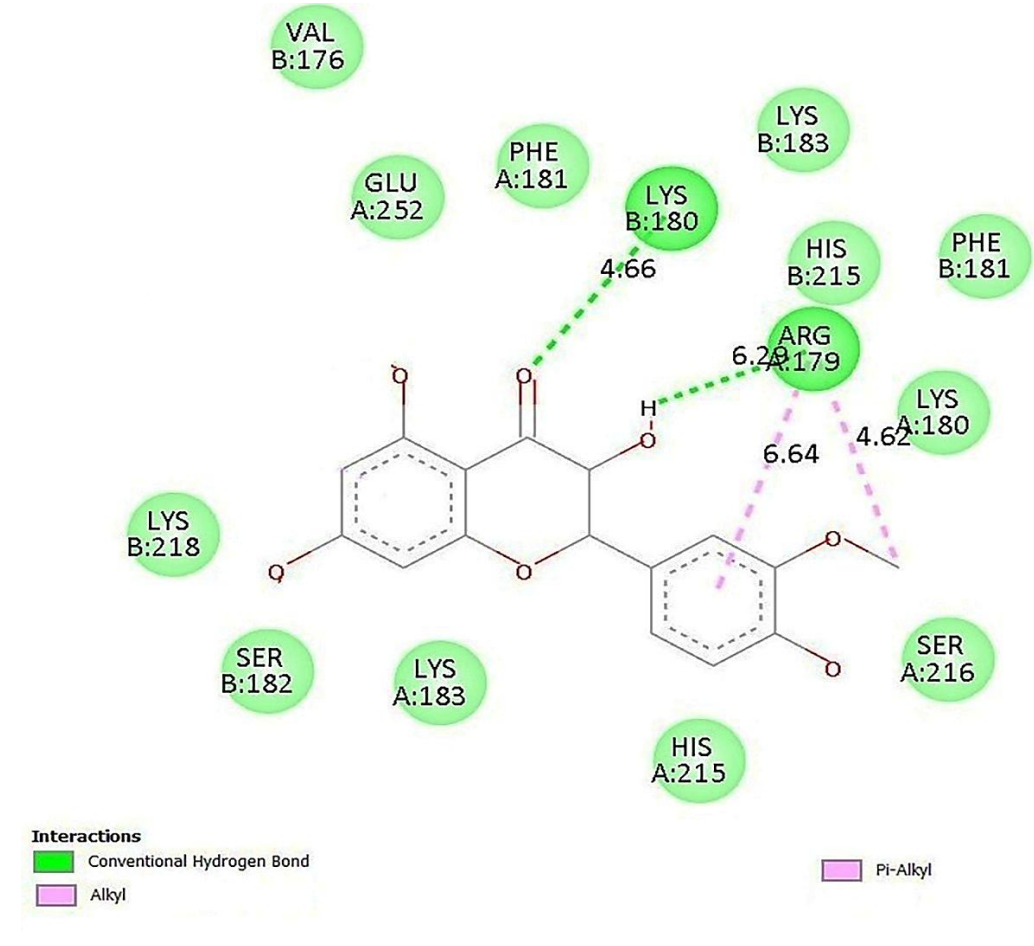
D2


LYS J:183
HIS E:215
PHE E:181
GLY F:220
SER E:182
VAL E:257
5.70
5.84
4.42
VAL E:256
ARG E:179
5.05
ARG F:179
LYS F:180
GLY F:219
4.86
3.90
GLU E:252
LYS E:180
SER J:187
VAL F:176
LEU J:208
GLN J:212
LYS F:218
Interactions
Conventional Hydrogen Bond
Pi-Alkyl
Alkyl

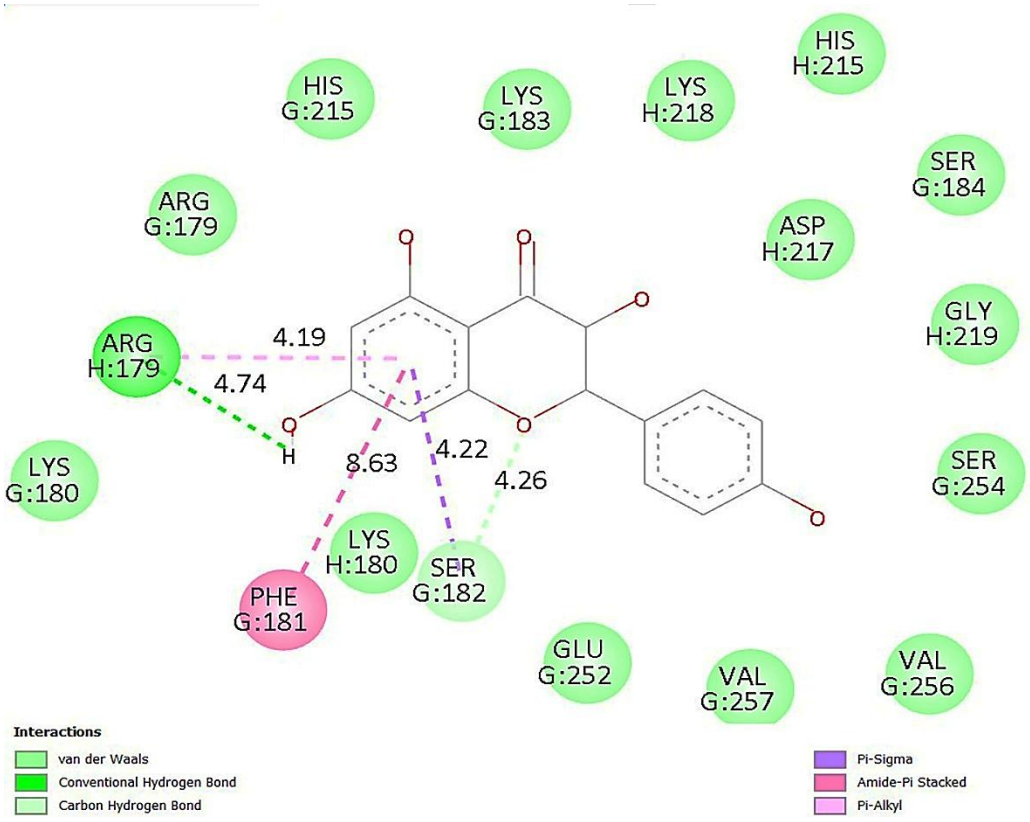
D3


LYS G:218
HIS H:215
SER H:184
ASP G:217
ARG H:179
LYS H:183
GLY G:220
LYS H:180
7.63
4.05
4.17
4.15
4.23
5.40
6.60
4.45
PHE H:181
LYS G:180
SER H:182
ARG G:179
GLU H:252
VAL H:257
SER H:254
Interactions
Conventional Hydrogen Bond
Pi-Cation
Pi-Alkyl
Pi-Anion
Pi-Sigma
Amide-Pi Stacked

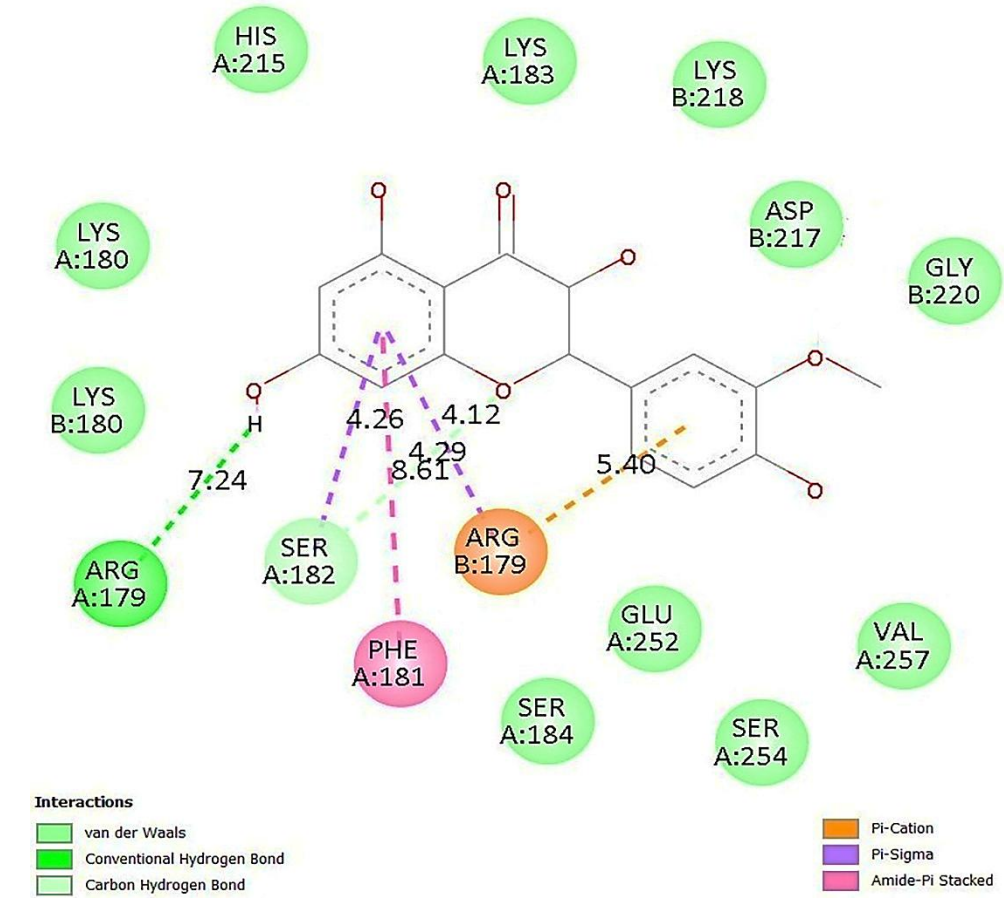
D4


VAL B:176
LYS B:183
PHE A:181
GLU A:252
LYS B:180
4.66
HIS B:215
PHE B:181
ARG A:179
6.29
H
LYS A:180
4.62
6.64
LYS B:218
SER B:182
LYS A:183
SER A:216
HIS A:215
Interactions
Conventional Hydrogen Bond
Alkyl
Pi-Alkyl

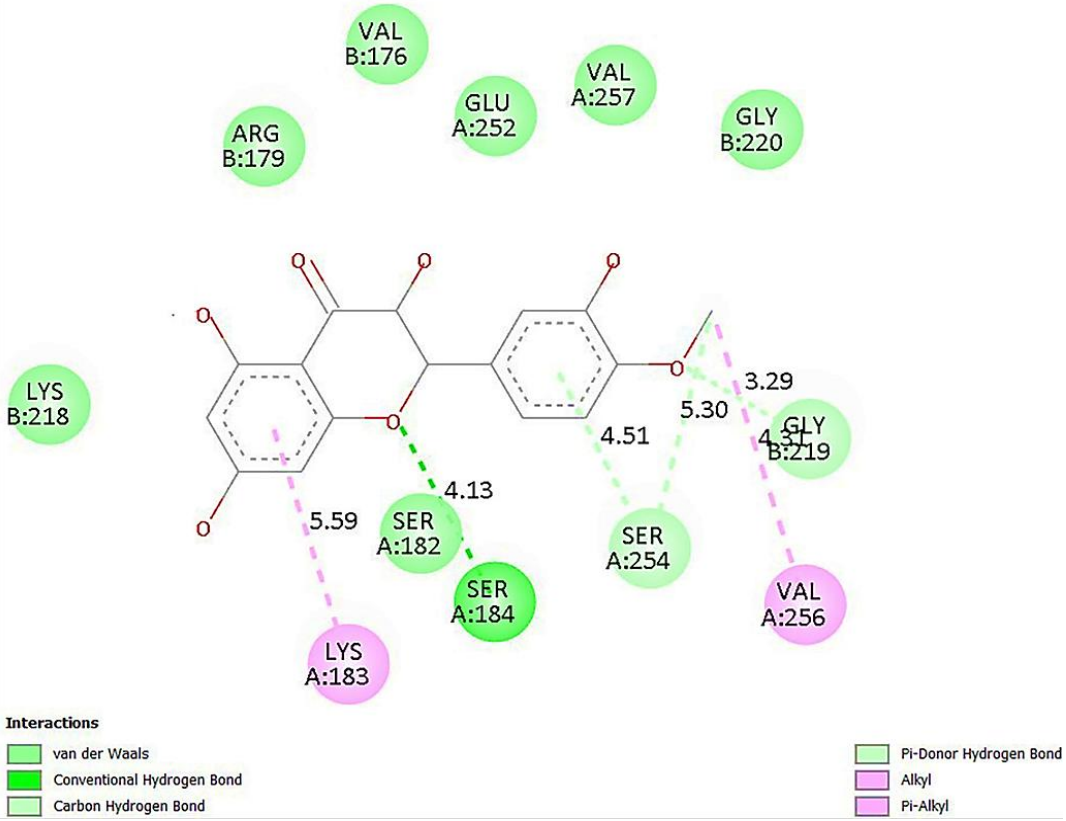
D5


HIS G:215
LYS G:183
LYS H:218
HIS H:215
SER G:184
ARG G:179
ASP H:217
GLY H:219
ARG H:179
4.19
4.74
H
8.63
4.22
4.26
LYS G:180
SER G:254
LYS H:180
SER G:182
PHE G:181
GLU G:252
VAL G:257
VAL G:256
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Pi-Sigma
Amide-Pi Stacked
Pi-Alkyl

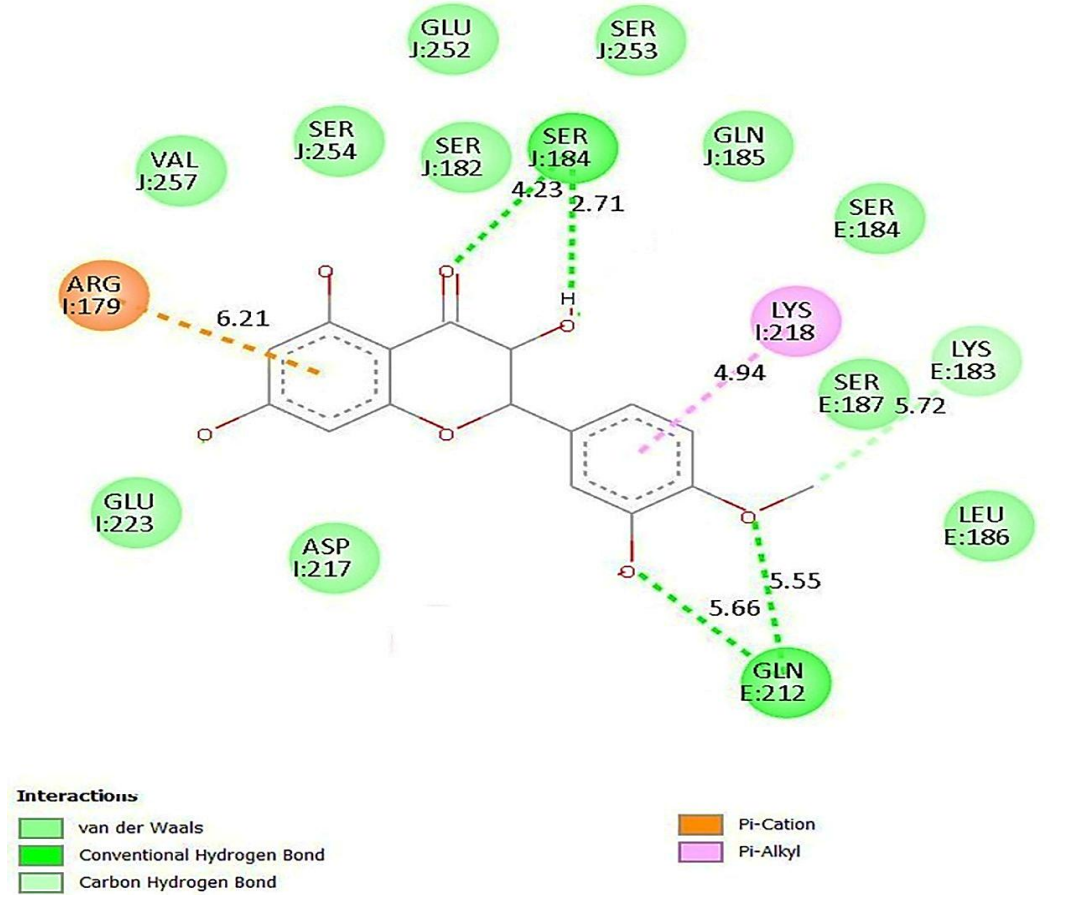
D6


HIS A:215
LYS A:183
LYS B:218
ASP B:217
LYS A:180
GLY B:220
LYS B:180
H
4.26
4.12
4.29
8.61
7.24
5.40
SER A:182
ARG B:179
ARG A:179
GLU A:252
VAL A:257
PHE A:181
SER A:184
SER A:254
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Pi-Cation
Pi-Sigma
Amide-Pi Stacked

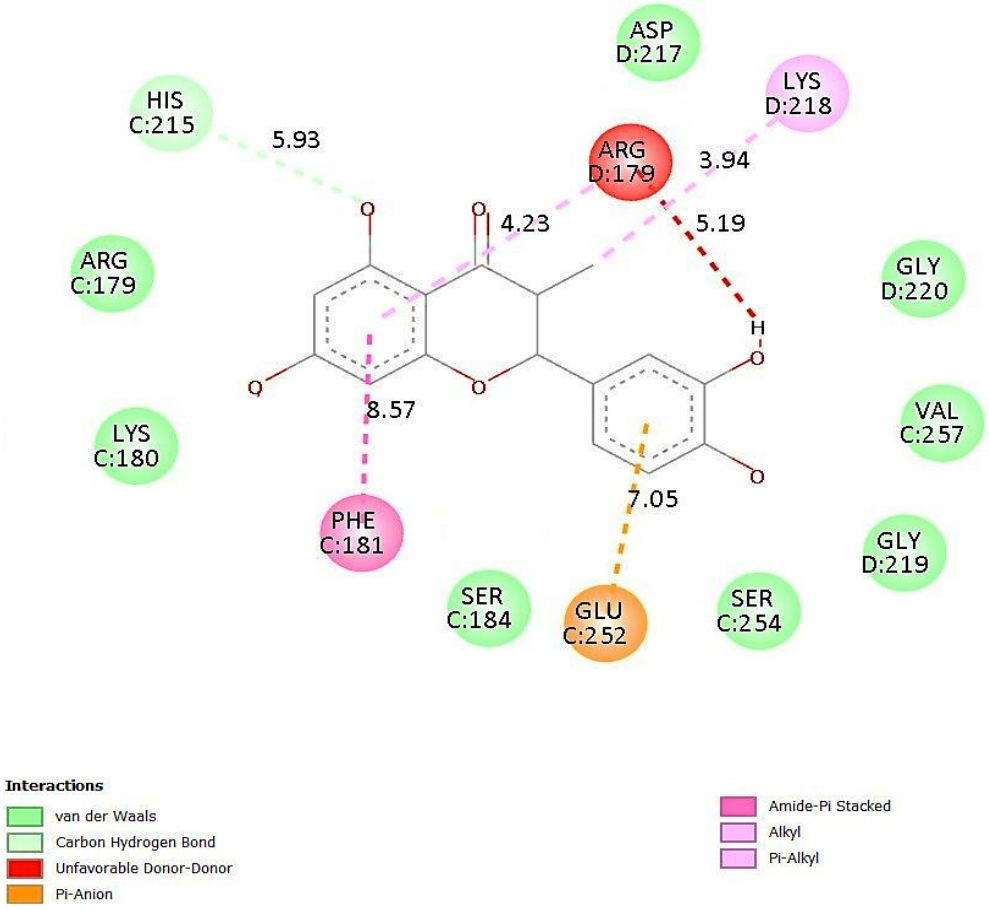
D7


VAL B:176
VAL A:257
GLU A:252
GLY B:220
ARG B:179
LYS B:218
3.29
5.30
4.51
4.31
GLY B:219
4.13
5.59
SER A:182
SER A:254
SER A:184
VAL A:256
LYS A:183
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Pi-Donor Hydrogen Bond
Alkyl
Pi-Alkyl

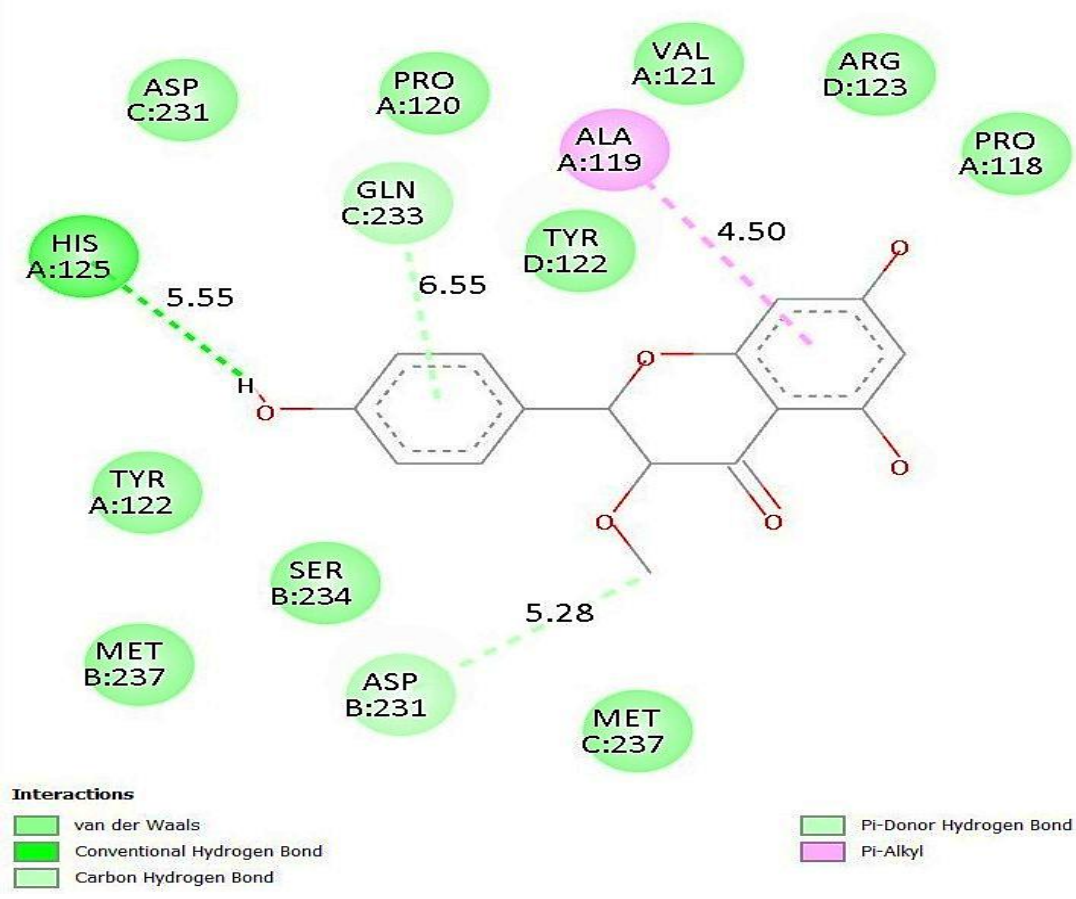
D8


GLU J:252
SER J:253
SER J:254
SER J:182
SER J:184
GLN J:185
VAL J:257
4.23
2.71
SER E:184
ARG I:179
6.21
LYS I:218
4.94
LYS E:183
SER E:187
5.72
GLU I:223
LEU E:186
ASP I:217
5.55
5.66
GLN E:212
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Pi-Cation
Pi-Alkyl

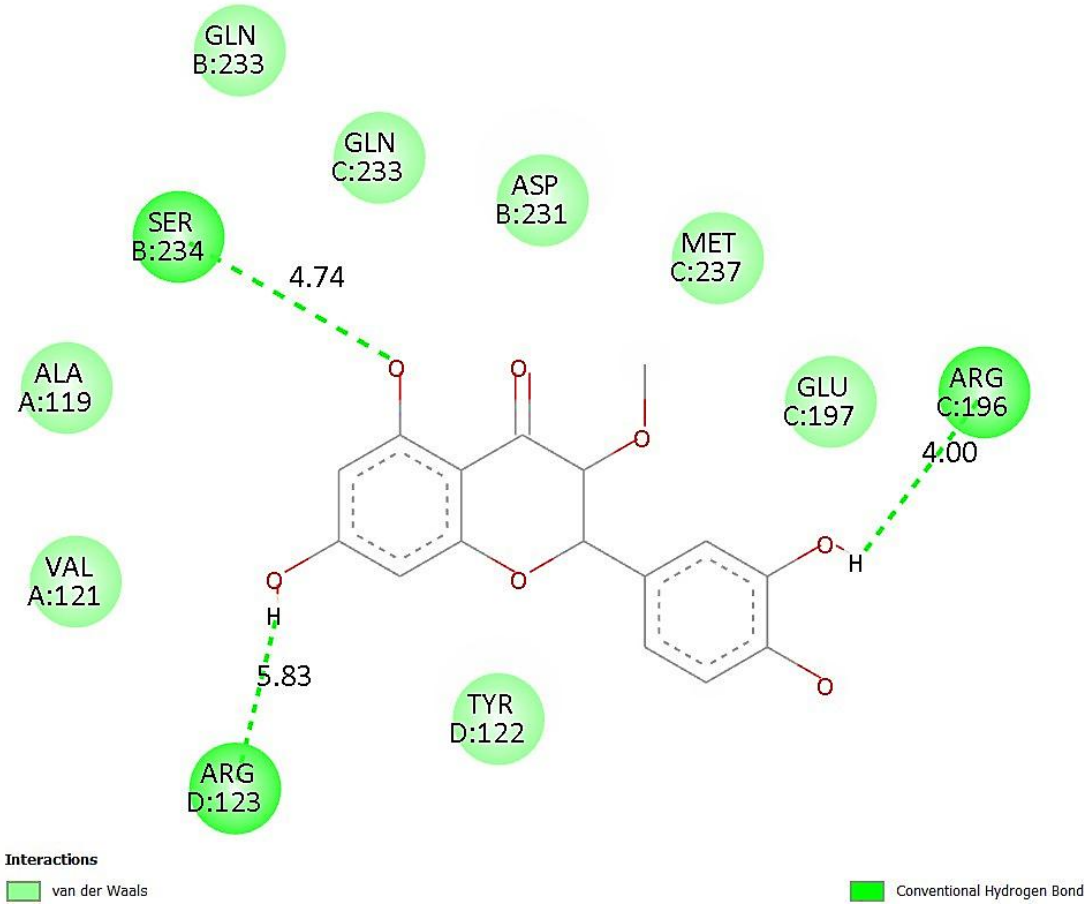
D9


ASP
D:217
LYS
D:218
HIS
C:215
5.93
ARG
D:179
3.94
4.23
5.19
ARG
C:179
GLY
D:220
H
O
8.57
LYS
C:180
VAL
C:257
7.05
PHE
C:181
GLY
D:219
SER
C:184
GLU
C:252
SER
C:254
Interactions
van der Waals
Carbon Hydrogen Bond
Unfavorable Donor-Donor
Pi-Anion
Amide-Pi Stacked
Alkyl
Pi-Alkyl

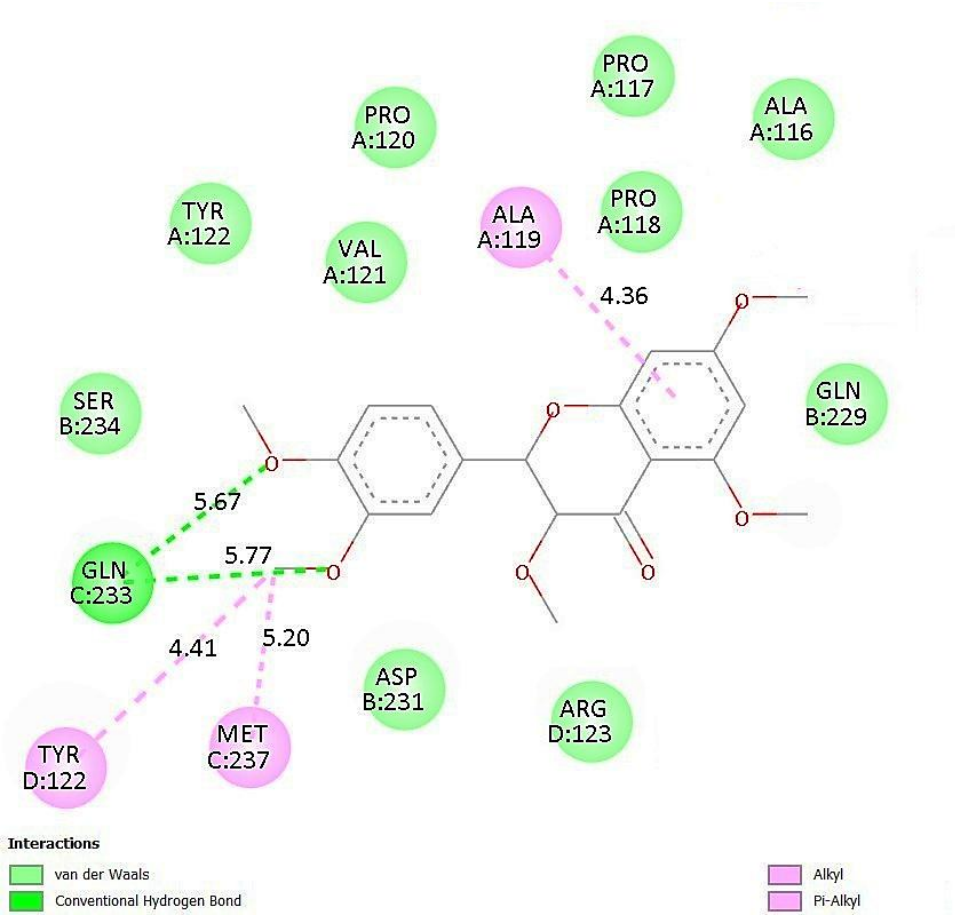
D10


ASP
C:231
PRO
A:120
VAL
A:121
ARG
D:123
ALA
A:119
PRO
A:118
GLN
C:233
HIS
A:125
TYR
D:122
4.50
5.55
6.55
H
O
TYR
A:122
SER
B:234
5.28
MET
B:237
ASP
B:231
MET
C:237
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Pi-Donor Hydrogen Bond
Pi-Alkyl

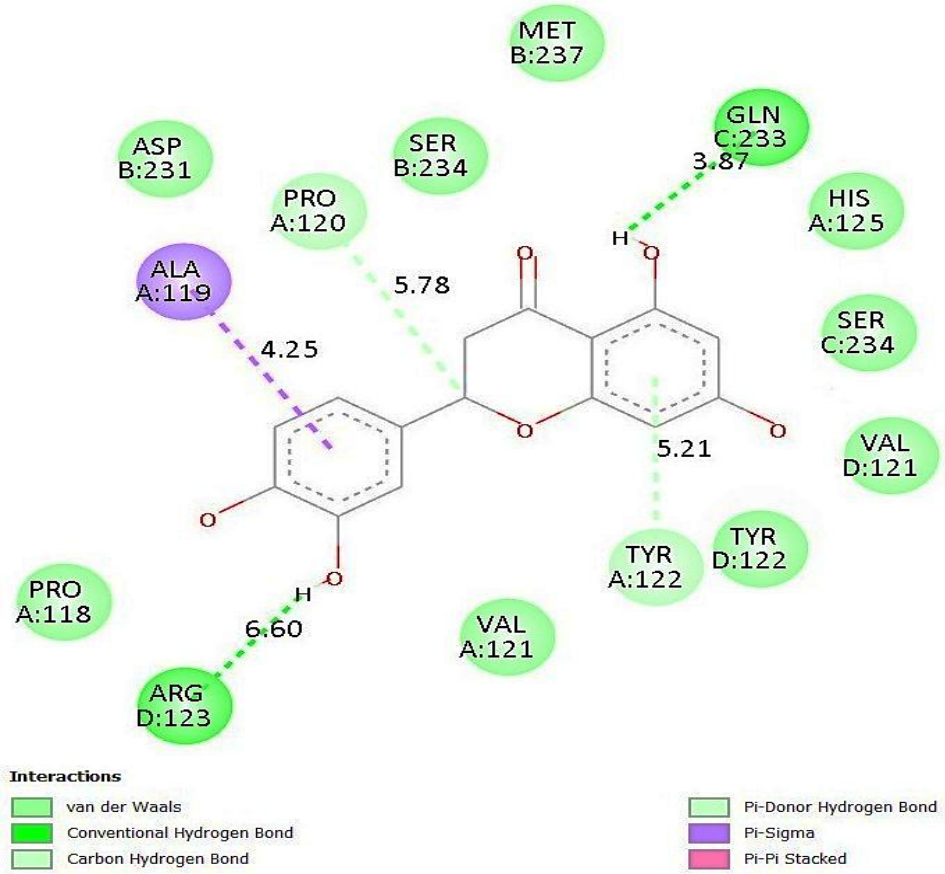
D11


GLN
B:233
GLN
C:233
ASP
B:231
SER
B:234
4.74
MET
C:237
ALA
A:119
GLU
C:197
ARG
C:196
4.00
VAL
A:121
5.83
TYR
D:122
ARG
D:123
Interactions
van der Waals
Conventional Hydrogen Bond

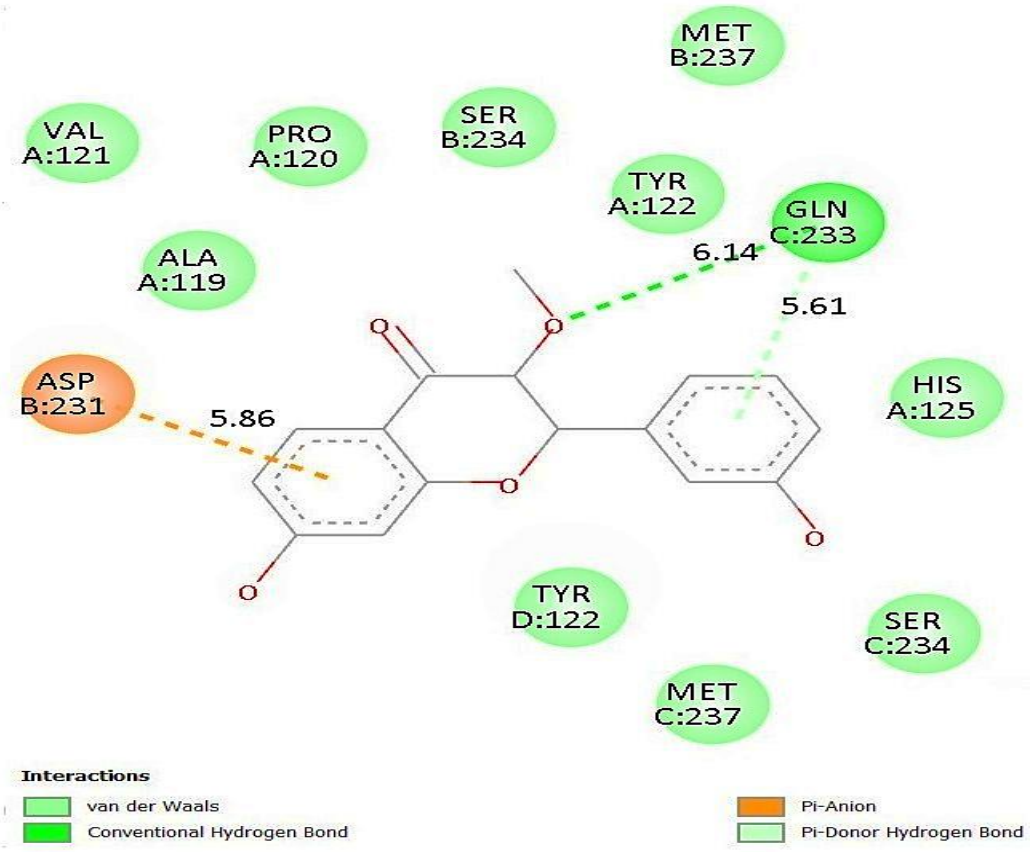
D12


PRO
A:117
PRO
A:120
ALA
A:116
TYR
A:122
ALA
A:119
PRO
A:118
VAL
A:121
4.36
SER
B:234
GLN
B:229
5.67
5.77
GLN
C:233
4.41
5.20
ASP
B:231
ARG
D:123
MET
C:237
TYR
D:122
Interactions
van der Waals
Conventional Hydrogen Bond
Alkyl
Pi-Alkyl

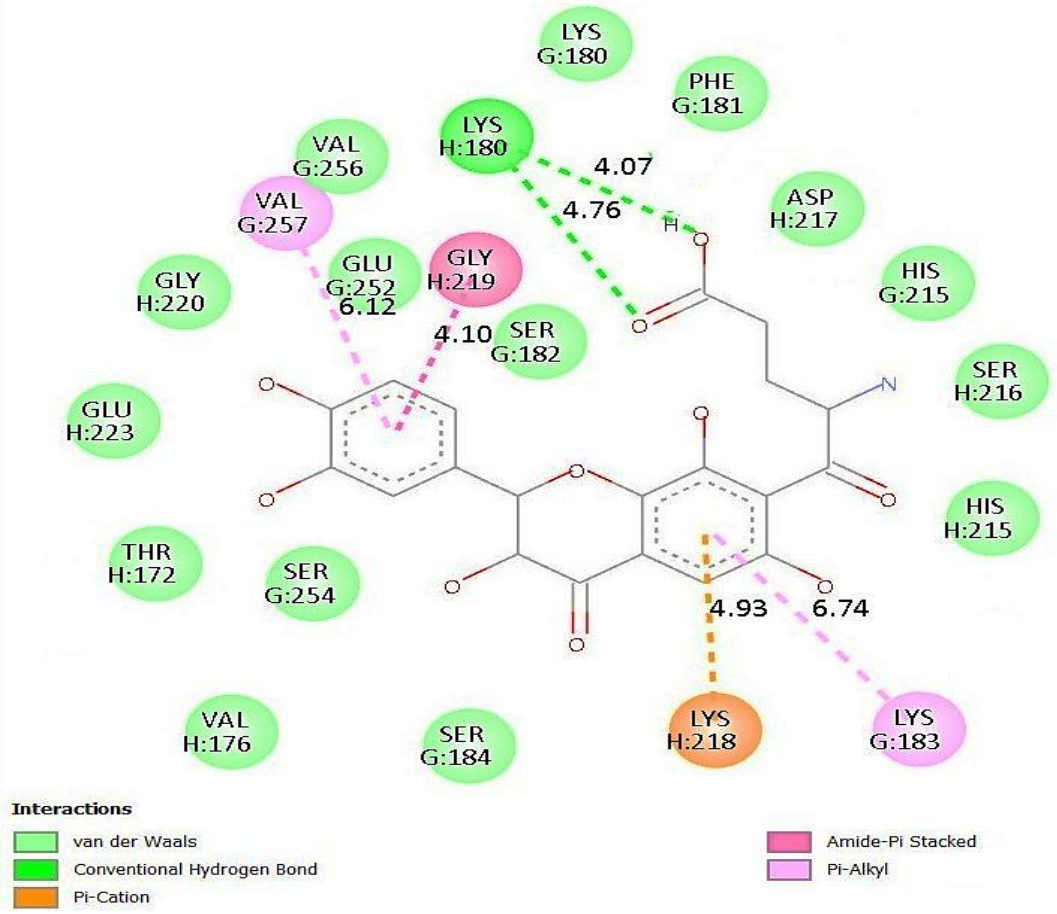
D13


MET
B:237
GLN
C:233
3.87
ASP
B:231
SER
B:234
PRO
A:120
HIS
A:125
ALA
A:119
5.78
4.25
SER
C:234
5.21
VAL
D:121
TYR
A:122
TYR
D:122
PRO
A:118
6.60
VAL
A:121
ARG
D:123
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Pi-Donor Hydrogen Bond
Pi-Sigma
Pi-Pi Stacked

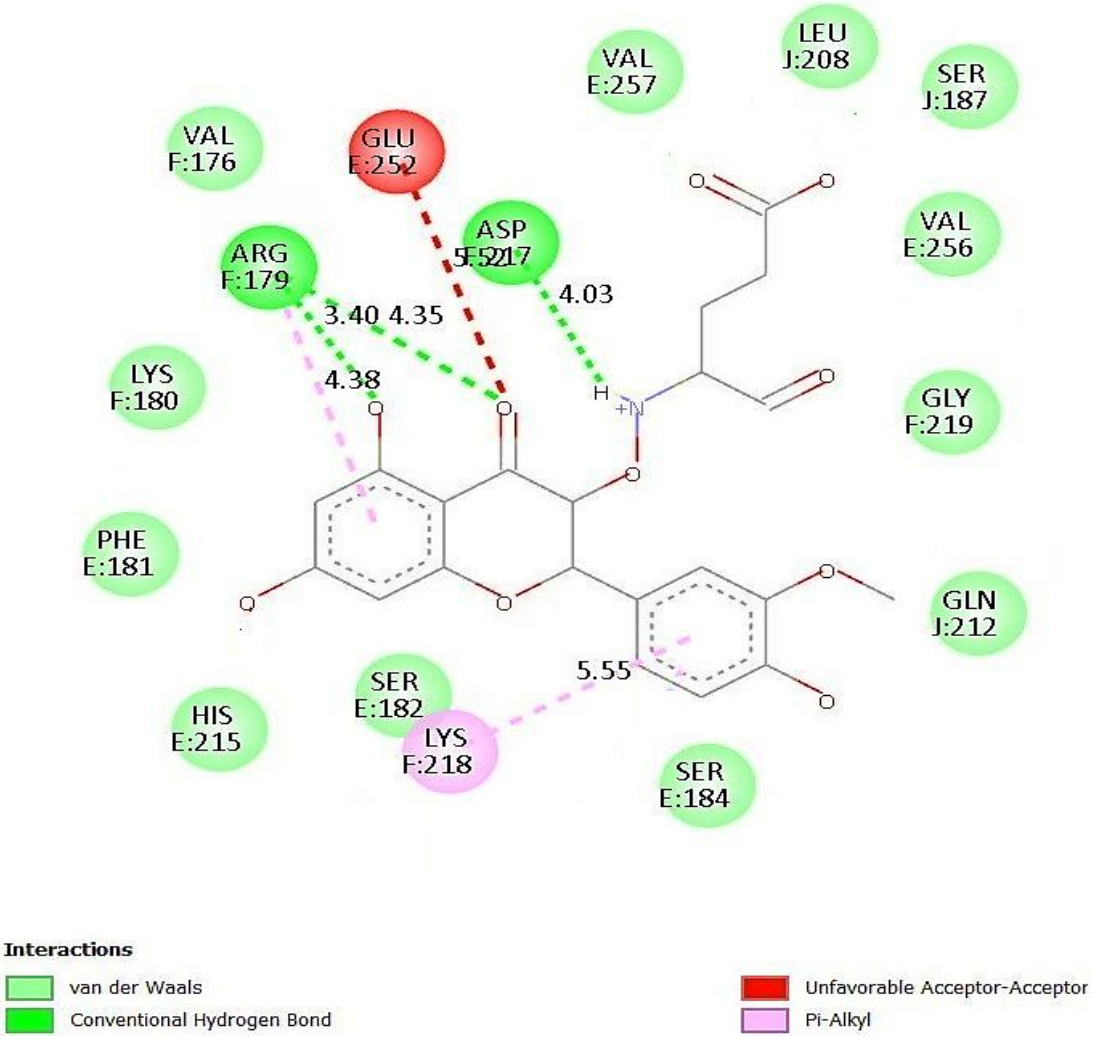
D14


MET
B:237
VAL
A:121
PRO
A:120
SER
B:234
TYR
A:122
GLN
C:233
6.14
ALA
A:119
5.61
ASP
B:231
5.86
HIS
A:125
TYR
D:122
SER
C:234
MET
C:237
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Anion
Pi-Donor Hydrogen Bond

D15


LYS G:180
PHE G:181
LYS H:180
4.07
4.76
VAL G:256
VAL G:257
ASP H:217
HIS G:215
GLY H:220
GLU G:252
6.12
GLY H:219
4.10
SER G:182
SER H:216
GLU H:223
HIS H:215
THR H:172
SER G:254
4.93
6.74
VAL H:176
SER G:184
LYS H:218
LYS G:183
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Cation
Amide-Pi Stacked
Pi-Alkyl

D16



D17

Figure S1. Docking interaction profiles in two dimensions of quercetin derivatives (D1-D17) at the active site of the Ebola virus (EBOV) VP30 protein. The docking interaction profiles give an overview of the orientations and binding modes of the derivatives at the active site, showing interactions between the ligands and the amino acid residues, such as hydrogen bonds, hydrophobic interactions, and aromatic interactions.