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Supplementary Materials

A Comprehensive Approach to Derivatization: Elemental Composition, Biochemical, and In Silico Studies of Metformin Derivatives Containing Copper and Zinc Complexes

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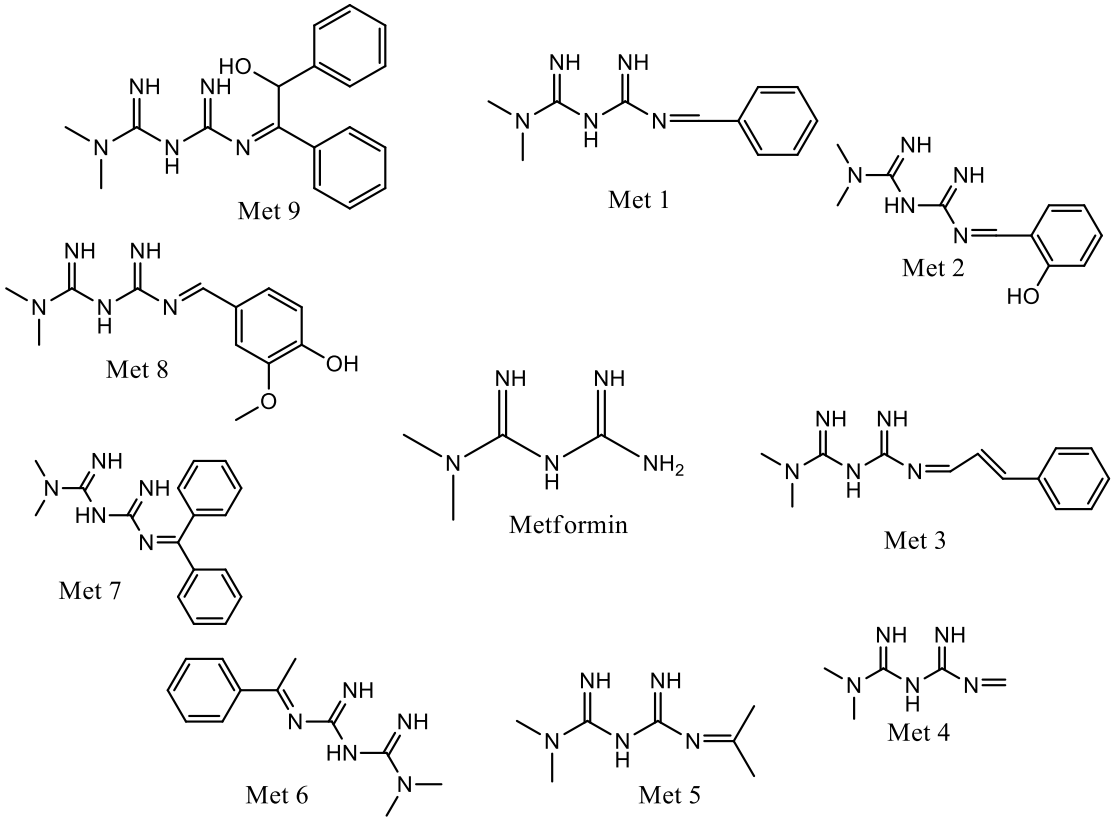
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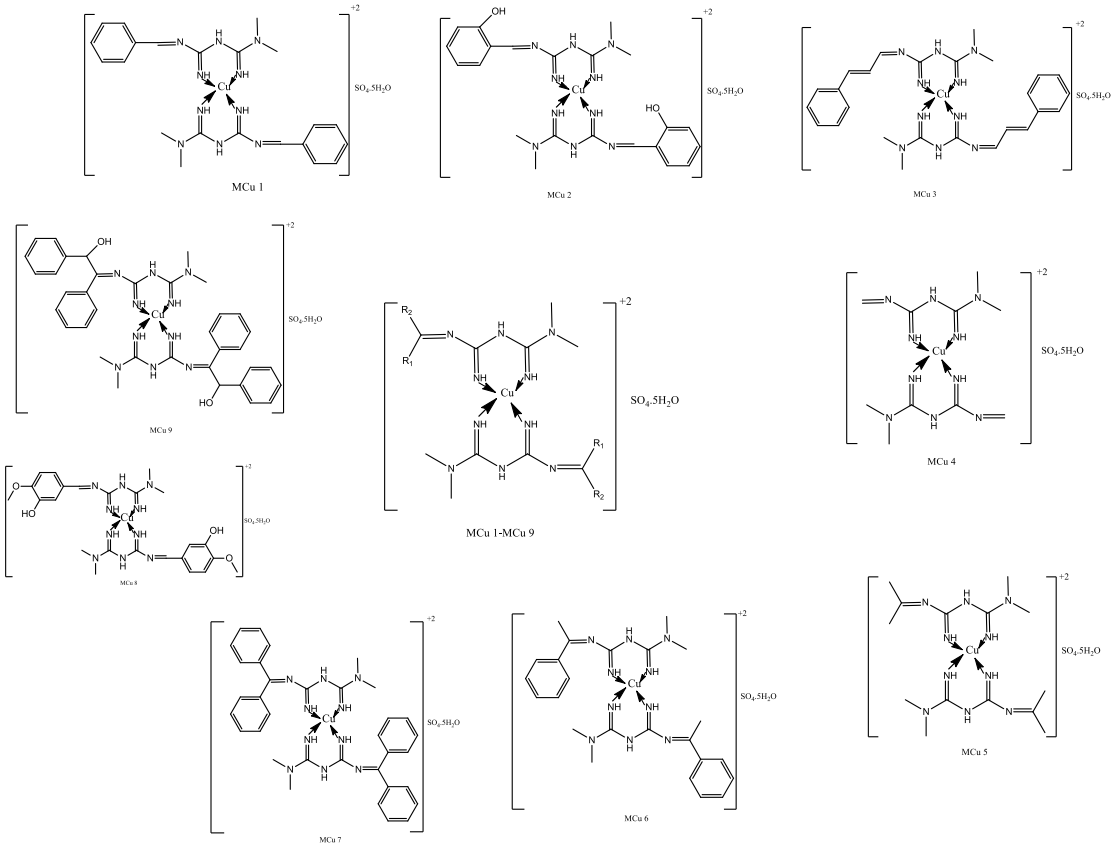
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Abstract: The current study was designed to synthesis, characterize, and screen molecular and biological activities of different metformin derivatives that possess potent anti-diabetic potential with minimal side effects. Copper II (MCu1 – Mcu9) and Zinc II (MZn1 – MZn9) metal complexes of metformin base derivatives were synthesized by aromatic aldehydes and ketones through template reaction. The novel metal complexes were characterized through elemental analysis, physical state, melting point, physical appearance, Fourier transform infrared (FTIR) spectroscopy, UV-Visible (UV-Vis) spectroscopy, 1H Nuclear Magnetic Resonance (NMR) spectroscopy, 13C NMR spectroscopy. Biological activities of the synthesized derivatives were evaluated through α-amylase and α-glucosidase enzyme inhibitory screening as well as further confirmation by molecular simulation studies through Schrödinger. Enzyme inhibition assay (α-amylase & α-glucosidase) revealed that MET1, MET2, MET3, and MET8 showed comparable activities with the standard. Molecular simulation studies supported the results of the enzyme inhibition assay and showed a competitive docking score with the standard. The ADME properties of metformin derivatives were calculated by using Swiss ADME online web server. All derivatives follow Lipinski rule of five and the percentage of absorption can be calculated. The results of the present study suggested that metformin derivatives presented significant antidiabetic properties against both targeted enzymes and could serve as lead molecules for further research and development.

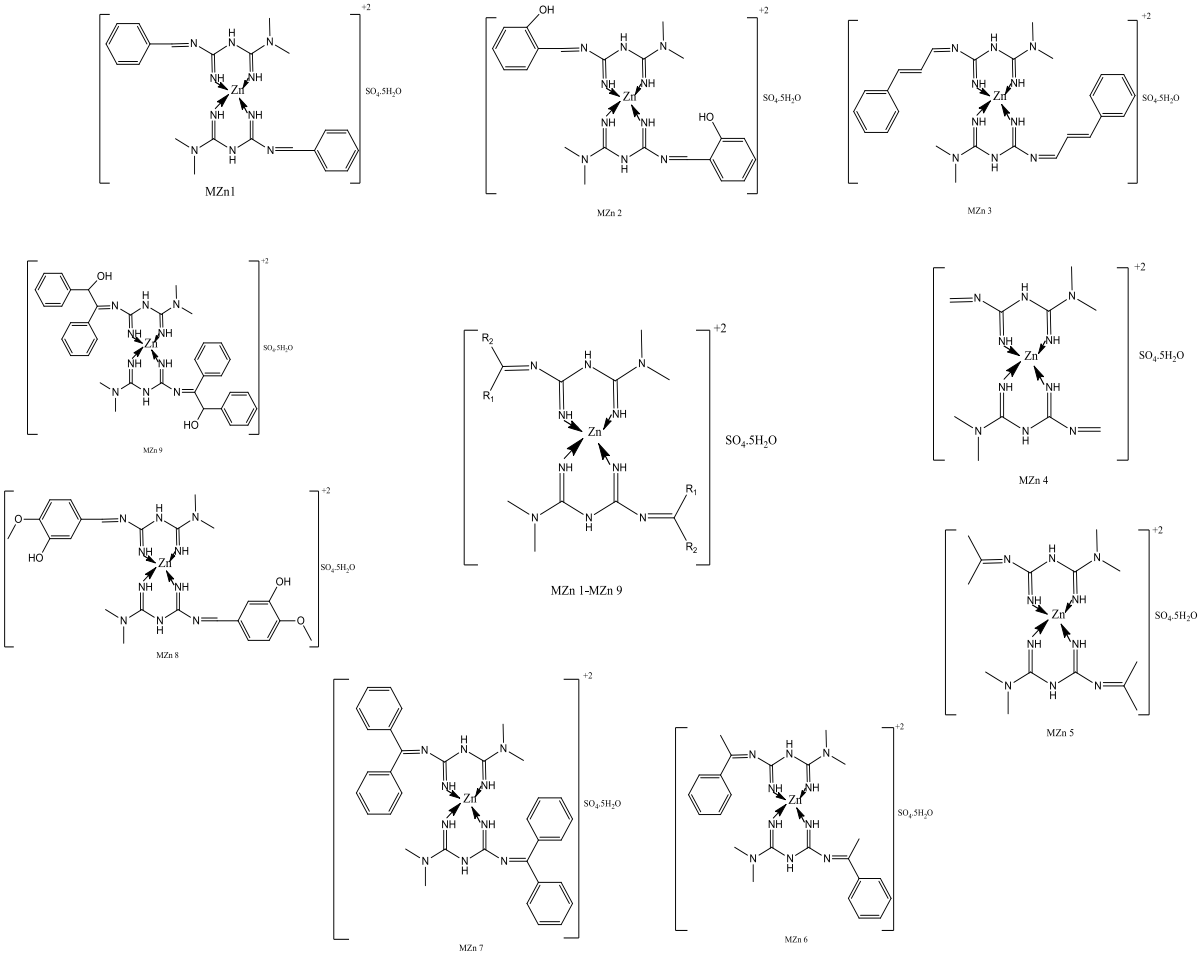
Keywords: Copper; Zinc; Metformin; FTIR; UV; NMR; Enzyme Inhibition Assay; Amylase; Glucosidase; Molecular Simulation; and Docking



Scheme S1. Characterization of (Met1 - Met9).

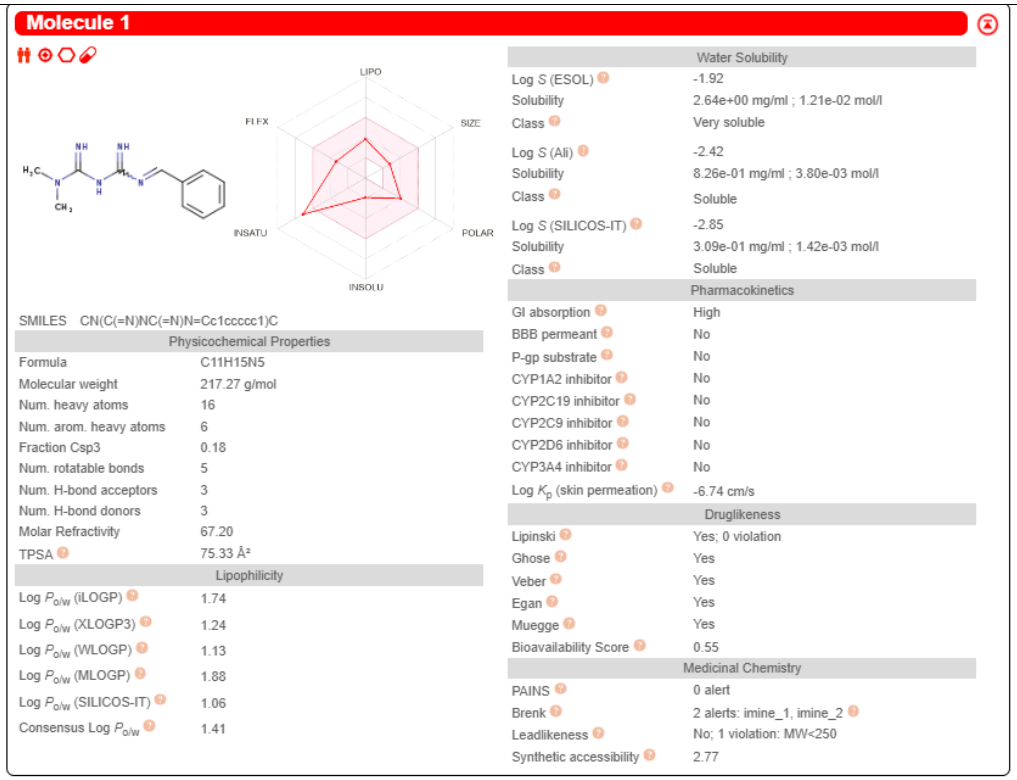
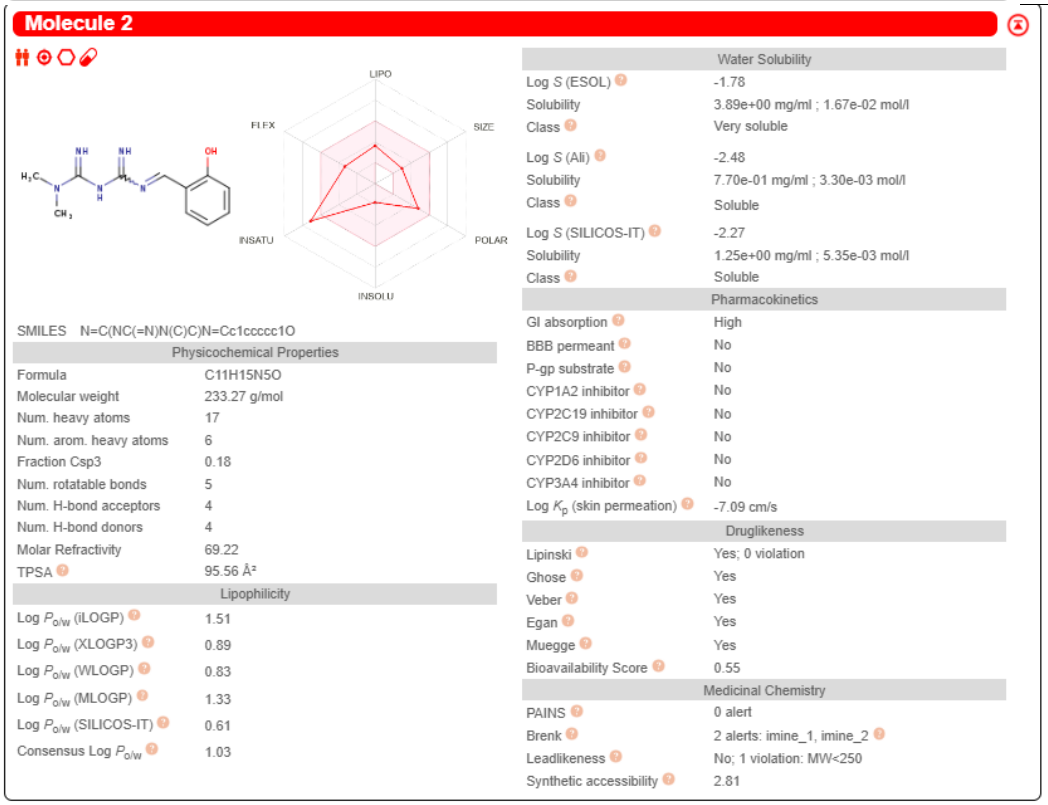


Scheme S2. Characterization of MCu1-MCu9.



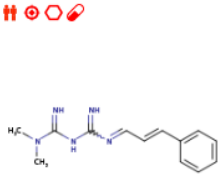
Scheme S3. Characterization of MZn1-MZn9.

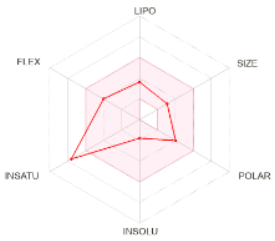
Table S1. ADME predictions of Metformin metabolites and metal complexes.

Derivative code	3D Pose
MET-1	
MET-2	

MET-3

Molecule 3





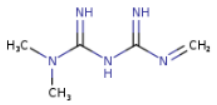
SMILES CN(C(=N)NC(=N)/N=C\C=C\c1ccccc1)C

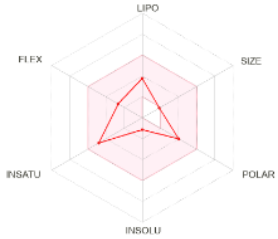
Physicochemical Properties	
Formula	C13H17N5
Molecular weight	243.31 g/mol
Num. heavy atoms	18
Num. arom. heavy atoms	6
Fraction Csp3	0.15
Num. rotatable bonds	6
Num. H-bond acceptors	3
Num. H-bond donors	3
Molar Refractivity	77.13
TPSA	75.33 Å²
Lipophilicity	
Log $P_{o/w}$ (iLOGP)	1.51
Log $P_{o/w}$ (XLOGP3)	0.89
Log $P_{o/w}$ (WLOGP)	1.68
Log $P_{o/w}$ (MLOGP)	1.33
Log $P_{o/w}$ (SILICOS-IT)	0.61
Consensus Log $P_{o/w}$	1.03

Water Solubility	
Log *S* (ESOL)	-1.78
Solubility	3.89e+00 mg/ml ; 1.67e-02 mol/l
Class	Very soluble
Log *S* (Ali)	-2.48
Solubility	7.70e-01 mg/ml ; 3.30e-03 mol/l
Class	Soluble
Log *S* (SILICOS-IT)	-2.27
Solubility	1.25e+00 mg/ml ; 5.35e-03 mol/l
Class	Soluble
Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-7.09 cm/s
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55
Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: imine_1, imine_2
Leadlikeness	No; 1 violation: MW<250
Synthetic accessibility	2.81

MET-4

Molecule 4





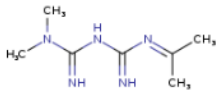
SMILES C=NC(=N)NC(=N)N(C)C

Physicochemical Properties	
Formula	C5H11N5
Molecular weight	141.17 g/mol
Num. heavy atoms	10
Num. arom. heavy atoms	0
Fraction Csp3	0.40
Num. rotatable bonds	4
Num. H-bond acceptors	3
Num. H-bond donors	3
Molar Refractivity	42.71
TPSA	75.33 Å²
Lipophilicity	
Log $P_{o/w}$ (iLOGP)	0.06
Log $P_{o/w}$ (XLOGP3)	1.10
Log $P_{o/w}$ (WLOGP)	-0.29
Log $P_{o/w}$ (MLOGP)	0.16
Log $P_{o/w}$ (SILICOS-IT)	-0.52
Consensus Log $P_{o/w}$	0.10

Water Solubility	
Log *S* (ESOL)	-1.14
Solubility	1.01e+01 mg/ml ; 7.17e-02 mol/l
Class	Very soluble
Log *S* (Ali)	-2.27
Solubility	7.50e-01 mg/ml ; 5.31e-03 mol/l
Class	Soluble
Log *S* (SILICOS-IT)	-0.65
Solubility	3.14e+01 mg/ml ; 2.22e-01 mol/l
Class	Soluble
Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-6.38 cm/s
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	No; 1 violation: MW<160
Veber	Yes
Egan	Yes
Muegge	No; 1 violation: MW<200
Bioavailability Score	0.55
Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: imine_1, imine_2
Leadlikeness	No; 1 violation: MW<250
Synthetic accessibility	3.41

MET-5

Molecule 5



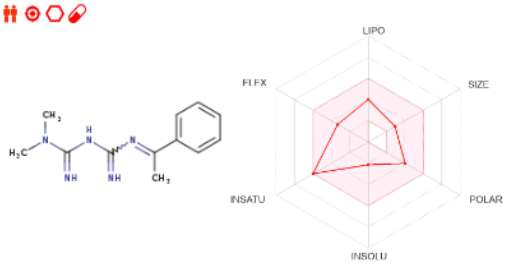
SMILES CC(=NC(=N)NC(=N)N(C)C)C

Physicochemical Properties	
Formula	C7H15N5
Molecular weight	169.23 g/mol
Num. heavy atoms	12
Num. arom. heavy atoms	0
Fraction Csp3	0.57
Num. rotatable bonds	4
Num. H-bond acceptors	3
Num. H-bond donors	3
Molar Refractivity	52.33
TPSA	75.33 Å²
Lipophilicity	
Log $P_{o/w}$ (iLOGP)	1.58
Log $P_{o/w}$ (XLOGP3)	-0.19
Log $P_{o/w}$ (WLOGP)	0.49
Log $P_{o/w}$ (MLOGP)	0.89
Log $P_{o/w}$ (SILICOS-IT)	-0.11
Consensus Log $P_{o/w}$	0.53

Water Solubility	
Log *S* (ESOL)	-0.51
Solubility	5.28e+01 mg/ml ; 3.12e-01 mol/l
Class	Very soluble
Log *S* (Ali)	-0.94
Solubility	1.96e+01 mg/ml ; 1.16e-01 mol/l
Class	Very soluble
Log *S* (SILICOS-IT)	-1.09
Solubility	1.37e+01 mg/ml ; 8.11e-02 mol/l
Class	Soluble
Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-7.47 cm/s
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	No; 1 violation: MW<200
Bioavailability Score	0.55
Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: imine_1, imine_2
Leadlikeness	No; 1 violation: MW<250
Synthetic accessibility	3.19

MET-6

Molecule 6



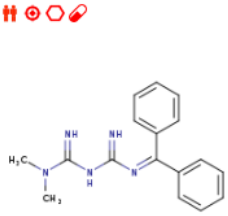
SMILES N=C(/N=C(/c1ccccc1)\C)NC(=N)N(C)C

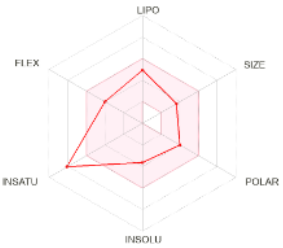
Physicochemical Properties	
Formula	C12H17N5
Molecular weight	231.30 g/mol
Num. heavy atoms	17
Num. arom. heavy atoms	6
Fraction Csp3	0.25
Num. rotatable bonds	5
Num. H-bond acceptors	3
Num. H-bond donors	3
Molar Refractivity	72.01
TPSA	75.33 Å²
Lipophilicity	
Log $P_{o/w}$ (iLOGP)	1.88
Log $P_{o/w}$ (XLOGP3)	1.47
Log $P_{o/w}$ (WLOGP)	1.52
Log $P_{o/w}$ (MLOGP)	2.16
Log $P_{o/w}$ (SILICOS-IT)	1.29
Consensus Log $P_{o/w}$	1.66

Water Solubility	
Log *S* (ESOL)	-2.13
Solubility	1.71e+00 mg/ml ; 7.39e-03 mol/l
Class	Soluble
Log *S* (Ali)	-2.66
Solubility	5.08e-01 mg/ml ; 2.20e-03 mol/l
Class	Soluble
Log *S* (SILICOS-IT)	-3.23
Solubility	1.35e-01 mg/ml ; 5.83e-04 mol/l
Class	Soluble
Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-6.67 cm/s
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55
Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: imine_1, imine_2
Leadlikeness	No; 1 violation: MW<250
Synthetic accessibility	2.74

MET-7

Molecule 7





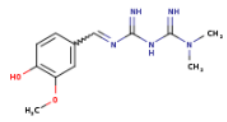
SMILES N=C(N=C(c1ccccc1)c1ccccc1)NC(=N)N(C)C

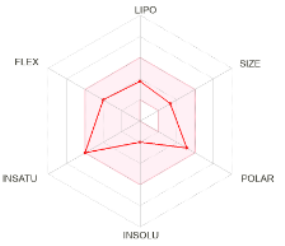
Physicochemical Properties	
Formula	C17H19N5
Molecular weight	293.37 g/mol
Num. heavy atoms	22
Num. arom. heavy atoms	12
Fraction Csp3	0.12
Num. rotatable bonds	6
Num. H-bond acceptors	3
Num. H-bond donors	3
Molar Refractivity	91.69
TPSA	75.33 Å²
Lipophilicity	
Log $P_{o/w}$ (iLOGP)	2.36
Log $P_{o/w}$ (XLOGP3)	3.12
Log $P_{o/w}$ (WLOGP)	2.54
Log $P_{o/w}$ (MLOGP)	3.21
Log $P_{o/w}$ (SILICOS-IT)	2.51
Consensus Log $P_{o/w}$	2.75

Water Solubility	
Log *S* (ESOL)	-3.63
Solubility	6.84e-02 mg/ml ; 2.33e-04 mol/l
Class	Soluble
Log *S* (Ali)	-4.37
Solubility	1.25e-02 mg/ml ; 4.26e-05 mol/l
Class	Moderately soluble
Log *S* (SILICOS-IT)	-5.35
Solubility	1.31e-03 mg/ml ; 4.48e-06 mol/l
Class	Moderately soluble
Pharmacokinetics	
GI absorption	High
BBB permeant	Yes
P-gp substrate	No
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-5.87 cm/s
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55
Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: imine_1, imine_2
Leadlikeness	Yes
Synthetic accessibility	3.08

MET-8

Molecule 8





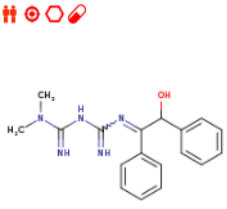
SMILES COc1cc(/C=N/C(=N)NC(=N)N(C)C)ccc1O

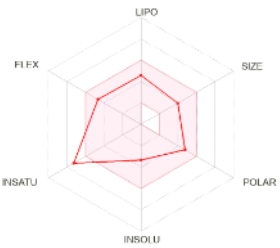
Physicochemical Properties	
Formula	C12H17N5O2
Molecular weight	263.30 g/mol
Num. heavy atoms	19
Num. arom. heavy atoms	6
Fraction Csp3	0.25
Num. rotatable bonds	6
Num. H-bond acceptors	5
Num. H-bond donors	4
Molar Refractivity	75.72
TPSA	104.79 Å²
Lipophilicity	
Log $P_{o/w}$ (iLOGP)	2.03
Log $P_{o/w}$ (XLOGP3)	1.07
Log $P_{o/w}$ (WLOGP)	0.84
Log $P_{o/w}$ (MLOGP)	1.08
Log $P_{o/w}$ (SILICOS-IT)	0.70
Consensus Log $P_{o/w}$	1.14

Water Solubility	
Log *S* (ESOL)	-1.98
Solubility	2.73e+00 mg/ml ; 1.04e-02 mol/l
Class	Very soluble
Log *S* (Ali)	-2.86
Solubility	3.62e-01 mg/ml ; 1.37e-03 mol/l
Class	Soluble
Log *S* (SILICOS-IT)	-2.40
Solubility	1.06e+00 mg/ml ; 4.03e-03 mol/l
Class	Soluble
Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-7.15 cm/s
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55
Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: imine_1, imine_2
Leadlikeness	Yes
Synthetic accessibility	2.81

MET-9

Molecule 9





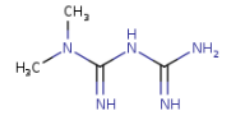
SMILES N=C(/N=C(\C(c1ccccc1)O)/c1ccccc1)NC(=N)N(C)C

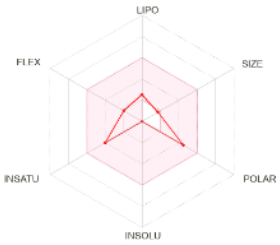
Physicochemical Properties	
Formula	C18H21N5O
Molecular weight	323.39 g/mol
Num. heavy atoms	24
Num. arom. heavy atoms	12
Fraction Csp3	0.17
Num. rotatable bonds	7
Num. H-bond acceptors	4
Num. H-bond donors	4
Molar Refractivity	97.66
TPSA	95.56 Å²
Lipophilicity	
Log $P_{o/w}$ (iLOGP)	2.10
Log $P_{o/w}$ (XLOGP3)	2.51
Log $P_{o/w}$ (WLOGP)	1.91
Log $P_{o/w}$ (MLOGP)	2.63
Log $P_{o/w}$ (SILICOS-IT)	2.13
Consensus Log $P_{o/w}$	2.26

Water Solubility	
Log *S* (ESOL)	-3.33
Solubility	1.50e-01 mg/ml ; 4.63e-04 mol/l
Class	Soluble
Log *S* (Ali)	-4.16
Solubility	2.22e-02 mg/ml ; 6.88e-05 mol/l
Class	Moderately soluble
Log *S* (SILICOS-IT)	-4.81
Solubility	5.04e-03 mg/ml ; 1.56e-05 mol/l
Class	Moderately soluble
Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-6.49 cm/s
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55
Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: imine_1, imine_2
Leadlikeness	Yes
Synthetic accessibility	3.76

MET

Molecule 10



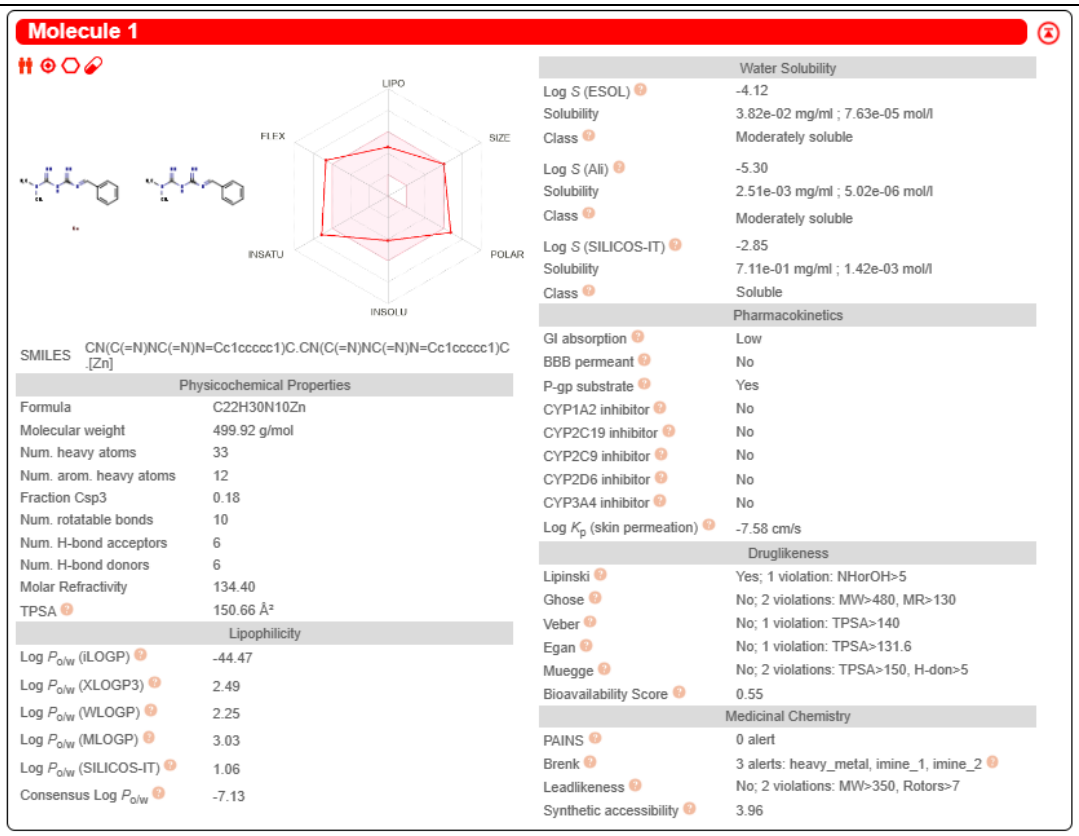


SMILES CN(C(=N)NC(=N)N)C

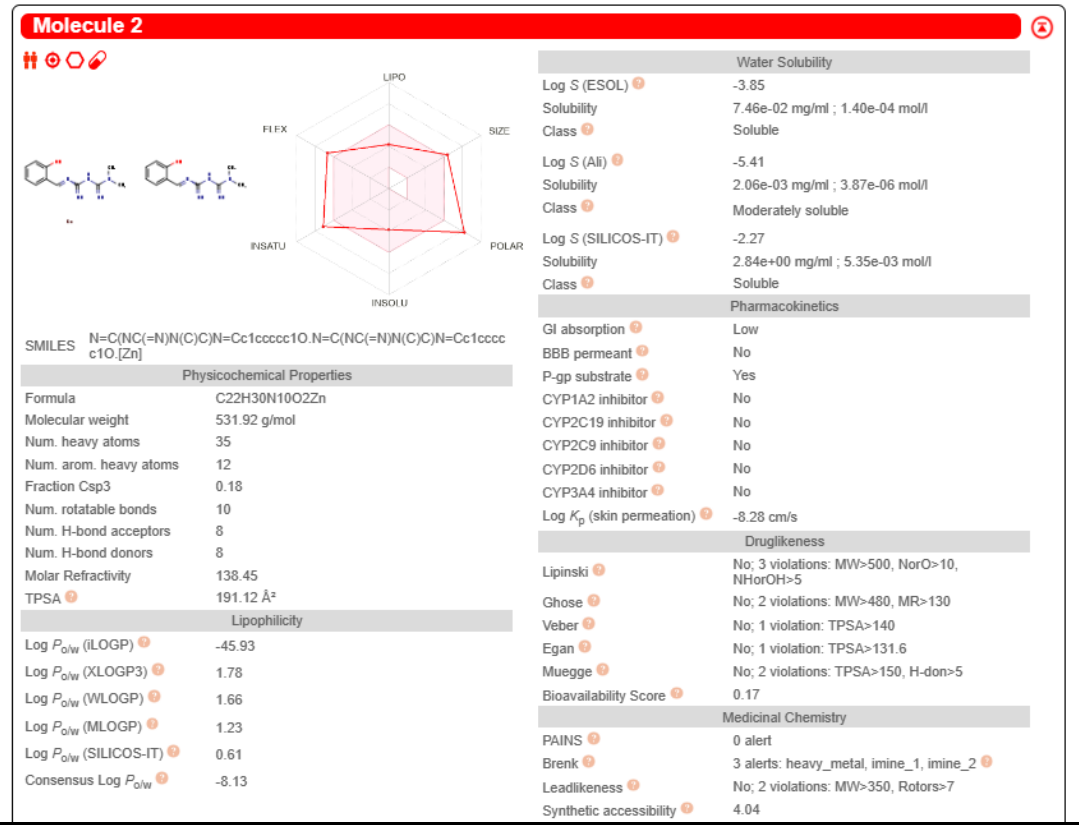
Physicochemical Properties	
Formula	C4H11N5
Molecular weight	129.16 g/mol
Num. heavy atoms	9
Num. arom. heavy atoms	0
Fraction Csp3	0.50
Num. rotatable bonds	3
Num. H-bond acceptors	2
Num. H-bond donors	4
Molar Refractivity	36.93
TPSA	88.99 Å²
Lipophilicity	
Log $P_{o/w}$ (iLOGP)	0.77
Log $P_{o/w}$ (XLOGP3)	-1.06
Log $P_{o/w}$ (WLOGP)	-1.03
Log $P_{o/w}$ (MLOGP)	-0.56
Log $P_{o/w}$ (SILICOS-IT)	-1.85
Consensus Log $P_{o/w}$	-0.75

Water Solubility	
Log *S* (ESOL)	0.22
Solubility	2.17e+02 mg/ml ; 1.68e+00 mol/l
Class	Highly soluble
Log *S* (Ali)	-0.32
Solubility	6.18e+01 mg/ml ; 4.79e-01 mol/l
Class	Very soluble
Log *S* (SILICOS-IT)	0.17
Solubility	1.90e+02 mg/ml ; 1.47e+00 mol/l
Class	Soluble
Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-7.84 cm/s
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	No; 3 violations: MW<160, WLOGP<-0.4, MR<40
Veber	Yes
Egan	Yes
Muegge	No; 2 violations: MW<200, #C<5
Bioavailability Score	0.55
Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: imine_1, imine_2
Leadlikeness	No; 1 violation: MW<250
Synthetic accessibility	3.11

MZN-1

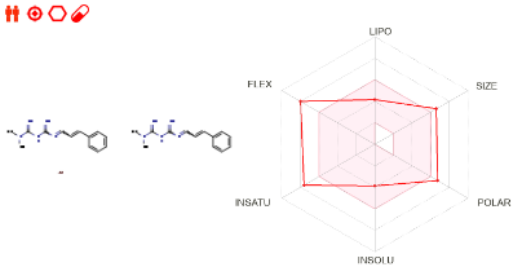

Molecule 1
LIPO
SIZE
POLAR
INSOLU
INSATU
FLEX
SMILES CN(C(=N)NC(=N)N=Cc1ccccc1)C.CN(C(=N)NC(=N)N=Cc1ccccc1)C.[Zn]
Physicochemical Properties
Formula C22H30N10Zn
Molecular weight 499.92 g/mol
Num. heavy atoms 33
Num. arom. heavy atoms 12
Fraction Csp3 0.18
Num. rotatable bonds 10
Num. H-bond acceptors 6
Num. H-bond donors 6
Molar Refractivity 134.40
TPSA 150.66 Å²
Lipophilicity
Log Po/w (iLOGP) -44.47
Log Po/w (XLOGP3) 2.49
Log Po/w (WLOGP) 2.25
Log Po/w (MLOGP) 3.03
Log Po/w (SILICOS-IT) 1.06
Consensus Log Po/w -7.13
Water Solubility
Log S (ESOL) -4.12
Solubility 3.82e-02 mg/ml ; 7.63e-05 mol/l
Class Moderately soluble
Log S (Ali) -5.30
Solubility 2.51e-03 mg/ml ; 5.02e-06 mol/l
Class Moderately soluble
Log S (SILICOS-IT) -2.85
Solubility 7.11e-01 mg/ml ; 1.42e-03 mol/l
Class Soluble
Pharmacokinetics
GI absorption Low
BBB permeant No
P-gp substrate Yes
CYP1A2 inhibitor No
CYP2C19 inhibitor No
CYP2C9 inhibitor No
CYP2D6 inhibitor No
CYP3A4 inhibitor No
Log Kp (skin permeation) -7.58 cm/s
Druglikeness
Lipinski Yes; 1 violation: NHorOH>5
Ghose No; 2 violations: MW>480, MR>130
Veber No; 1 violation: TPSA>140
Egan No; 1 violation: TPSA>131.6
Muegge No; 2 violations: TPSA>150, H-don>5
Bioavailability Score 0.55
Medicinal Chemistry
PAINS 0 alert
Brenk 3 alerts: heavy_metal, imine_1, imine_2
Leadlikeness No; 2 violations: MW>350, Rotors>7
Synthetic accessibility 3.96

MZN-2


Molecule 2
LIPO
SIZE
POLAR
INSOLU
INSATU
FLEX
SMILES N=C(NC(=N)N(C)C)N=Cc1ccccc1O.N=C(NC(=N)N(C)C)N=Cc1ccccc1O.[Zn]
Physicochemical Properties
Formula C22H30N10O2Zn
Molecular weight 531.92 g/mol
Num. heavy atoms 35
Num. arom. heavy atoms 12
Fraction Csp3 0.18
Num. rotatable bonds 10
Num. H-bond acceptors 8
Num. H-bond donors 8
Molar Refractivity 138.45
TPSA 191.12 Å²
Lipophilicity
Log Po/w (iLOGP) -45.93
Log Po/w (XLOGP3) 1.78
Log Po/w (WLOGP) 1.66
Log Po/w (MLOGP) 1.23
Log Po/w (SILICOS-IT) 0.61
Consensus Log Po/w -8.13
Water Solubility
Log S (ESOL) -3.85
Solubility 7.46e-02 mg/ml ; 1.40e-04 mol/l
Class Soluble
Log S (Ali) -5.41
Solubility 2.06e-03 mg/ml ; 3.87e-06 mol/l
Class Moderately soluble
Log S (SILICOS-IT) -2.27
Solubility 2.84e+00 mg/ml ; 5.35e-03 mol/l
Class Soluble
Pharmacokinetics
GI absorption Low
BBB permeant No
P-gp substrate Yes
CYP1A2 inhibitor No
CYP2C19 inhibitor No
CYP2C9 inhibitor No
CYP2D6 inhibitor No
CYP3A4 inhibitor No
Log Kp (skin permeation) -8.28 cm/s
Druglikeness
Lipinski No; 3 violations: MW>500, NorO>10, NHorOH>5
Ghose No; 2 violations: MW>480, MR>130
Veber No; 1 violation: TPSA>140
Egan No; 1 violation: TPSA>131.6
Muegge No; 2 violations: TPSA>150, H-don>5
Bioavailability Score 0.17
Medicinal Chemistry
PAINS 0 alert
Brenk 3 alerts: heavy_metal, imine_1, imine_2
Leadlikeness No; 2 violations: MW>350, Rotors>7
Synthetic accessibility 4.04

MZN-3

Molecule 3



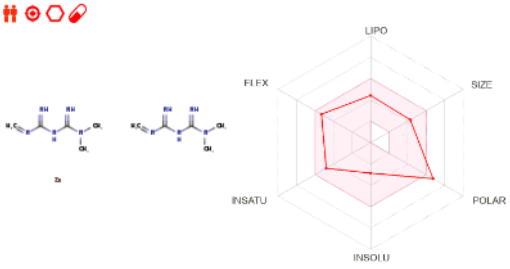
SMILES CN(C(=N)NC(=N)/N=C\C=C\c1ccccc1)C.CN(C(=N)NC(=N)/N=C\C=C\c1ccccc1)C.[Zn]

Physicochemical Properties	
Formula	C26H34N10Zn
Molecular weight	552.00 g/mol
Num. heavy atoms	37
Num. arom. heavy atoms	12
Fraction Csp3	0.15
Num. rotatable bonds	12
Num. H-bond acceptors	6
Num. H-bond donors	6
Molar Refractivity	154.26
TPSA	150.66 Å²
Lipophilicity	
Log $P_{o/w}$ (iLOGP)	-45.93
Log $P_{o/w}$ (XLOGP3)	1.78
Log $P_{o/w}$ (WLOGP)	3.36
Log $P_{o/w}$ (MLOGP)	1.23
Log $P_{o/w}$ (SILICOS-IT)	0.61
Consensus Log $P_{o/w}$	-8.13

Water Solubility	
Log *S* (ESOL)	-3.85
Solubility	7.46e-02 mg/ml ; 1.40e-04 mol/l
Class	Soluble
Log *S* (Ali)	-5.41
Solubility	2.06e-03 mg/ml ; 3.87e-06 mol/l
Class	Moderately soluble
Log *S* (SILICOS-IT)	-2.27
Solubility	2.84e+00 mg/ml ; 5.35e-03 mol/l
Class	Soluble
Pharmacokinetics	
GI absorption	Low
BBB permeant	No
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-8.28 cm/s
Druglikeness	
Lipinski	No; 3 violations: MW>500, NorO>10, NHorOH>5
Ghose	No; 2 violations: MW>480, MR>130
Veber	No; 1 violation: TPSA>140
Egan	No; 1 violation: TPSA>131.6
Muegge	No; 2 violations: TPSA>150, H-don>5
Bioavailability Score	0.17
Medicinal Chemistry	
PAINS	0 alert
Brenk	3 alerts: heavy_metal, imine_1, imine_2
Leadlikeness	No; 2 violations: MW>350, Rotors>7
Synthetic accessibility	4.04

MZN-4

Molecule 4



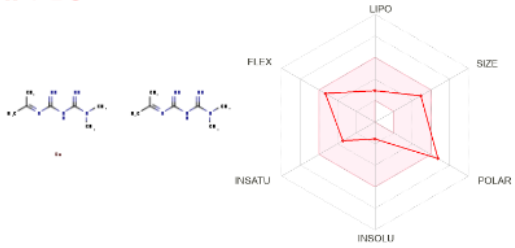
SMILES C=NC(=N)NC(=N)N(C)C.C=NC(=N)NC(=N)N(C)C.[Zn]

Physicochemical Properties	
Formula	C10H22N10Zn
Molecular weight	347.73 g/mol
Num. heavy atoms	21
Num. arom. heavy atoms	0
Fraction Csp3	0.40
Num. rotatable bonds	8
Num. H-bond acceptors	6
Num. H-bond donors	6
Molar Refractivity	85.43
TPSA	150.66 Å²
Lipophilicity	
Log $P_{o/w}$ (iLOGP)	-47.13
Log $P_{o/w}$ (XLOGP3)	2.21
Log $P_{o/w}$ (WLOGP)	-0.59
Log $P_{o/w}$ (MLOGP)	0.48
Log $P_{o/w}$ (SILICOS-IT)	-0.52
Consensus Log $P_{o/w}$	-9.11

Water Solubility	
Log *S* (ESOL)	-2.86
Solubility	4.80e-01 mg/ml ; 1.38e-03 mol/l
Class	Soluble
Log *S* (Ali)	-5.01
Solubility	3.41e-03 mg/ml ; 9.81e-06 mol/l
Class	Moderately soluble
Log *S* (SILICOS-IT)	-0.65
Solubility	7.73e+01 mg/ml ; 2.22e-01 mol/l
Class	Soluble
Pharmacokinetics	
GI absorption	Low
BBB permeant	No
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-6.85 cm/s
Druglikeness	
Lipinski	Yes; 1 violation: NHorOH>5
Ghose	No; 1 violation: WLOGP<-0.4
Veber	No; 1 violation: TPSA>140
Egan	No; 1 violation: TPSA>131.6
Muegge	No; 2 violations: TPSA>150, H-don>5
Bioavailability Score	0.55
Medicinal Chemistry	
PAINS	0 alert
Brenk	3 alerts: heavy_metal, imine_1, imine_2
Leadlikeness	No; 1 violation: Rotors>7
Synthetic accessibility	4.14

MZN-5

Molecule 5



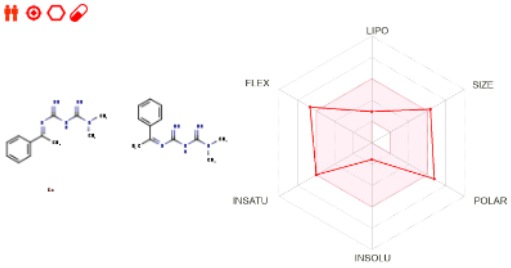
SMILES CC(=NC(=N)NC(=N)N(C)C)C.CC(=NC(=N)NC(=N)N(C)C)C.[Zn]

Physicochemical Properties	
Formula	C14H30N10Zn
Molecular weight	403.84 g/mol
Num. heavy atoms	25
Num. arom. heavy atoms	0
Fraction Csp3	0.57
Num. rotatable bonds	8
Num. H-bond acceptors	6
Num. H-bond donors	6
Molar Refractivity	104.65
TPSA	150.66 Å²
Lipophilicity	
Log $P_{o/w}$ (iLOGP)	-46.14
Log $P_{o/w}$ (XLOGP3)	-0.39
Log $P_{o/w}$ (WLOGP)	0.97
Log $P_{o/w}$ (MLOGP)	1.59
Log $P_{o/w}$ (SILICOS-IT)	-0.11
Consensus Log $P_{o/w}$	-8.82

Water Solubility	
Log *S* (ESOL)	-1.57
Solubility	1.09e+01 mg/ml ; 2.69e-02 mol/l
Class	Very soluble
Log *S* (Ali)	-2.31
Solubility	1.98e+00 mg/ml ; 4.89e-03 mol/l
Class	Soluble
Log *S* (SILICOS-IT)	-1.09
Solubility	3.27e+01 mg/ml ; 8.11e-02 mol/l
Class	Soluble
Pharmacokinetics	
GI absorption	Low
BBB permeant	No
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-9.04 cm/s
Druglikeness	
Lipinski	Yes; 1 violation: NHorOH>5
Ghose	Yes
Veber	No; 1 violation: TPSA>140
Egan	No; 1 violation: TPSA>131.6
Muegge	No; 2 violations: TPSA>150, H-don>5
Bioavailability Score	0.55
Medicinal Chemistry	
PAINS	0 alert
Brenk	3 alerts: heavy_metal, imine_1, imine_2
Leadlikeness	No; 2 violations: MW>350, Rotors>7
Synthetic accessibility	4.19

MZN-6

Molecule 6



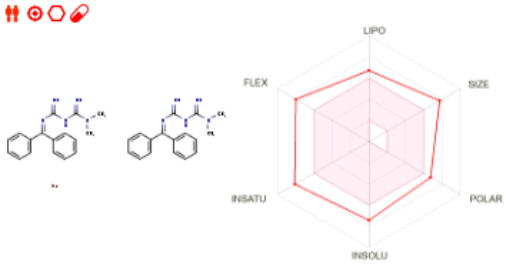
SMILES N=C(/N=C(/c1ccccc1)\C)NC(=N)N(C)C.N=C(/N=C(\c1ccccc1)/C)NC(=N)N(C)C.[Zn]

Physicochemical Properties	
Formula	C24H34N10Zn
Molecular weight	527.97 g/mol
Num. heavy atoms	35
Num. arom. heavy atoms	12
Fraction Csp3	0.25
Num. rotatable bonds	10
Num. H-bond acceptors	6
Num. H-bond donors	6
Molar Refractivity	144.01
TPSA	150.66 Å²
Lipophilicity	
Log $P_{o/w}$ (iLOGP)	-46.14
Log $P_{o/w}$ (XLOGP3)	-0.39
Log $P_{o/w}$ (WLOGP)	3.03
Log $P_{o/w}$ (MLOGP)	1.59
Log $P_{o/w}$ (SILICOS-IT)	-0.11
Consensus Log $P_{o/w}$	-8.82

Water Solubility	
Log *S* (ESOL)	-1.57
Solubility	1.09e+01 mg/ml ; 2.69e-02 mol/l
Class	Very soluble
Log *S* (Ali)	-2.31
Solubility	1.98e+00 mg/ml ; 4.89e-03 mol/l
Class	Soluble
Log *S* (SILICOS-IT)	-1.09
Solubility	3.27e+01 mg/ml ; 8.11e-02 mol/l
Class	Soluble
Pharmacokinetics	
GI absorption	Low
BBB permeant	No
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-9.04 cm/s
Druglikeness	
Lipinski	Yes; 1 violation: NHorOH>5
Ghose	Yes
Veber	No; 1 violation: TPSA>140
Egan	No; 1 violation: TPSA>131.6
Muegge	No; 2 violations: TPSA>150, H-don>5
Bioavailability Score	0.55
Medicinal Chemistry	
PAINS	0 alert
Brenk	3 alerts: heavy_metal, imine_1, imine_2
Leadlikeness	No; 2 violations: MW>350, Rotors>7
Synthetic accessibility	4.19

MZN-7

Molecule 7



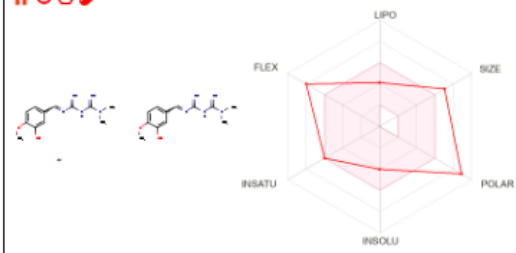
SMILES N=C(N=C(c1ccccc1)c1ccccc1)NC(=N)N(C)C.N=C(N=C(c1ccccc1)c1ccccc1)NC(=N)N(C)C.[Zn]

Physicochemical Properties	
Formula	C34H38N10Zn
Molecular weight	652.11 g/mol
Num. heavy atoms	45
Num. arom. heavy atoms	24
Fraction Csp3	0.12
Num. rotatable bonds	12
Num. H-bond acceptors	6
Num. H-bond donors	6
Molar Refractivity	183.37
TPSA	150.66 Å²
Lipophilicity	
Log $P_{o/w}$ (iLOGP)	-45.39
Log $P_{o/w}$ (XLOGP3)	6.25
Log $P_{o/w}$ (WLOGP)	5.09
Log $P_{o/w}$ (MLOGP)	4.99
Log $P_{o/w}$ (SILICOS-IT)	2.51
Consensus Log $P_{o/w}$	-5.31

Water Solubility	
Log *S* (ESOL)	-7.42
Solubility	2.46e-05 mg/ml ; 3.77e-08 mol/l
Class	Poorly soluble
Log *S* (Ali)	-9.20
Solubility	4.11e-07 mg/ml ; 6.30e-10 mol/l
Class	Poorly soluble
Log *S* (SILICOS-IT)	-5.35
Solubility	2.92e-03 mg/ml ; 4.48e-06 mol/l
Class	Moderately soluble
Pharmacokinetics	
GI absorption	Low
BBB permeant	No
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-5.84 cm/s
Druglikeness	
Lipinski	No; 3 violations: MW>500, MLOGP>4.15, NHorOH>5
Ghose	No; 3 violations: MW>480, MR>130, #atoms>70
Veber	No; 2 violations: Rotors>10, TPSA>140
Egan	No; 1 violation: TPSA>131.6
Muegge	No; 4 violations: MW>600, XLOGP3>5, TPSA>150, H-don>5
Bioavailability Score	0.17
Medicinal Chemistry	
PAINS	0 alert
Brenk	3 alerts: heavy_metal, imine_1, imine_2
Leadlikeness	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5
Synthetic accessibility	4.73

MZN-8

Molecule 8

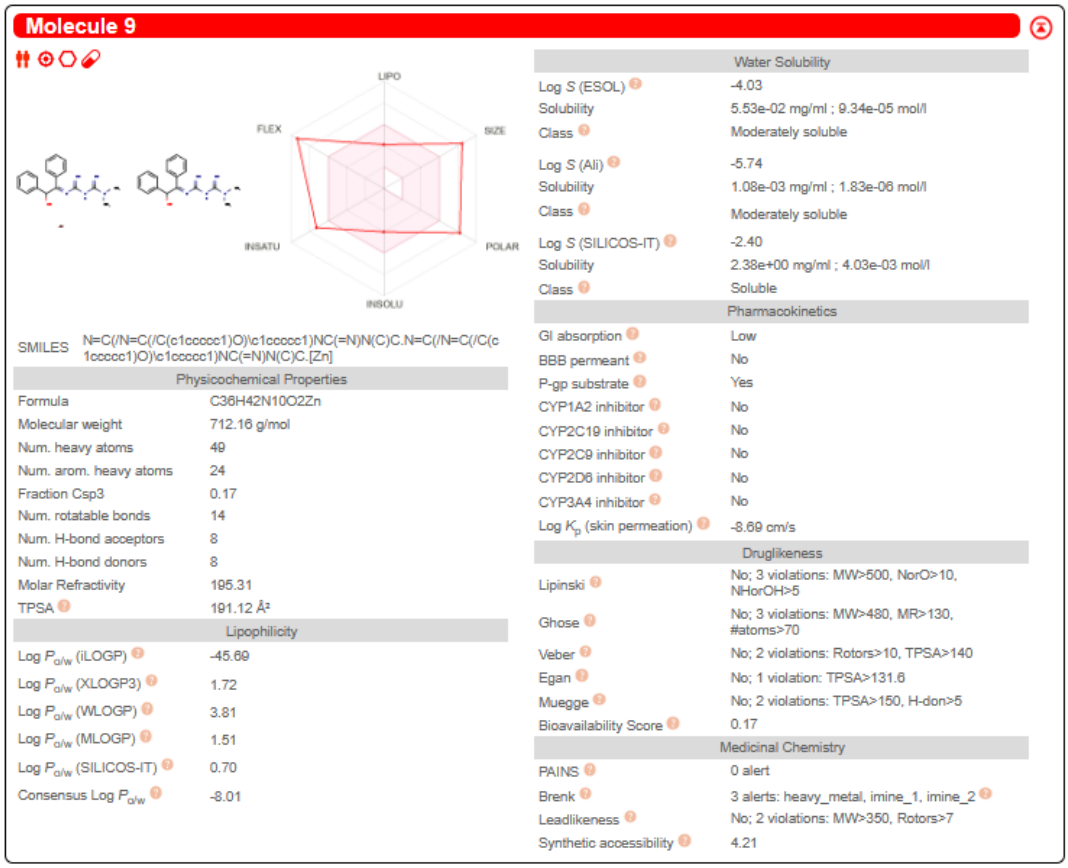


SMILES COc1ccc(cc1O)C=NC(=N)NC(=N)N(C)C.COc1ccc(cc1O)C=NC(=N)NC(=N)N(C)C.[Zn]

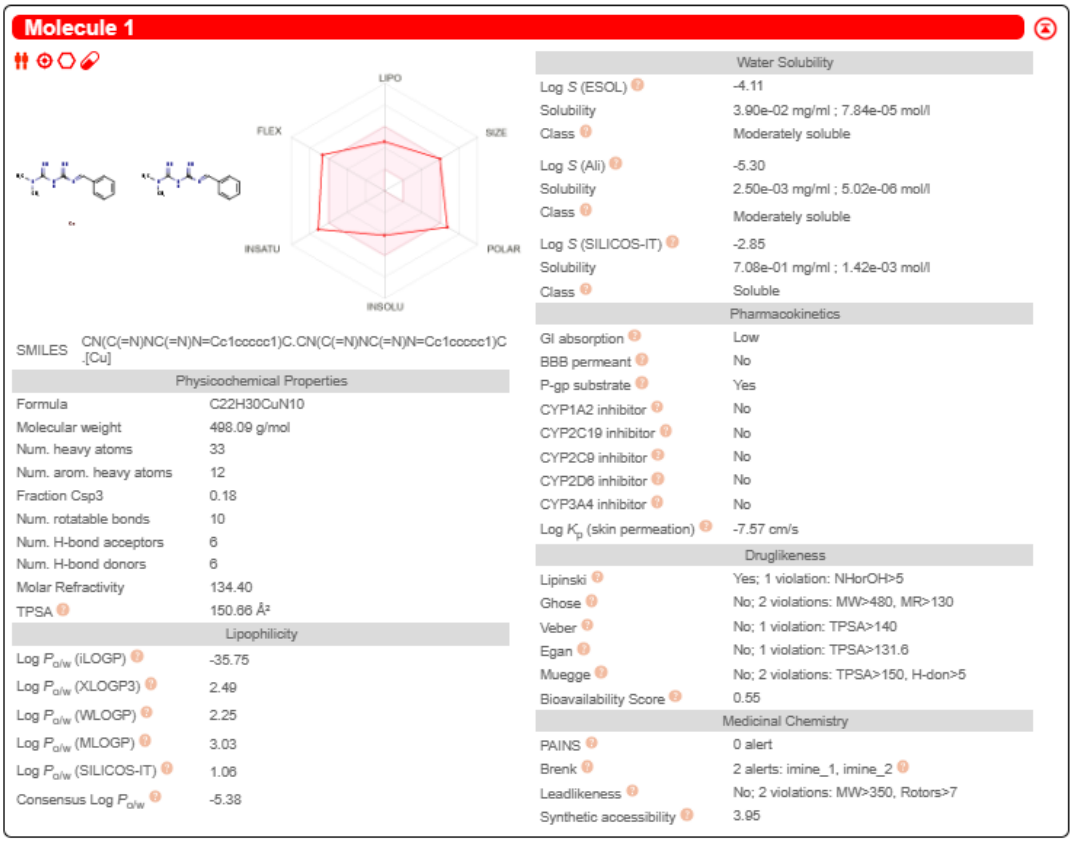
Physicochemical Properties	
Formula	C24H34N10O4Zn
Molecular weight	591.97 g/mol
Num. heavy atoms	39
Num. arom. heavy atoms	12
Fraction Csp3	0.25
Num. rotatable bonds	12
Num. H-bond acceptors	10
Num. H-bond donors	8
Molar Refractivity	151.43
TPSA	209.58 Å²
Lipophilicity	
Log $P_{o/w}$ (iLOGP)	-45.69
Log $P_{o/w}$ (XLOGP3)	1.72
Log $P_{o/w}$ (WLOGP)	1.68
Log $P_{o/w}$ (MLOGP)	1.51
Log $P_{o/w}$ (SILICOS-IT)	0.70
Consensus Log $P_{o/w}$	-8.01

Water Solubility	
Log *S* (ESOL)	-4.03
Solubility	5.53e-02 mg/ml ; 9.34e-05 mol/l
Class	Moderately soluble
Log *S* (Ali)	-5.74
Solubility	1.08e-03 mg/ml ; 1.83e-06 mol/l
Class	Moderately soluble
Log *S* (SILICOS-IT)	-2.40
Solubility	2.38e+00 mg/ml ; 4.03e-03 mol/l
Class	Soluble
Pharmacokinetics	
GI absorption	Low
BBB permeant	No
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-8.69 cm/s
Druglikeness	
Lipinski	No; 3 violations: MW>500, NorO>10, NHorOH>5
Ghose	No; 3 violations: MW>480, MR>130, #atoms>70
Veber	No; 2 violations: Rotors>10, TPSA>140
Egan	No; 1 violation: TPSA>131.6
Muegge	No; 2 violations: TPSA>150, H-don>5
Bioavailability Score	0.17
Medicinal Chemistry	
PAINS	0 alert
Brenk	3 alerts: heavy_metal, imine_1, imine_2
Leadlikeness	No; 2 violations: MW>350, Rotors>7
Synthetic accessibility	4.21

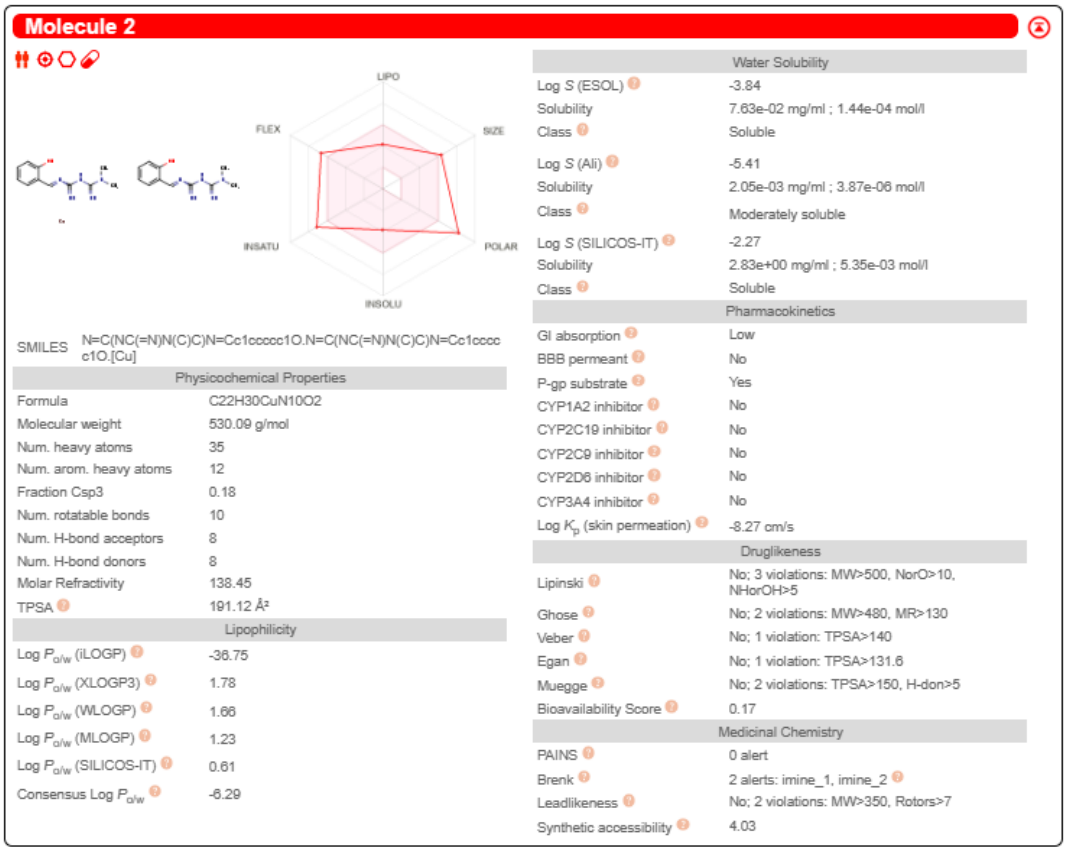
MZN-9


Molecule 9
LIPO
SIZE
POLAR
INSOLU
INSATU
FLEX
SMILES N=C(/N=C(/C(c1ccccc1)O)\c1ccccc1)NC(=N)N(C)C.N=C(/N=C(/C(c1ccccc1)O)\c1ccccc1)NC(=N)N(C)C.[Zn]
Physicochemical Properties
Formula C36H42N10O2Zn
Molecular weight 712.16 g/mol
Num. heavy atoms 49
Num. arom. heavy atoms 24
Fraction Csp3 0.17
Num. rotatable bonds 14
Num. H-bond acceptors 8
Num. H-bond donors 8
Molar Refractivity 195.31
TPSA 191.12 Å²
Lipophilicity
Log Po/w (iLOGP) -45.69
Log Po/w (XLOGP3) 1.72
Log Po/w (WLOGP) 3.81
Log Po/w (MLOGP) 1.51
Log Po/w (SILICOS-IT) 0.70
Consensus Log Po/w -8.01
Water Solubility
Log S (ESOL) -4.03
Solubility 5.53e-02 mg/ml ; 9.34e-05 mol/l
Class Moderately soluble
Log S (Ali) -5.74
Solubility 1.08e-03 mg/ml ; 1.83e-06 mol/l
Class Moderately soluble
Log S (SILICOS-IT) -2.40
Solubility 2.38e+00 mg/ml ; 4.03e-03 mol/l
Class Soluble
Pharmacokinetics
GI absorption Low
BBB permeant No
P-gp substrate Yes
CYP1A2 inhibitor No
CYP2C19 inhibitor No
CYP2C9 inhibitor No
CYP2D6 inhibitor No
CYP3A4 inhibitor No
Log Kp (skin permeation) -8.69 cm/s
Druglikeness
Lipinski No; 3 violations: MW>500, NorO>10, NHorOH>5
Ghose No; 3 violations: MW>480, MR>130, #atoms>70
Veber No; 2 violations: Rotors>10, TPSA>140
Egan No; 1 violation: TPSA>131.6
Muegge No; 2 violations: TPSA>150, H-don>5
Bioavailability Score 0.17
Medicinal Chemistry
PAINS 0 alert
Brenk 3 alerts: heavy_metal, imine_1, imine_2
Leadlikeness No; 2 violations: MW>350, Rotors>7
Synthetic accessibility 4.21

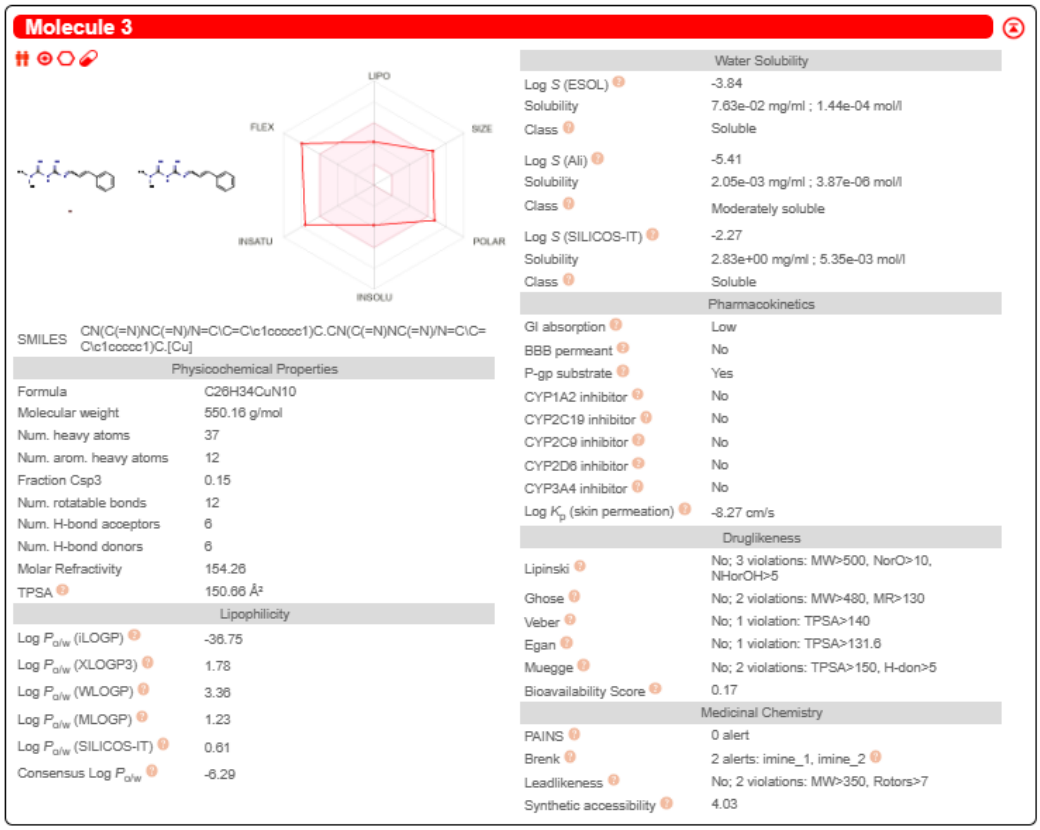
MCu-1


Molecule 1
LIPO
SIZE
POLAR
INSOLU
INSATU
FLEX
SMILES CN(C(=N)NC(=N)Nc1ccccc1)C.CN(C(=N)NC(=N)N=Cc1ccccc1)C.[Cu]
Physicochemical Properties
Formula C22H30CuN10
Molecular weight 498.09 g/mol
Num. heavy atoms 33
Num. arom. heavy atoms 12
Fraction Csp3 0.18
Num. rotatable bonds 10
Num. H-bond acceptors 6
Num. H-bond donors 6
Molar Refractivity 134.40
TPSA 150.66 Å²
Lipophilicity
Log Po/w (iLOGP) -35.75
Log Po/w (XLOGP3) 2.49
Log Po/w (WLOGP) 2.25
Log Po/w (MLOGP) 3.03
Log Po/w (SILICOS-IT) 1.06
Consensus Log Po/w -5.38
Water Solubility
Log S (ESOL) -4.11
Solubility 3.90e-02 mg/ml ; 7.84e-05 mol/l
Class Moderately soluble
Log S (Ali) -5.30
Solubility 2.50e-03 mg/ml ; 5.02e-06 mol/l
Class Moderately soluble
Log S (SILICOS-IT) -2.85
Solubility 7.08e-01 mg/ml ; 1.42e-03 mol/l
Class Soluble
Pharmacokinetics
GI absorption Low
BBB permeant No
P-gp substrate Yes
CYP1A2 inhibitor No
CYP2C19 inhibitor No
CYP2C9 inhibitor No
CYP2D6 inhibitor No
CYP3A4 inhibitor No
Log Kp (skin permeation) -7.57 cm/s
Druglikeness
Lipinski Yes; 1 violation: NHorOH>5
Ghose No; 2 violations: MW>480, MR>130
Veber No; 1 violation: TPSA>140
Egan No; 1 violation: TPSA>131.6
Muegge No; 2 violations: TPSA>150, H-don>5
Bioavailability Score 0.55
Medicinal Chemistry
PAINS 0 alert
Brenk 2 alerts: imine_1, imine_2
Leadlikeness No; 2 violations: MW>350, Rotors>7
Synthetic accessibility 3.95

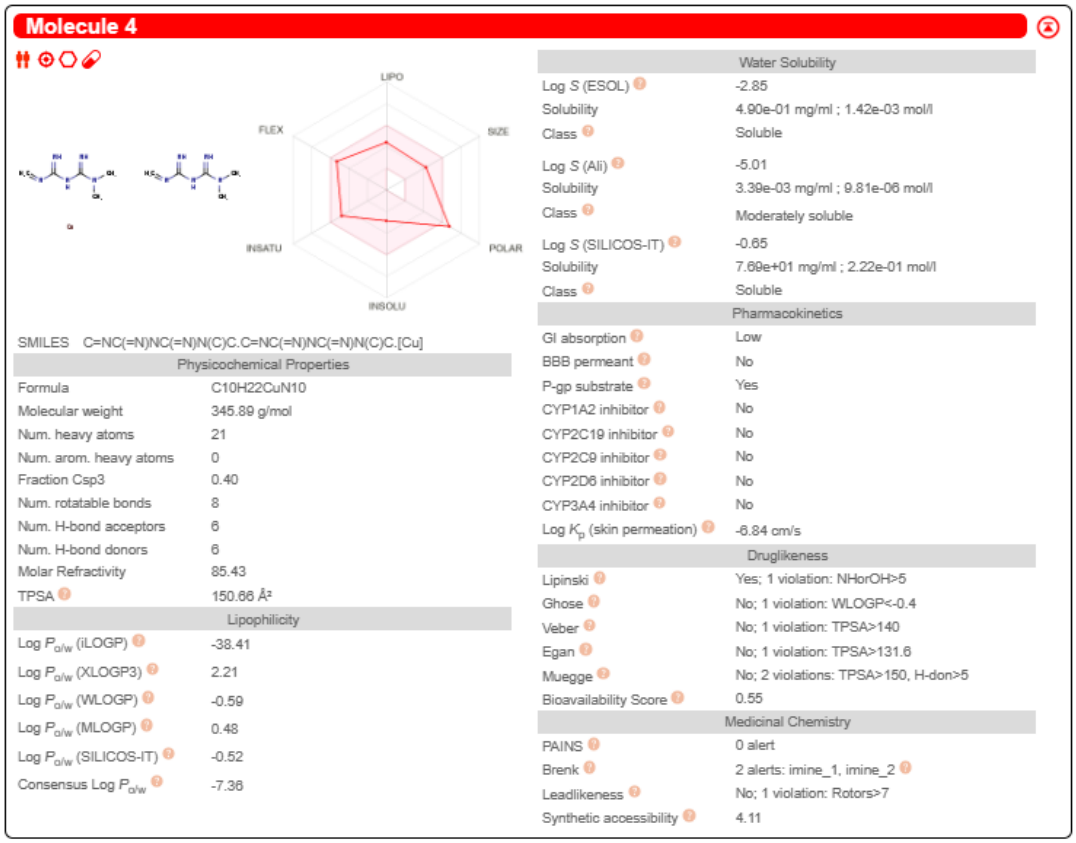
MCu-2


Molecule 2
LIPO
SIZE
POLAR
INSOLU
INSATU
FLEX
SMILES N=C(NC(=N)N(C)C)N=Cc1ccccc1O.N=C(NC(=N)N(C)C)N=Cc1ccccc1O.[Cu]
Physicochemical Properties
Formula C22H30CuN10O2
Molecular weight 530.09 g/mol
Num. heavy atoms 35
Num. arom. heavy atoms 12
Fraction Csp3 0.18
Num. rotatable bonds 10
Num. H-bond acceptors 8
Num. H-bond donors 8
Molar Refractivity 138.45
TPSA 191.12 Å²
Lipophilicity
Log Po/w (iLOGP) -36.75
Log Po/w (XLOGP3) 1.78
Log Po/w (WLOGP) 1.66
Log Po/w (MLOGP) 1.23
Log Po/w (SILICOS-IT) 0.61
Consensus Log Po/w -6.29
Water Solubility
Log S (ESOL) -3.84
Solubility 7.63e-02 mg/ml ; 1.44e-04 mol/l
Class Soluble
Log S (Ali) -5.41
Solubility 2.05e-03 mg/ml ; 3.87e-06 mol/l
Class Moderately soluble
Log S (SILICOS-IT) -2.27
Solubility 2.83e+00 mg/ml ; 5.35e-03 mol/l
Class Soluble
Pharmacokinetics
GI absorption Low
BBB permeant No
P-gp substrate Yes
CYP1A2 inhibitor No
CYP2C19 inhibitor No
CYP2C9 inhibitor No
CYP2D6 inhibitor No
CYP3A4 inhibitor No
Log Kp (skin permeation) -8.27 cm/s
Druglikeness
Lipinski No; 3 violations: MW>500, NorO>10, NHorOH>5
Ghose No; 2 violations: MW>480, MR>130
Veber No; 1 violation: TPSA>140
Egan No; 1 violation: TPSA>131.6
Muegge No; 2 violations: TPSA>150, H-don>5
Bioavailability Score 0.17
Medicinal Chemistry
PAINS 0 alert
Brenk 2 alerts: imine_1, imine_2
Leadlikeness No; 2 violations: MW>350, Rotors>7
Synthetic accessibility 4.03

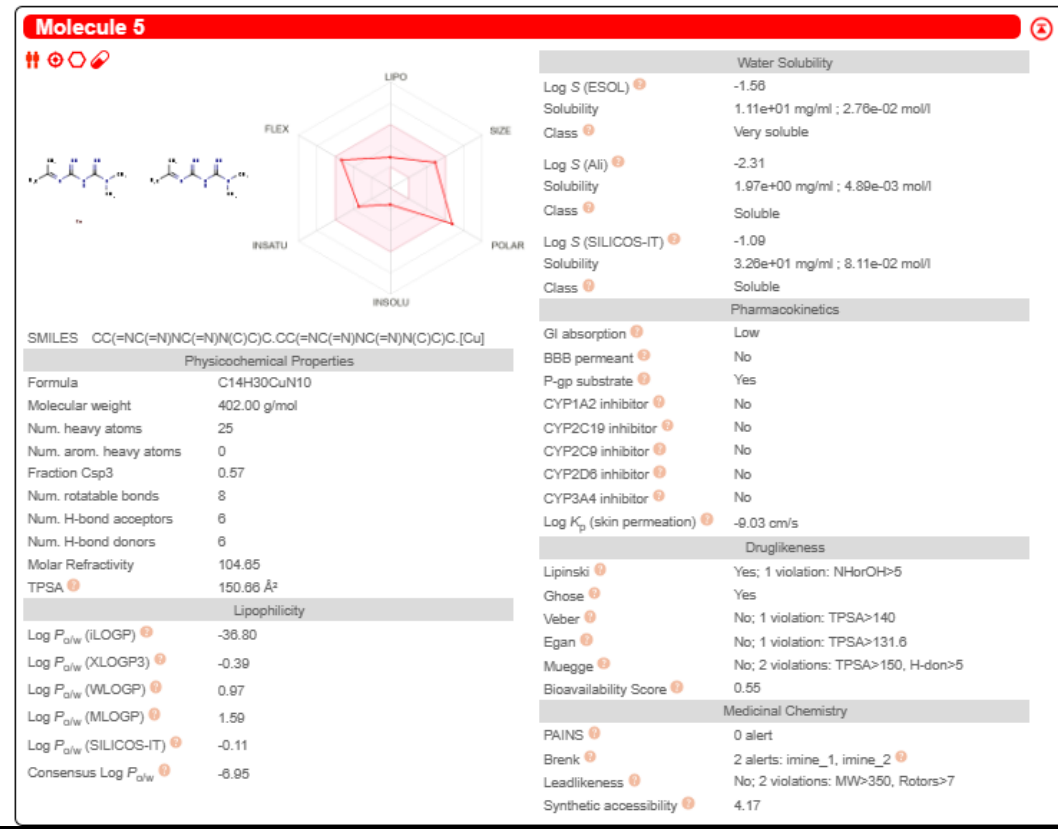
MCu-3


Molecule 3
LIPO
SIZE
POLAR
INSOLU
INSATU
FLEX
SMILES CN(C(=N)NC(=N)/N=C\C=C\c1ccccc1)C.CN(C(=N)NC(=N)/N=C\C=C\c1ccccc1)C.[Cu]
Physicochemical Properties
Formula C26H34CuN10
Molecular weight 550.16 g/mol
Num. heavy atoms 37
Num. arom. heavy atoms 12
Fraction Csp3 0.15
Num. rotatable bonds 12
Num. H-bond acceptors 6
Num. H-bond donors 6
Molar Refractivity 154.26
TPSA 150.66 Å²
Lipophilicity
Log Po/w (iLOGP) -36.75
Log Po/w (XLOGP3) 1.78
Log Po/w (WLOGP) 3.36
Log Po/w (MLOGP) 1.23
Log Po/w (SILICOS-IT) 0.61
Consensus Log Po/w -6.29
Water Solubility
Log S (ESOL) -3.84
Solubility 7.63e-02 mg/ml ; 1.44e-04 mol/l
Class Soluble
Log S (Ali) -5.41
Solubility 2.05e-03 mg/ml ; 3.87e-06 mol/l
Class Moderately soluble
Log S (SILICOS-IT) -2.27
Solubility 2.83e+00 mg/ml ; 5.35e-03 mol/l
Class Soluble
Pharmacokinetics
GI absorption Low
BBB permeant No
P-gp substrate Yes
CYP1A2 inhibitor No
CYP2C19 inhibitor No
CYP2C9 inhibitor No
CYP2D6 inhibitor No
CYP3A4 inhibitor No
Log Kp (skin permeation) -8.27 cm/s
Druglikeness
Lipinski No; 3 violations: MW>500, NorO>10, NHorOH>5
Ghose No; 2 violations: MW>480, MR>130
Veber No; 1 violation: TPSA>140
Egan No; 1 violation: TPSA>131.6
Muegge No; 2 violations: TPSA>150, H-don>5
Bioavailability Score 0.17
Medicinal Chemistry
PAINS 0 alert
Brenk 2 alerts: imine_1, imine_2
Leadlikeness No; 2 violations: MW>350, Rotors>7
Synthetic accessibility 4.03

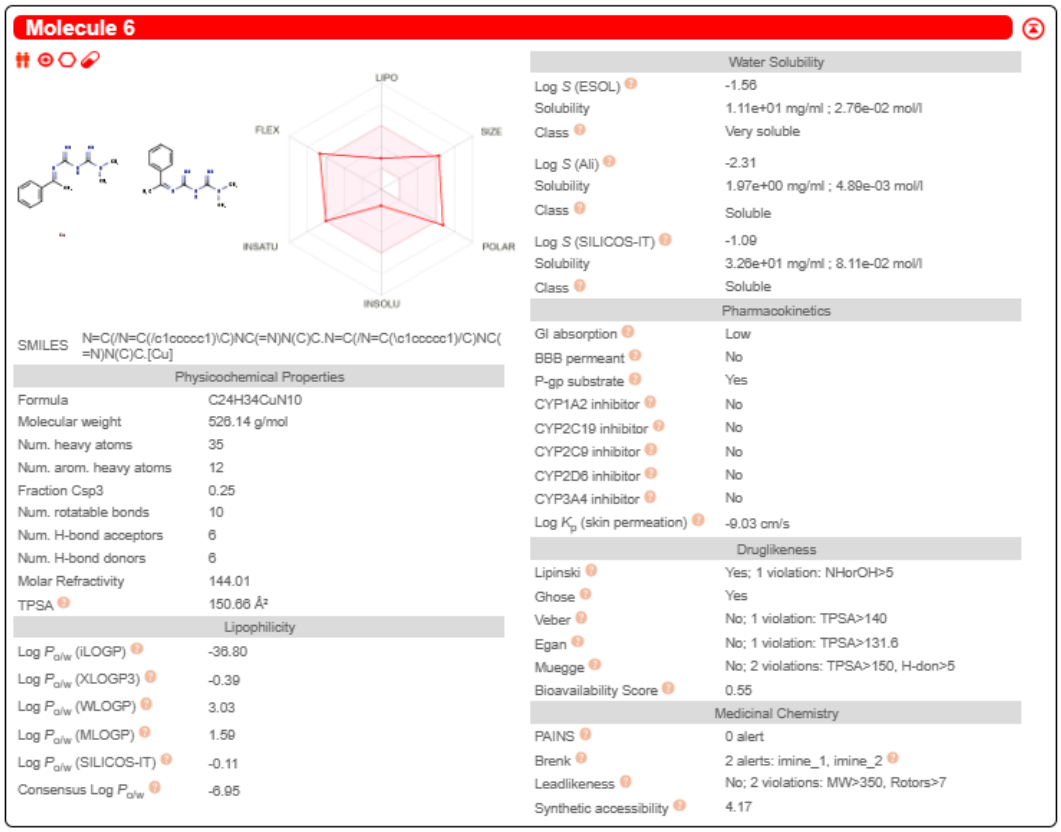
MCu-4


Molecule 4
LIPO
SIZE
POLAR
INSOLU
INSATU
FLEX
SMILES C=NC(=N)NC(=N)N(C)C.C=NC(=N)NC(=N)N(C)C.[Cu]
Physicochemical Properties
Formula C10H22CuN10
Molecular weight 345.89 g/mol
Num. heavy atoms 21
Num. arom. heavy atoms 0
Fraction Csp3 0.40
Num. rotatable bonds 8
Num. H-bond acceptors 6
Num. H-bond donors 6
Molar Refractivity 85.43
TPSA 150.66 Å²
Lipophilicity
Log Po/w (iLOGP) -38.41
Log Po/w (XLOGP3) 2.21
Log Po/w (WLOGP) -0.59
Log Po/w (MLOGP) 0.48
Log Po/w (SILICOS-IT) -0.52
Consensus Log Po/w -7.36
Water Solubility
Log S (ESOL) -2.85
Solubility 4.90e-01 mg/ml ; 1.42e-03 mol/l
Class Soluble
Log S (Ali) -5.01
Solubility 3.39e-03 mg/ml ; 9.81e-06 mol/l
Class Moderately soluble
Log S (SILICOS-IT) -0.65
Solubility 7.69e+01 mg/ml ; 2.22e-01 mol/l
Class Soluble
Pharmacokinetics
GI absorption Low
BBB permeant No
P-gp substrate Yes
CYP1A2 inhibitor No
CYP2C19 inhibitor No
CYP2C9 inhibitor No
CYP2D6 inhibitor No
CYP3A4 inhibitor No
Log Kp (skin permeation) -6.84 cm/s
Druglikeness
Lipinski Yes; 1 violation: NHorOH>5
Ghose No; 1 violation: WLOGP<-0.4
Veber No; 1 violation: TPSA>140
Egan No; 1 violation: TPSA>131.6
Muegge No; 2 violations: TPSA>150, H-don>5
Bioavailability Score 0.55
Medicinal Chemistry
PAINS 0 alert
Brenk 2 alerts: imine_1, imine_2
Leadlikeness No; 1 violation: Rotors>7
Synthetic accessibility 4.11

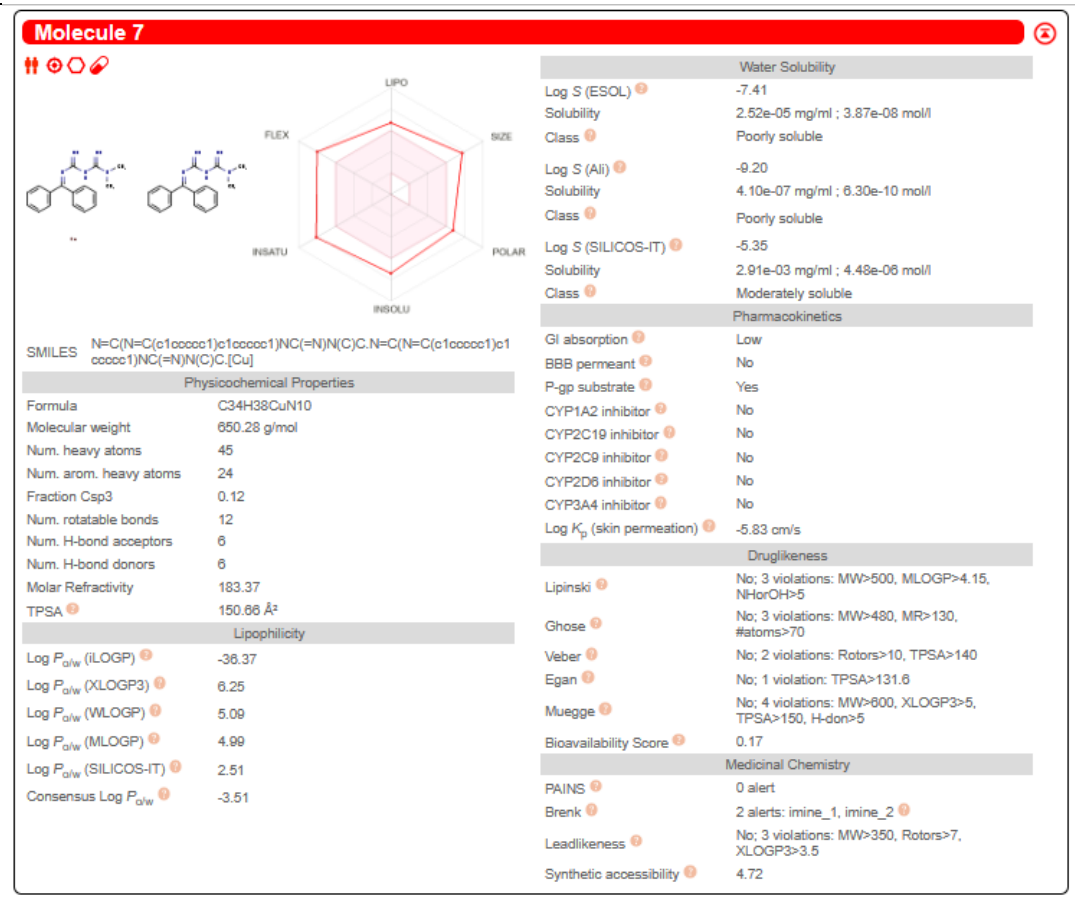
MCu-5


Molecule 5
LIPO
SIZE
POLAR
INSOLU
INSATU
FLEX
SMILES CC(=NC(=N)NC(=N)N(C)C)C.CC(=NC(=N)NC(=N)N(C)C)C.[Cu]
Physicochemical Properties
Formula C14H30CuN10
Molecular weight 402.00 g/mol
Num. heavy atoms 25
Num. arom. heavy atoms 0
Fraction Csp3 0.57
Num. rotatable bonds 8
Num. H-bond acceptors 6
Num. H-bond donors 6
Molar Refractivity 104.65
TPSA 150.66 Å²
Lipophilicity
Log Po/w (iLOGP) -36.80
Log Po/w (XLOGP3) -0.39
Log Po/w (WLOGP) 0.97
Log Po/w (MLOGP) 1.59
Log Po/w (SILICOS-IT) -0.11
Consensus Log Po/w -6.95
Water Solubility
Log S (ESOL) -1.56
Solubility 1.11e+01 mg/ml ; 2.76e-02 mol/l
Class Very soluble
Log S (Ali) -2.31
Solubility 1.97e+00 mg/ml ; 4.89e-03 mol/l
Class Soluble
Log S (SILICOS-IT) -1.09
Solubility 3.26e+01 mg/ml ; 8.11e-02 mol/l
Class Soluble
Pharmacokinetics
GI absorption Low
BBB permeant No
P-gp substrate Yes
CYP1A2 inhibitor No
CYP2C19 inhibitor No
CYP2C9 inhibitor No
CYP2D6 inhibitor No
CYP3A4 inhibitor No
Log Kp (skin permeation) -9.03 cm/s
Druglikeness
Lipinski Yes; 1 violation: NHorOH>5
Ghose Yes
Veber No; 1 violation: TPSA>140
Egan No; 1 violation: TPSA>131.6
Muegge No; 2 violations: TPSA>150, H-don>5
Bioavailability Score 0.55
Medicinal Chemistry
PAINS 0 alert
Brenk 2 alerts: imine_1, imine_2
Leadlikeness No; 2 violations: MW>350, Rotors>7
Synthetic accessibility 4.17

MCu-6

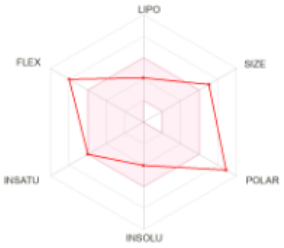

Molecule 6
LIPO
SIZE
POLAR
INSOLU
INSATU
FLEX
SMILES N=C(/N=C(/c1ccccc1)\C)NC(=N)N(C)C.N=C(/N=C(\c1ccccc1)/C)NC(=N)N(C)C.[Cu]
Physicochemical Properties
Formula C24H34CuN10
Molecular weight 526.14 g/mol
Num. heavy atoms 35
Num. arom. heavy atoms 12
Fraction Csp3 0.25
Num. rotatable bonds 10
Num. H-bond acceptors 6
Num. H-bond donors 6
Molar Refractivity 144.01
TPSA 150.66 Å²
Lipophilicity
Log Po/w (iLOGP) -36.80
Log Po/w (XLOGP3) -0.39
Log Po/w (WLOGP) 3.03
Log Po/w (MLOGP) 1.59
Log Po/w (SILICOS-IT) -0.11
Consensus Log Po/w -6.95
Water Solubility
Log S (ESOL) -1.56
Solubility 1.11e+01 mg/ml ; 2.76e-02 mol/l
Class Very soluble
Log S (Ali) -2.31
Solubility 1.97e+00 mg/ml ; 4.89e-03 mol/l
Class Soluble
Log S (SILICOS-IT) -1.09
Solubility 3.26e+01 mg/ml ; 8.11e-02 mol/l
Class Soluble
Pharmacokinetics
GI absorption Low
BBB permeant No
P-gp substrate Yes
CYP1A2 inhibitor No
CYP2C19 inhibitor No
CYP2C9 inhibitor No
CYP2D6 inhibitor No
CYP3A4 inhibitor No
Log Kp (skin permeation) -9.03 cm/s
Druglikeness
Lipinski Yes; 1 violation: NHorOH>5
Ghose Yes
Veber No; 1 violation: TPSA>140
Egan No; 1 violation: TPSA>131.6
Muegge No; 2 violations: TPSA>150, H-don>5
Bioavailability Score 0.55
Medicinal Chemistry
PAINS 0 alert
Brenk 2 alerts: imine_1, imine_2
Leadlikeness No; 2 violations: MW>350, Rotors>7
Synthetic accessibility 4.17

MCu-7


Molecule 7
LIPO
SIZE
POLAR
INSOLU
INSATU
FLEX
SMILES N=C(N=C(c1ccccc1)c1ccccc1)NC(=N)N(C)C.N=C(N=C(c1ccccc1)c1ccccc1)NC(=N)N(C)C.[Cu]
Physicochemical Properties
Formula C34H38CuN10
Molecular weight 650.28 g/mol
Num. heavy atoms 45
Num. arom. heavy atoms 24
Fraction Csp3 0.12
Num. rotatable bonds 12
Num. H-bond acceptors 6
Num. H-bond donors 6
Molar Refractivity 183.37
TPSA 150.66 Å²
Lipophilicity
Log Po/w (iLOGP) -36.37
Log Po/w (XLOGP3) 6.25
Log Po/w (WLOGP) 5.09
Log Po/w (MLOGP) 4.99
Log Po/w (SILICOS-IT) 2.51
Consensus Log Po/w -3.51
Water Solubility
Log S (ESOL) -7.41
Solubility 2.52e-05 mg/ml ; 3.87e-08 mol/l
Class Poorly soluble
Log S (Ali) -9.20
Solubility 4.10e-07 mg/ml ; 6.30e-10 mol/l
Class Poorly soluble
Log S (SILICOS-IT) -5.35
Solubility 2.91e-03 mg/ml ; 4.48e-06 mol/l
Class Moderately soluble
Pharmacokinetics
GI absorption Low
BBB permeant No
P-gp substrate Yes
CYP1A2 inhibitor No
CYP2C19 inhibitor No
CYP2C9 inhibitor No
CYP2D6 inhibitor No
CYP3A4 inhibitor No
Log Kp (skin permeation) -5.83 cm/s
Druglikeness
Lipinski No; 3 violations: MW>500, MLOGP>4.15, NHorOH>5
Ghose No; 3 violations: MW>480, MR>130, #atoms>70
Veber No; 2 violations: Rotors>10, TPSA>140
Egan No; 1 violation: TPSA>131.6
Muegge No; 4 violations: MW>600, XLOGP3>5, TPSA>150, H-don>5
Bioavailability Score 0.17
Medicinal Chemistry
PAINS 0 alert
Brenk 2 alerts: imine_1, imine_2
Leadlikeness No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5
Synthetic accessibility 4.72

MCu-8

Molecule 8



SMILES COc1ccc(cc1O)C=NC(=N)NC(=N)N(C)C.COc1ccc(cc1O)C=NC(=N)NC(=N)N(C)C.[Cu]

Physicochemical Properties	
Formula	C24H34CuN10O4
Molecular weight	590.14 g/mol
Num. heavy atoms	39
Num. arom. heavy atoms	12
Fraction Csp3	0.25
Num. rotatable bonds	12
Num. H-bond acceptors	10
Num. H-bond donors	8
Molar Refractivity	151.43
TPSA	209.58 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	-36.71
Log $P_{o/w}$ (XLOGP3)	1.72
Log $P_{o/w}$ (WLOGP)	1.68
Log $P_{o/w}$ (MLOGP)	1.51
Log $P_{o/w}$ (SILICOS-IT)	0.70
Consensus Log $P_{o/w}$	-6.22

Water Solubility	
Log *S* (ESOL)	-4.02
Solubility	5.66e-02 mg/ml ; 9.59e-05 mol/l
Class	Moderately soluble
Log *S* (Ali)	-5.74
Solubility	1.08e-03 mg/ml ; 1.83e-06 mol/l
Class	Moderately soluble
Log *S* (SILICOS-IT)	-2.40
Solubility	2.38e+00 mg/ml ; 4.03e-03 mol/l
Class	Soluble

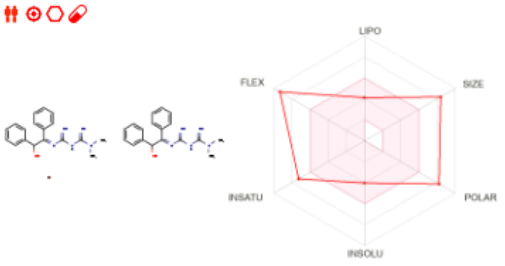
Pharmacokinetics	
GI absorption	Low
BBB permeant	No
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-8.68 cm/s

Druglikeness	
Lipinski	No; 3 violations: MW>500, NorO>10, NHorOH>5
Ghose	No; 3 violations: MW>480, MR>130, #atoms>70
Veber	No; 2 violations: Rotors>10, TPSA>140
Egan	No; 1 violation: TPSA>131.6
Muegge	No; 2 violations: TPSA>150, H-don>5
Bioavailability Score	0.17

Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: imine_1, imine_2
Leadlikeness	No; 2 violations: MW>350, Rotors>7
Synthetic accessibility	4.21

MCu-9

Molecule 9



SMILES N=C(/N=C(/C(c1ccccc1)O)\c1ccccc1)NC(=N)N(C)C.N=C(/N=C(/C(c1ccccc1)O)\c1ccccc1)NC(=N)N(C)C.[Cu]

Physicochemical Properties	
Formula	C36H42CuN10O2
Molecular weight	710.33 g/mol
Num. heavy atoms	49
Num. arom. heavy atoms	24
Fraction Csp3	0.17
Num. rotatable bonds	14
Num. H-bond acceptors	8
Num. H-bond donors	8
Molar Refractivity	195.31
TPSA	191.12 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	-36.71
Log $P_{o/w}$ (XLOGP3)	1.72
Log $P_{o/w}$ (WLOGP)	3.81
Log $P_{o/w}$ (MLOGP)	1.51
Log $P_{o/w}$ (SILICOS-IT)	0.70
Consensus Log $P_{o/w}$	-6.22

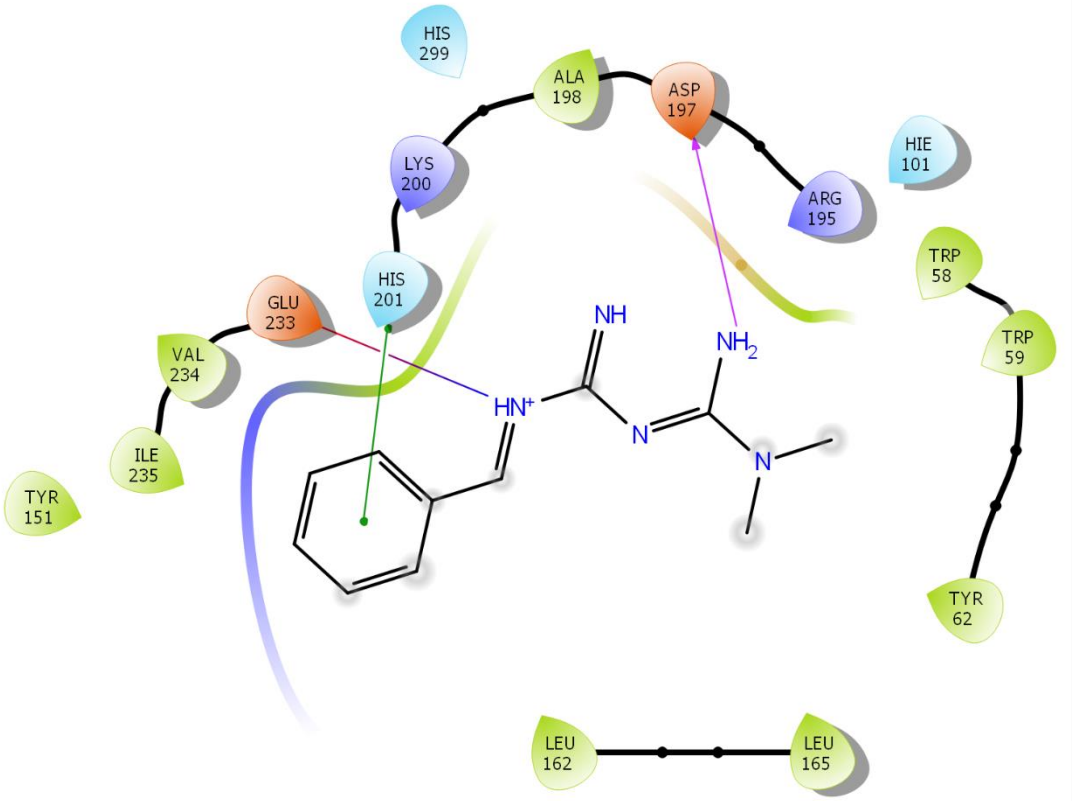
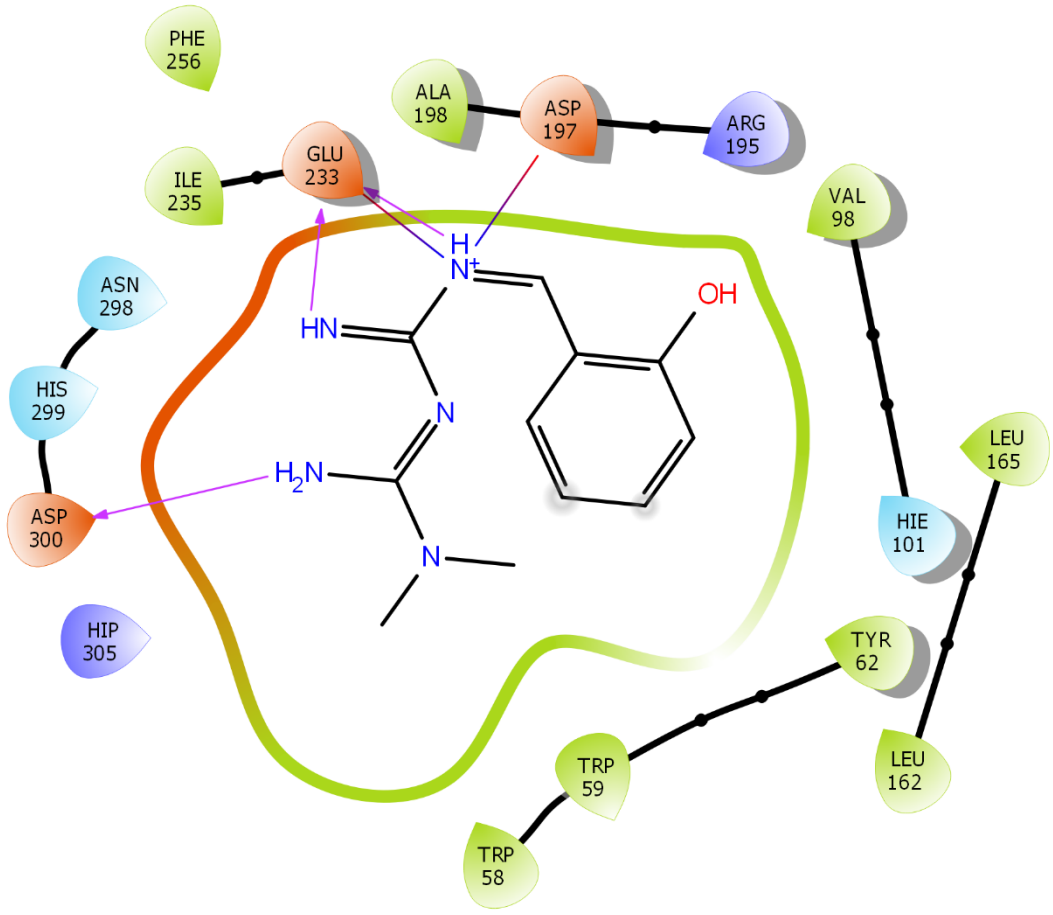
Water Solubility	
Log *S* (ESOL)	-4.02
Solubility	5.66e-02 mg/ml ; 9.59e-05 mol/l
Class	Moderately soluble
Log *S* (Ali)	-5.74
Solubility	1.08e-03 mg/ml ; 1.83e-06 mol/l
Class	Moderately soluble
Log *S* (SILICOS-IT)	-2.40
Solubility	2.38e+00 mg/ml ; 4.03e-03 mol/l
Class	Soluble

Pharmacokinetics	
GI absorption	Low
BBB permeant	No
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-8.68 cm/s

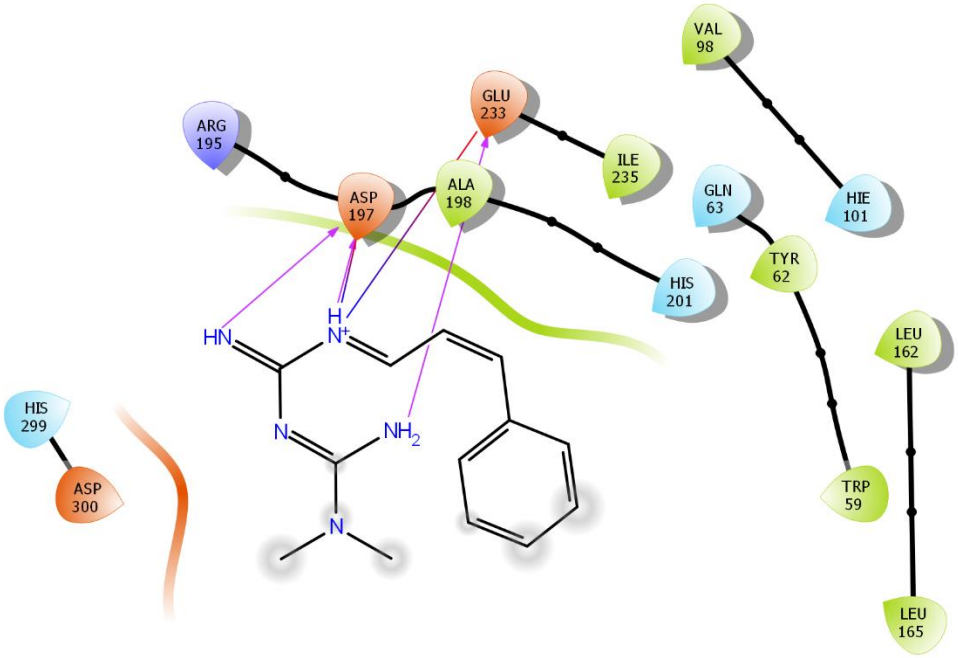
Druglikeness	
Lipinski	No; 3 violations: MW>500, NorO>10, NHorOH>5
Ghose	No; 3 violations: MW>480, MR>130, #atoms>70
Veber	No; 2 violations: Rotors>10, TPSA>140
Egan	No; 1 violation: TPSA>131.6
Muegge	No; 2 violations: TPSA>150, H-don>5
Bioavailability Score	0.17

Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: imine_1, imine_2
Leadlikeness	No; 2 violations: MW>350, Rotors>7
Synthetic accessibility	4.21

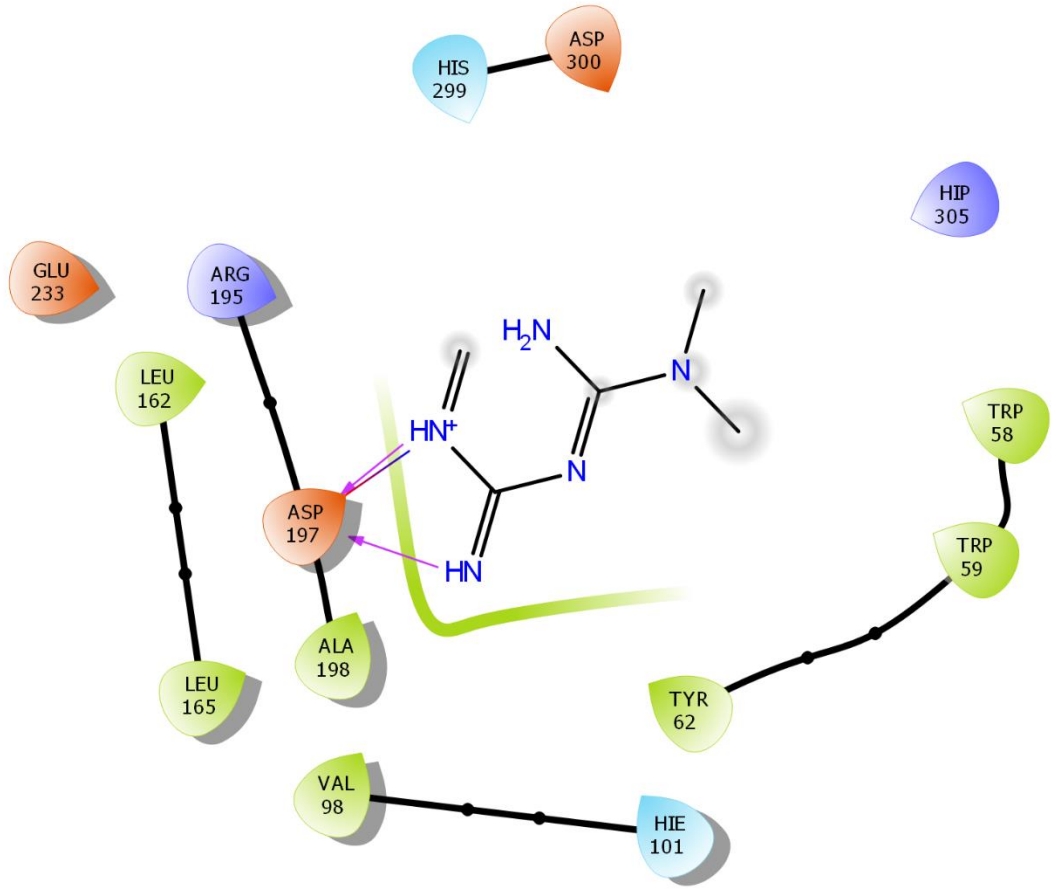
Table S2. 2D structures of all Metformin derivatives with respect to amylase enzyme.

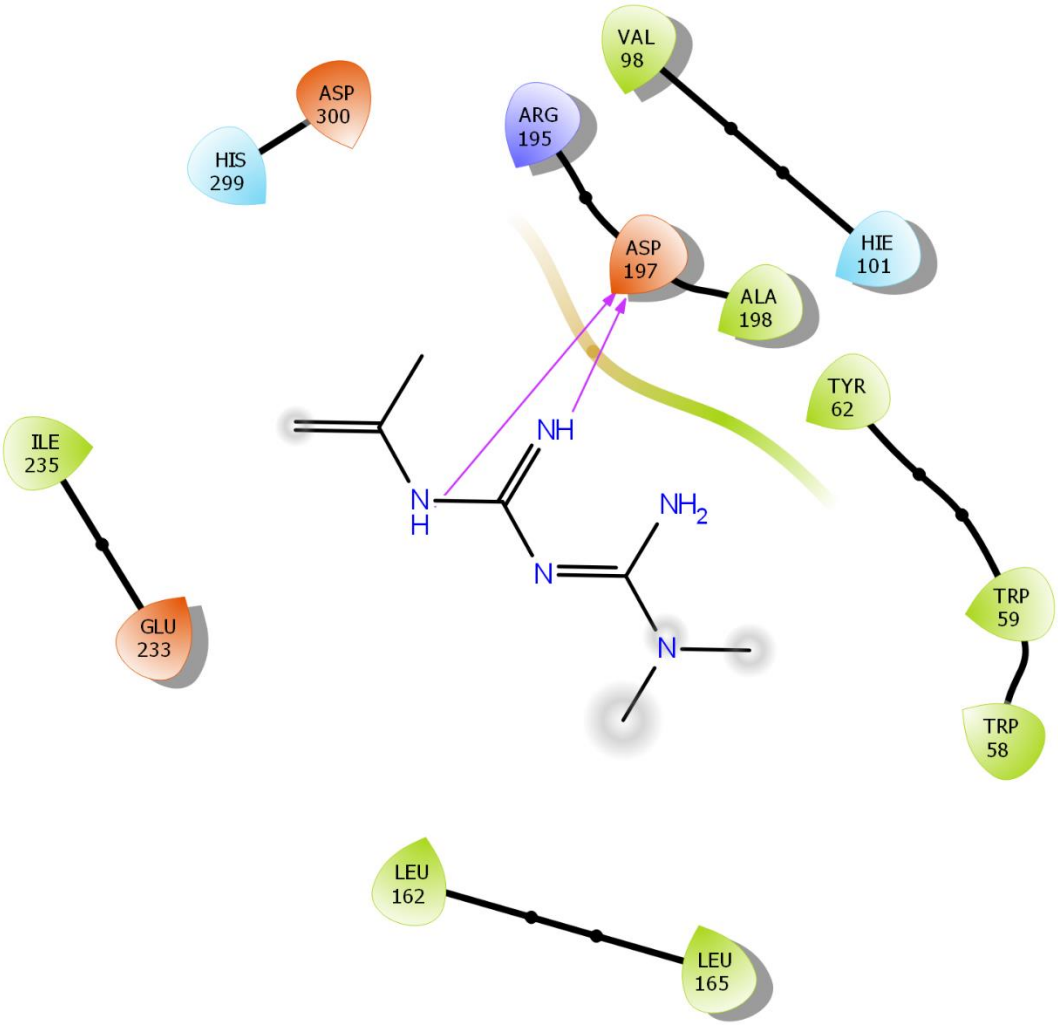
Derivative code	2D Pose
MET-1	
MET-2	

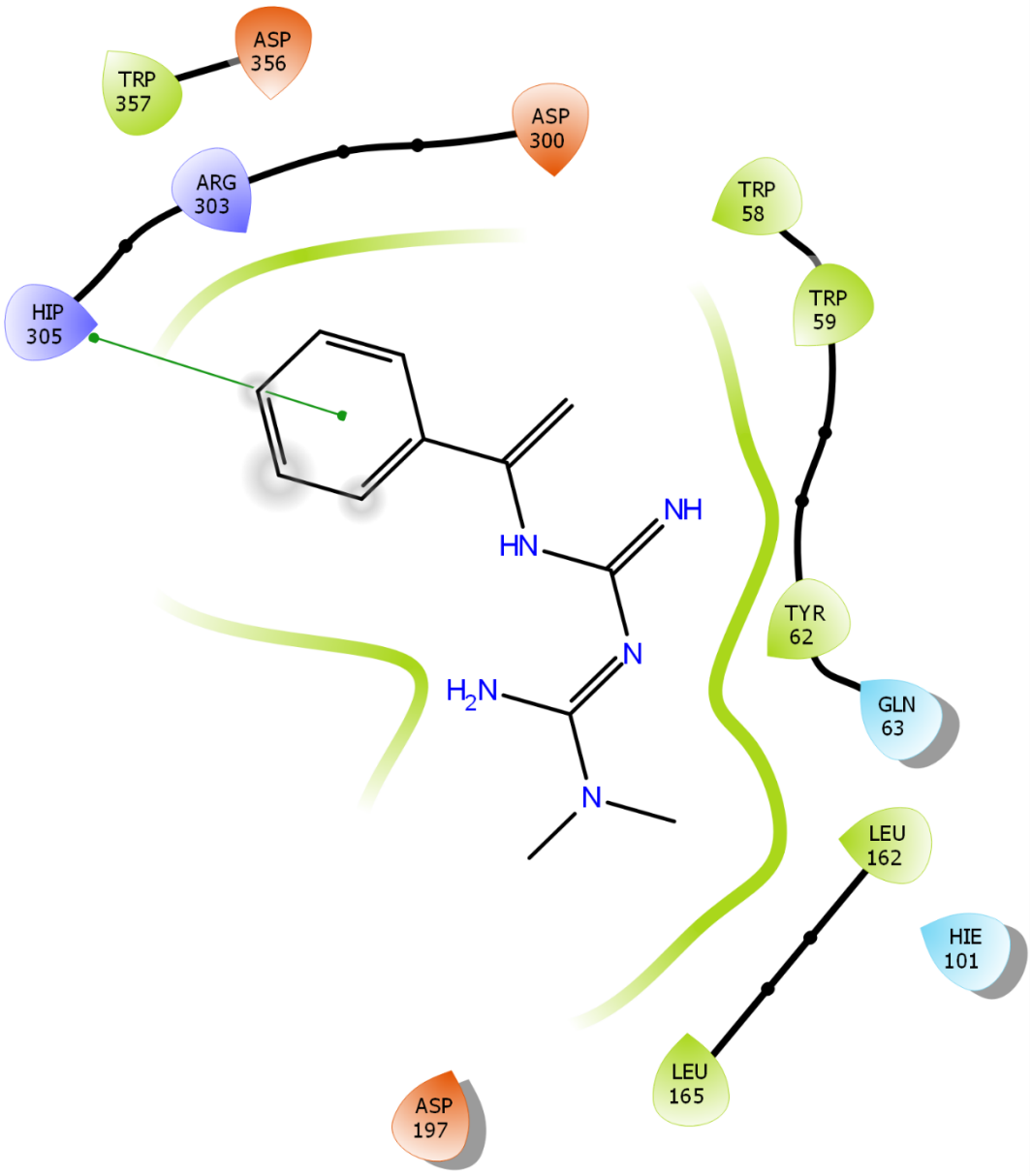
MET-3

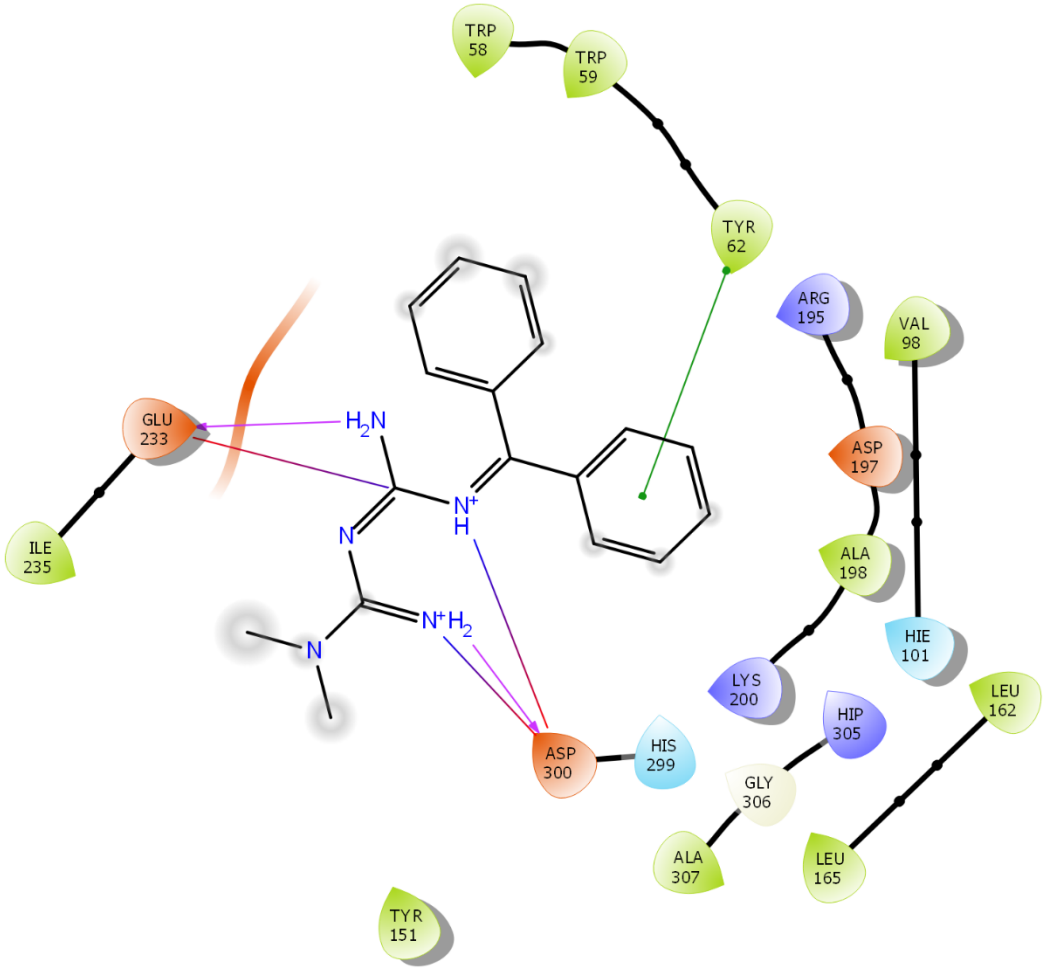

VAL
98
GLU
233
ARG
195
ILE
235
ASP
197
ALA
198
GLN
63
HIE
101
TYR
62
HIS
201
H
HN
N+
LEU
162
HIS
299
N
NH2
ASP
300
N
TRP
59
LEU
165

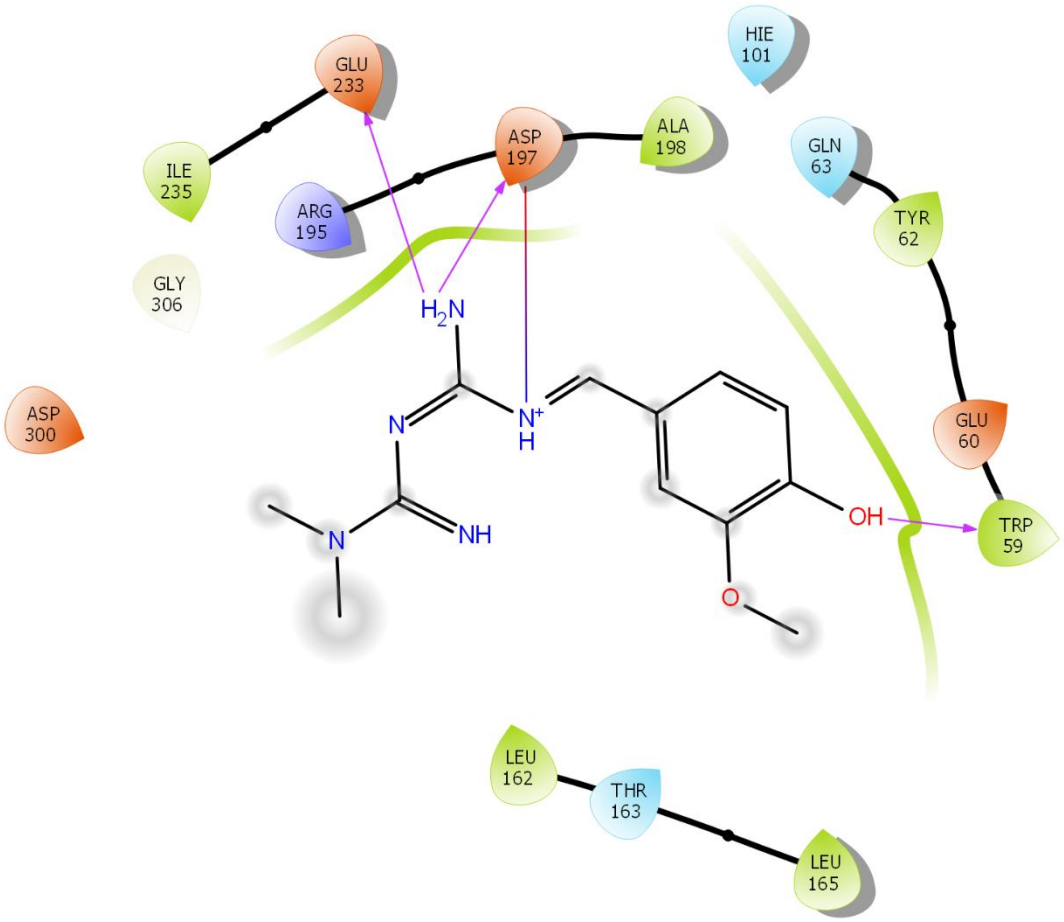
MET-4

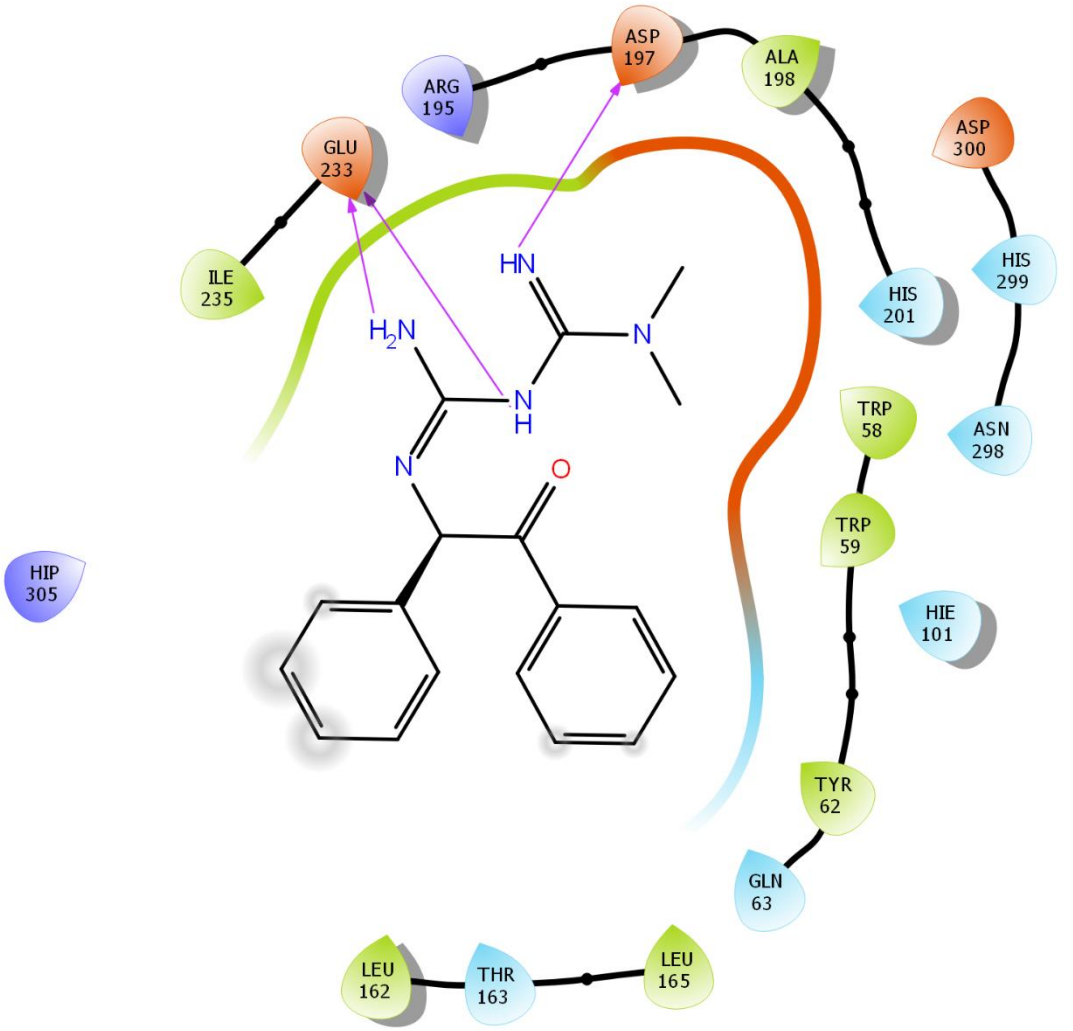

HIS
299
ASP
300
HIP
305
GLU
233
ARG
195
H2N
N
LEU
162
HN+
TRP
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ASP
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HN
TRP
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ALA
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TYR
62
LEU
165
VAL
98
HIE
101

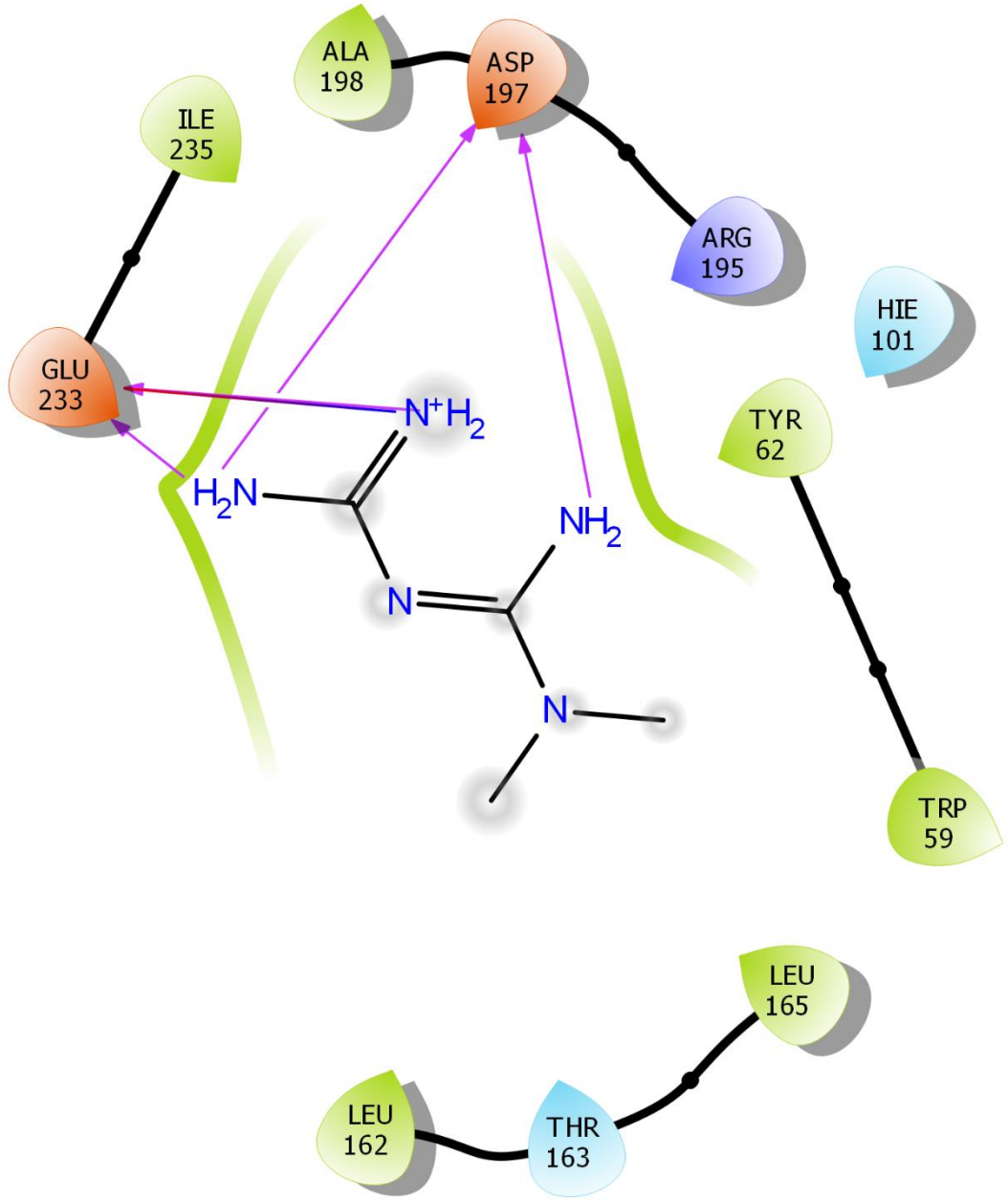
MET-5	VAL 98 ASP 300 ARG 195 HIS 299 ASP 197 HIE 101 ALA 198 TYR 62 ILE 235 NH N H NH2 N TRP 59 GLU 233 N TRP 58 LEU 162 LEU 165

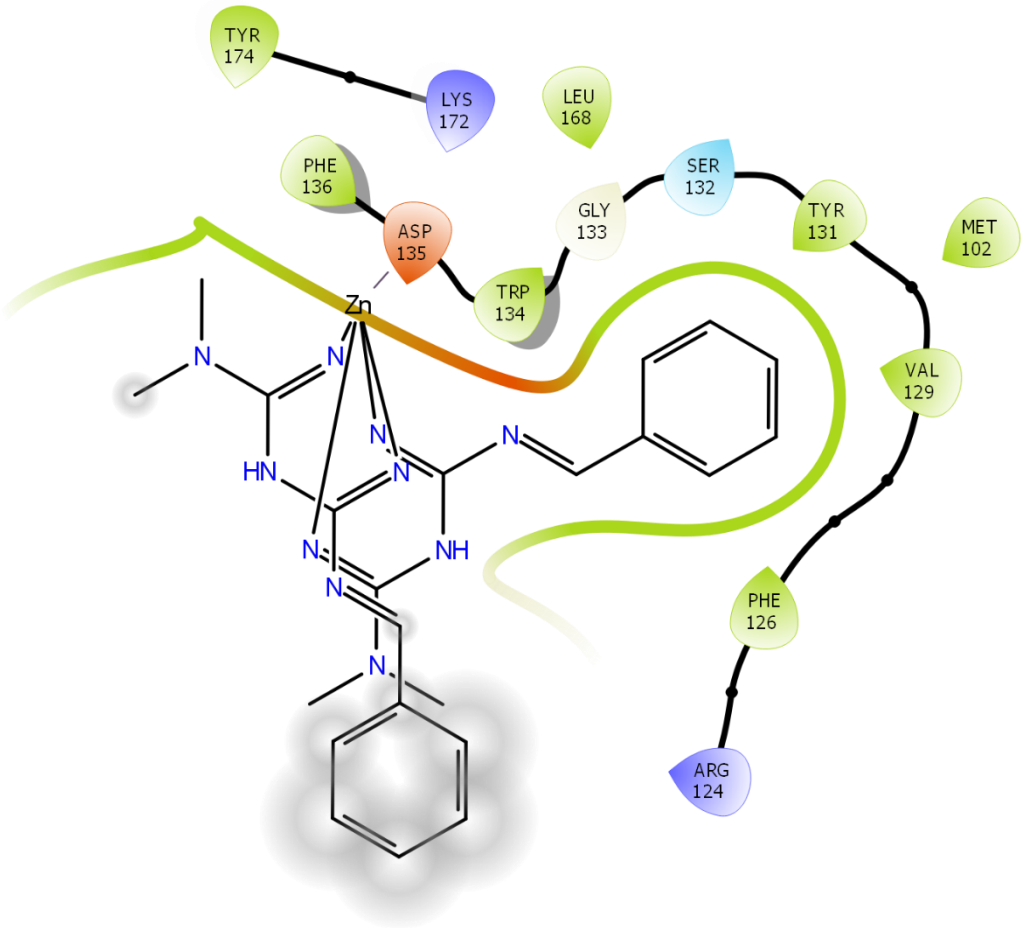
MET-6	ASP 356 TRP 357 ASP 300 ARG 303 HIP 305 TRP 58 TRP 59 TYR 62 GLN 63 LEU 162 HIE 101 LEU 165 ASP 197 NH HN N H_2N N

MET-7	TRP 58 TRP 59 TYR 62 ARG 195 VAL 98 GLU 233 H_2N ASP 197 N^+ H N ILE 235 ALA 198 N^+H_2 HIE 101 N LYS 200 LEU 162 HIP 305 ASP 300 HIS 299 GLY 306 ALA 307 LEU 165 TYR 151

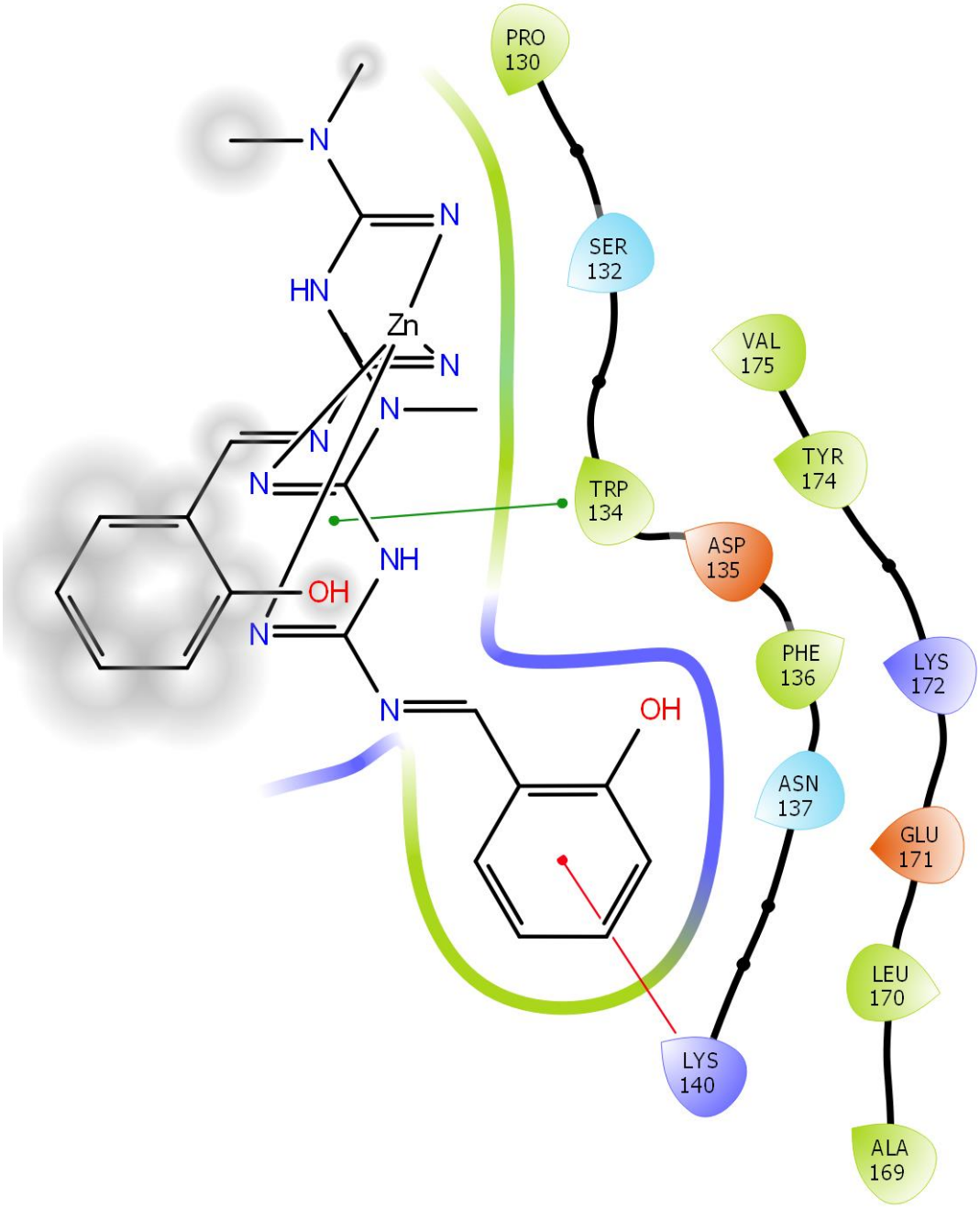
MET-8	GLU 233 HIE 101 ASP 197 ALA 198 GLN 63 ILE 235 ARG 195 TYR 62 GLY 306 H_2N ASP 300 N N^+ H GLU 60 OH TRP 59 N NH O LEU 162 THR 163 LEU 165

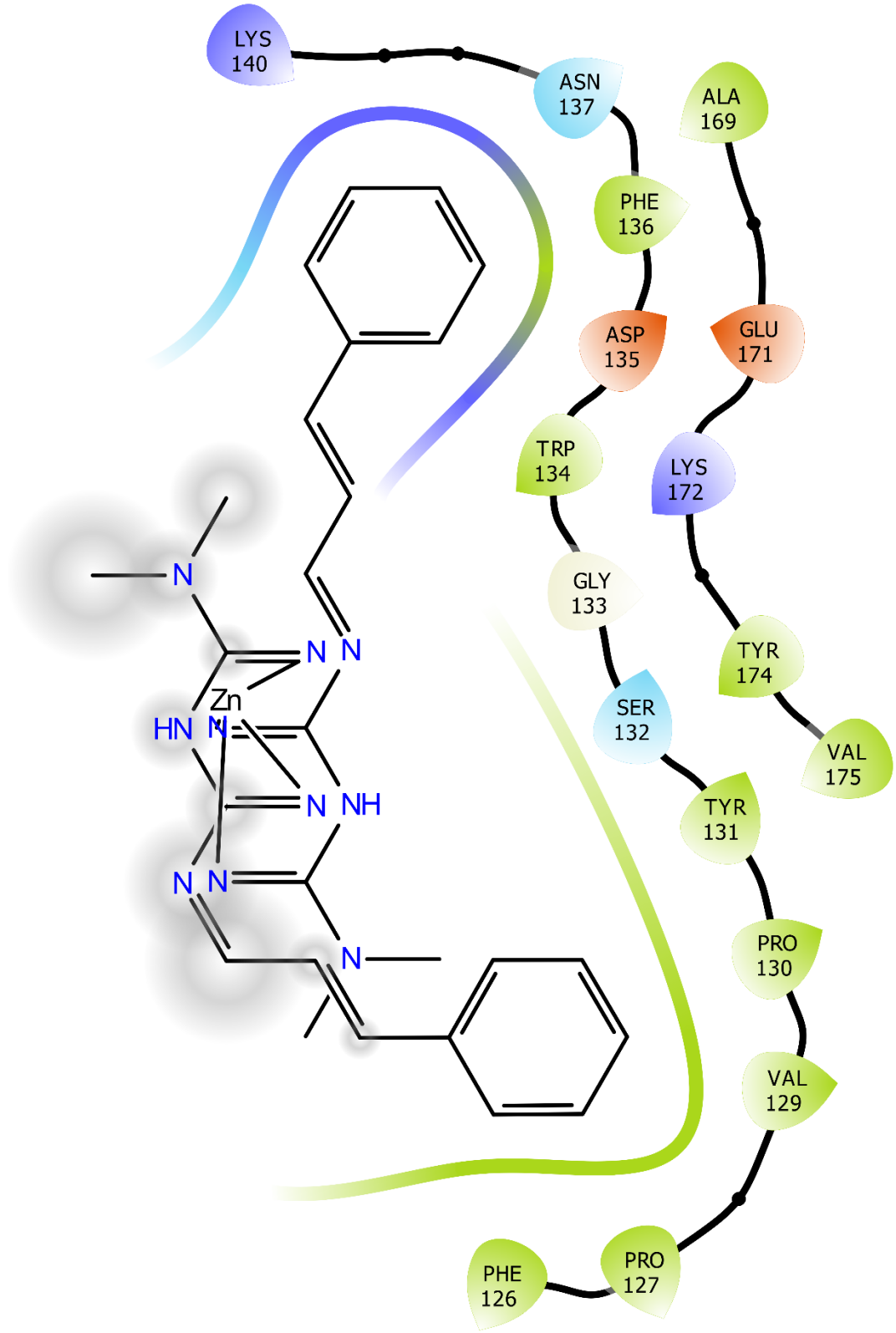
MET-9	ASP 197 ALA 198 ARG 195 ASP 300 GLU 233 HIS 299 ILE 235 HIS 201 HN H_2N N N H TRP 58 ASN 298 N O TRP 59 HIP 305 HIE 101 TYR 62 GLN 63 LEU 162 THR 163 LEU 165

MET	ALA 198 ASP 197 ILE 235 ARG 195 HIE 101 GLU 233 TYR 62 TRP 59 LEU 165 LEU 162 THR 163

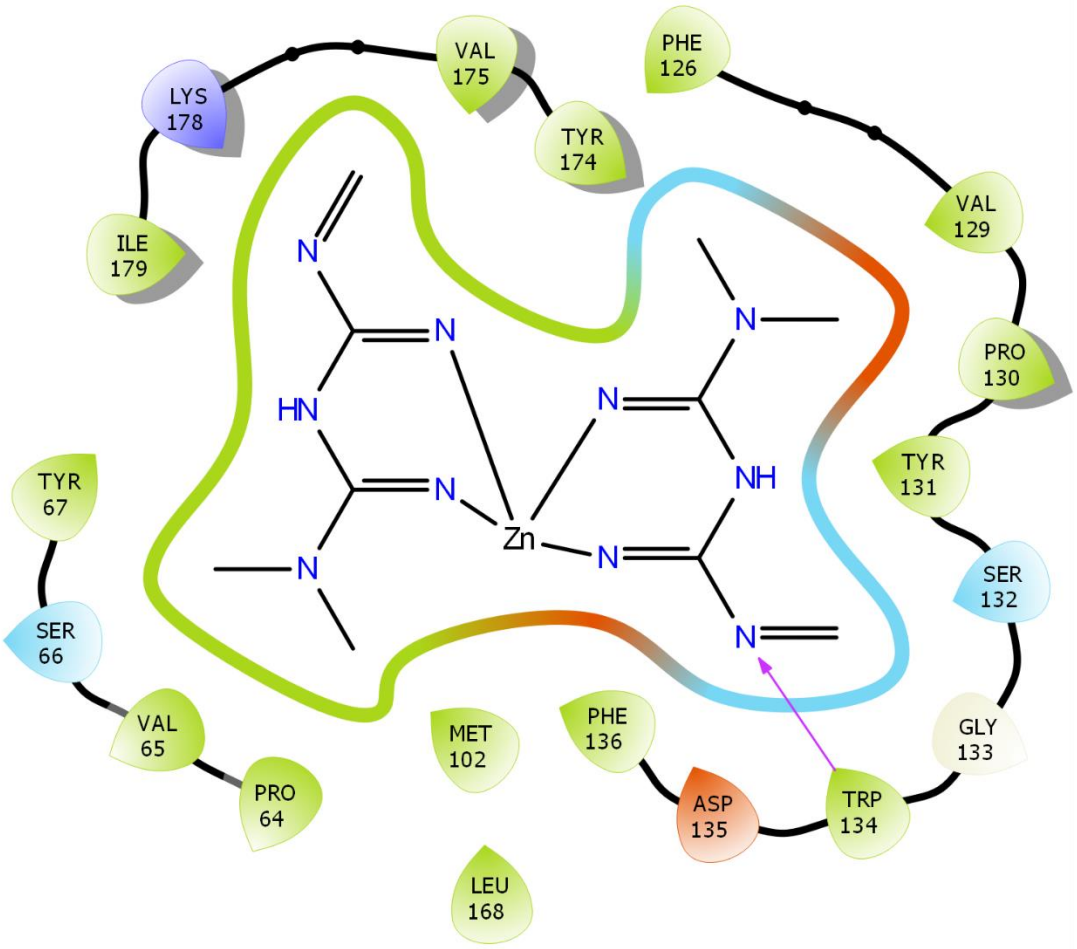
MZN-1	TYR 174 LYS 172 LEU 168 PHE 136 SER 132 GLY 133 TYR 131 MET 102 ASP 135 TRP 134 Zn VAL 129 PHE 126 ARG 124 N HN NH

MZN-2

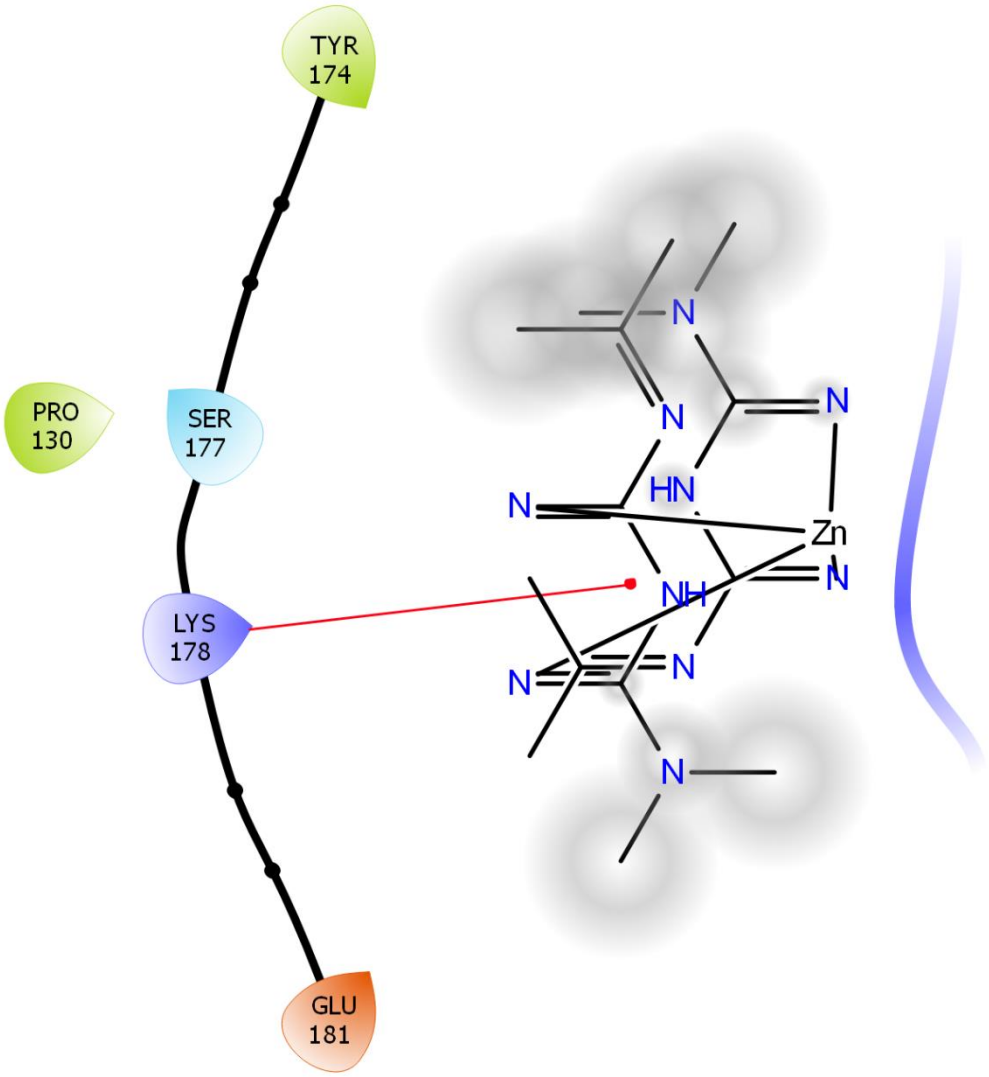

PRO
130
SER
132
VAL
175
TYR
174
TRP
134
ASP
135
PHE
136
LYS
172
ASN
137
GLU
171
LEU
170
LYS
140
ALA
169
N
N
HN
Zn
N
N
N
N
NH
OH
N
N
OH

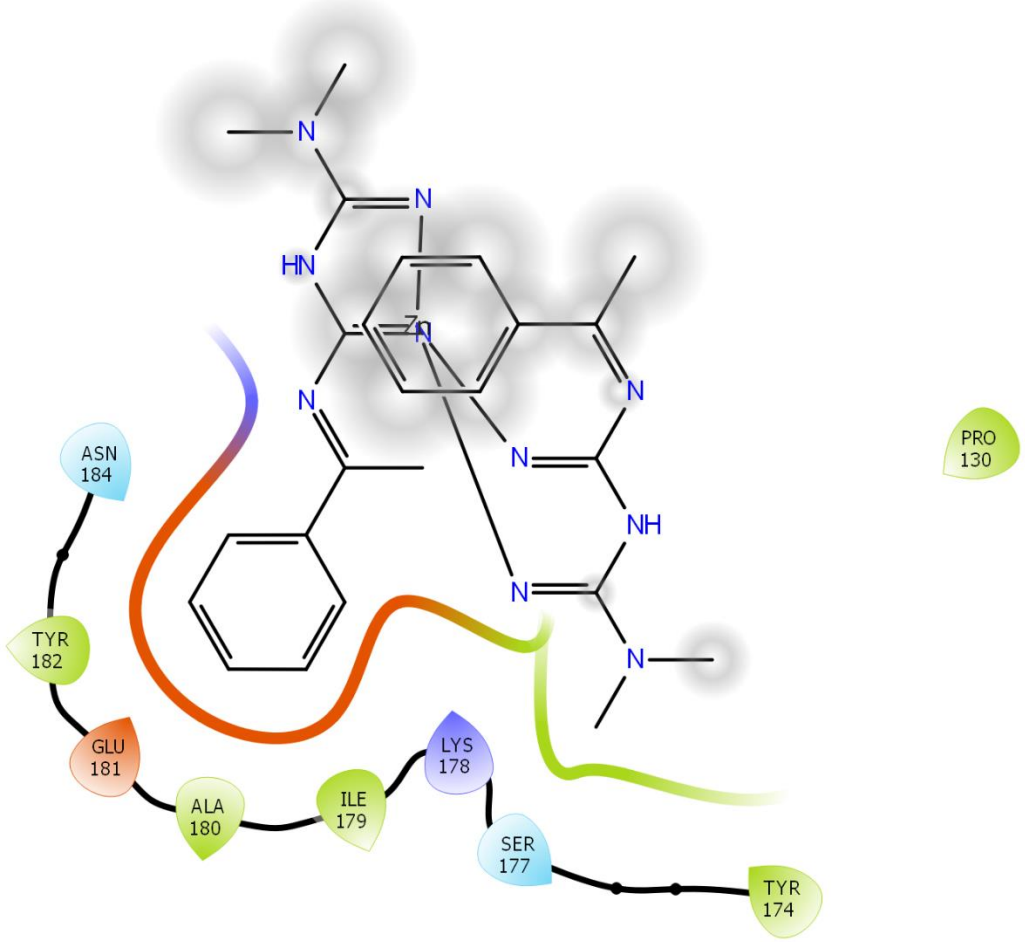

LYS
140
ASN
137
ALA
169
PHE
136
ASP
135
GLU
171
TRP
134
LYS
172
GLY
133
TYR
174
SER
132
VAL
175
TYR
131
PRO
130
VAL
129
PRO
127
PHE
126
N
N N
Zn
HN N
N NH
N N
N

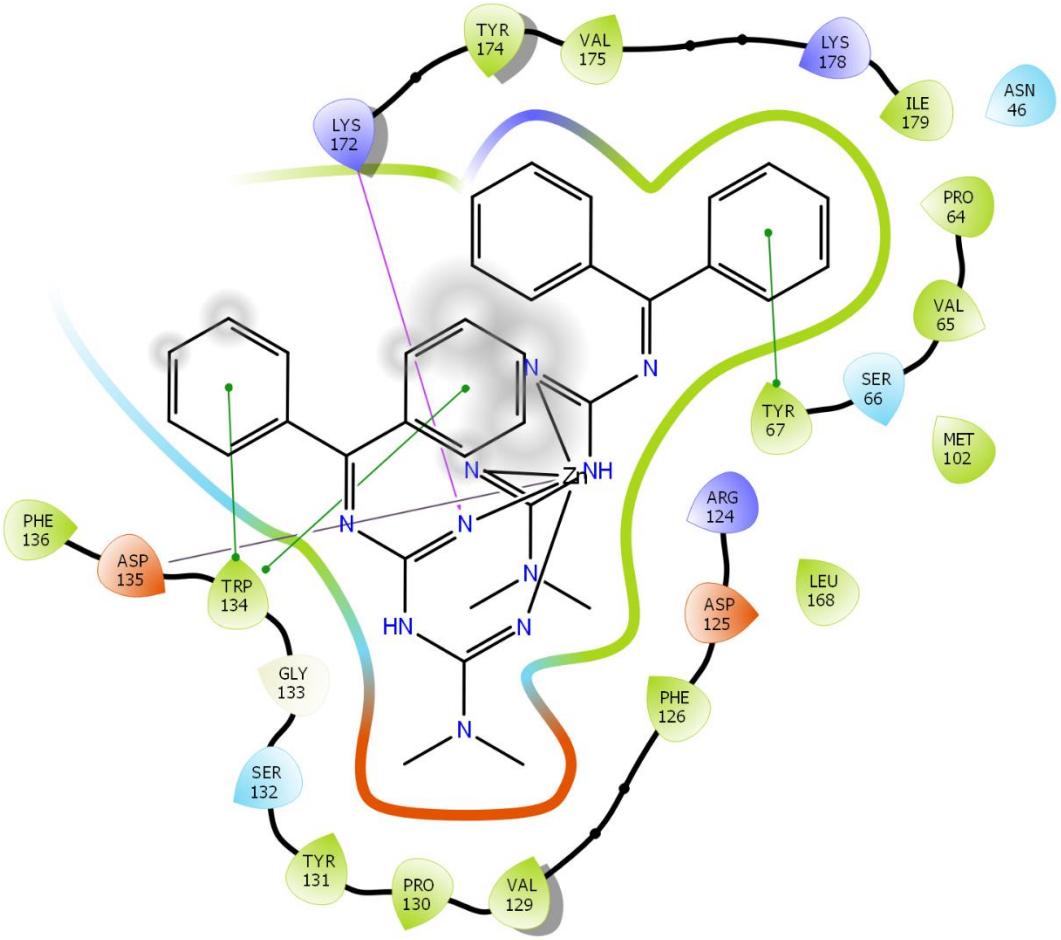
MZN-3

MZN-4	VAL 175 PHE 126 LYS 178 TYR 174 VAL 129 ILE 179 PRO 130 TYR 131 SER 132 TYR 67 SER 66 VAL 65 PRO 64 MET 102 PHE 136 GLY 133 ASP 135 TRP 134 LEU 168 N HN Zn NH

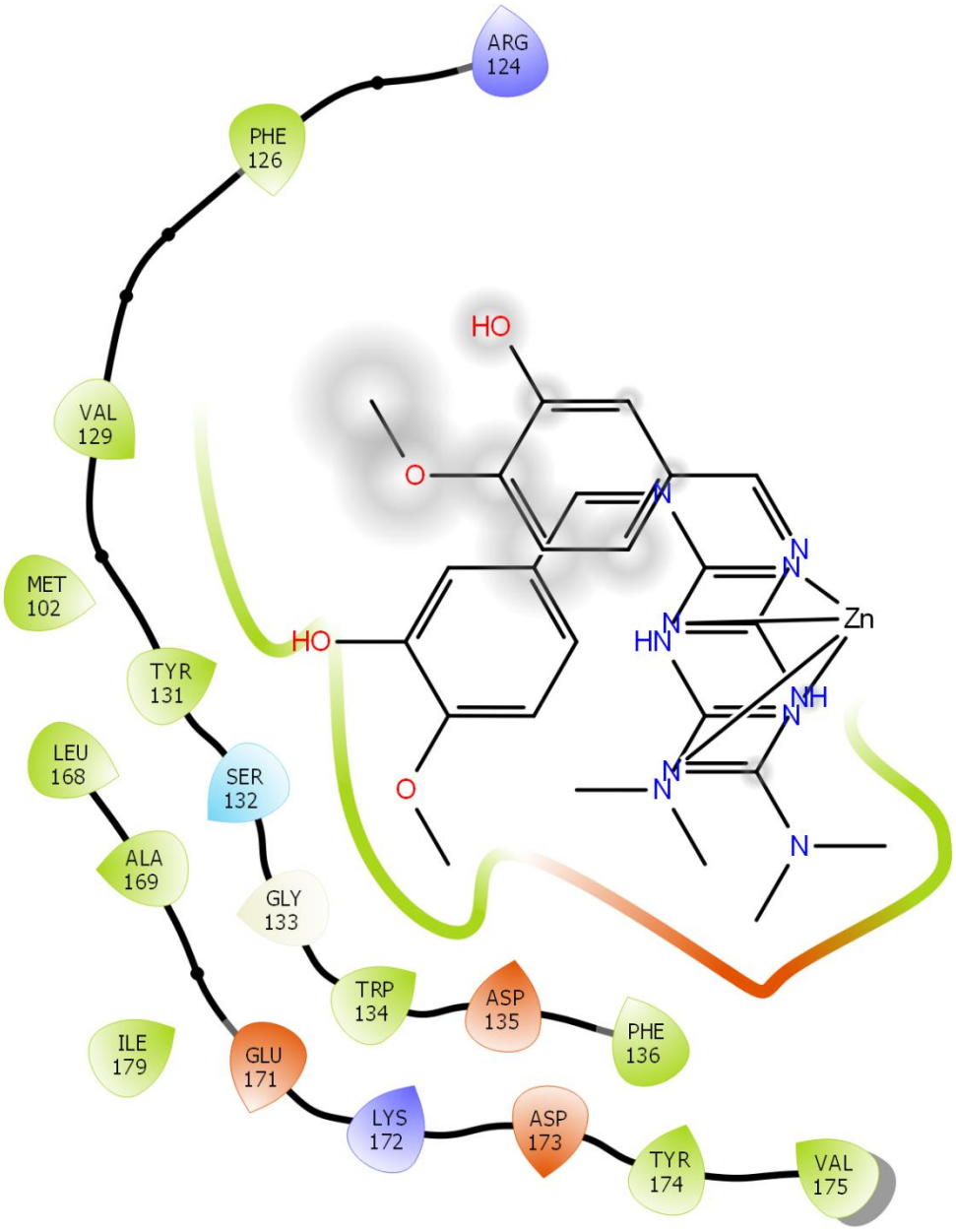
MZN-5



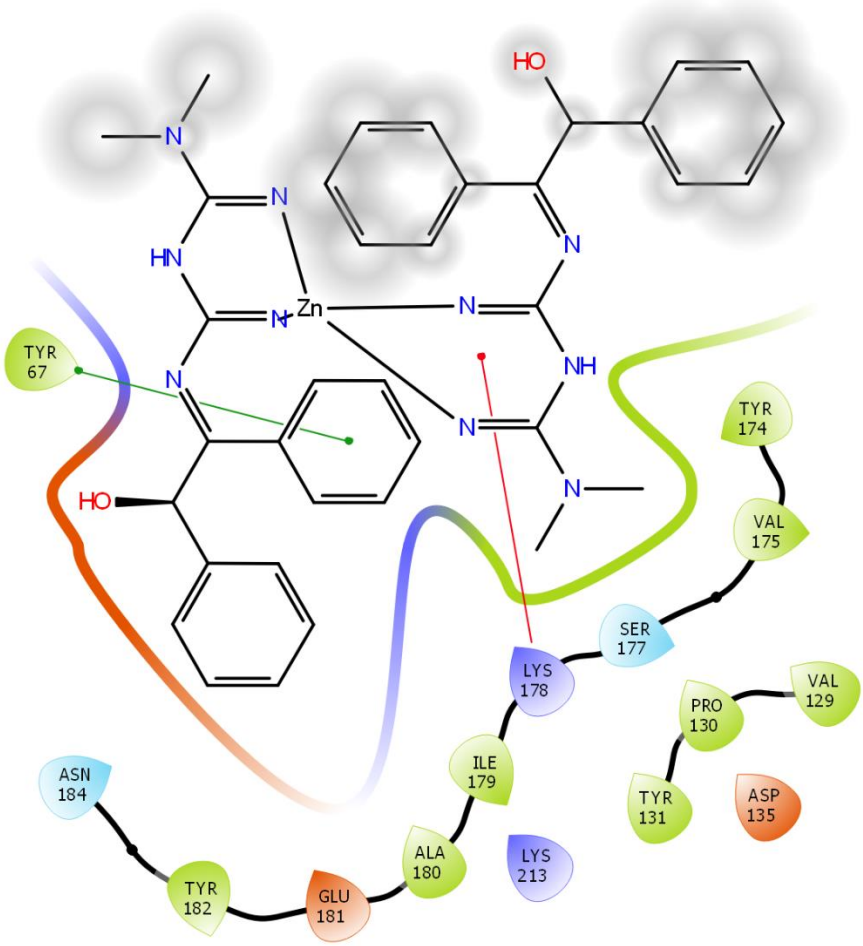
MZN-6	N N HN Zn N N N NH N N ASN 184 TYR 182 GLU 181 ALA 180 ILE 179 LYS 178 SER 177 TYR 174 PRO 130

MZN-7	TYR 174 VAL 175 LYS 178 ILE 179 ASN 46 LYS 172 PRO 64 VAL 65 SER 66 TYR 67 MET 102 ARG 124 LEU 168 ASP 125 PHE 126 PHE 136 ASP 135 TRP 134 GLY 133 SER 132 TYR 131 PRO 130 VAL 129 N NH HN

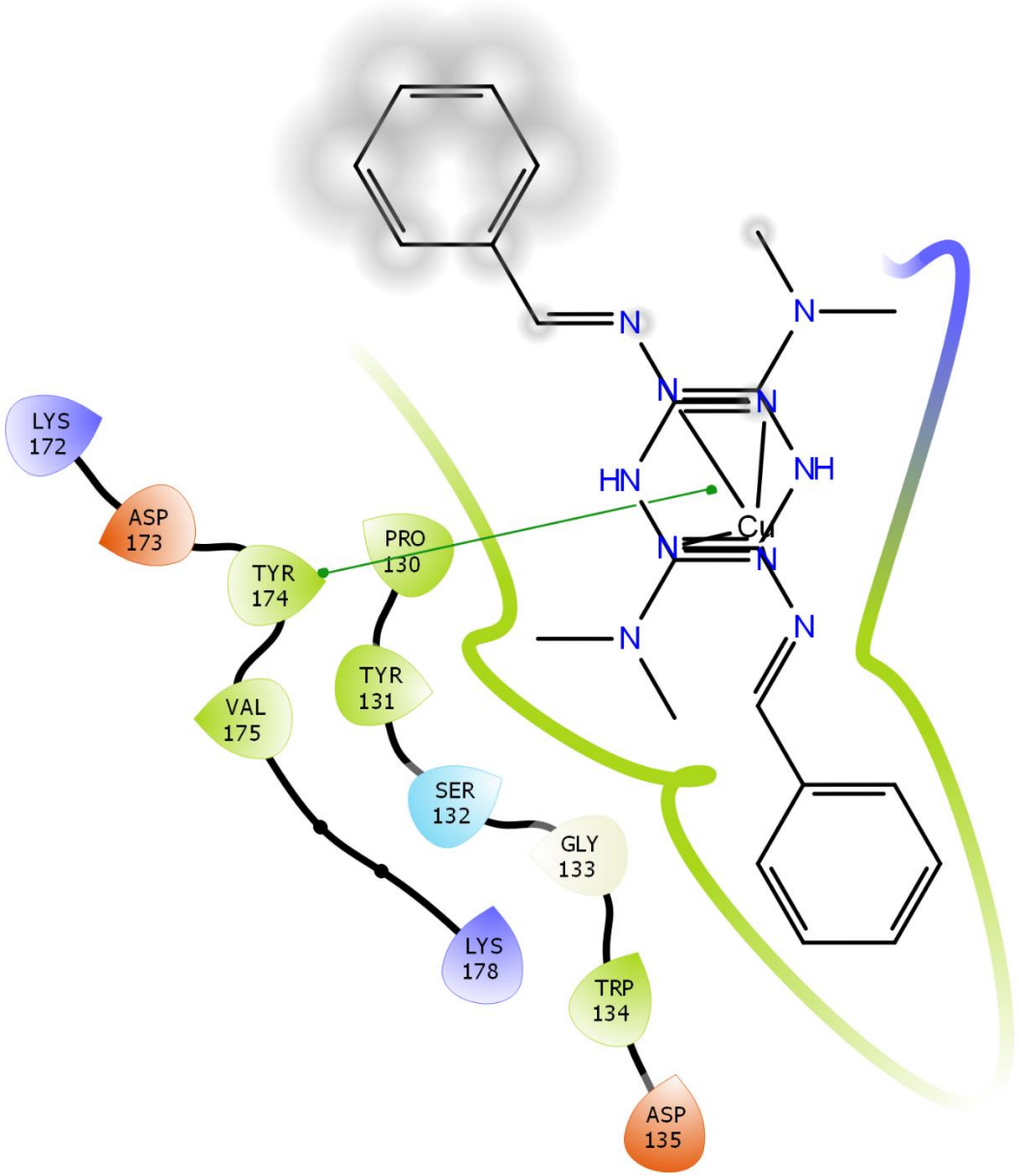
MZN-8

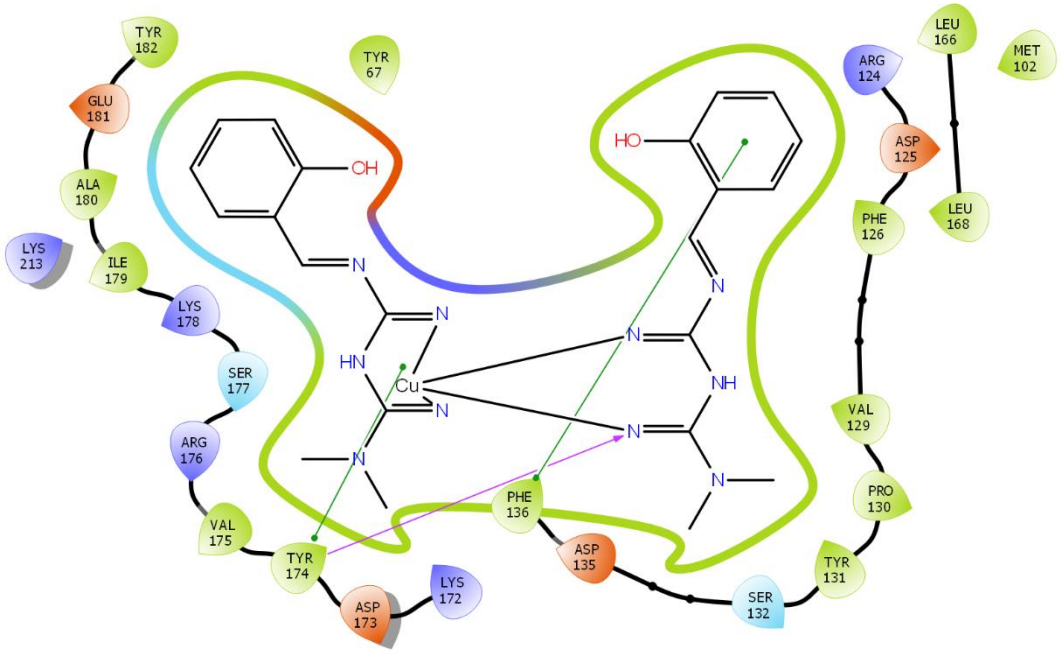

ARG
124
PHE
126
VAL
129
MET
102
TYR
131
LEU
168
SER
132
ALA
169
GLY
133
TRP
134
ASP
135
PHE
136
ILE
179
GLU
171
LYS
172
ASP
173
TYR
174
VAL
175
HO
O
HO
O
N
N
HN
N
Zn
NH
N
N
N

MZN-9

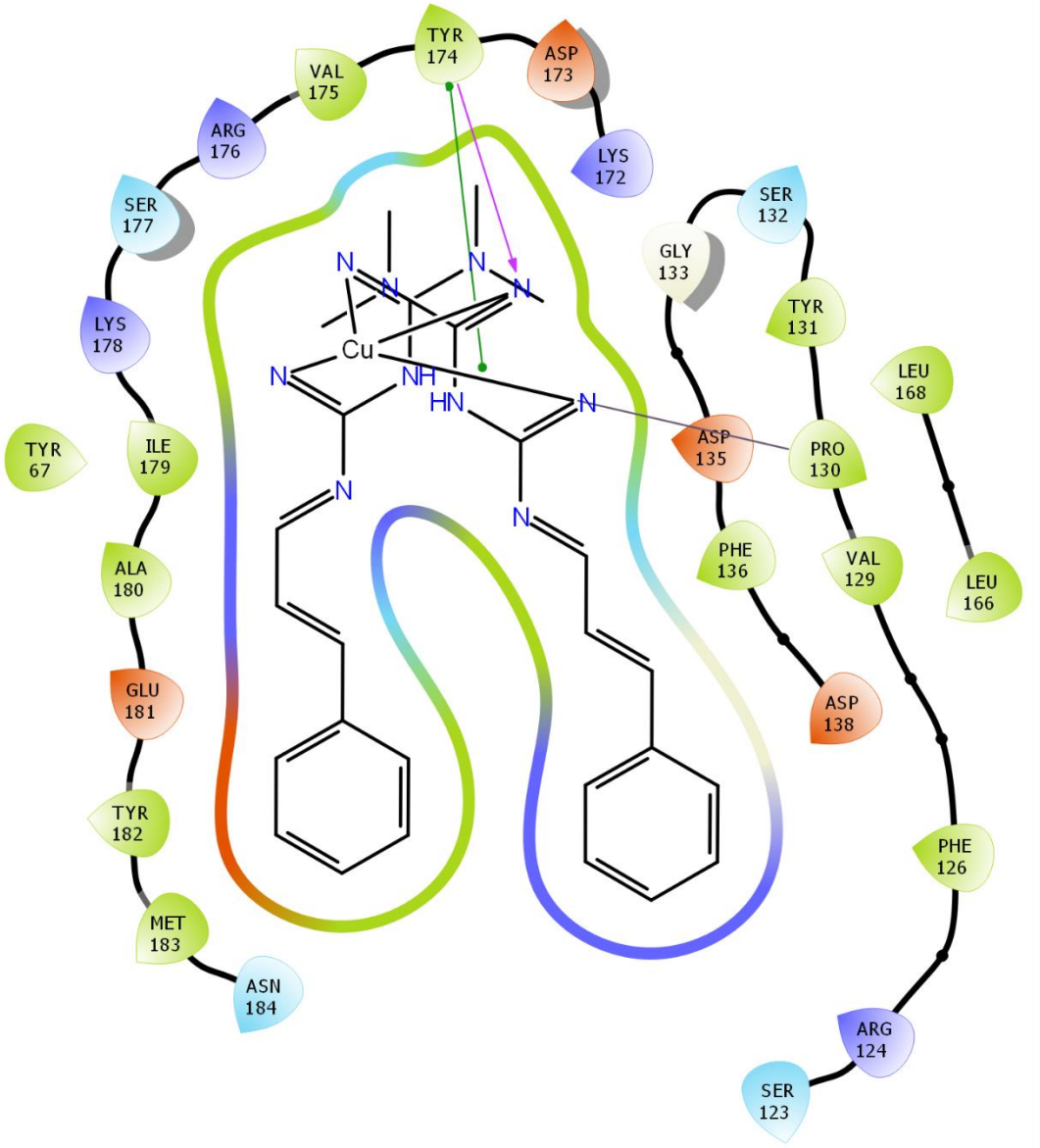

HO
N
N
HN
N
Zn
N
N
NH
N
N
HO
TYR
67
TYR
174
VAL
175
SER
177
LYS
178
PRO
130
VAL
129
ILE
179
TYR
131
ASP
135
ASN
184
ALA
180
LYS
213
TYR
182
GLU
181

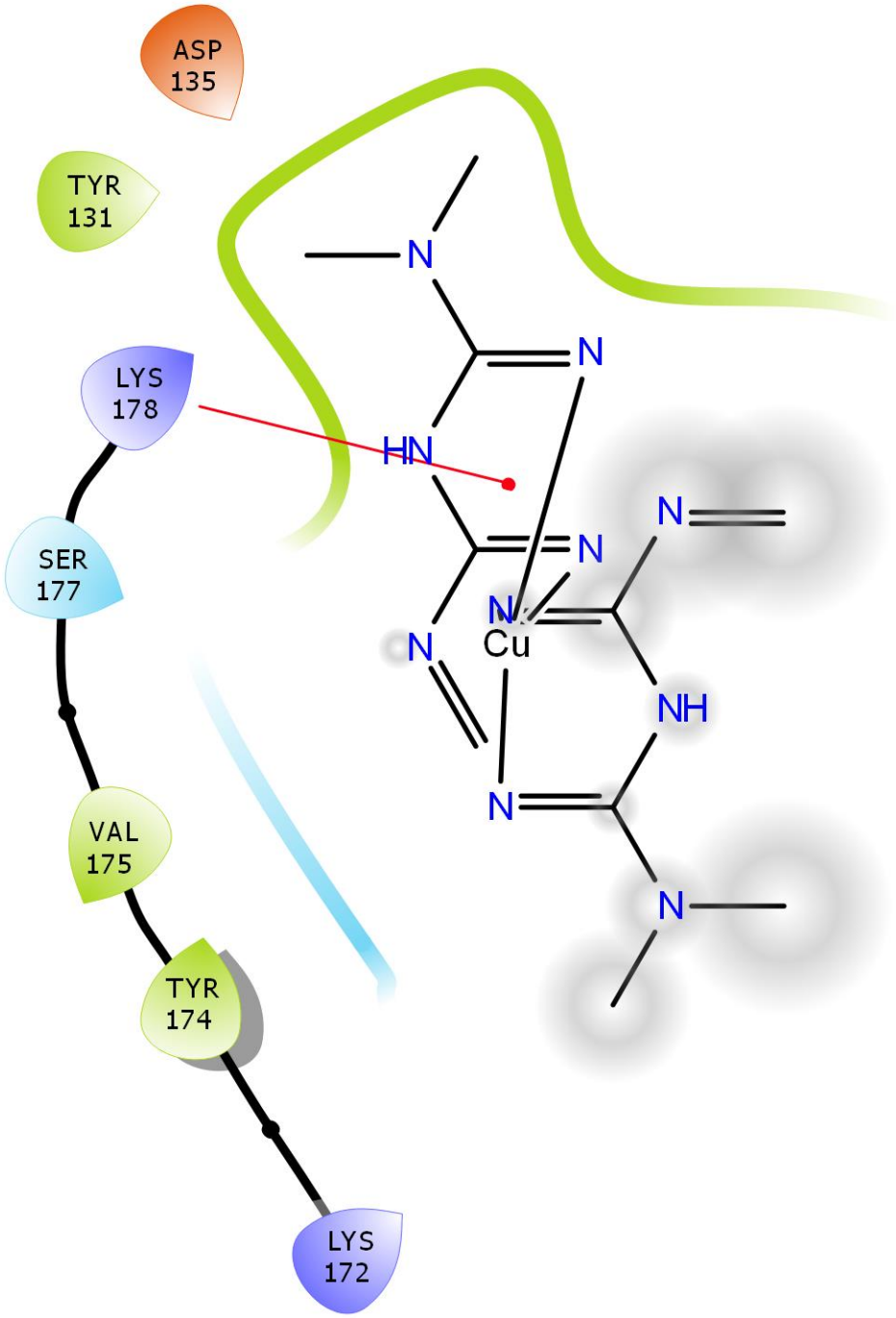
MCu-1


LYS
172
ASP
173
TYR
174
PRO
130
TYR
131
VAL
175
SER
132
GLY
133
LYS
178
TRP
134
ASP
135
N
N
N
N
HN
NH
Cu
N
N
N
N

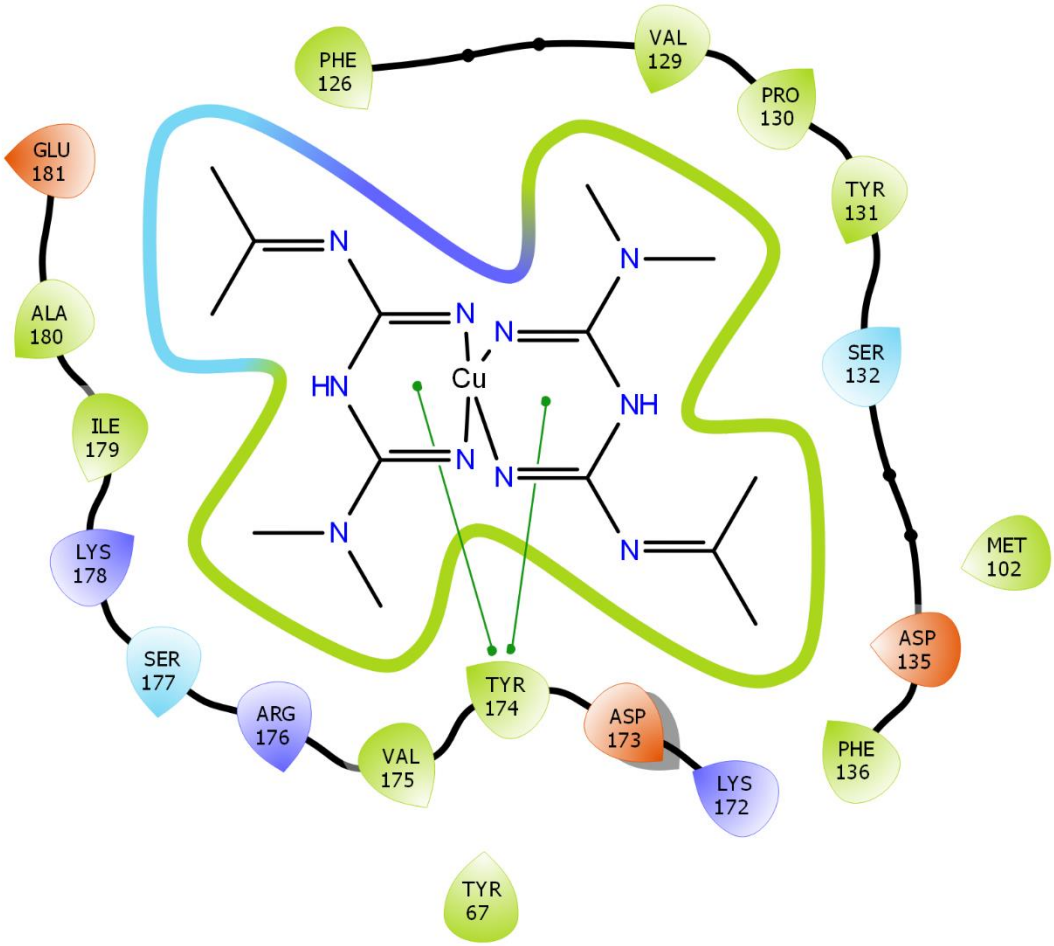
MCu-2	TYR 182 GLU 181 ALA 180 LYS 213 ILE 179 LYS 178 SER 177 ARG 176 VAL 175 TYR 174 ASP 173 LYS 172 TYR 67 OH HO N HN Cu NH PHE 136 ASP 135 SER 132 TYR 131 PRO 130 VAL 129 PHE 126 ASP 125 ARG 124 LEU 168 LEU 166 MET 102

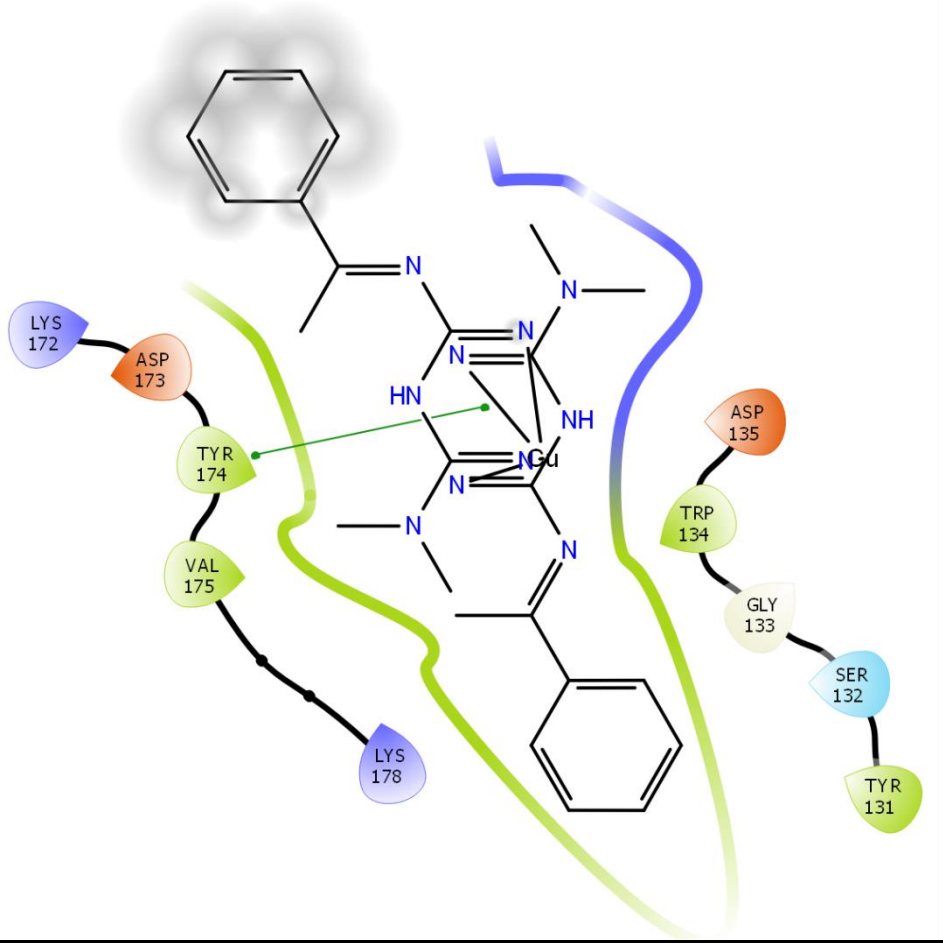
MCu-3


TYR 174
ASP 173
VAL 175
ARG 176
LYS 172
SER 177
SER 132
GLY 133
LYS 178
TYR 131
LEU 168
TYR 67
ILE 179
ASP 135
PRO 130
ALA 180
PHE 136
VAL 129
LEU 166
GLU 181
ASP 138
TYR 182
PHE 126
MET 183
ASN 184
ARG 124
SER 123
Cu
N
NH
HN

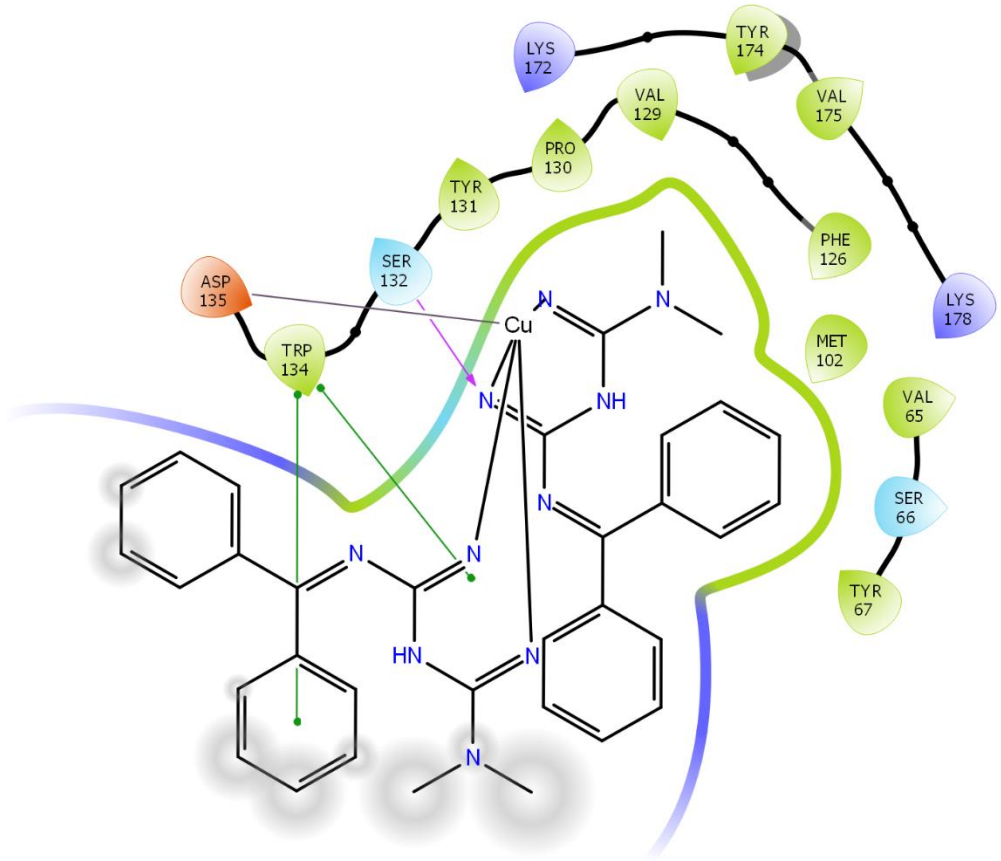

ASP
135
TYR
131
LYS
178
SER
177
VAL
175
TYR
174
LYS
172
N
N
HN
N
N
N
Cu
N
NH
N
N

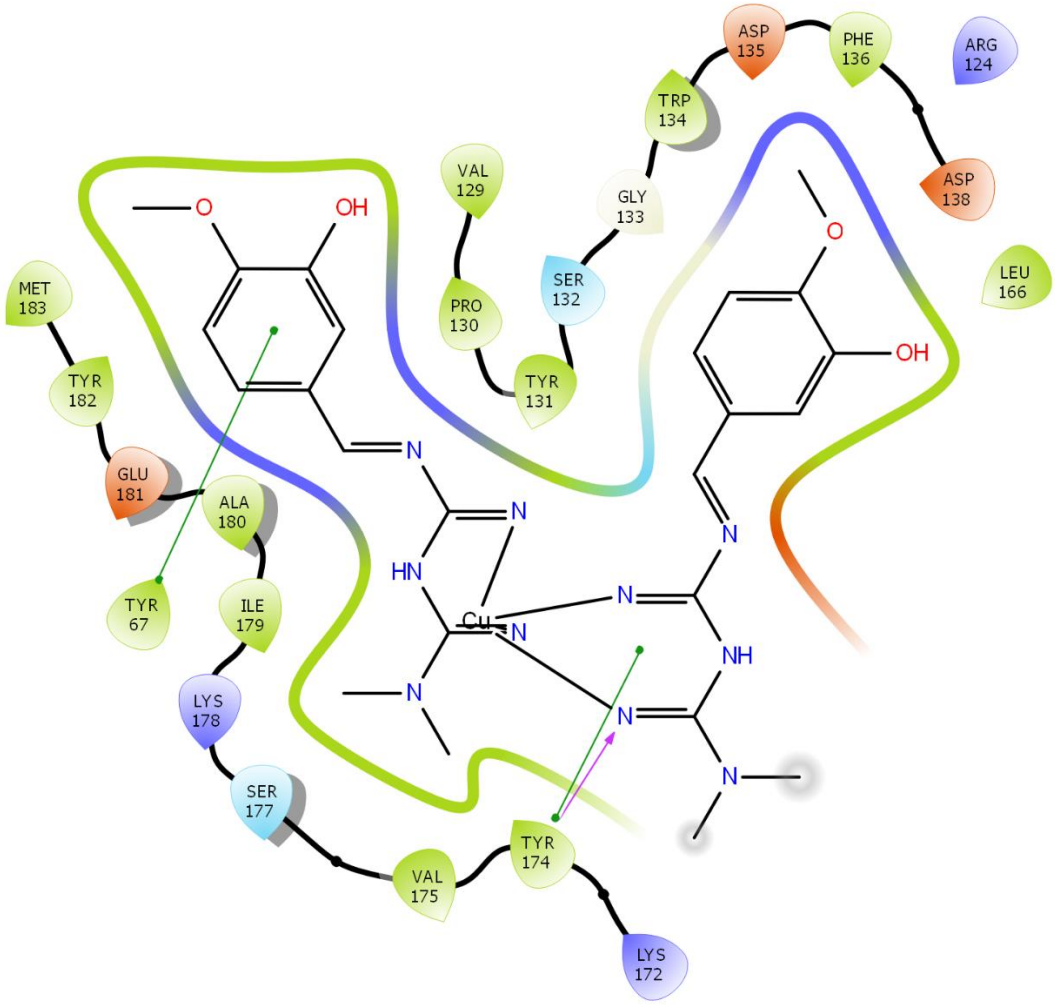
MCu-4

MCu-5	PHE 126 VAL 129 PRO 130 TYR 131 SER 132 MET 102 ASP 135 PHE 136 LYS 172 ASP 173 TYR 174 VAL 175 ARG 176 SER 177 LYS 178 ILE 179 ALA 180 GLU 181 TYR 67 N HN Cu NH

MCu-6	LYS 172 ASP 173 TYR 174 VAL 175 LYS 178 HN NH Cu ASP 135 TRP 134 GLY 133 SER 132 TYR 131

MCu-7


LYS
172
TYR
174
VAL
175
VAL
129
PRO
130
TYR
131
PHE
126
SER
132
ASP
135
LYS
178
Cu
TRP
134
MET
102
VAL
65
NH
SER
66
TYR
67
HN

MCu-8	

ASP 135
PHE 136
ARG 124
TRP 134
ASP 138
VAL 129
GLY 133
LEU 166
SER 132
PRO 130
TYR 131
MET 183
TYR 182
GLU 181
ALA 180
TYR 67
ILE 179
LYS 178
SER 177
VAL 175
TYR 174
LYS 172
O
OH
N
HN
Cu
NH

MCu-9

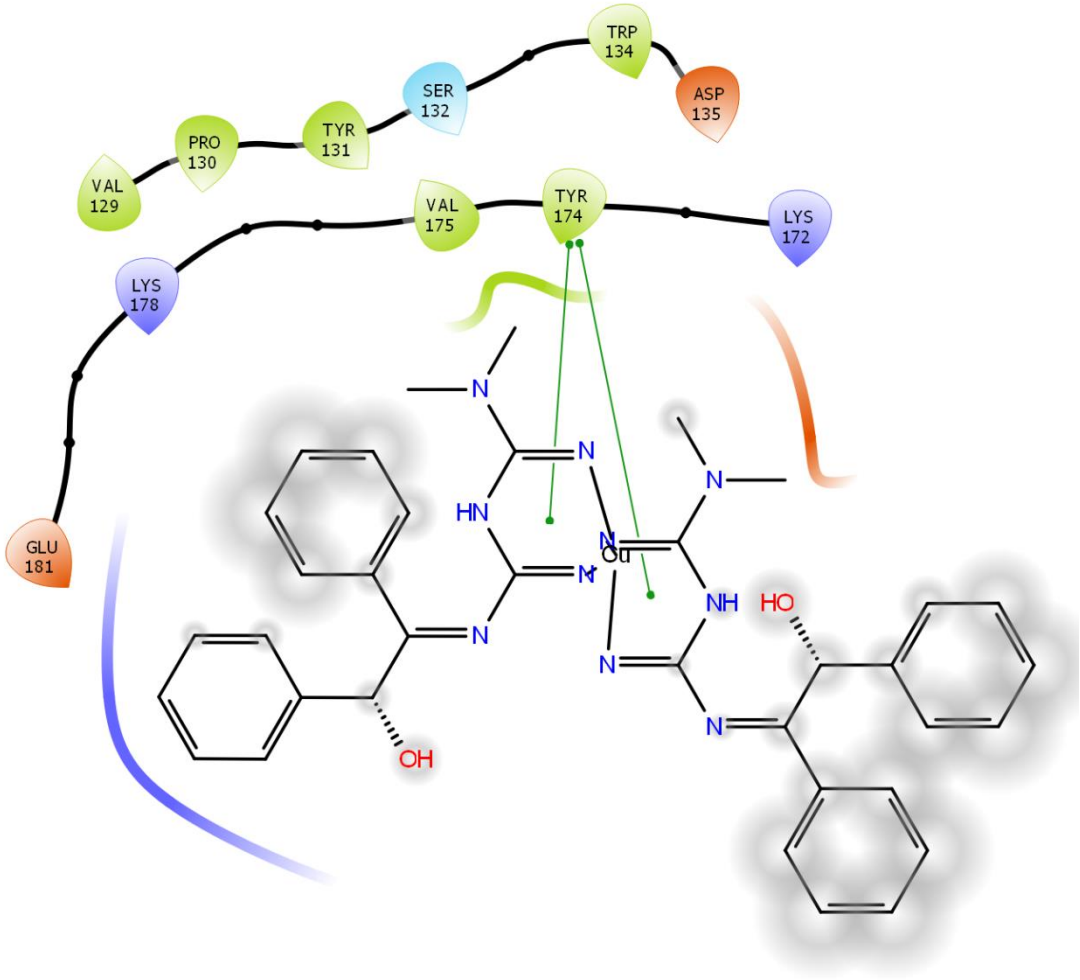
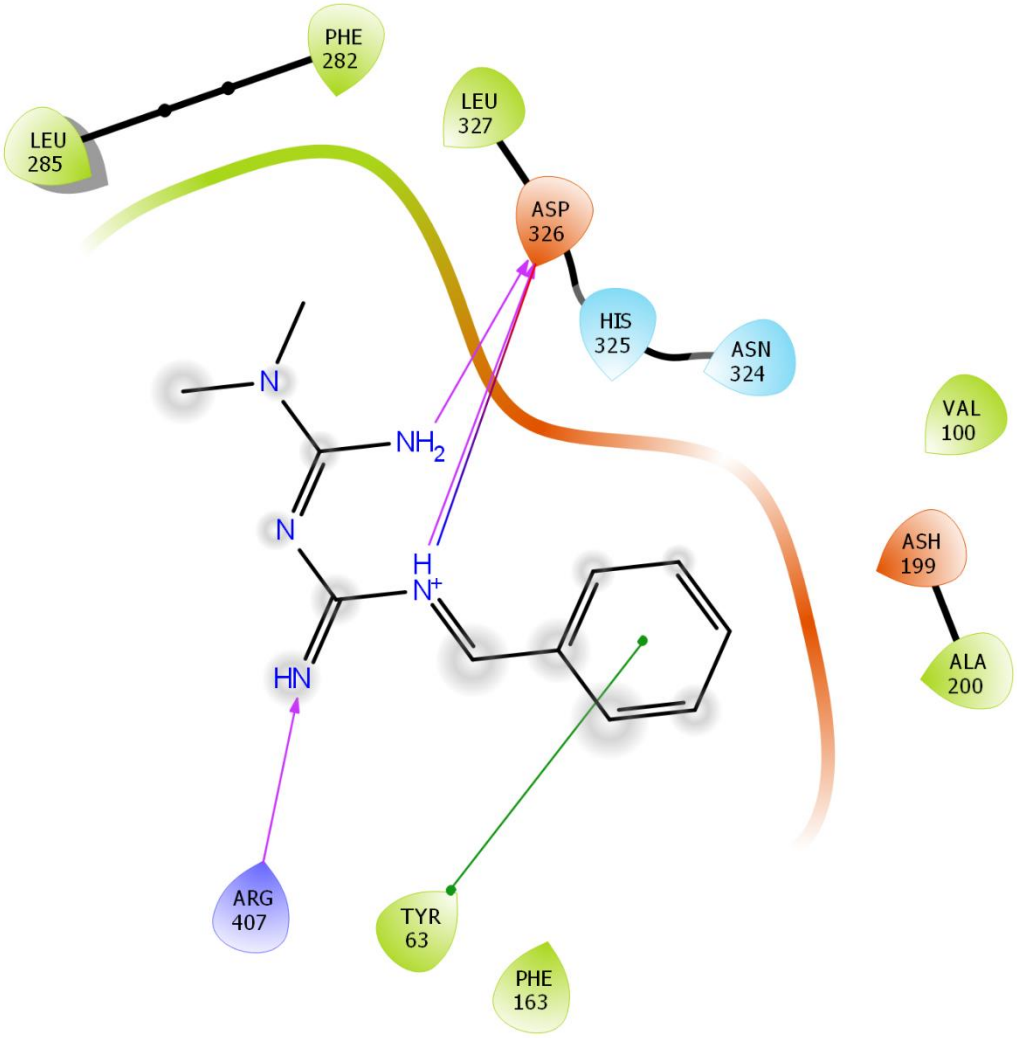
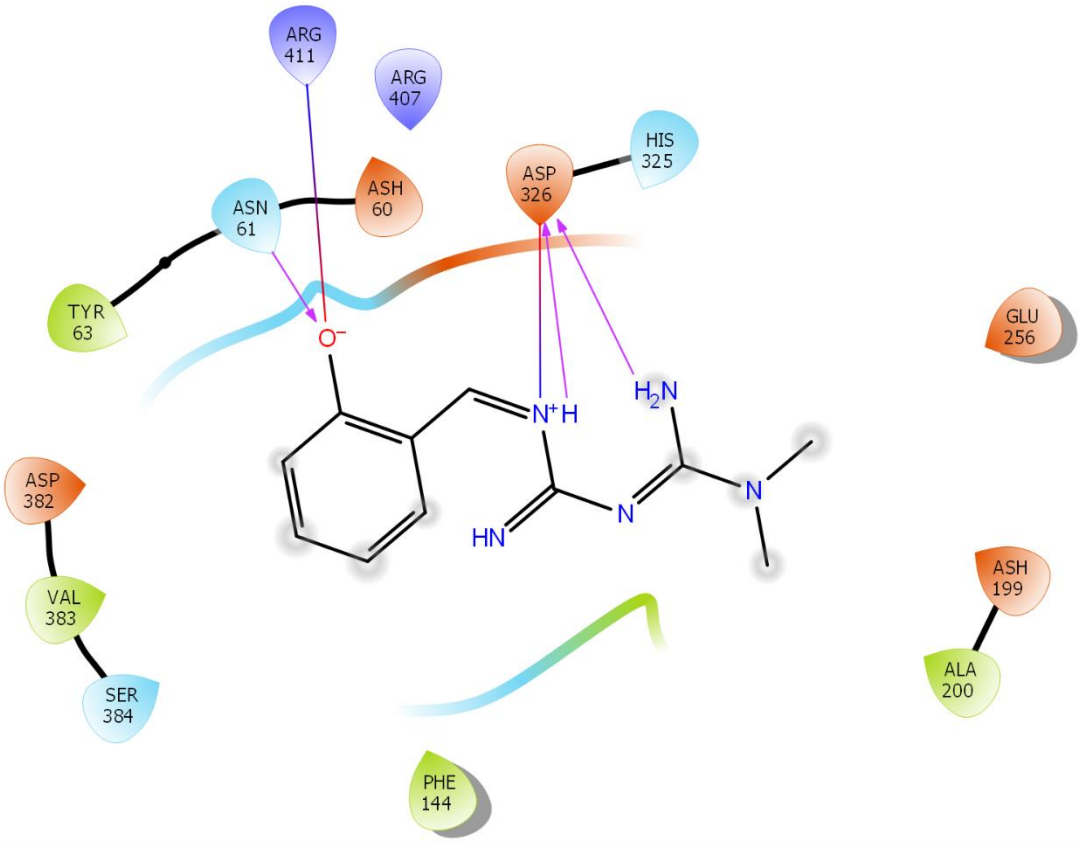
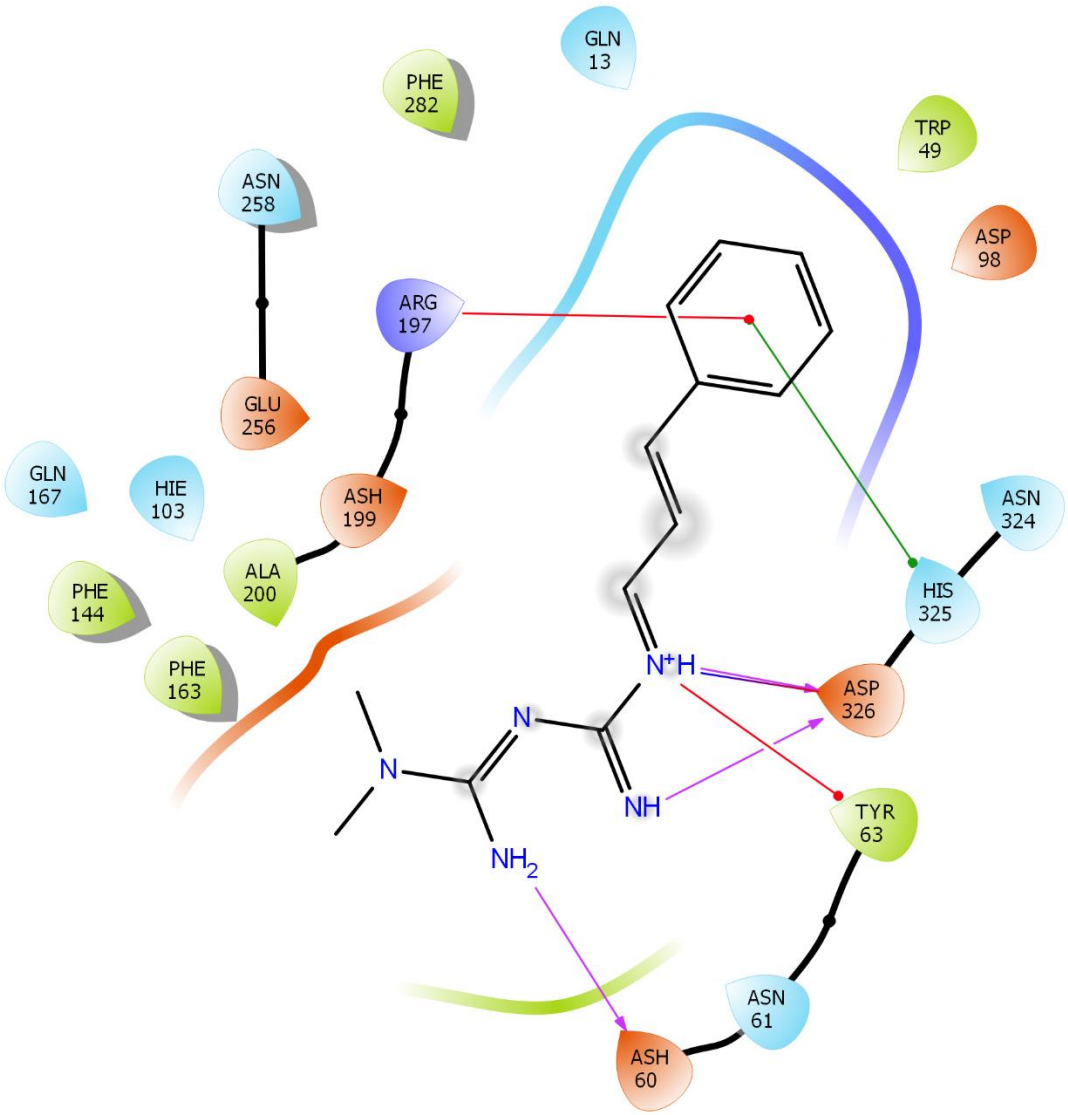
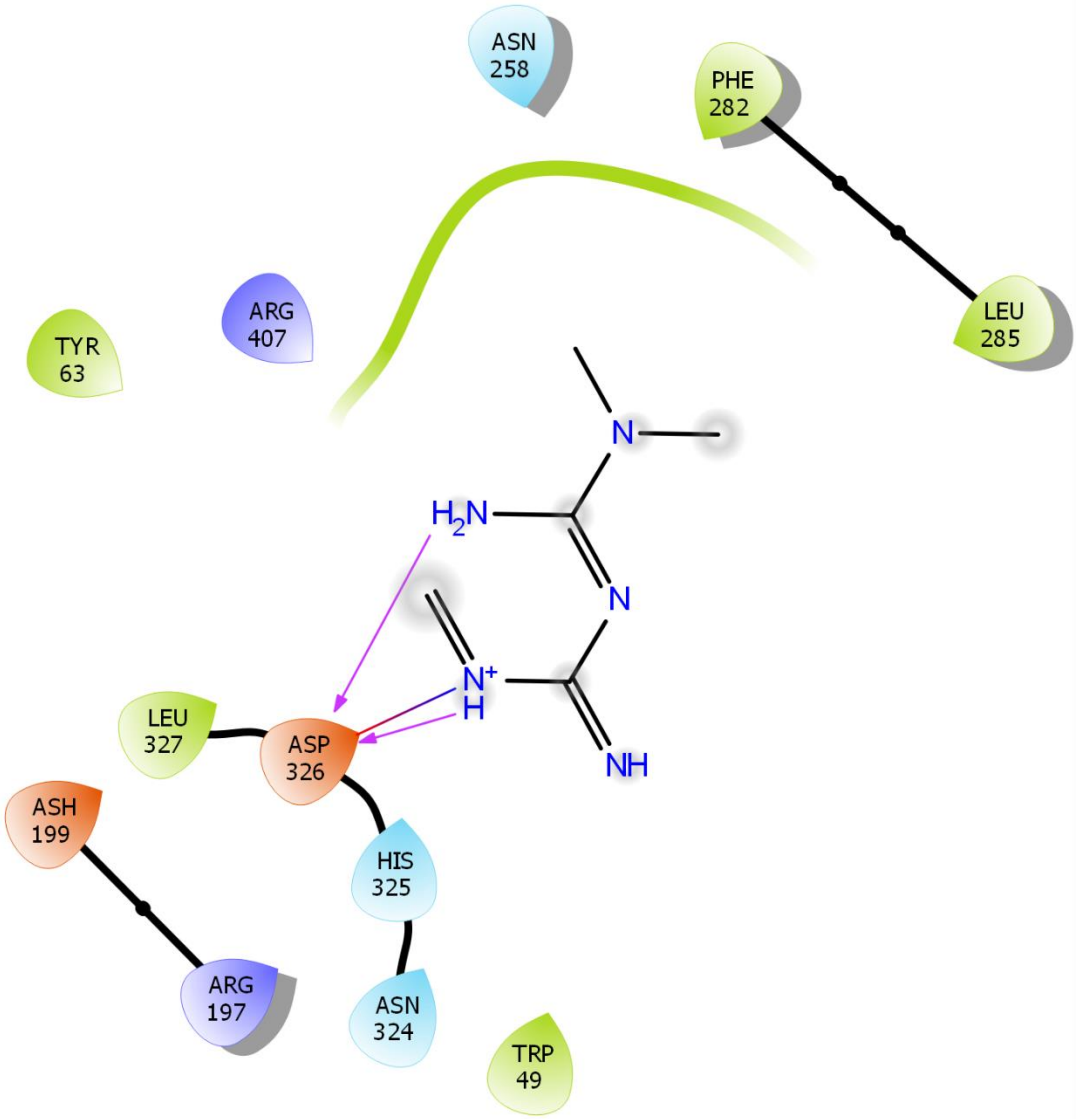

TRP 134
ASP 135
SER 132
TYR 131
PRO 130
VAL 129
VAL 175
TYR 174
LYS 172
LYS 178
GLU 181
N
HN
N
Cu
NH
HO
OH

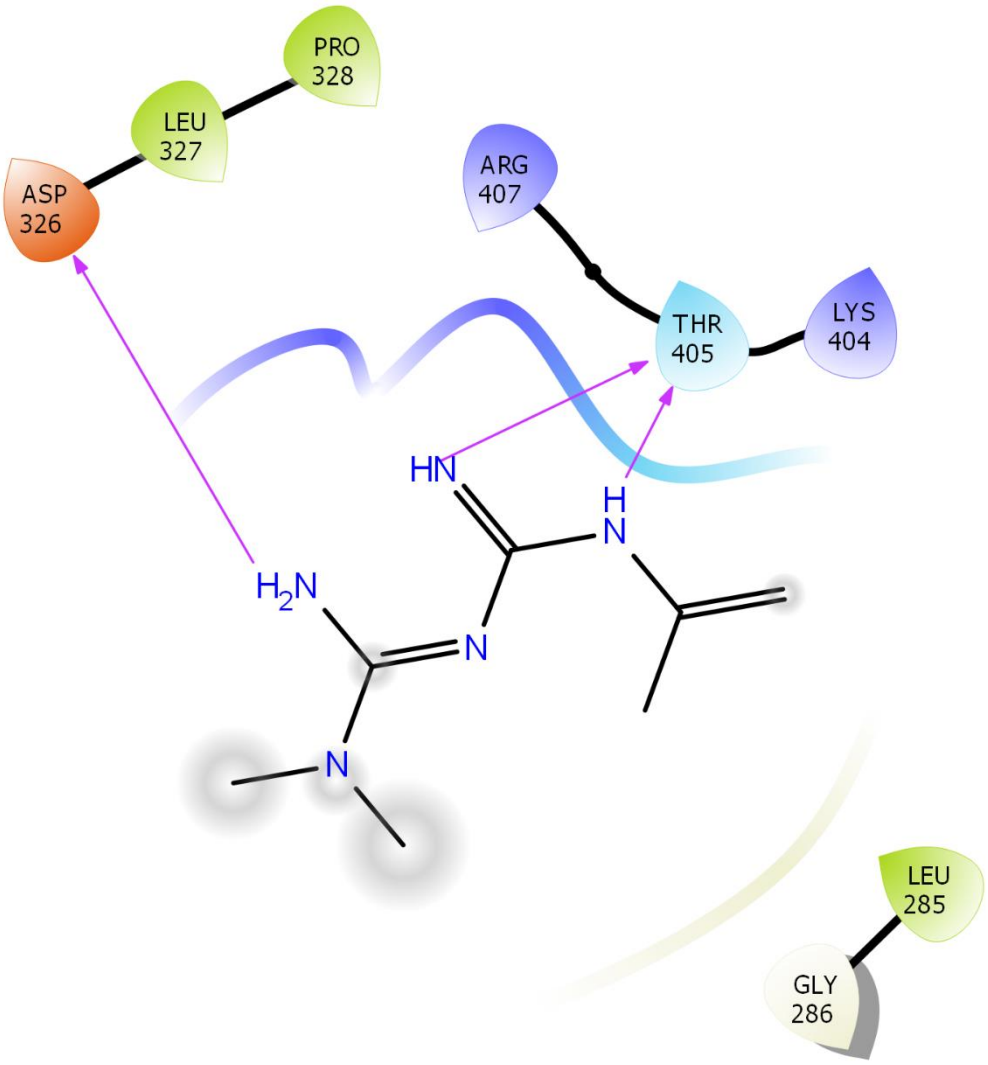
Table S3. 2D structures of all Metformin derivatives with respect to glucosidase enzyme.

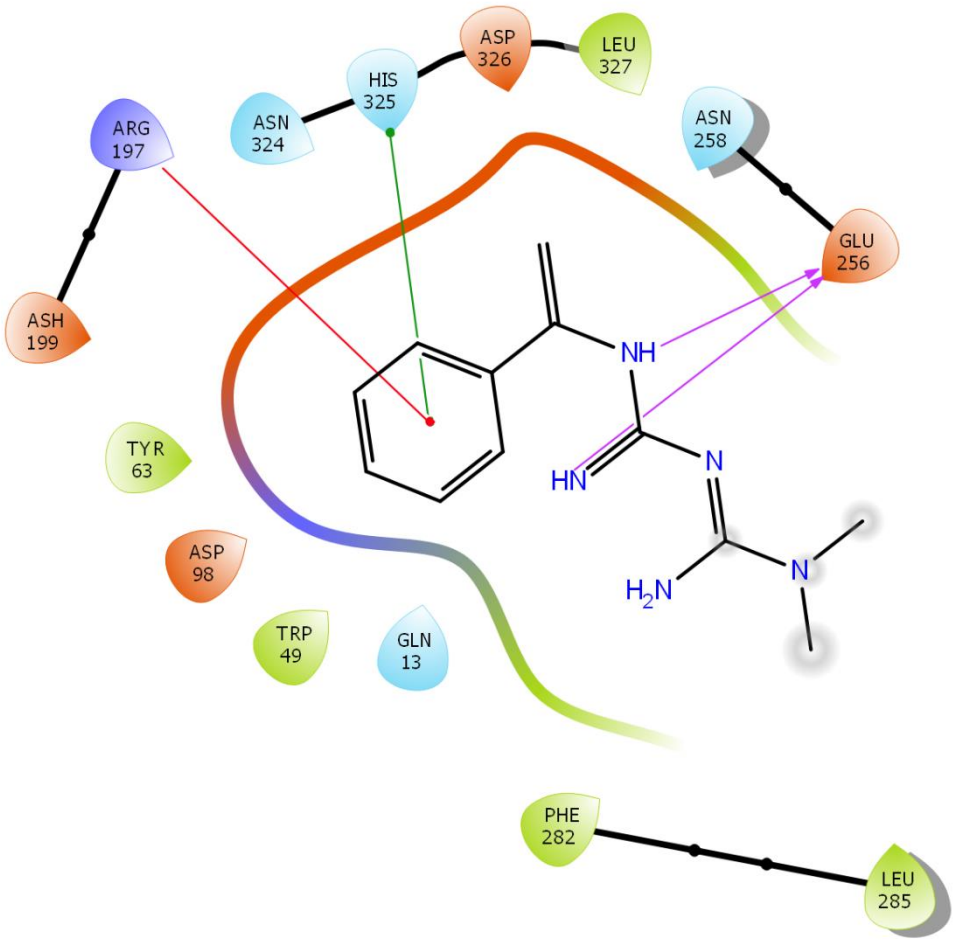
Derivative code	2D Pose
MET-1	

MET-2	ARG 411 ARG 407 HIS 325 ASP 326 ASH 60 ASN 61 TYR 63 GLU 256 O⁻ N⁺H H₂N N N HN ASP 382 VAL 383 SER 384 ASH 199 ALA 200 PHE 144

MET-3	GLN 13 PHE 282 TRP 49 ASN 258 ASP 98 ARG 197 GLU 256 GLN 167 HIE 103 ASH 199 ASN 324 ALA 200 HIS 325 PHE 144 PHE 163 N+H ASP 326 N N NH TYR 63 NH2 ASN 61 ASH 60

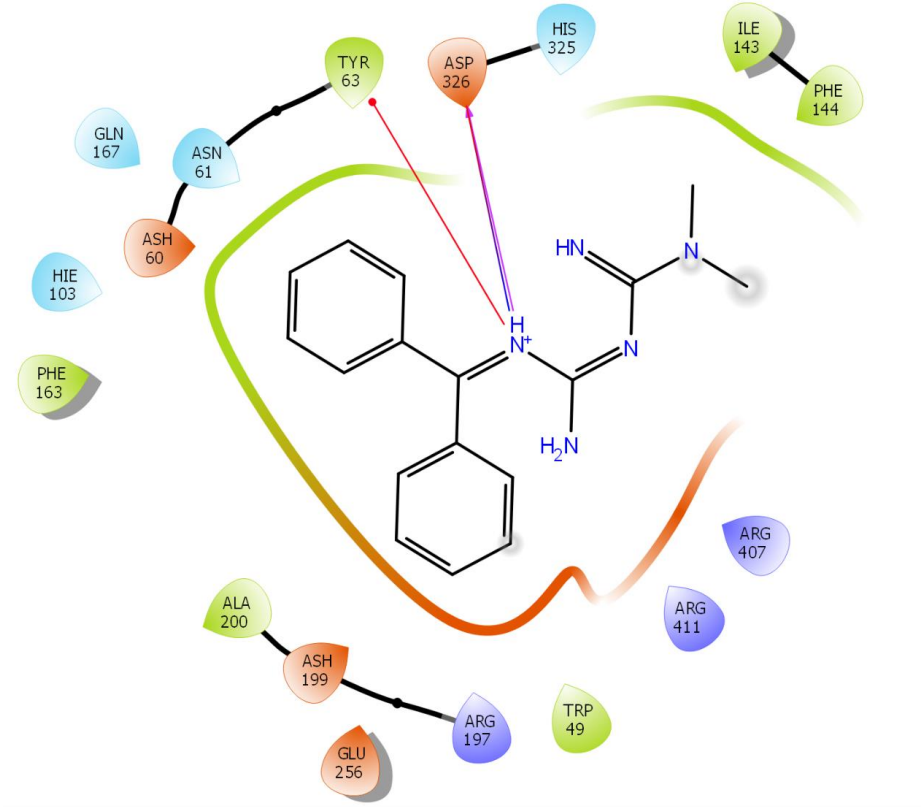
MET-4	ASN 258 PHE 282 LEU 285 ARG 407 TYR 63 N H_2N N N^+ H NH LEU 327 ASP 326 ASH 199 HIS 325 ARG 197 ASN 324 TRP 49

MET-5	PRO 328 LEU 327 ASP 326 ARG 407 THR 405 LYS 404 HN H N H_2N N N LEU 285 GLY 286

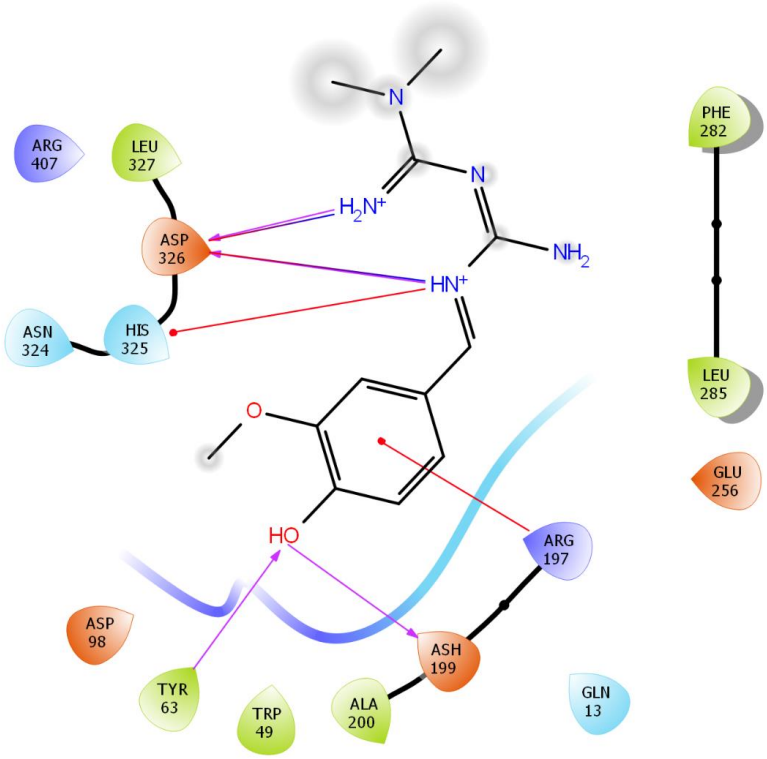

ASP
326
LEU
327
HIS
325
ASN
324
ARG
197
ASN
258
GLU
256
ASH
199
NH
HN
N
N
H_2N
TYR
63
ASP
98
TRP
49
GLN
13
PHE
282
LEU
285

MET-6

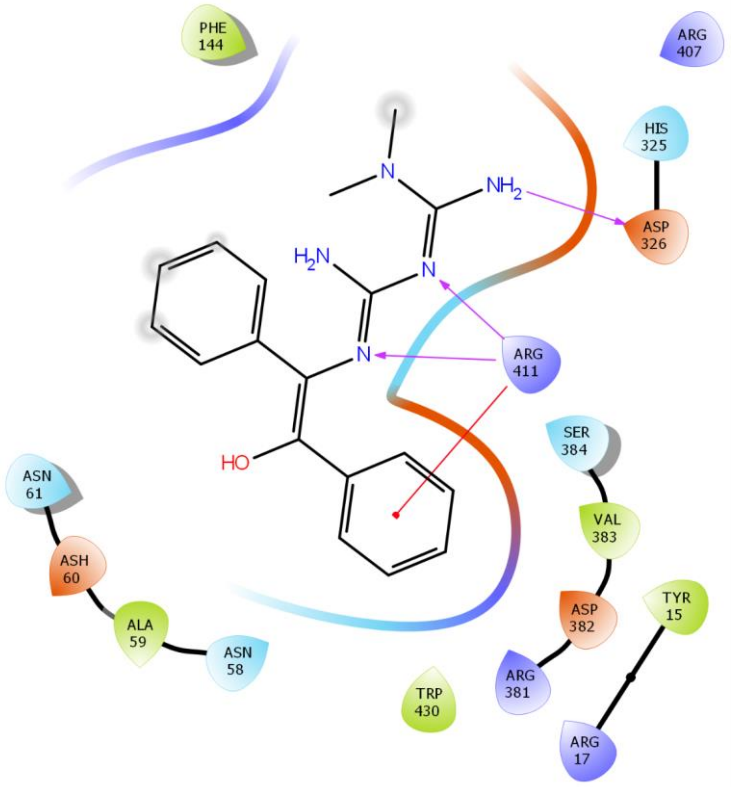
MET-7


TYR 63
ASP 326
HIS 325
ILE 143
PHE 144
GLN 167
ASN 61
ASH 60
HIE 103
PHE 163
HN
N
H
N+
N
H2N
ARG 407
ARG 411
ALA 200
ASH 199
ARG 197
TRP 49
GLU 256

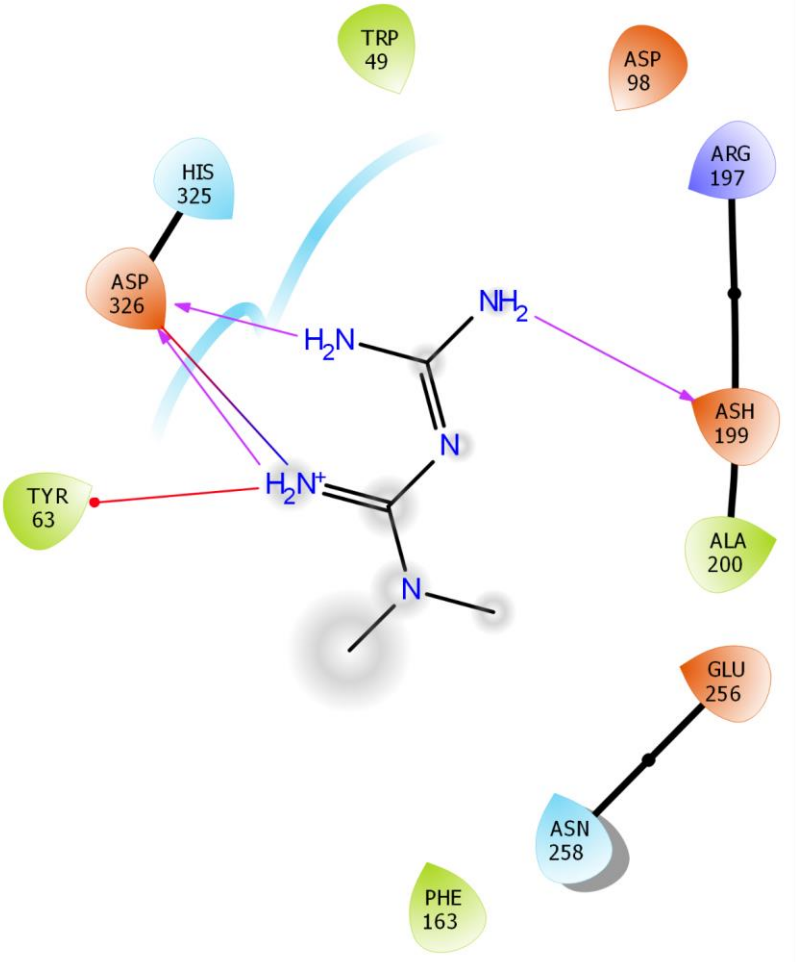
MET-8


N
ARG 407
LEU 327
H2N+
N
NH2
ASP 326
HN+
ASN 324
HIS 325
PHE 282
O
LEU 285
GLU 256
HO
ARG 197
ASP 98
ASH 199
TYR 63
TRP 49
ALA 200
GLN 13

MET-9

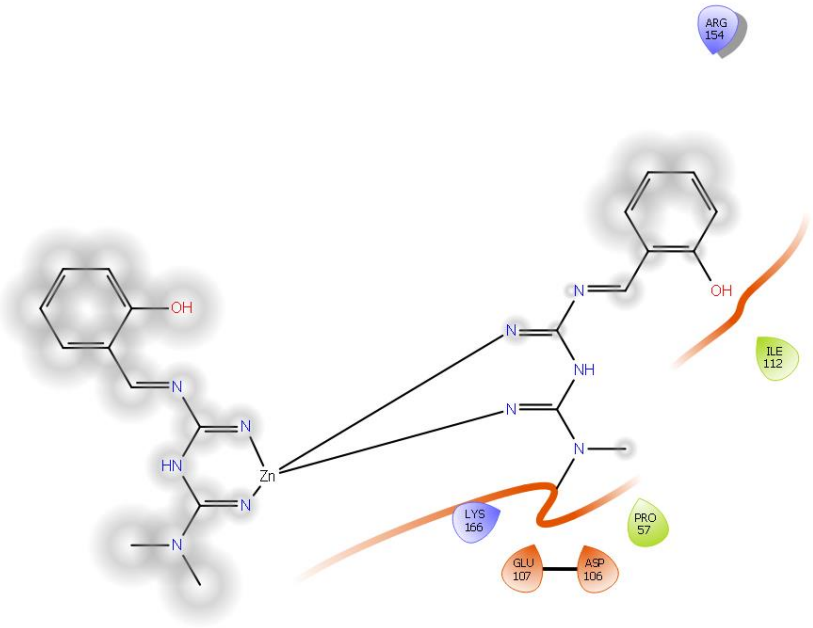

PHE 144
ARG 407
HIS 325
ASP 326
NH2
H2N
N
N
N
ARG 411
HO
SER 384
VAL 383
ASP 382
TYR 15
ARG 381
ARG 17
TRP 430
ASN 61
ASH 60
ALA 59
ASN 58

MET

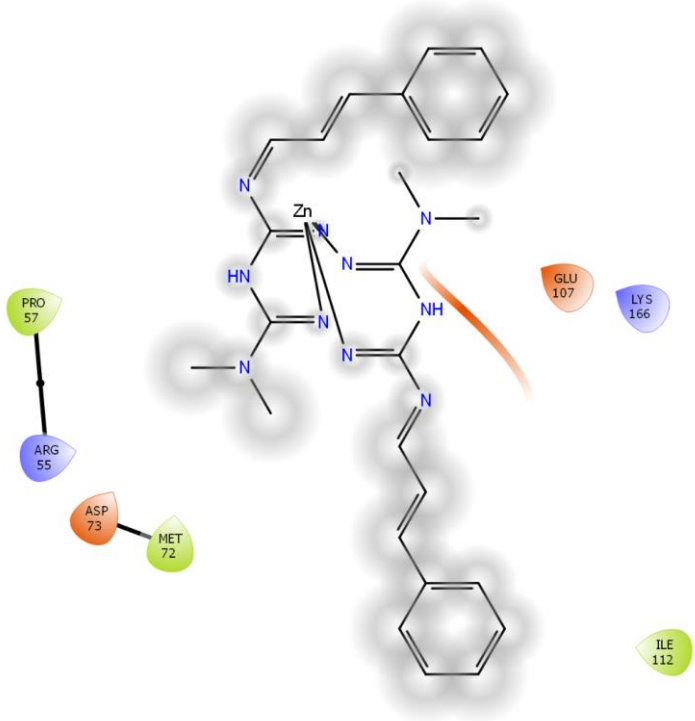

TRP 49
ASP 98
ARG 197
HIS 325
ASP 326
NH2
H2N
N
H2N+
TYR 63
ASH 199
ALA 200
N
GLU 256
ASN 258
PHE 163

MZN-1

MZN-2

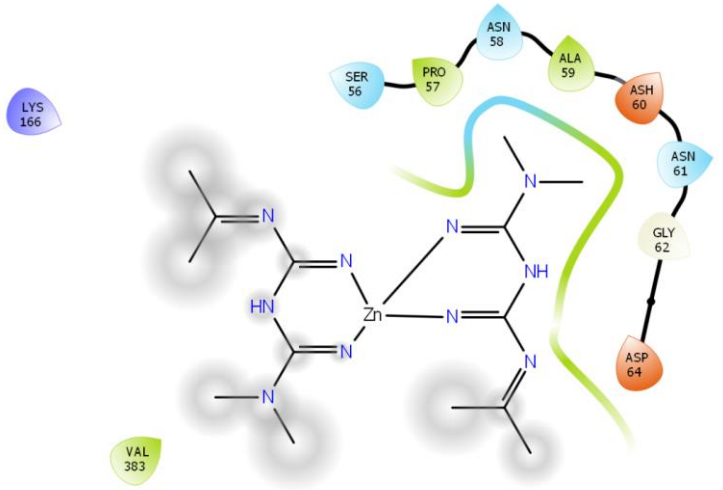


MZN-3

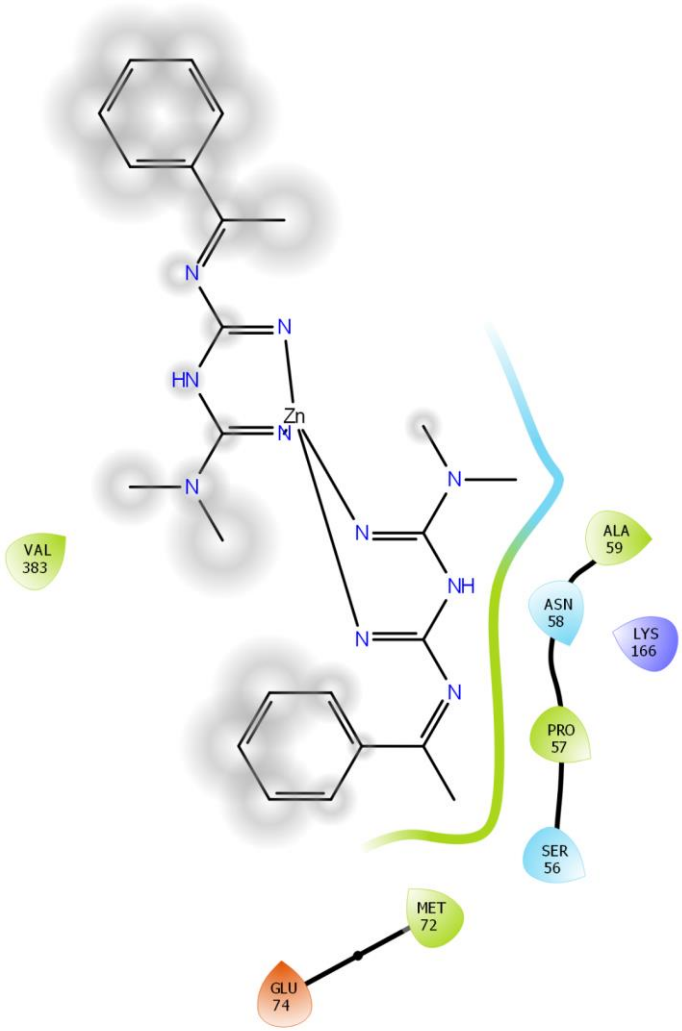


MZN-4

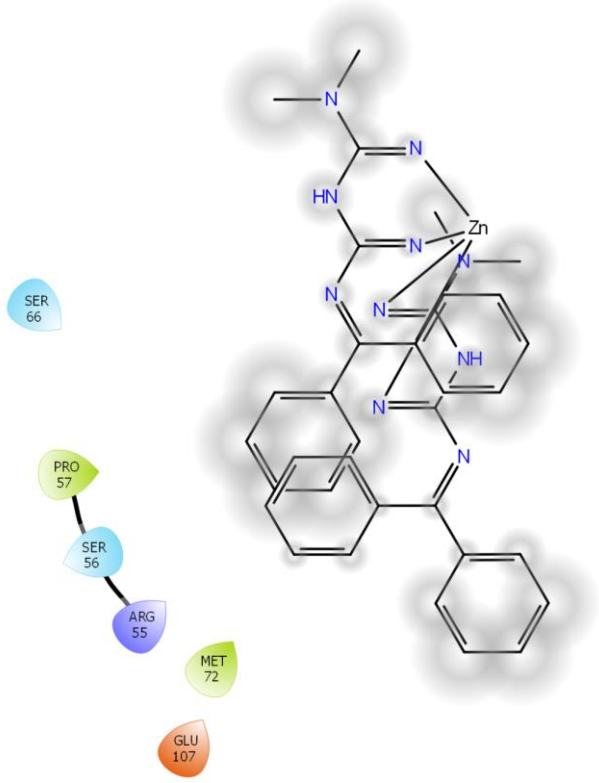
MZN-5


ASN
58
SER
56
PRO
57
ALA
59
ASH
60
LYS
166
ASN
61
GLY
62
N
N
N
NH
HN
Zn
N
N
N
N
ASP
64
VAL
383

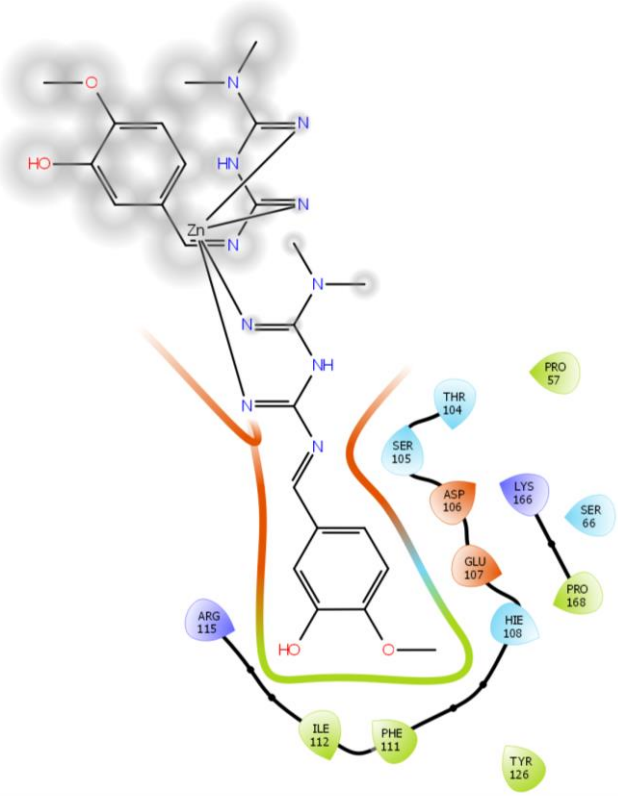
MZN-6


N
N
HN
Zn
N
N
N
N
N
NH
N
VAL
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ALA
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ASN
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LYS
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PRO
57
SER
56
MET
72
GLU
74

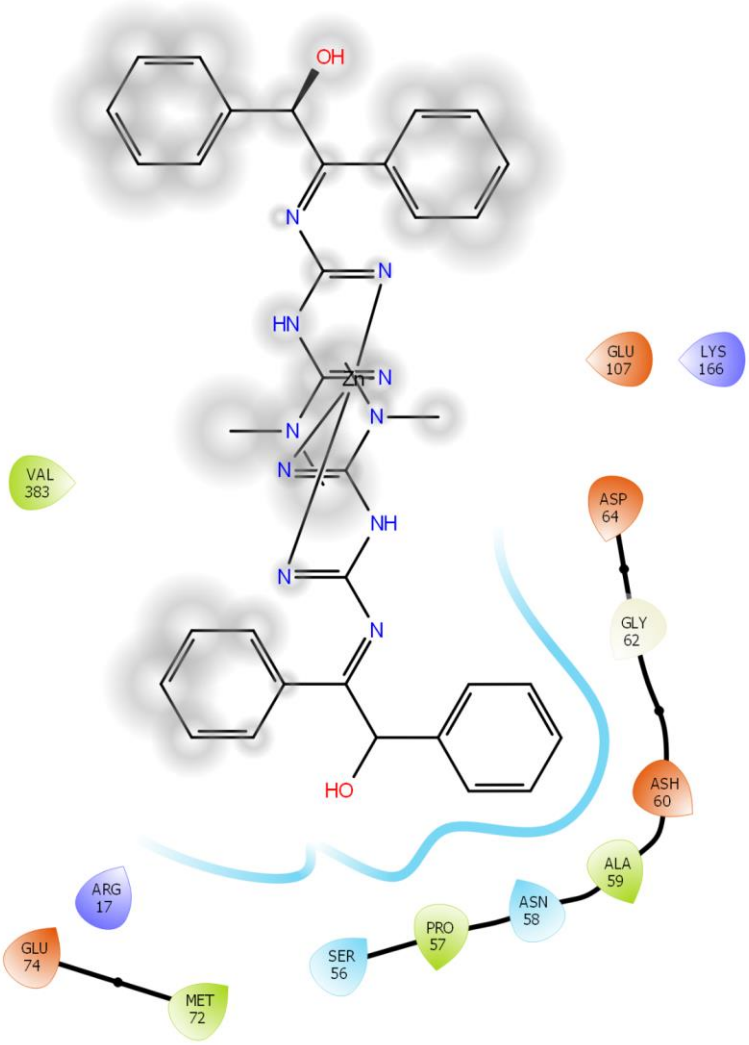
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PRO
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SER
56
ARG
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MET
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GLU
107
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HN
NH

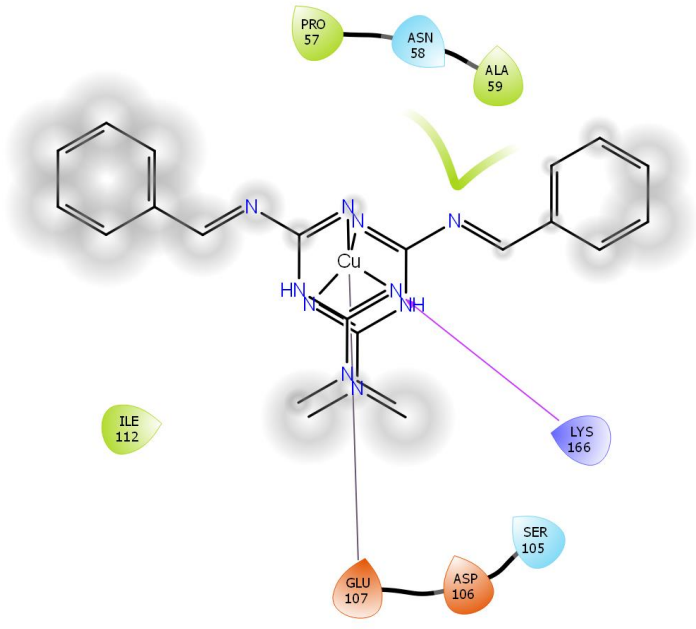
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Zn
HN
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PRO
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THR
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SER
105
ASP
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SER
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GLU
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PRO
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HIE
108
ARG
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HO
ILE
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PHE
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TYR
126

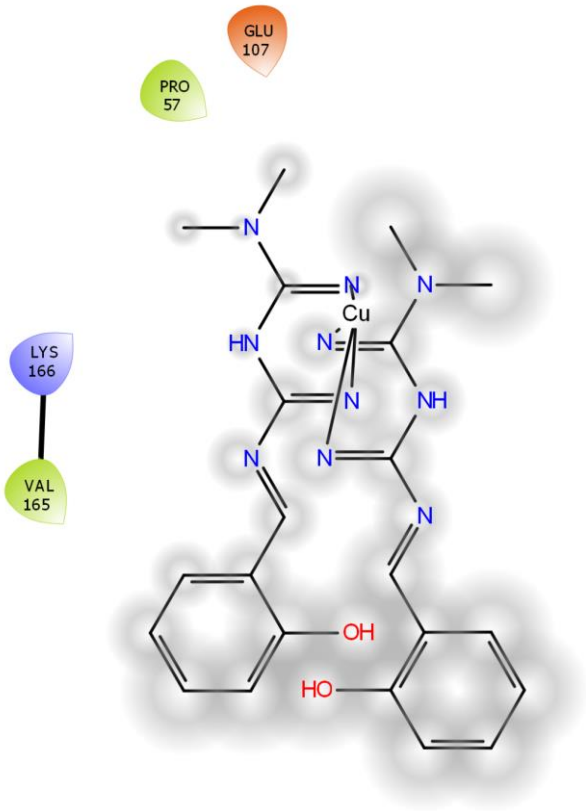
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Zn
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NH
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HO
GLU
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LYS
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VAL
383
ASP
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GLY
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ASH
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ALA
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ASN
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PRO
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SER
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ARG
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GLU
74
MET
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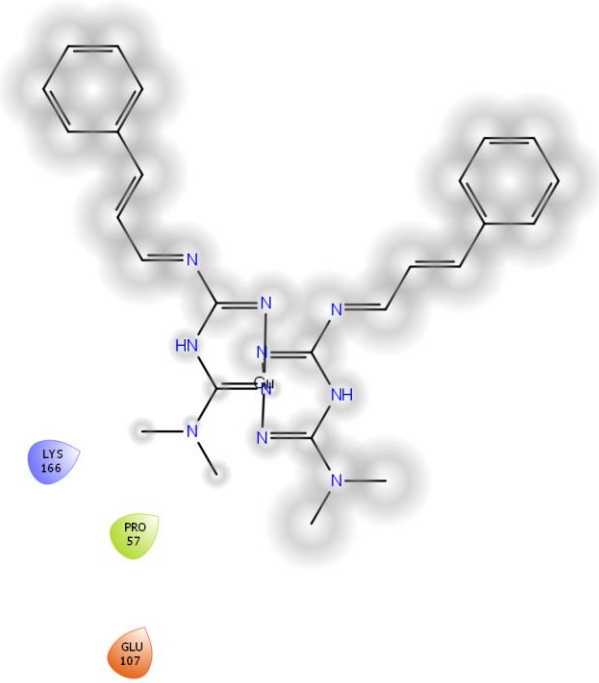
MCu-1


PRO
57
ASN
58
ALA
59
N
N
N
N
Cu
HN
N
N
NH
N
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105
GLU
107
ASP
106

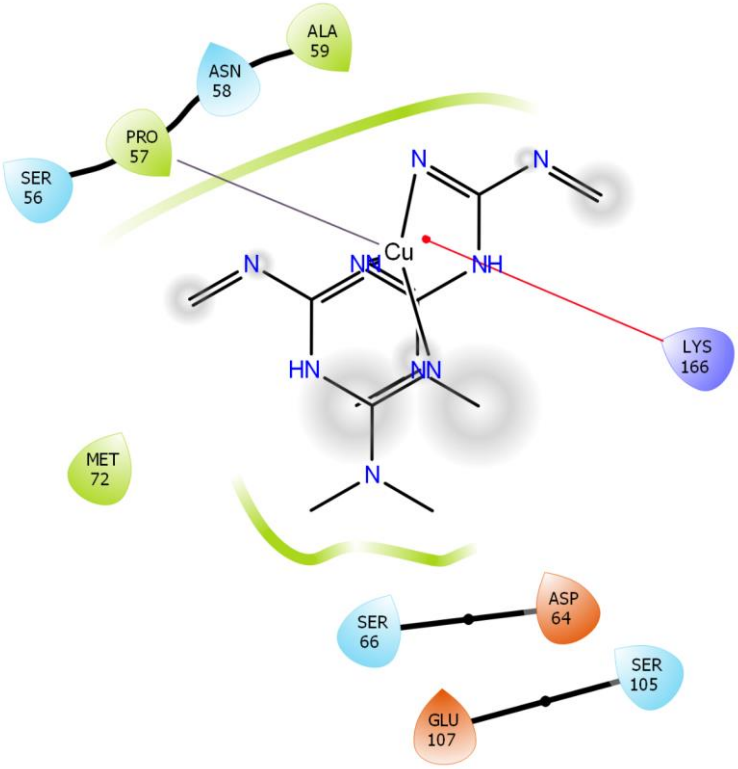
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PRO
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LYS
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VAL
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Cu
NH
OH
HO

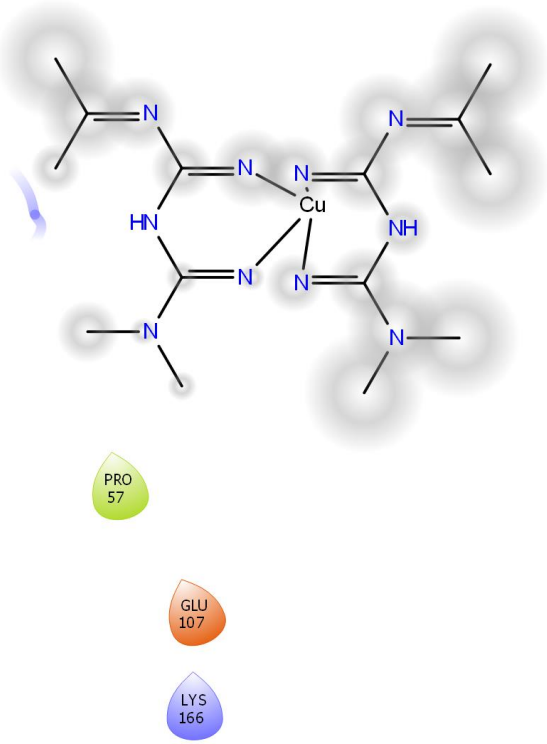
MCu-3


N
HN
Cu
NH
LYS
166
PRO
57
GLU
107

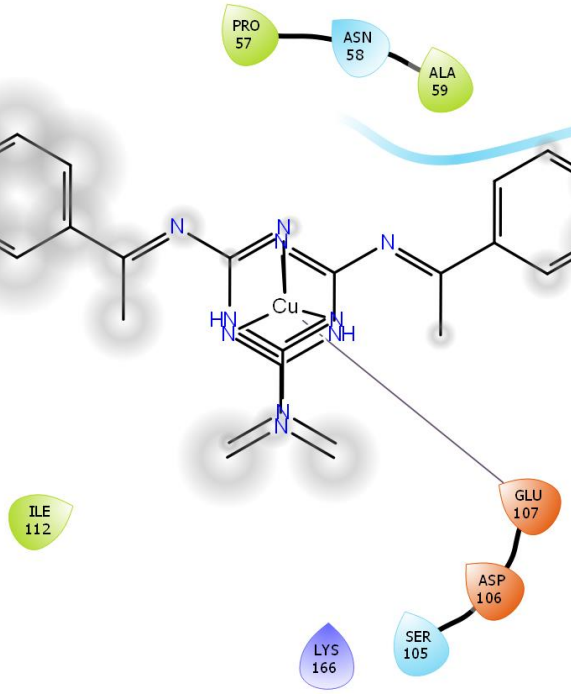
MCu-4


ALA
59
ASN
58
PRO
57
SER
56
N
N
Cu
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NH
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LYS
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HN
NN
MET
72
N
SER
66
ASP
64
SER
105
GLU
107

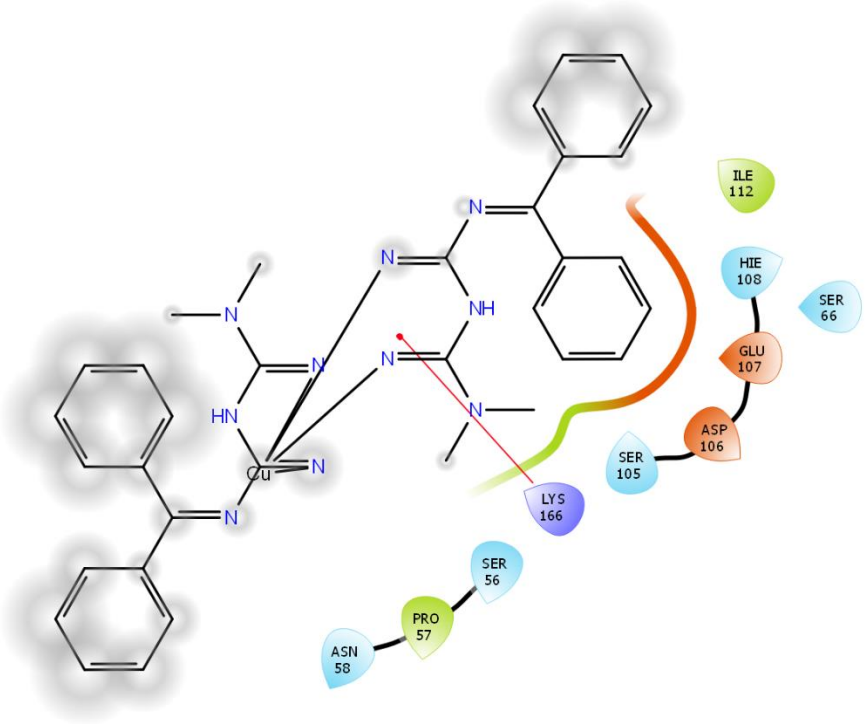
MCu-5


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N
N
N
Cu
HN
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N
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N
N
PRO
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GLU
107
LYS
166

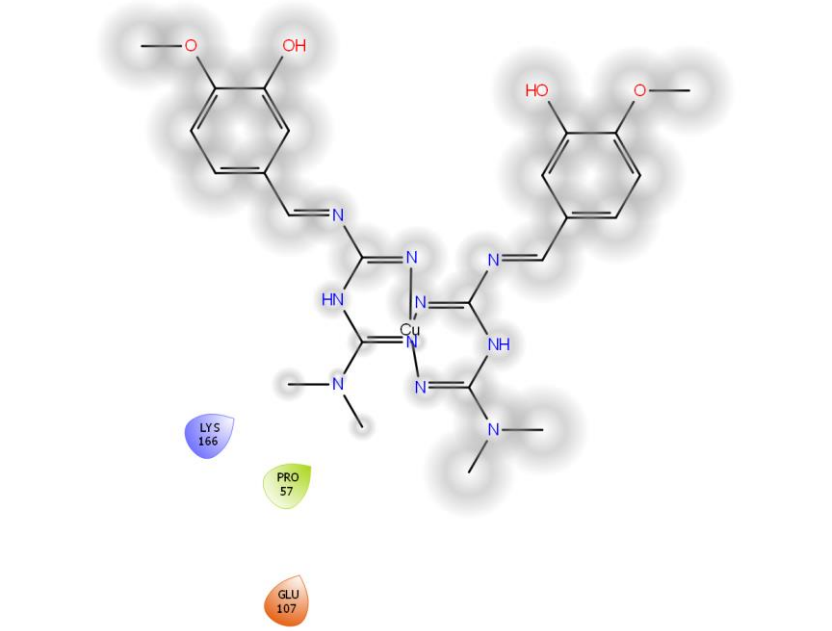
MCu-6


PRO
57
ASN
58
ALA
59
N
N
N
N
HN
Cu
N
NH
N
N
ILE
112
GLU
107
ASP
106
SER
105
LYS
166

MCu-7


ILE
112
N
N
NH
HIE
108
SER
66
GLU
107
N
N
HN
N
Cu
N
ASP
106
SER
105
N
LYS
166
SER
56
PRO
57
ASN
58

MCu-8


O
OH
HO
O
N
N
N
HN
N
Cu
N
NH
N
N
N
LYS
166
PRO
57
GLU
107

MCu-9

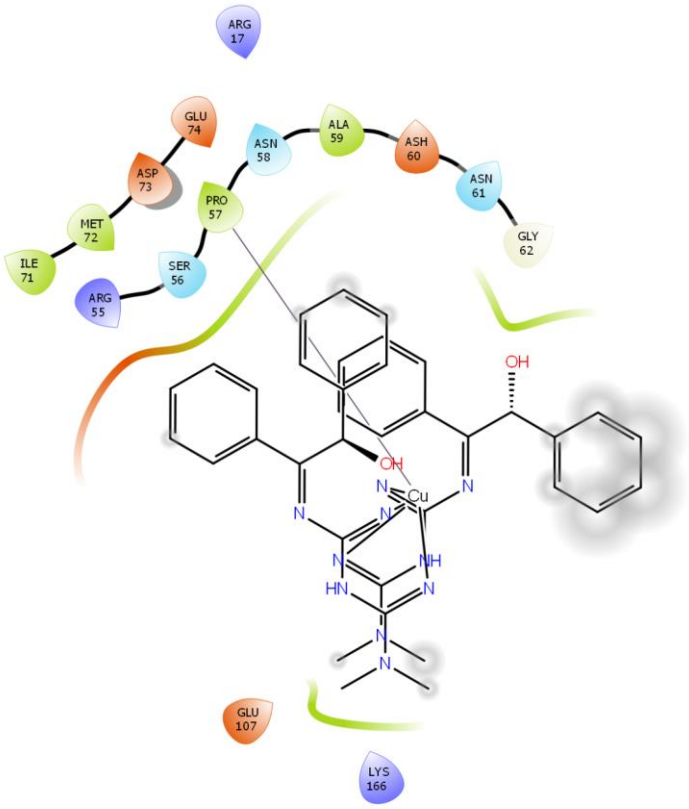
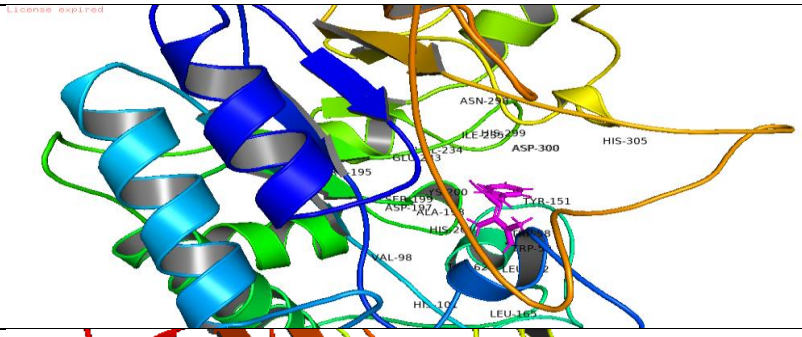
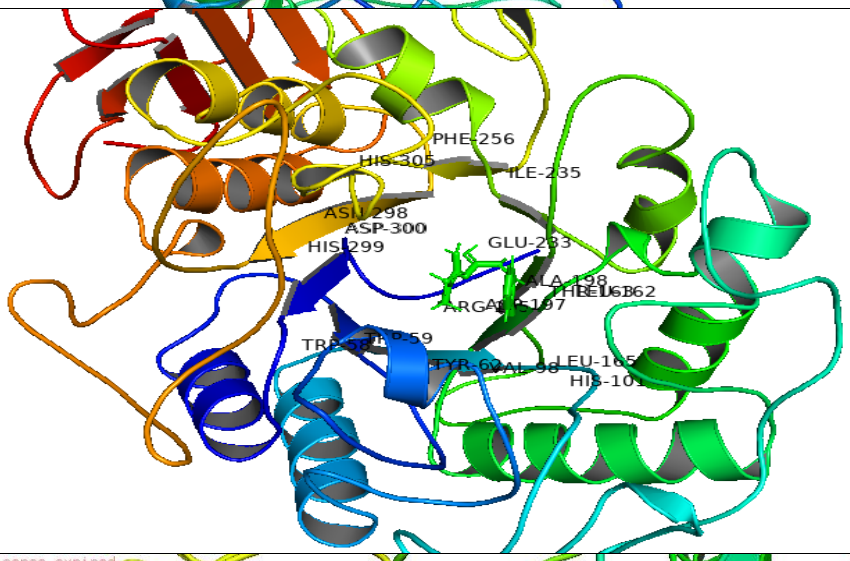
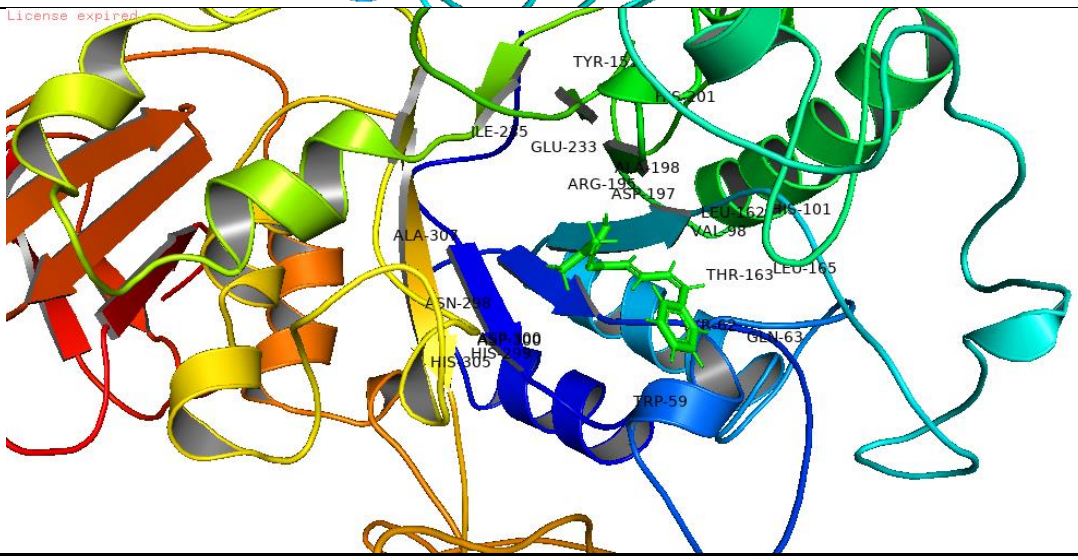
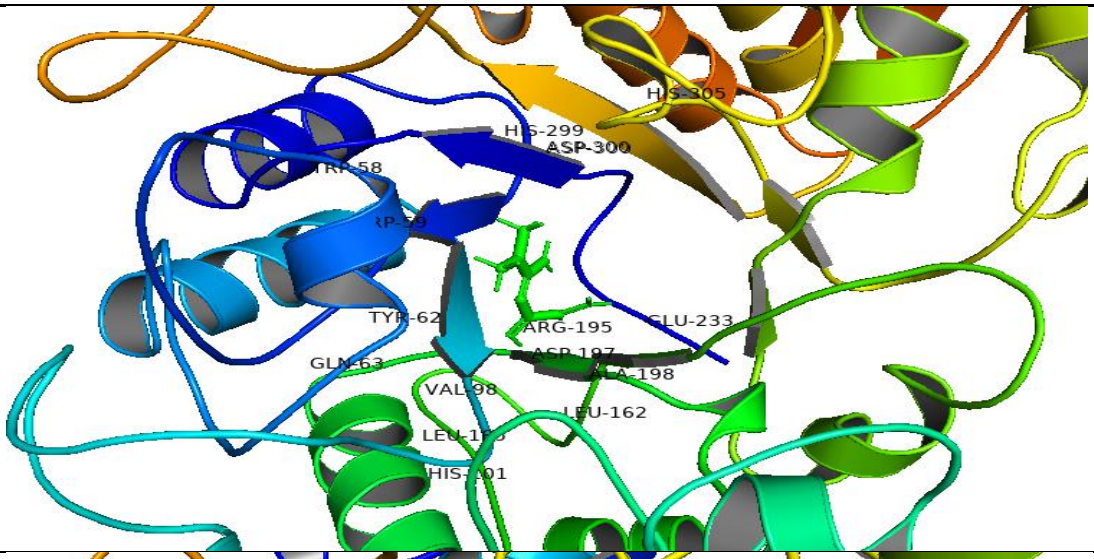

ARG
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GLU
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ASN
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ALA
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ASH
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ASN
61
GLY
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ASP
73
PRO
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MET
72
ILE
71
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HN
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GLU
107
LYS
166

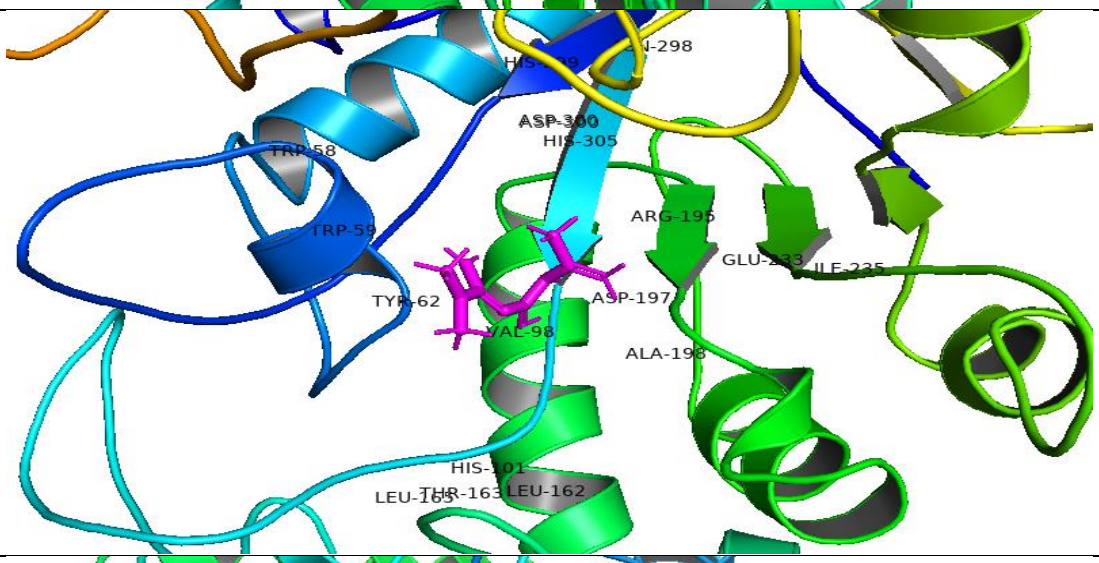
Table S4. 3D pose and geometries of all the metformin derivatives.

Derivative code	3D Pose
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MET-2	
MET-3	

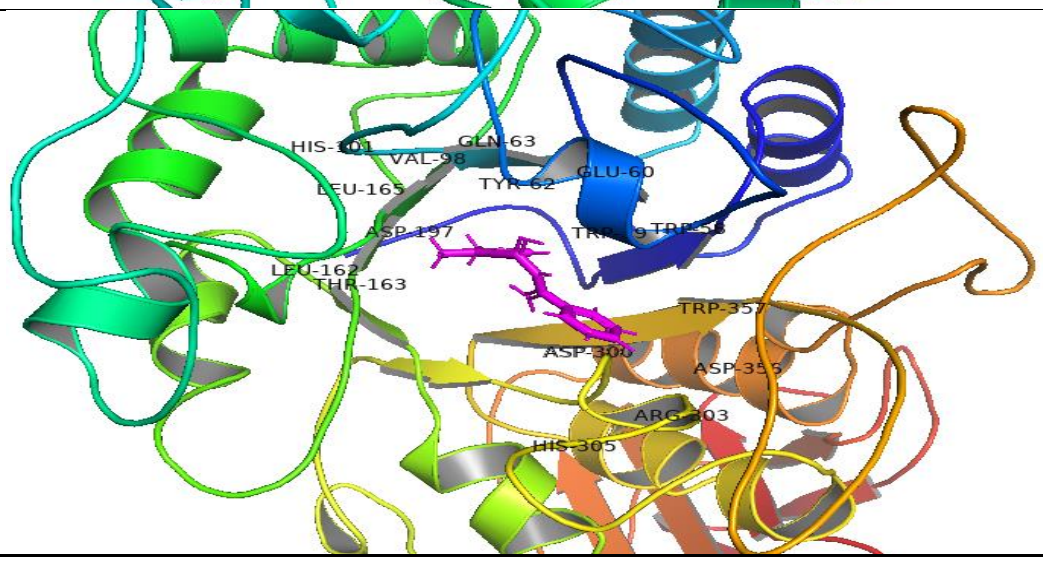
MET-4



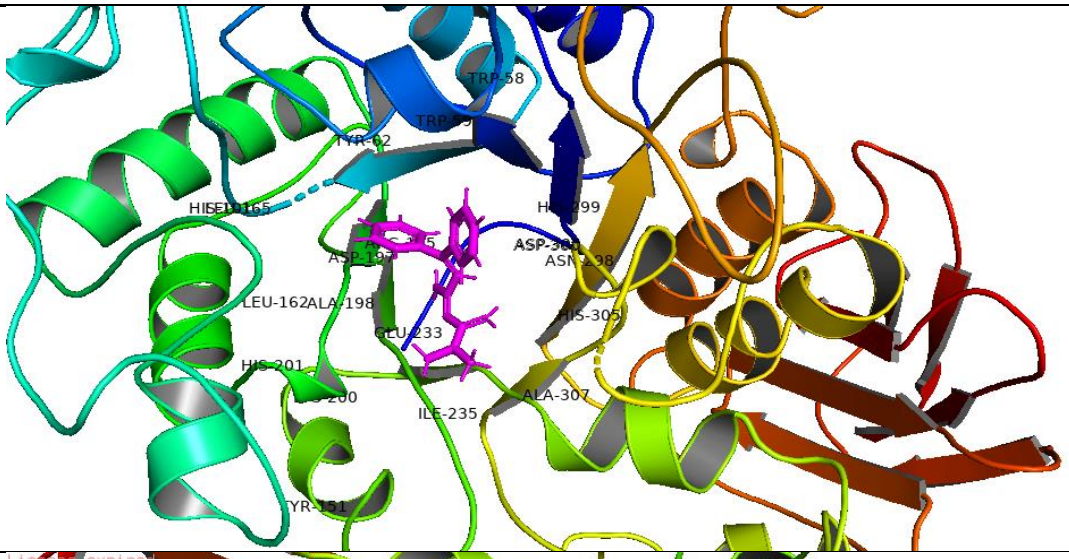
MET-5



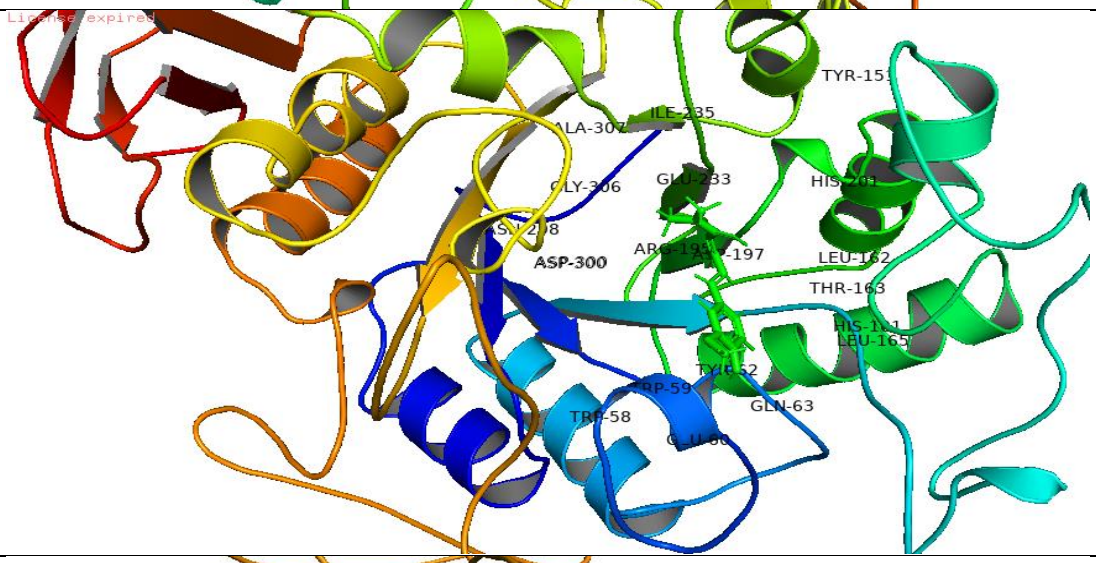
MET-6



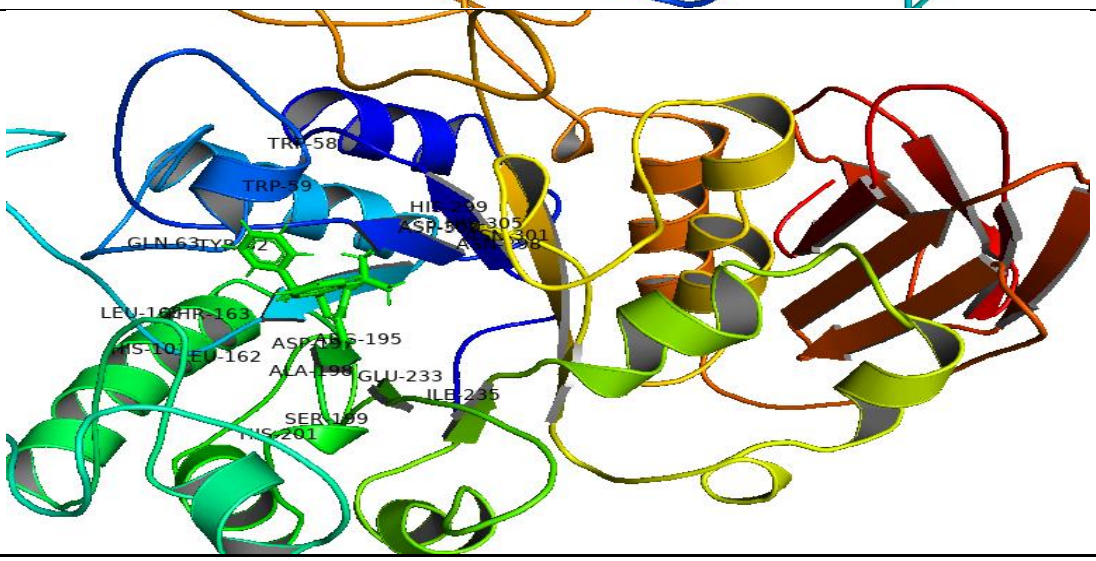
MET-7



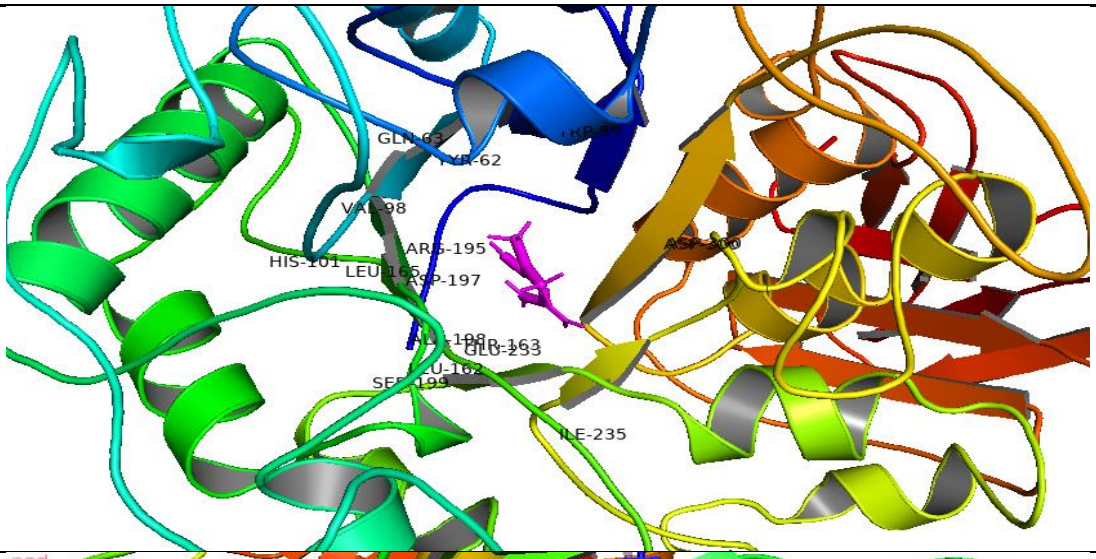
MET-8



MET-9



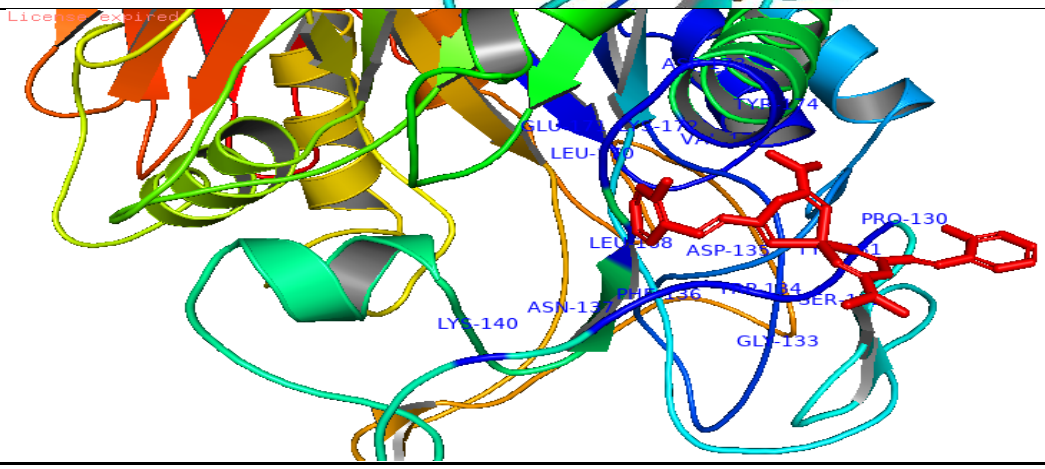
MET

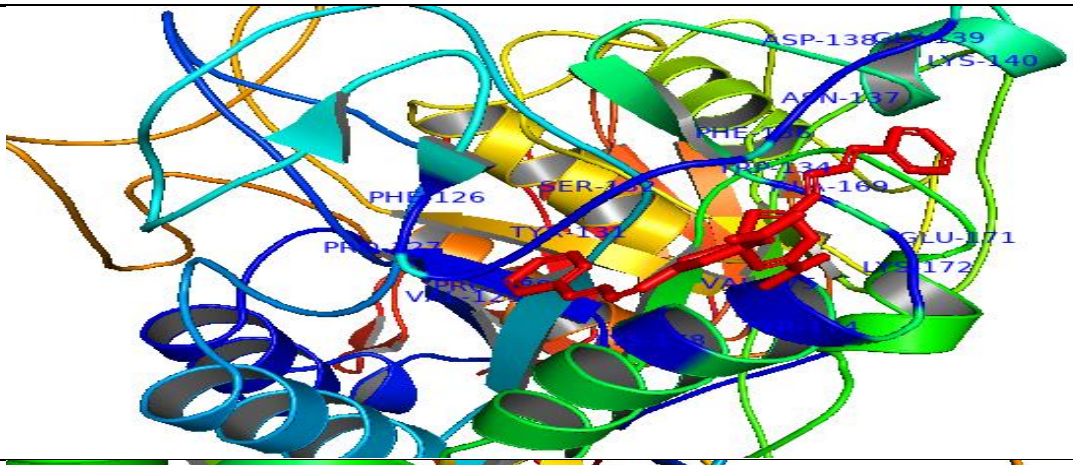
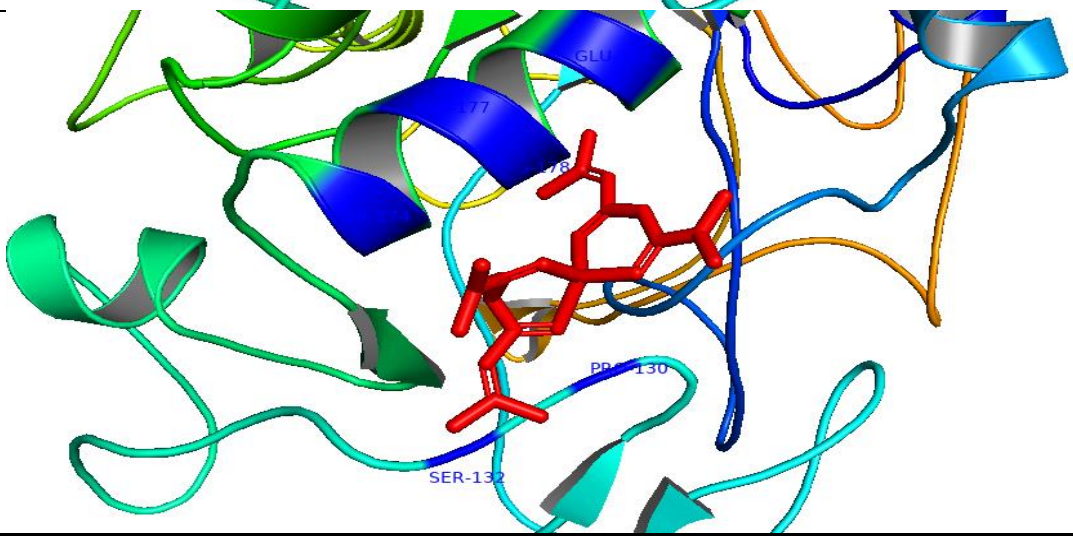


MZN-1

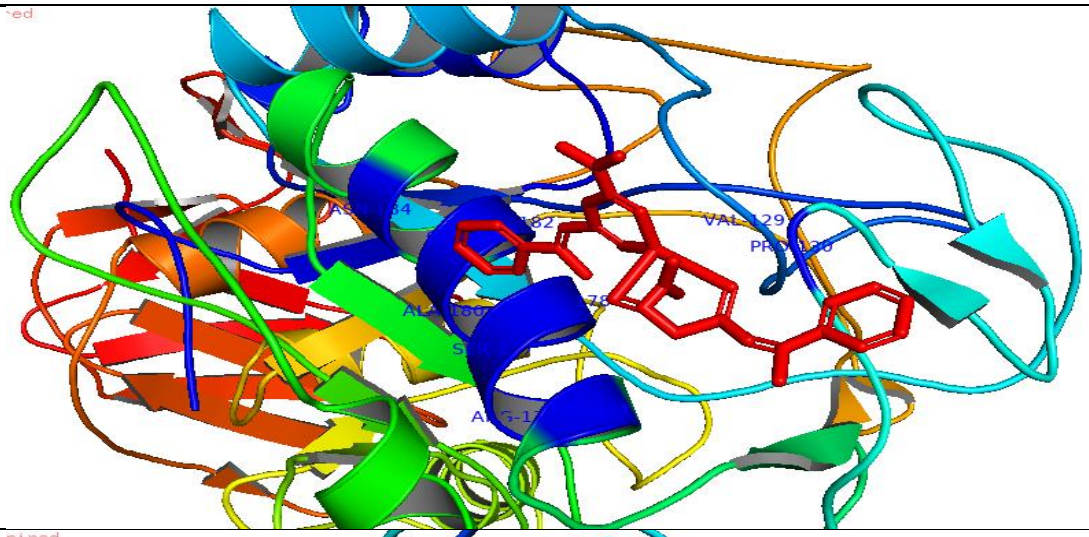


MZN-2

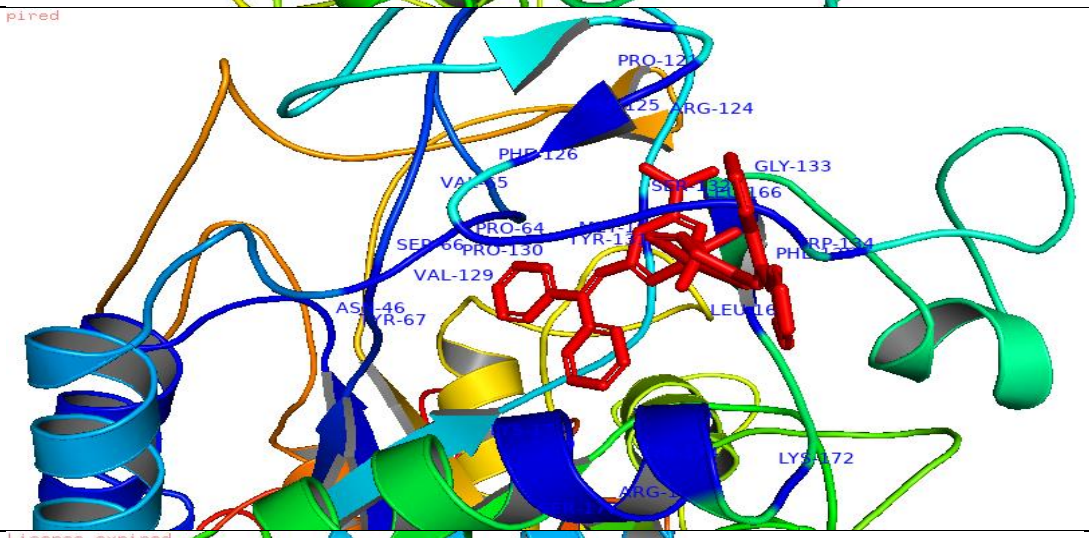


MZN-3	
MZN-4	
MZN-5	

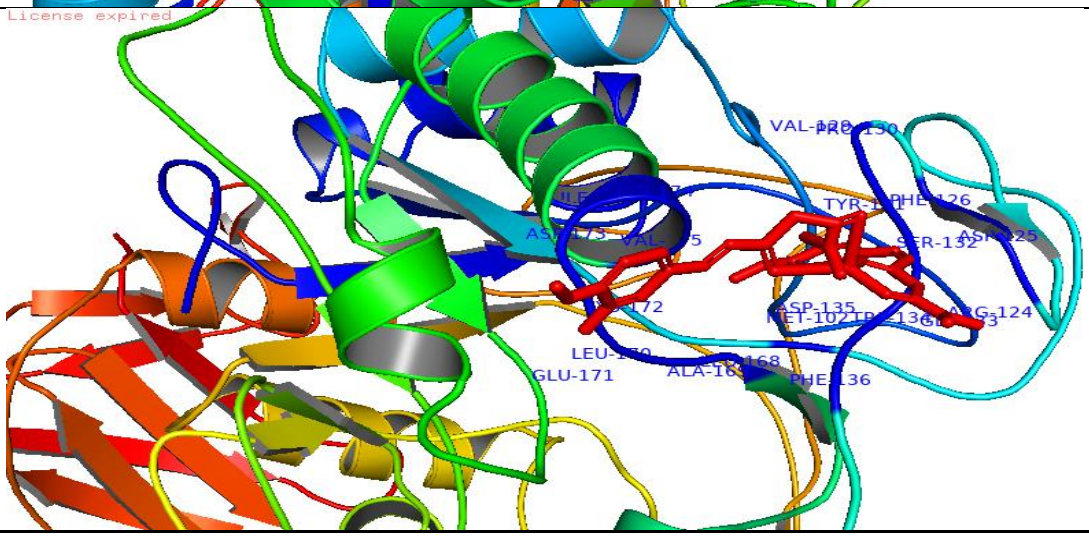
MZN-6

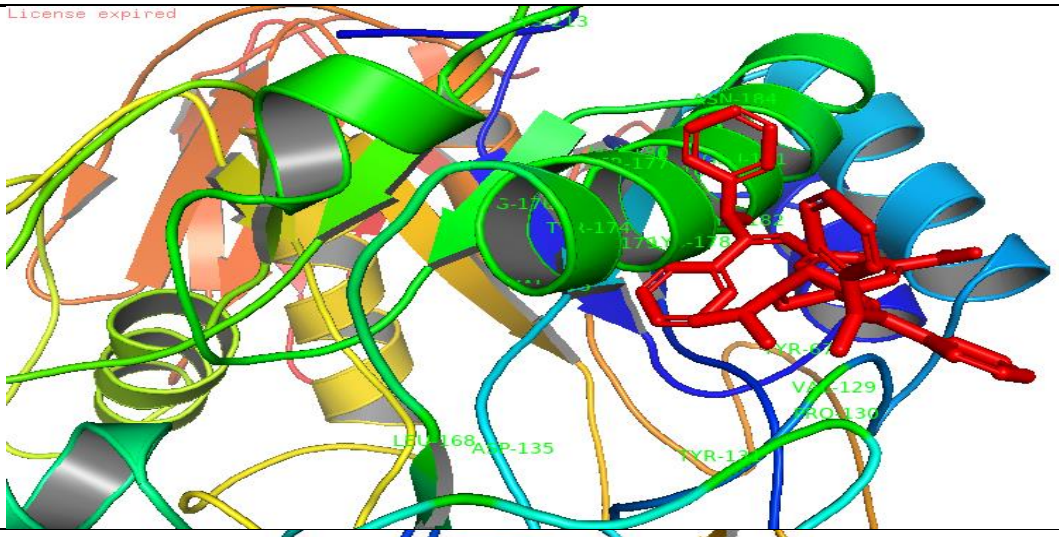
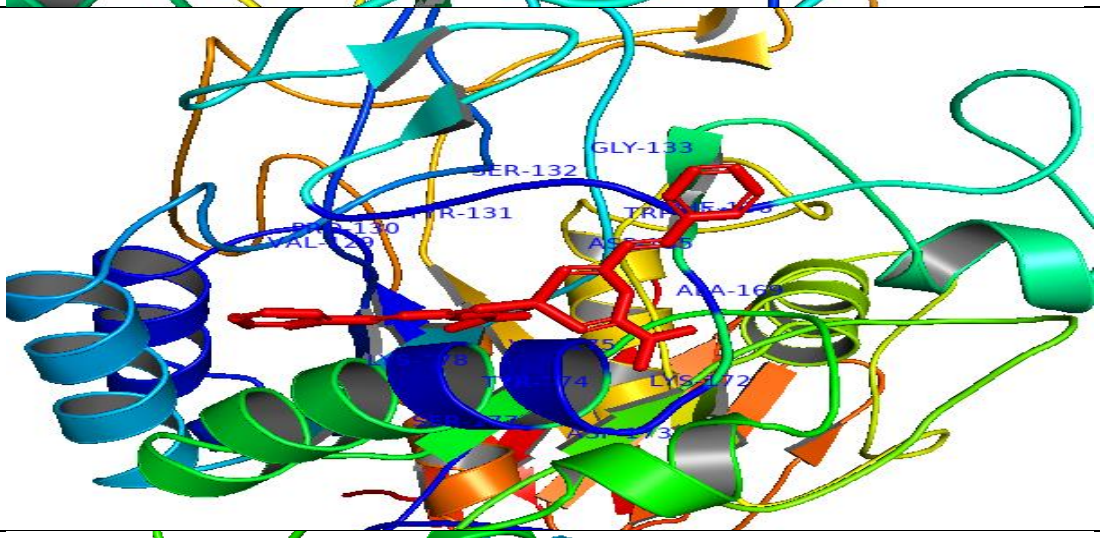
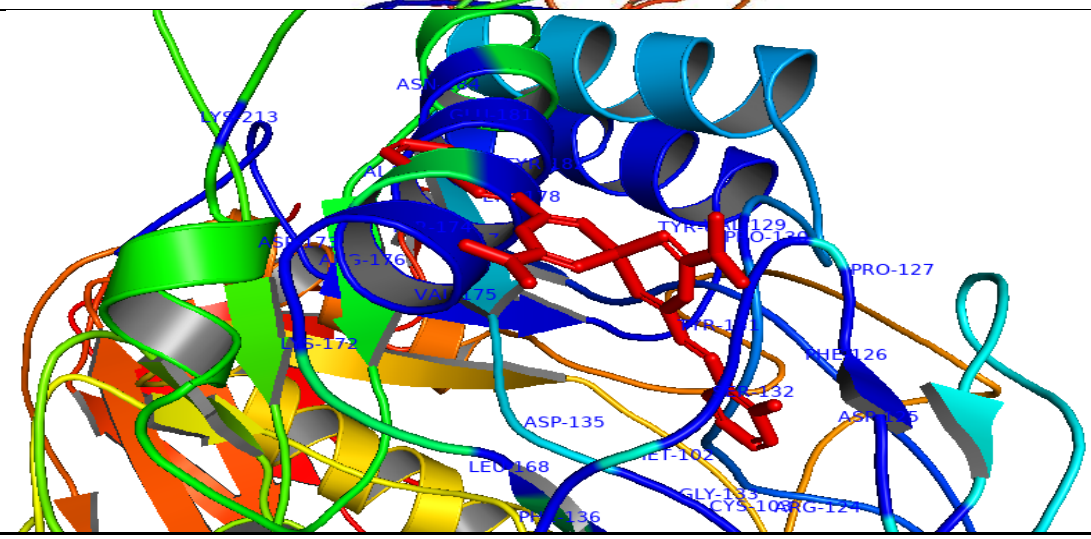


MZN-7

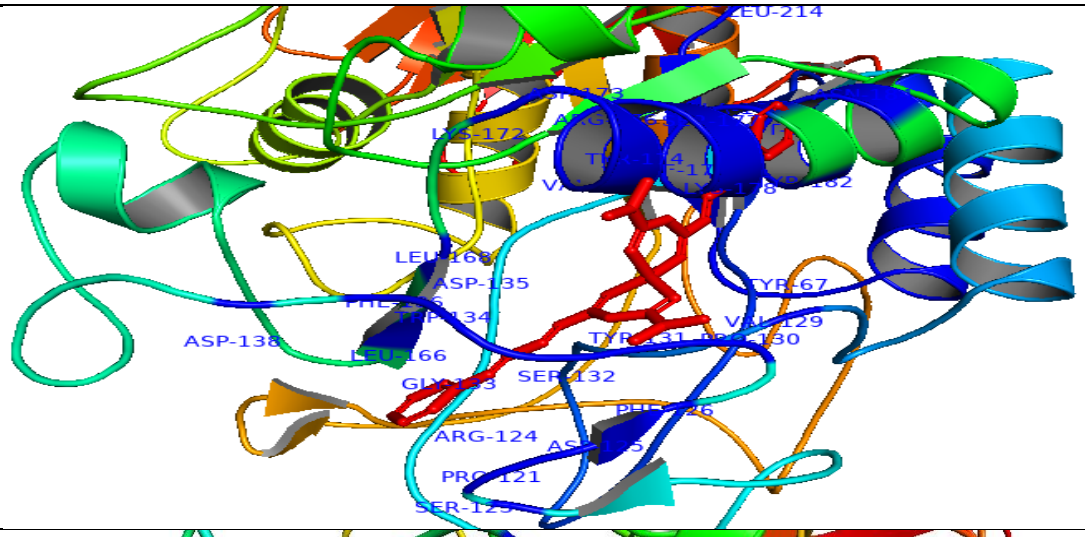


MZN-8

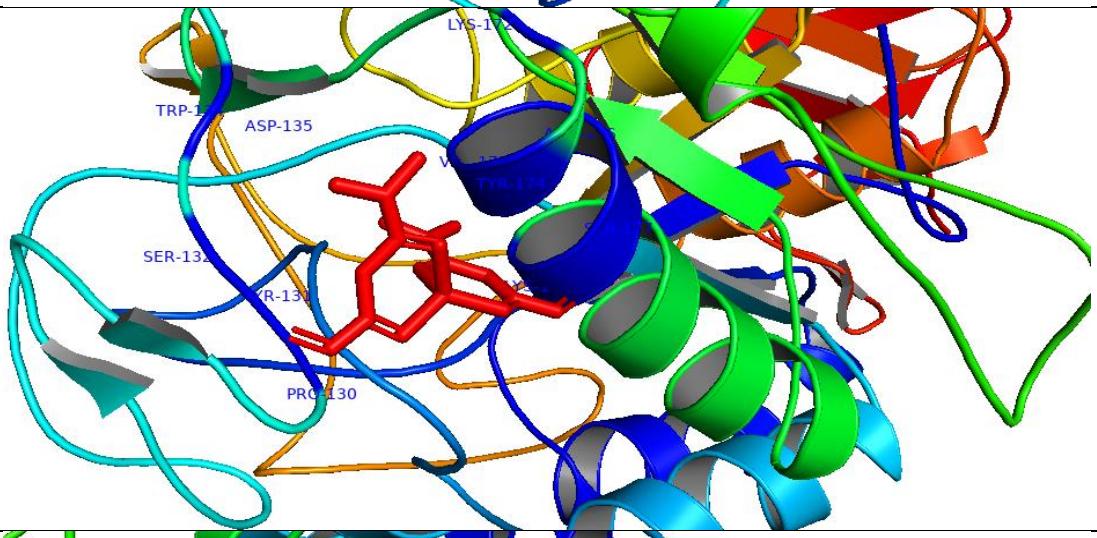


MZN-9	
MCu-1	
MCu-2	

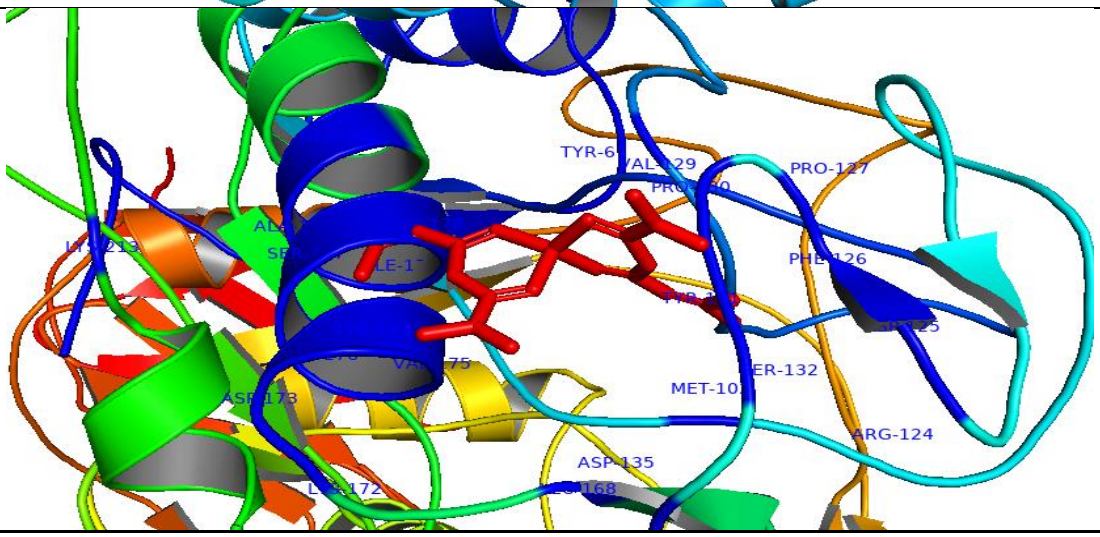
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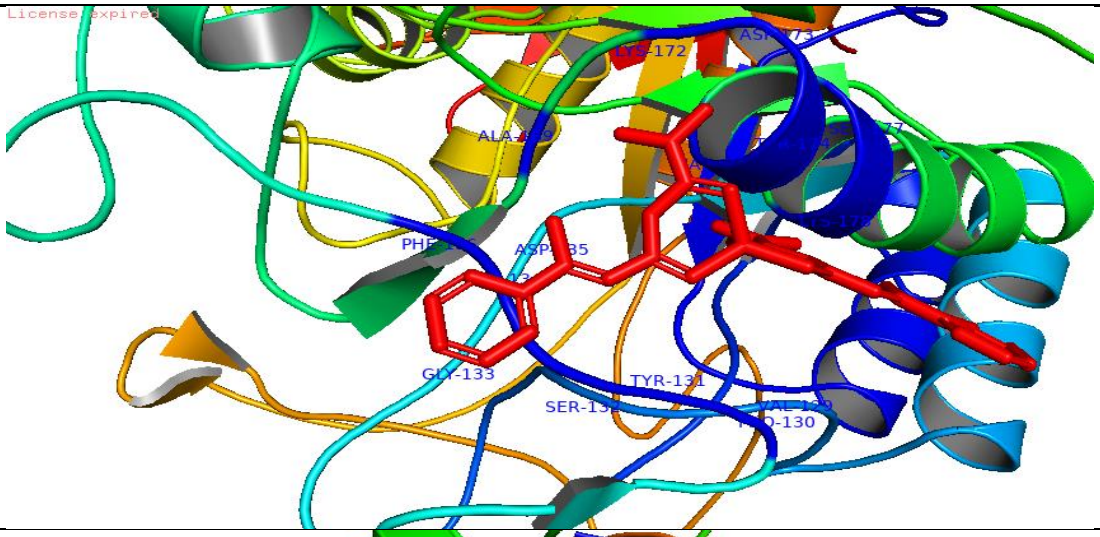
MCu-4



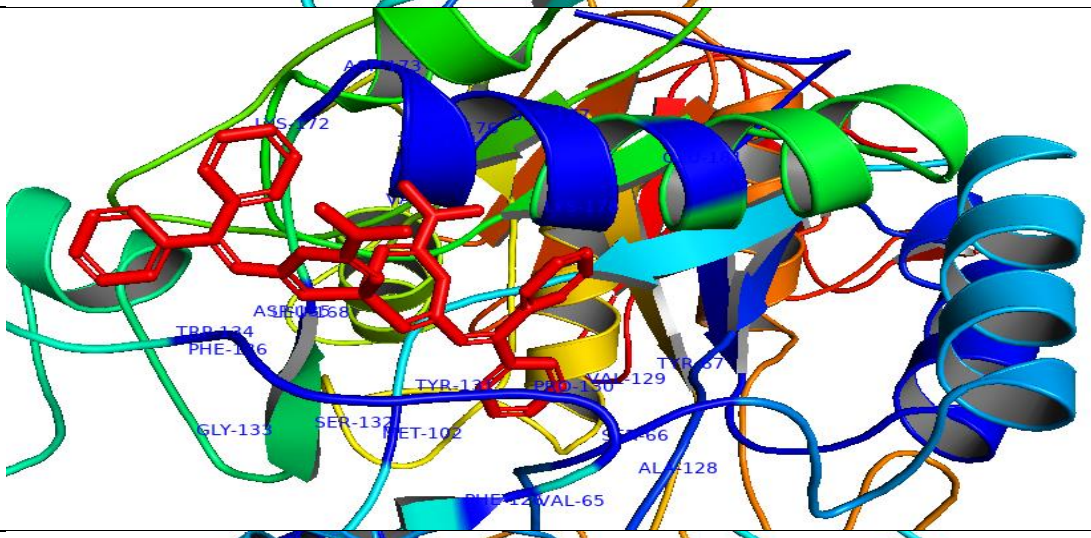
MCu-5



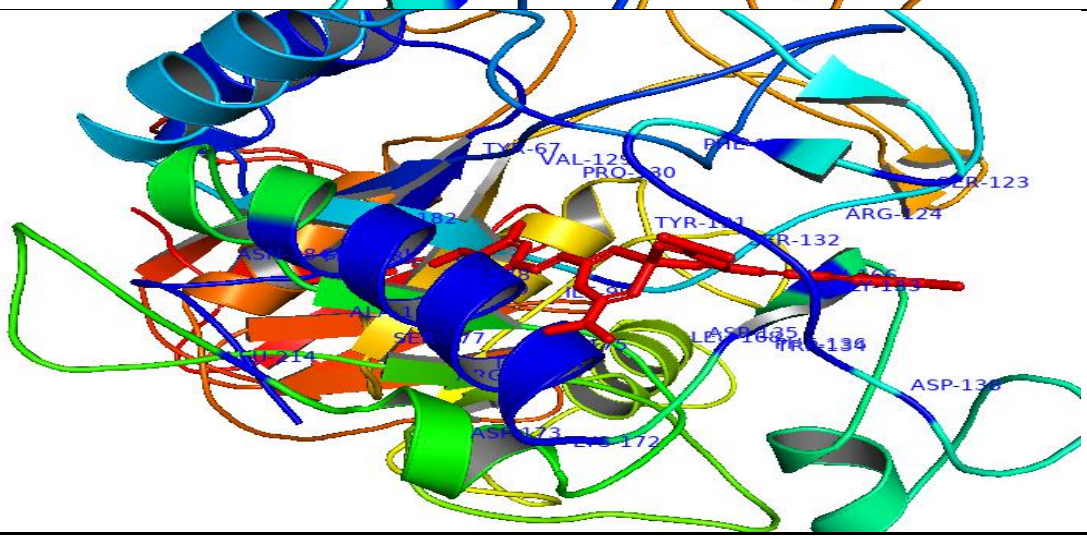
MCu-6



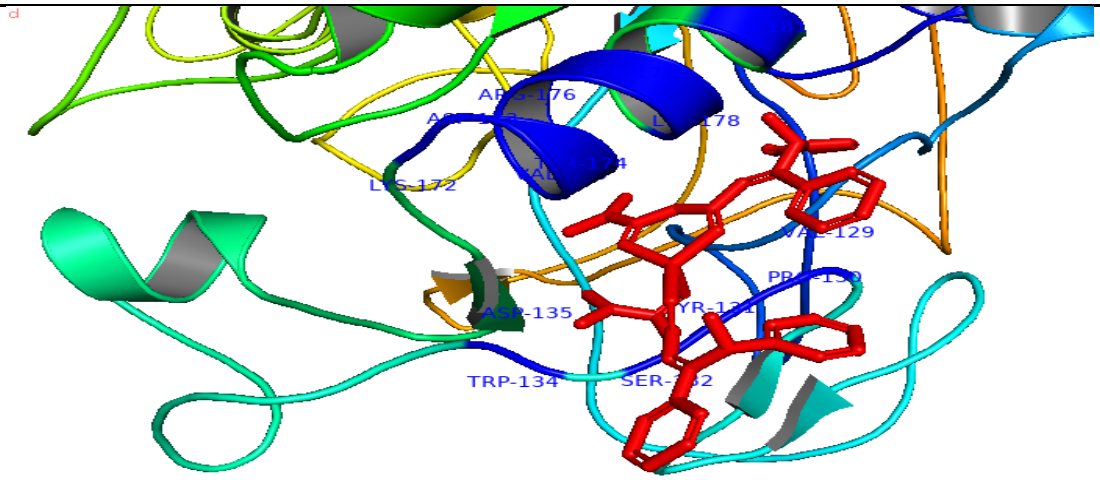
MCu-7



MCu-8



MCu-9



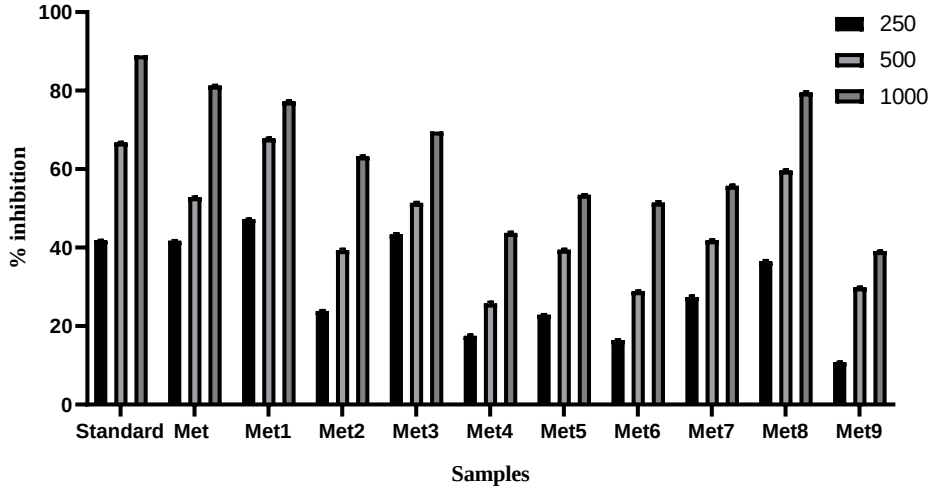


Figure S1. Graphical representation of α-glucosidase activity of Met-1-Met-9.

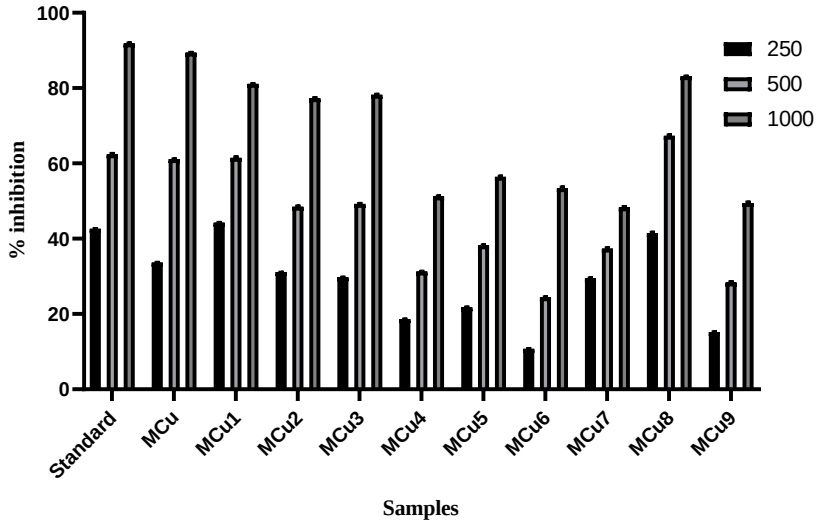


Figure S2. Graphical representation of α-glucosidase activity of MCu1-MCu9.

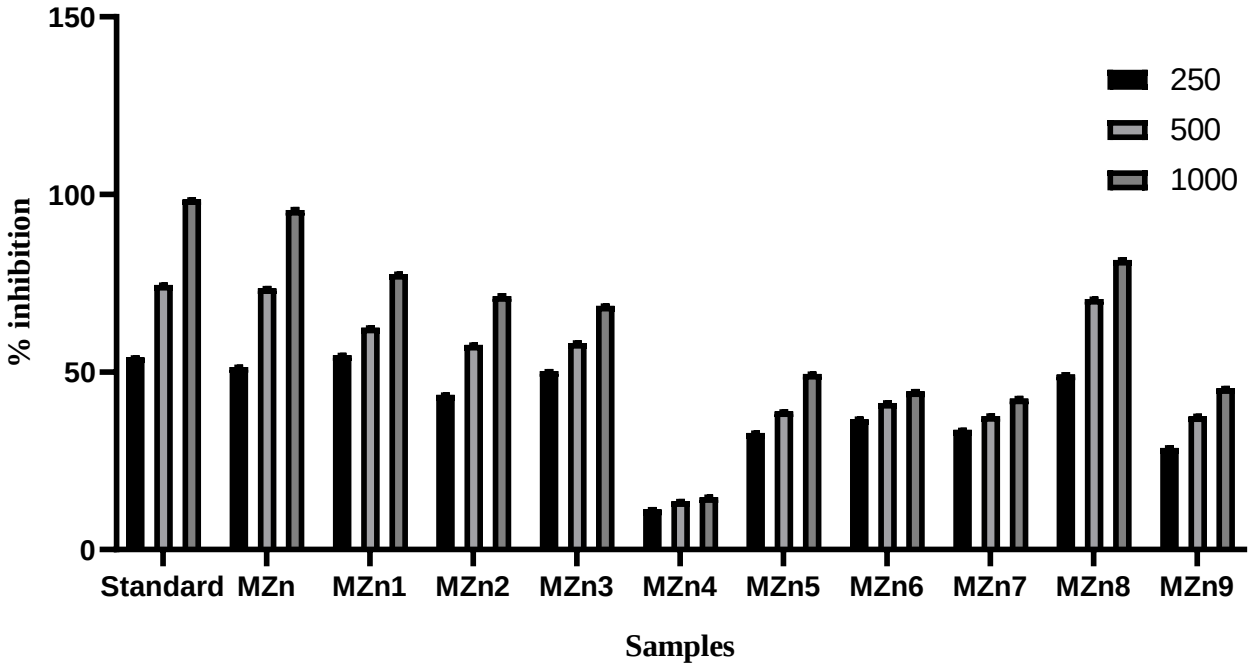


Figure S3. Graphical representation of α-glucosidase activity of MZn1-MZn9.

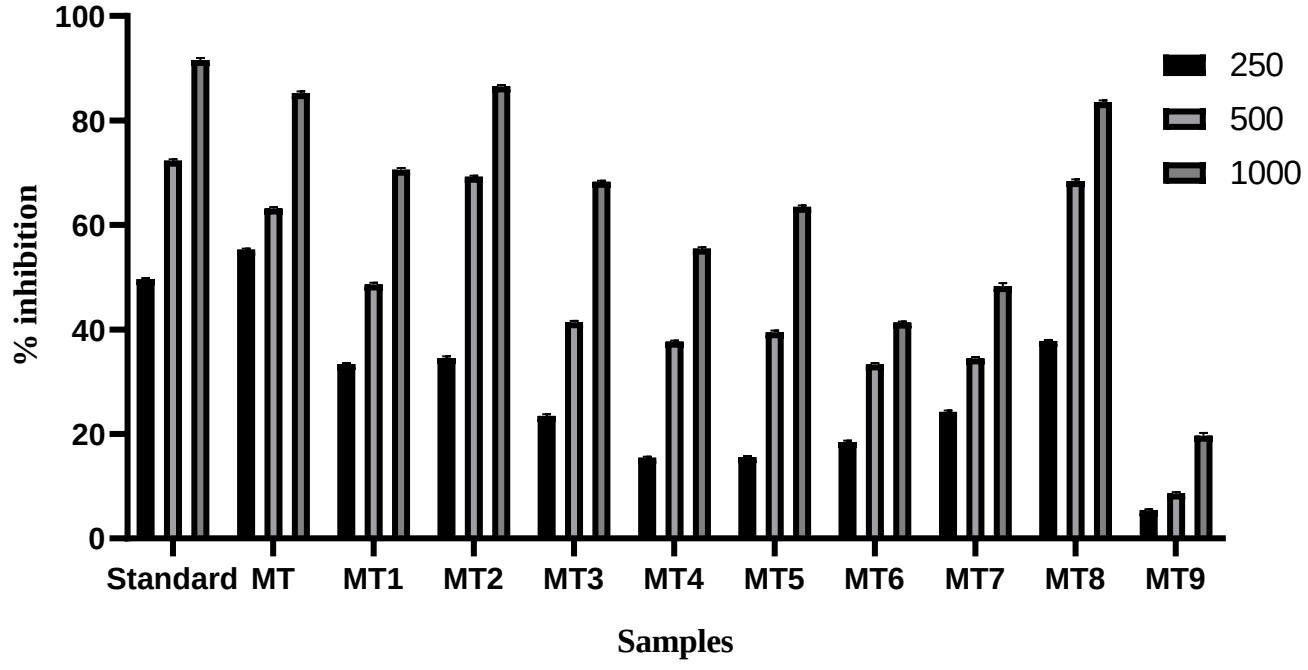


Figure S4. Graphical representation of α-amylase activity of Met1-Met9.

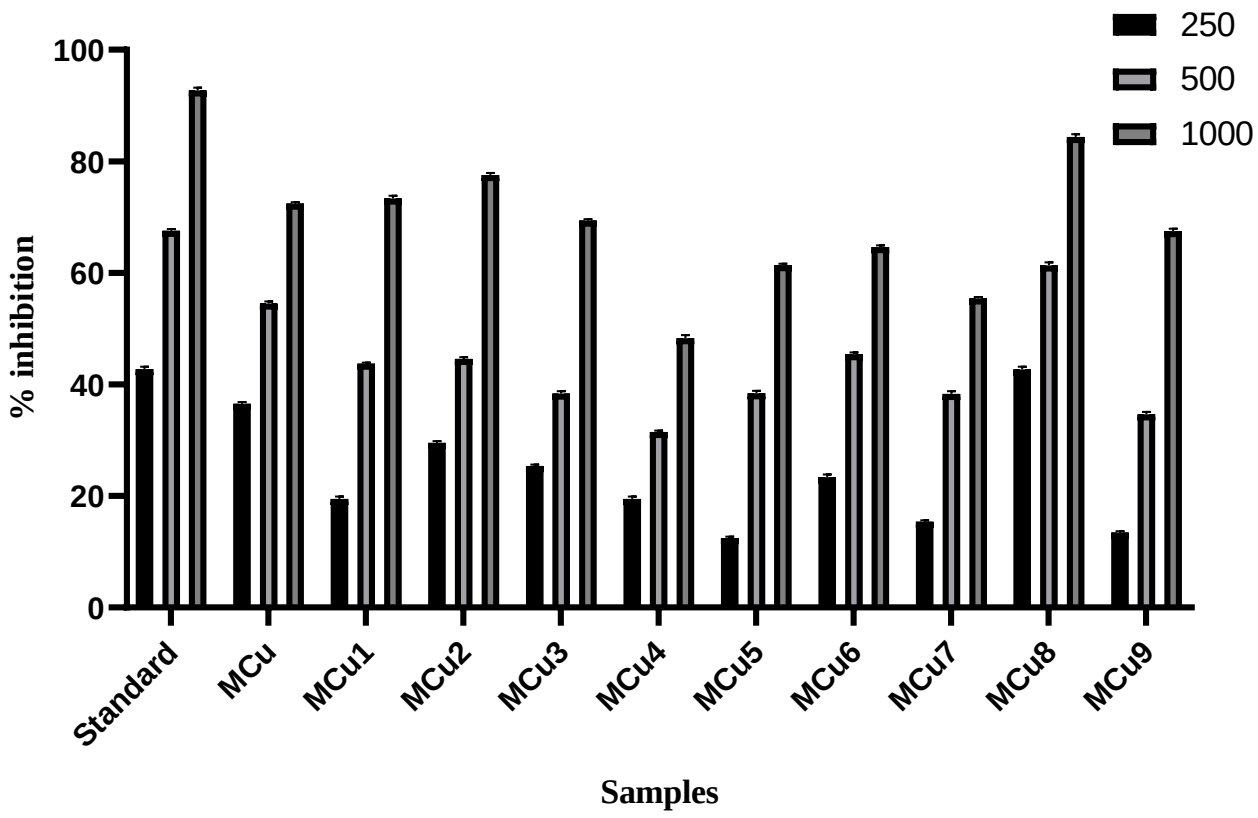


Figure S5. Graphical representation of α-amylase activity of MCu1-MCu9.

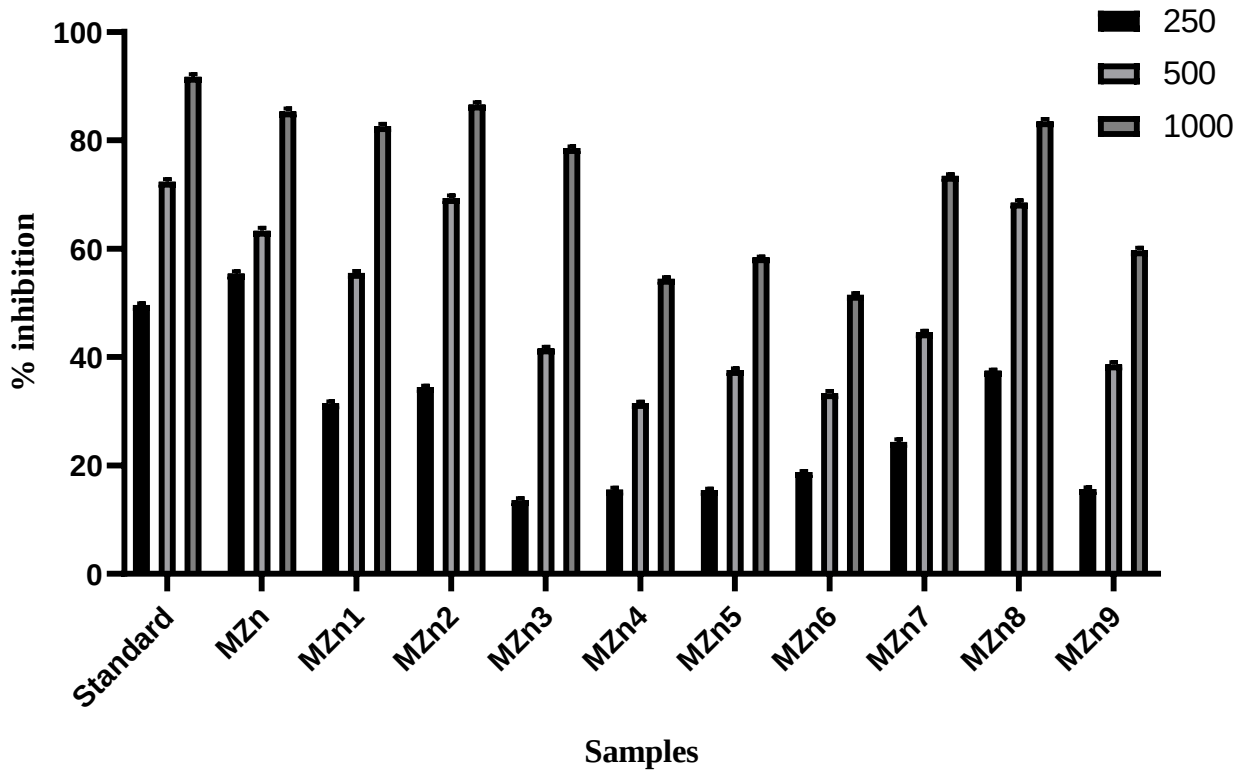


Figure S6. Graphical representation of α-amylase activity of MZn1-MZn9.

NMR Spectra of Metformin Derivatives:

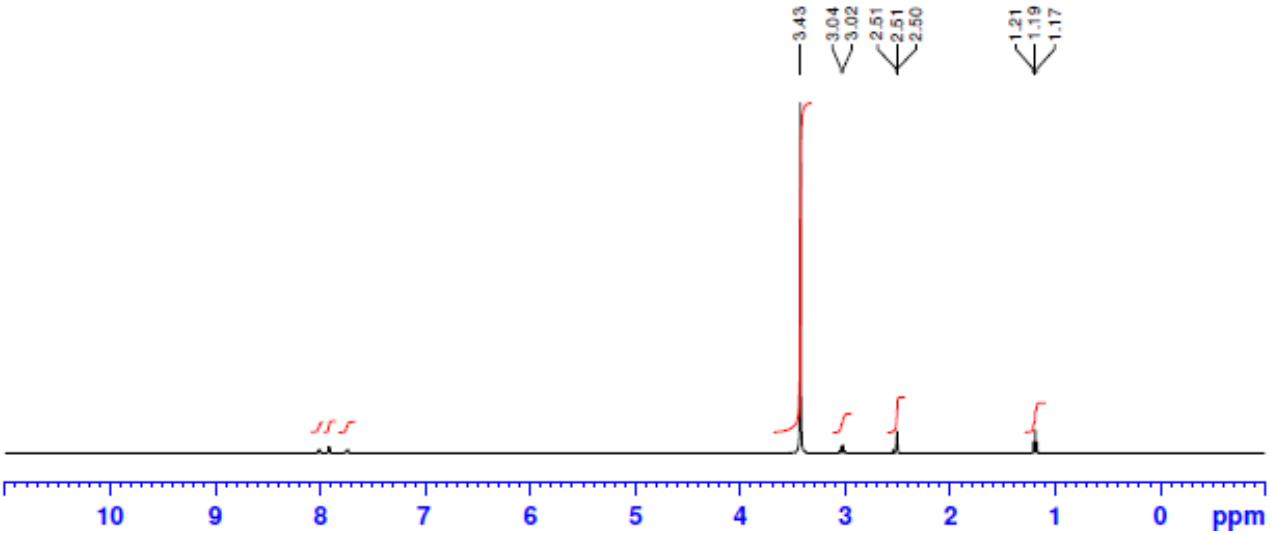


Figure S7. H^1 spectra of Metformin.

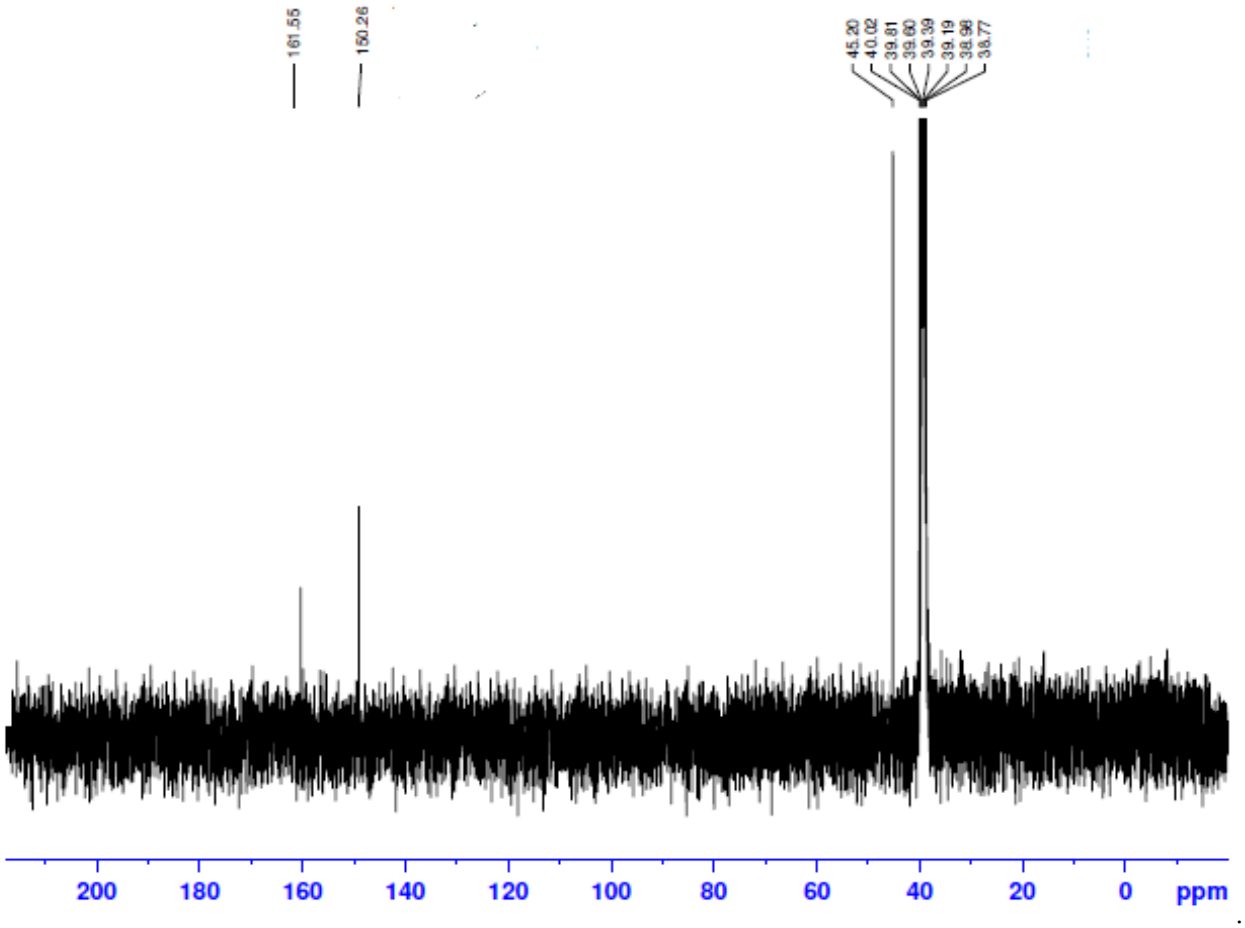


Figure S8. C^{13} spectra of Metformin.

Met1;

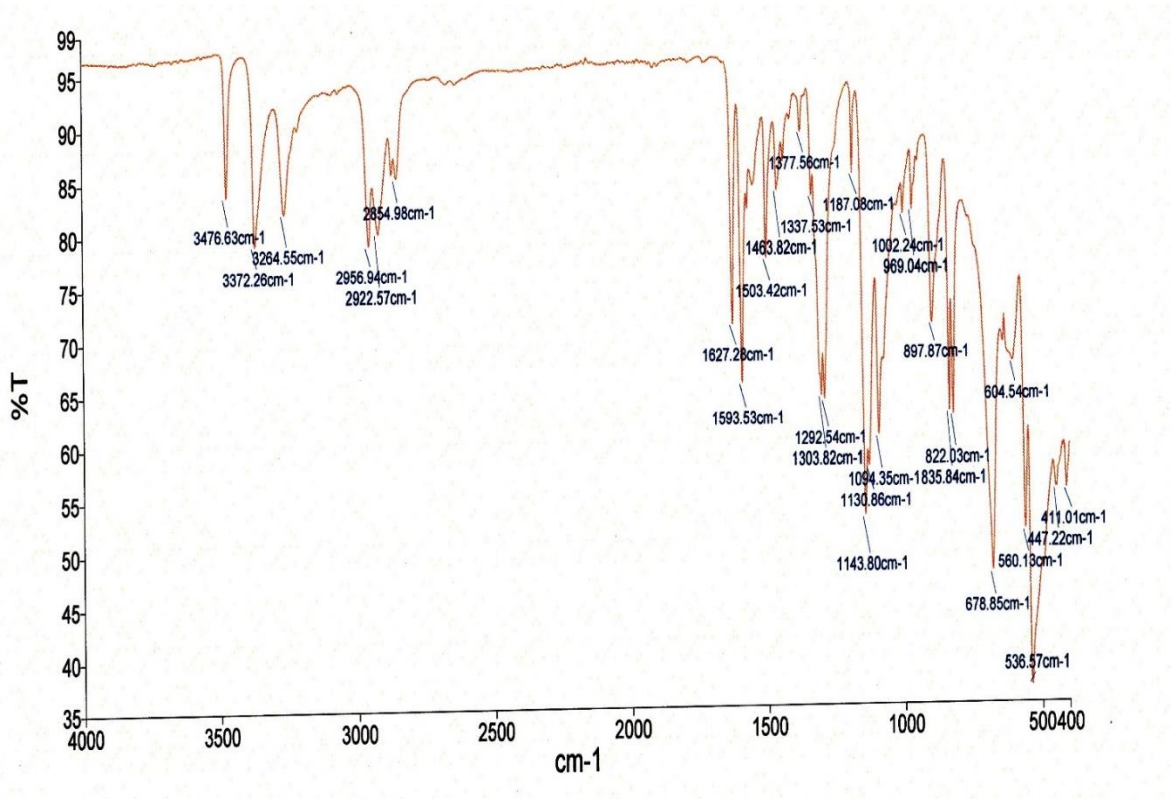


Figure S9. IR spectra of Metformin derivative Met1.

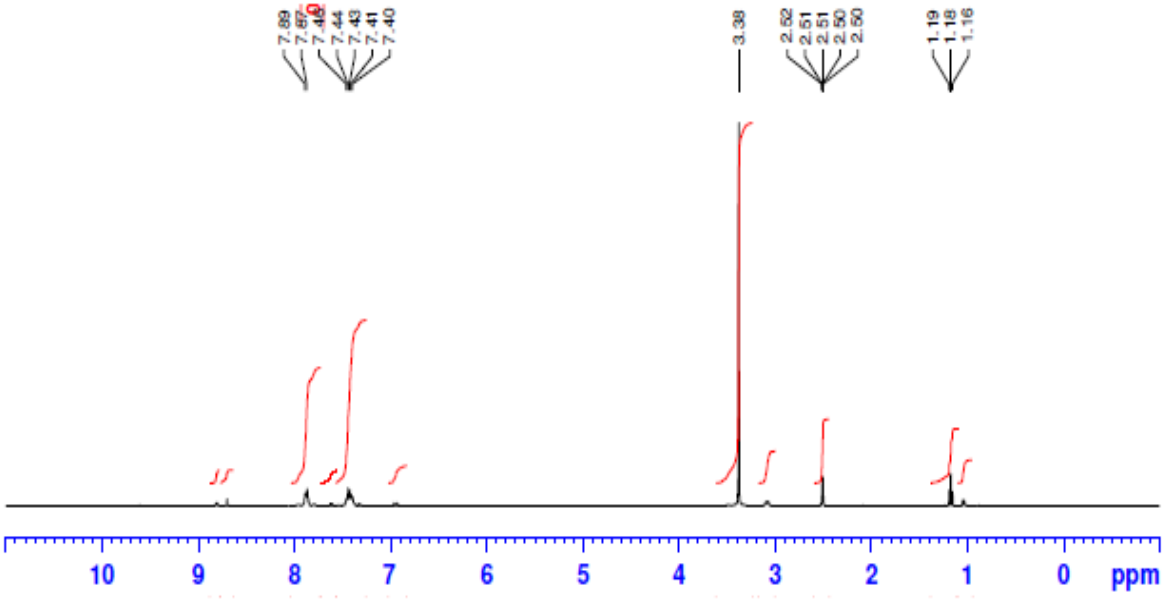


Figure S10. H^1 spectra of Metformin derivative Met1.

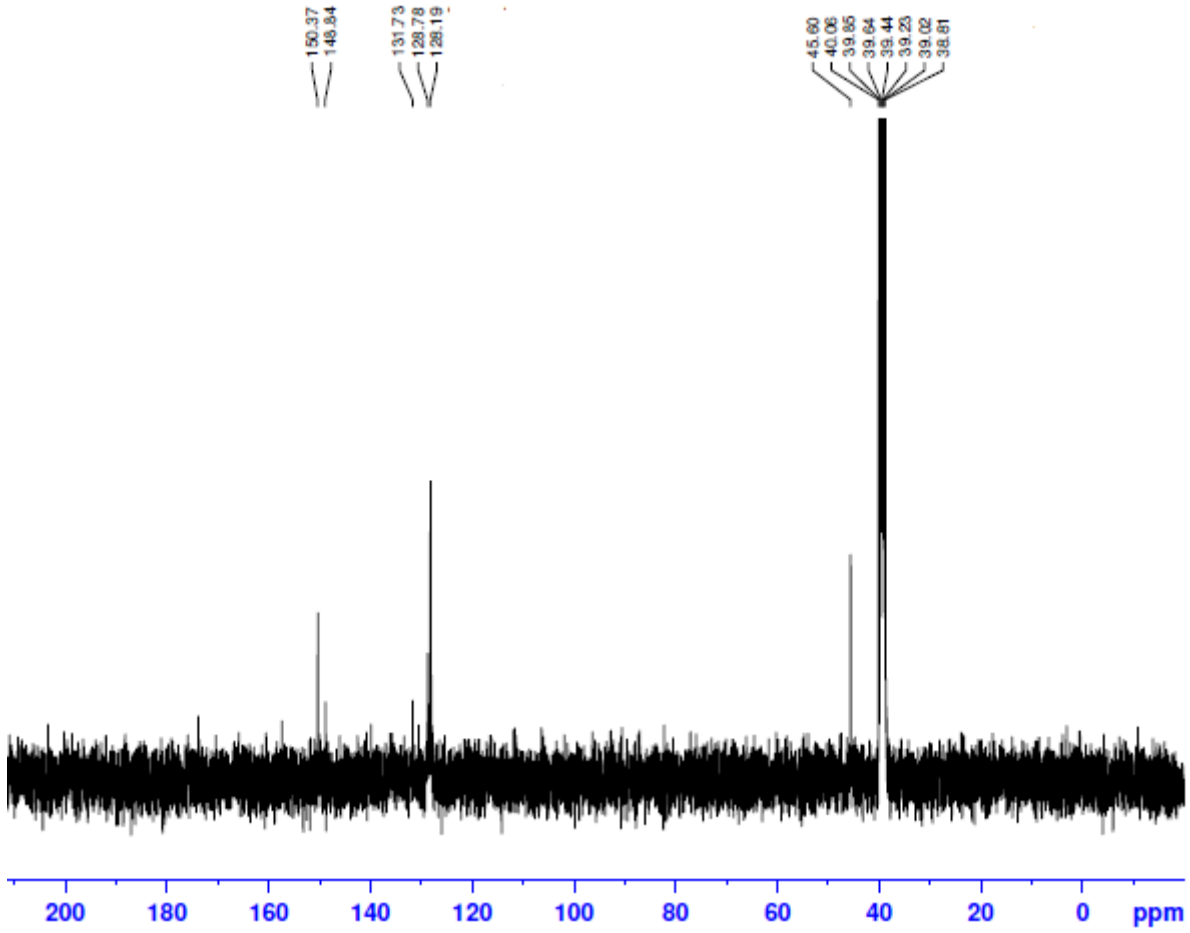


Figure S11. C^{13} spectra of Metformin derivative Met1.

Met 2;

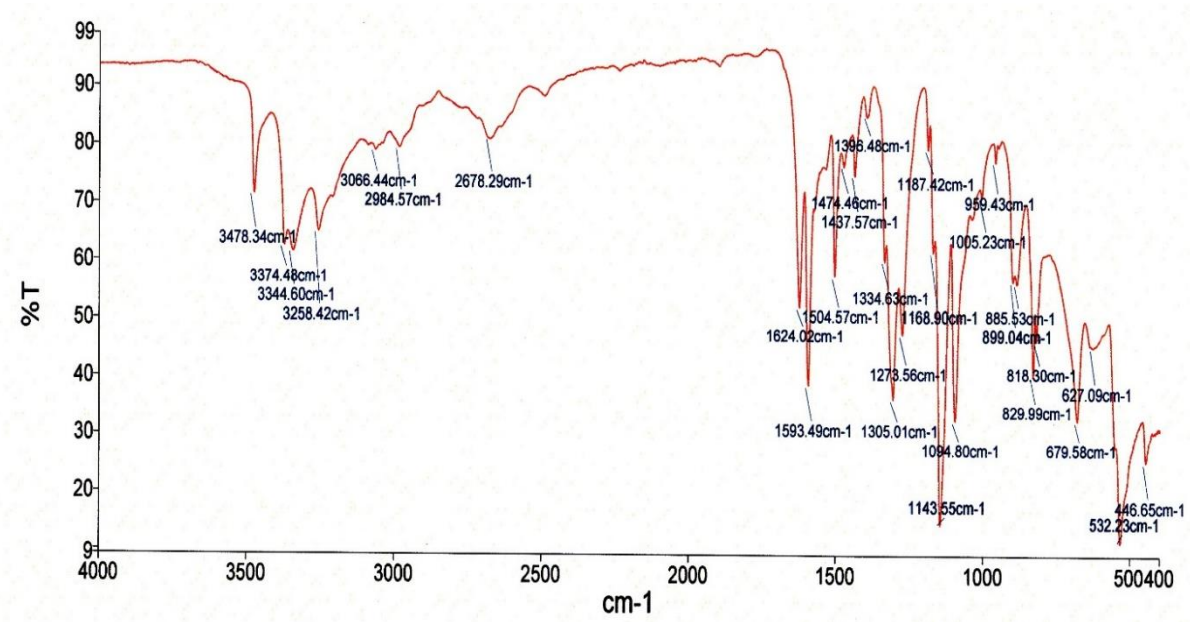


Figure S12. IR spectra of Metformin derivative Met2.

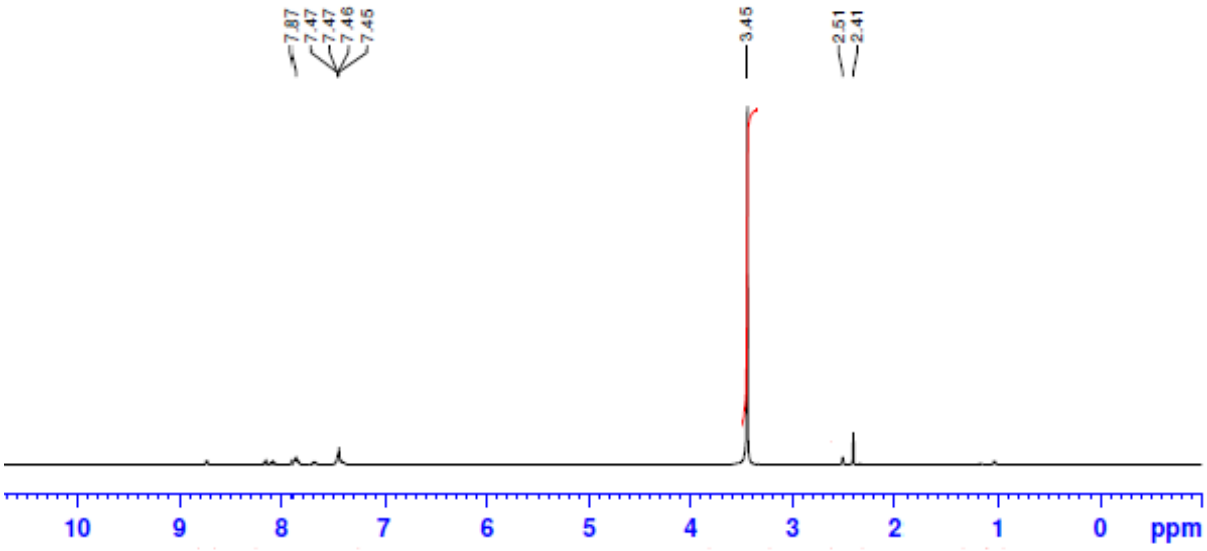


Figure S13. H^1 spectra of Metformin derivative Met2.

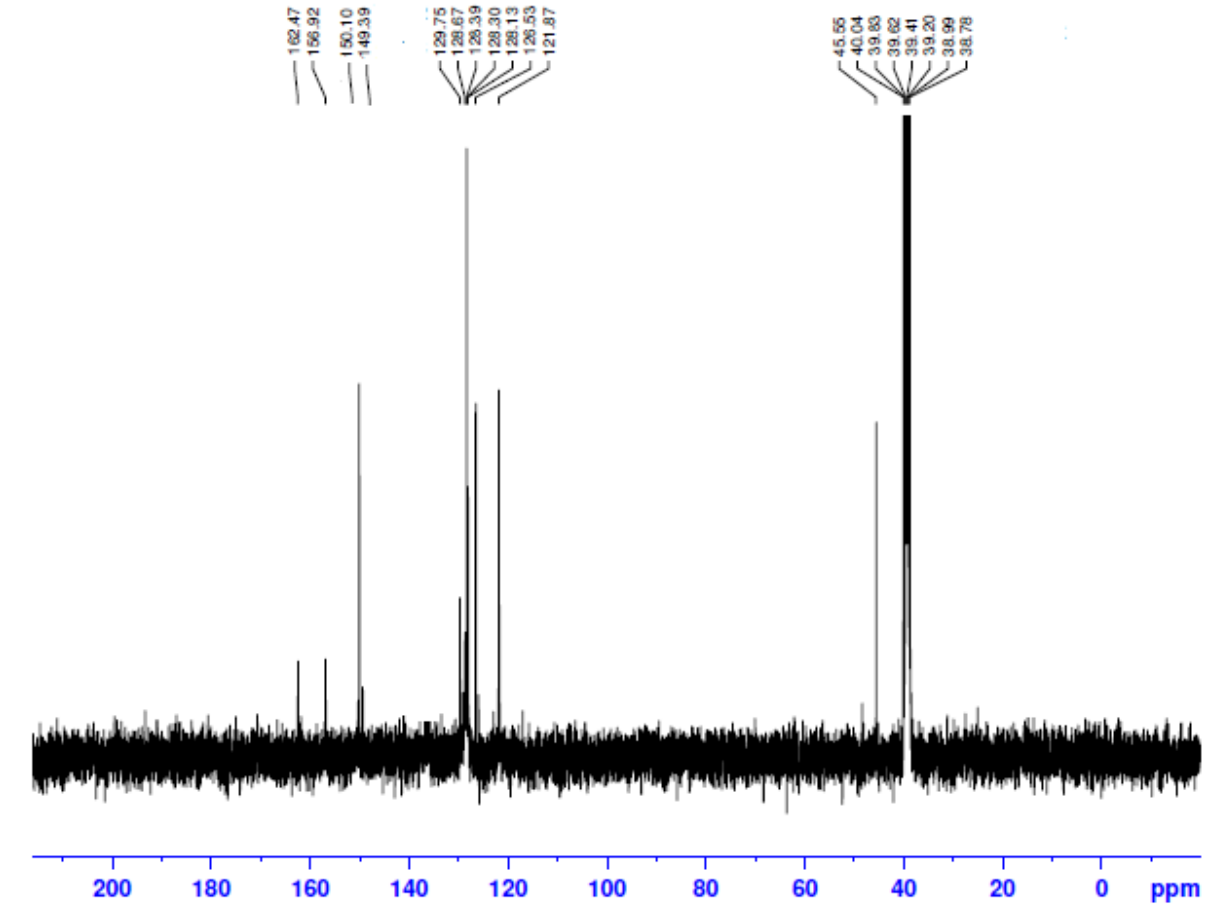


Figure S14. C^{13} spectra of Metformin derivative Met2.

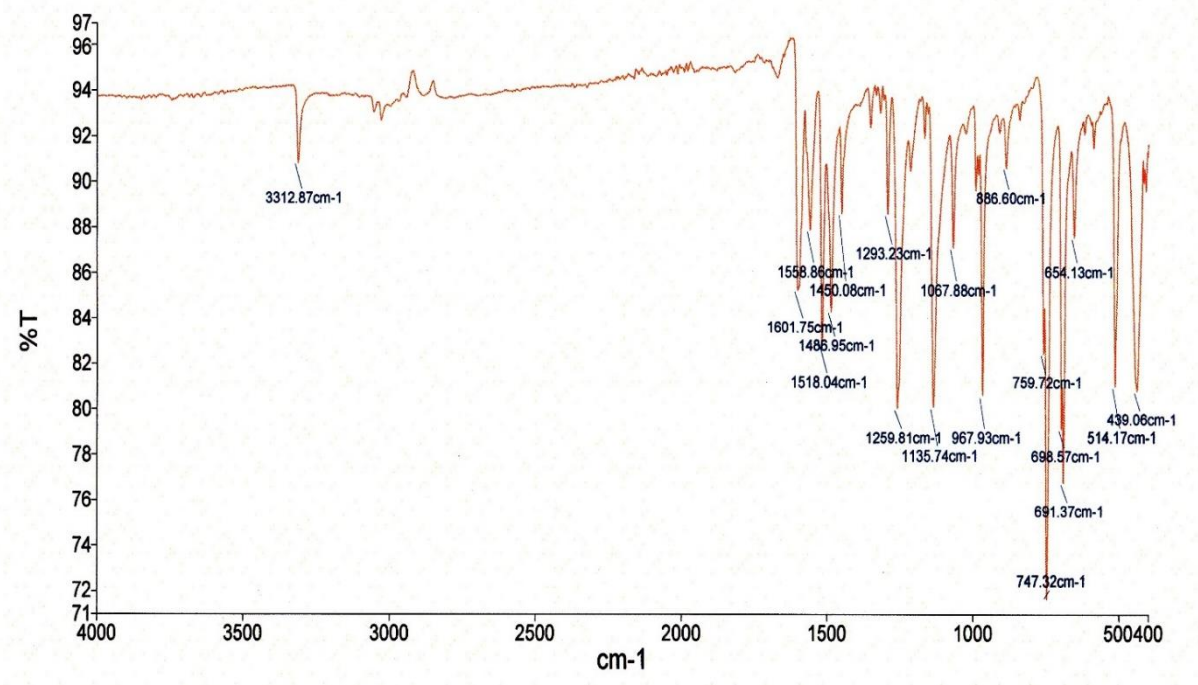


Figure S15. IR spectra of Metformin derivative Met3.

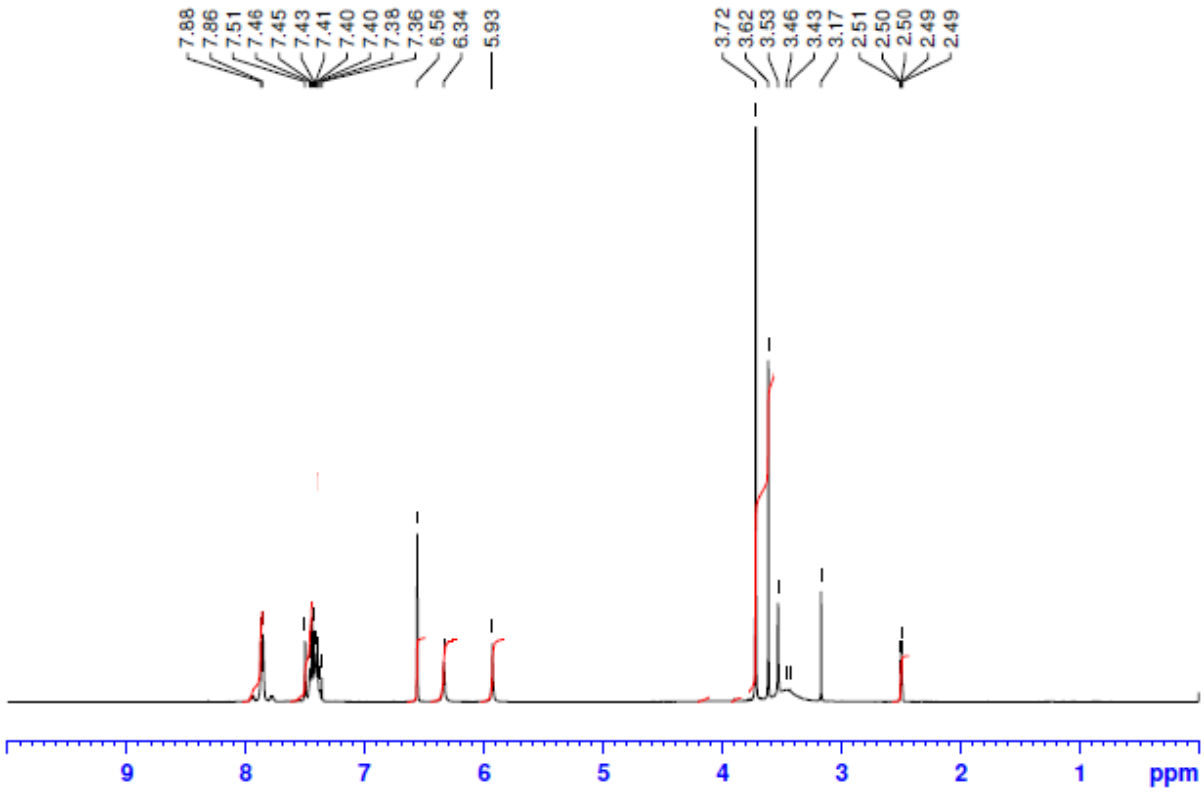


Figure S16. H^1 spectra of Metformin derivative Met3.

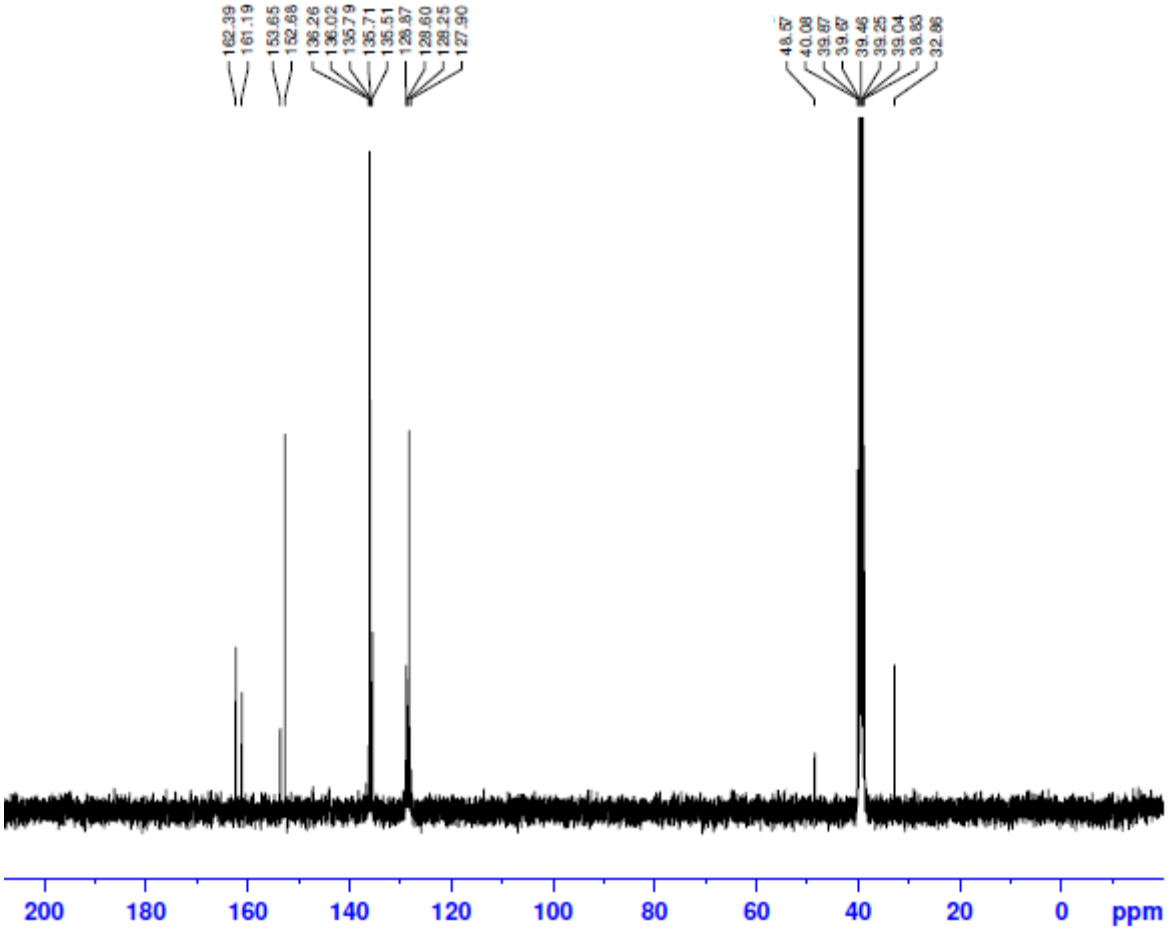


Figure S17. C^{13} spectra of Metformin derivative Met3.

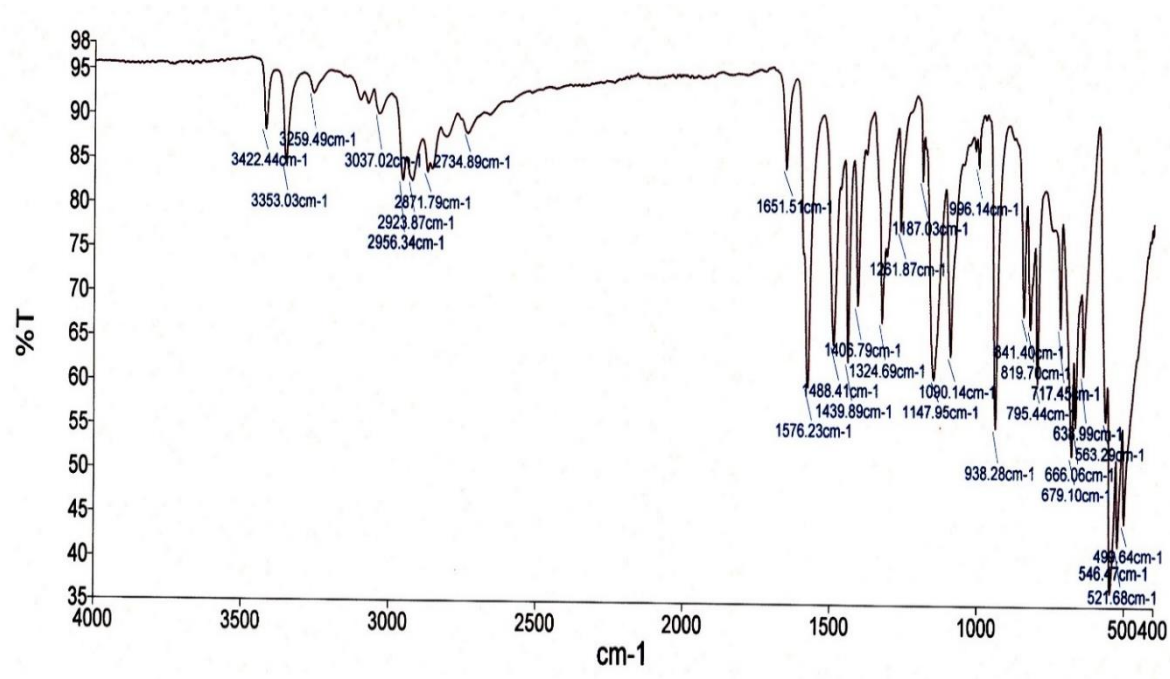


Figure S18. IR spectra of Metformin derivative Met4.

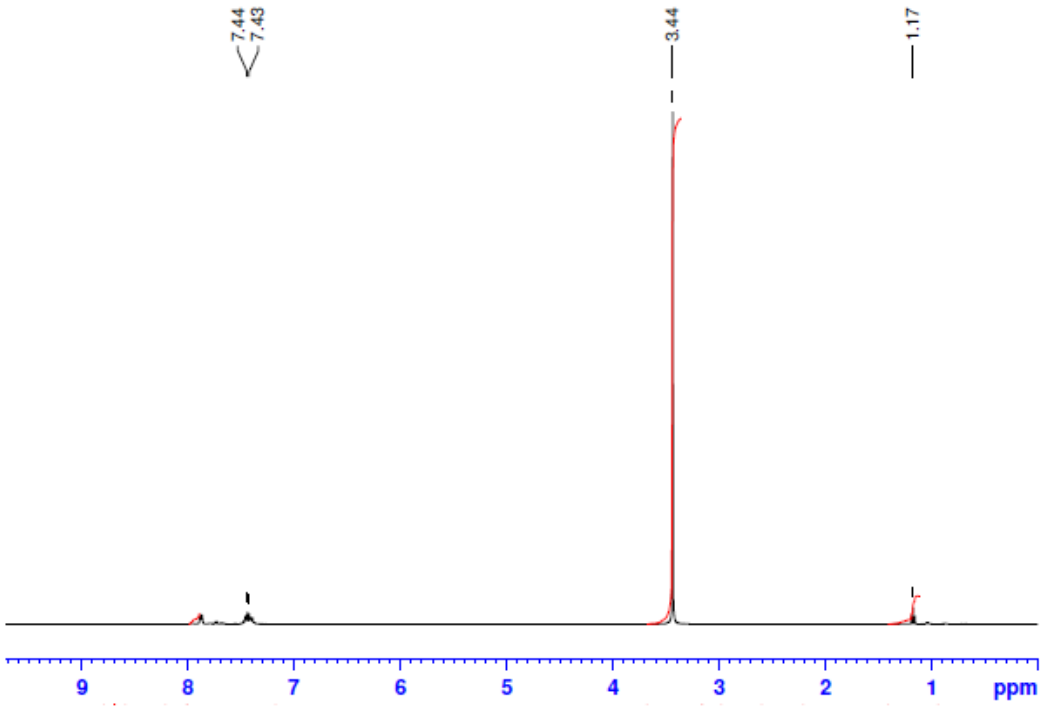


Figure S19. H^1 spectra of Metformin derivative Met4.

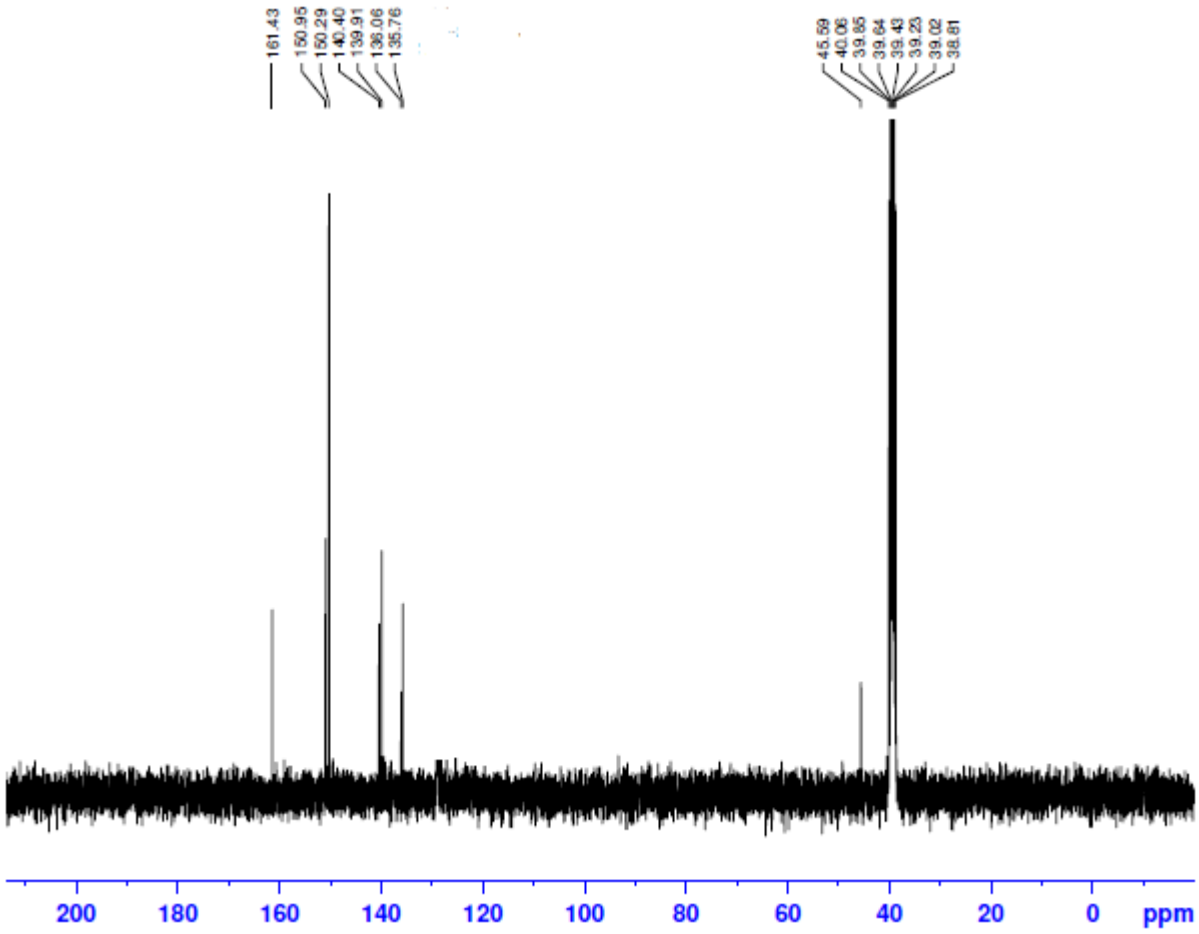


Figure S20. C^{13} spectra of Metformin derivative Met4.

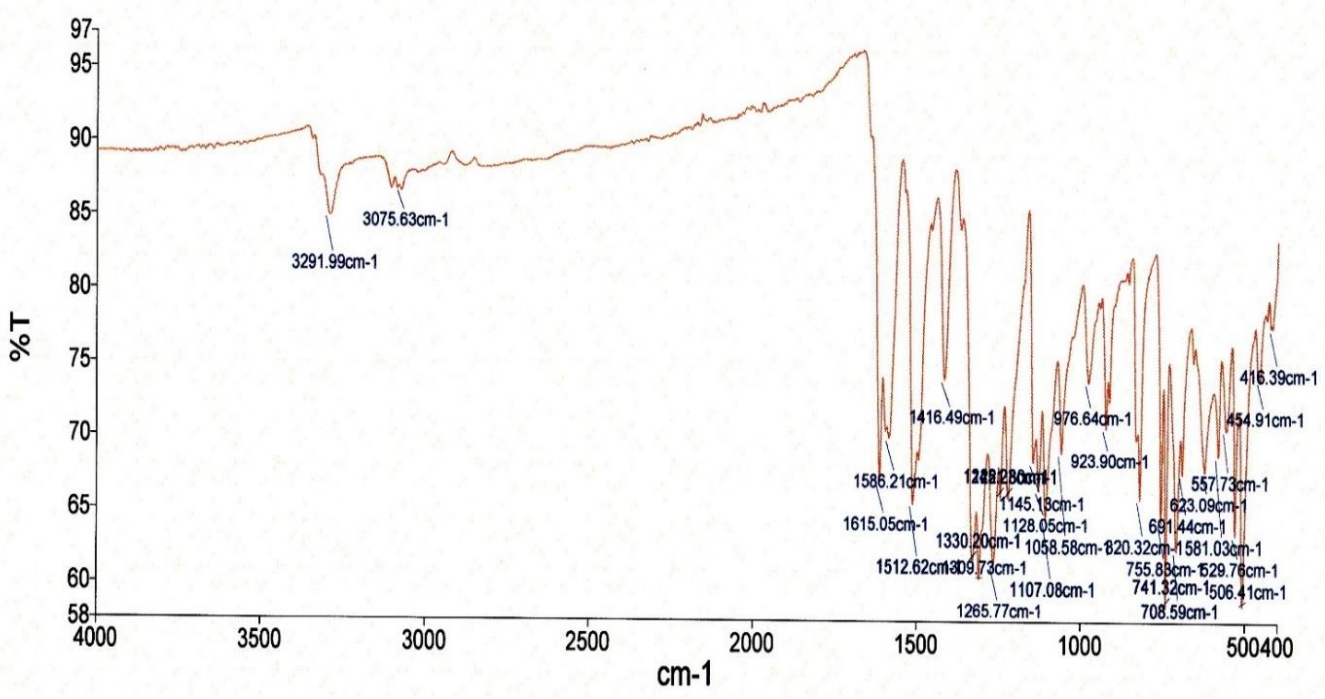


Figure S21. IR spectra of Metformin derivative Met5.

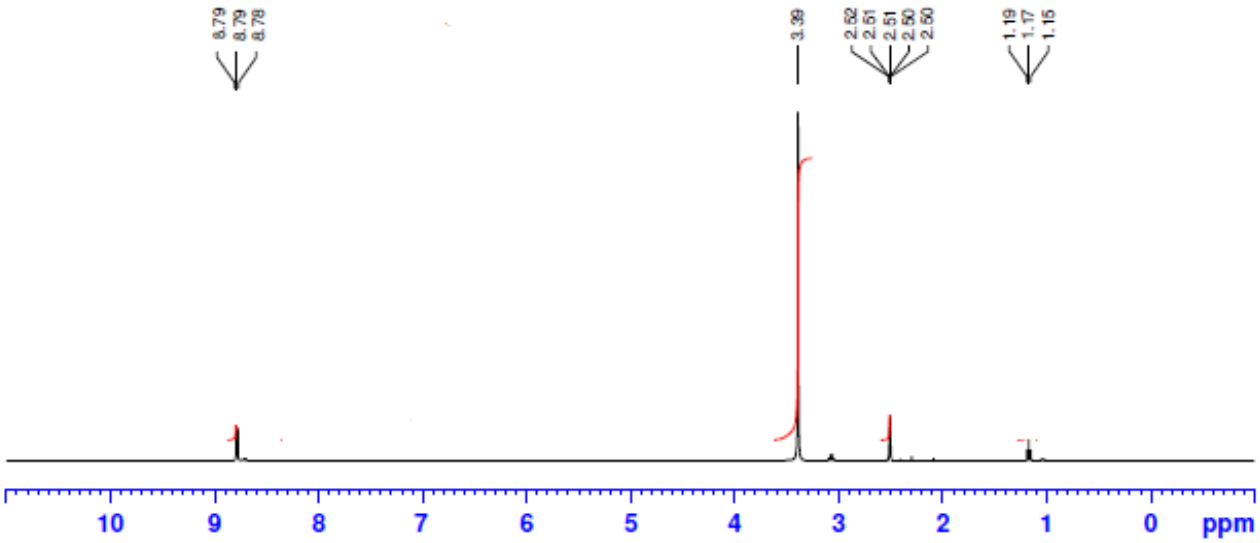


Figure S22. H^1 spectra of Metformin derivative Met5.

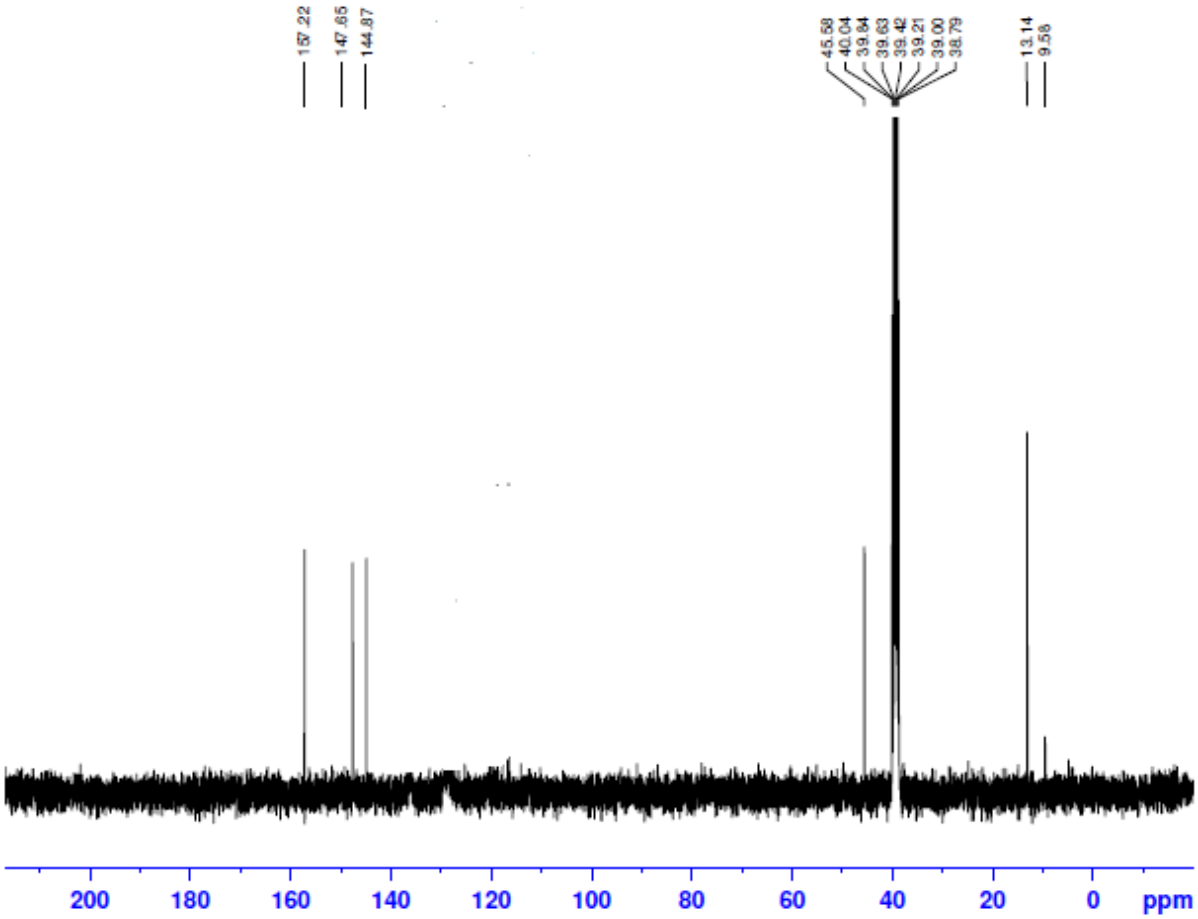


Figure S23. C^{13} spectra of Metformin derivative Met5.

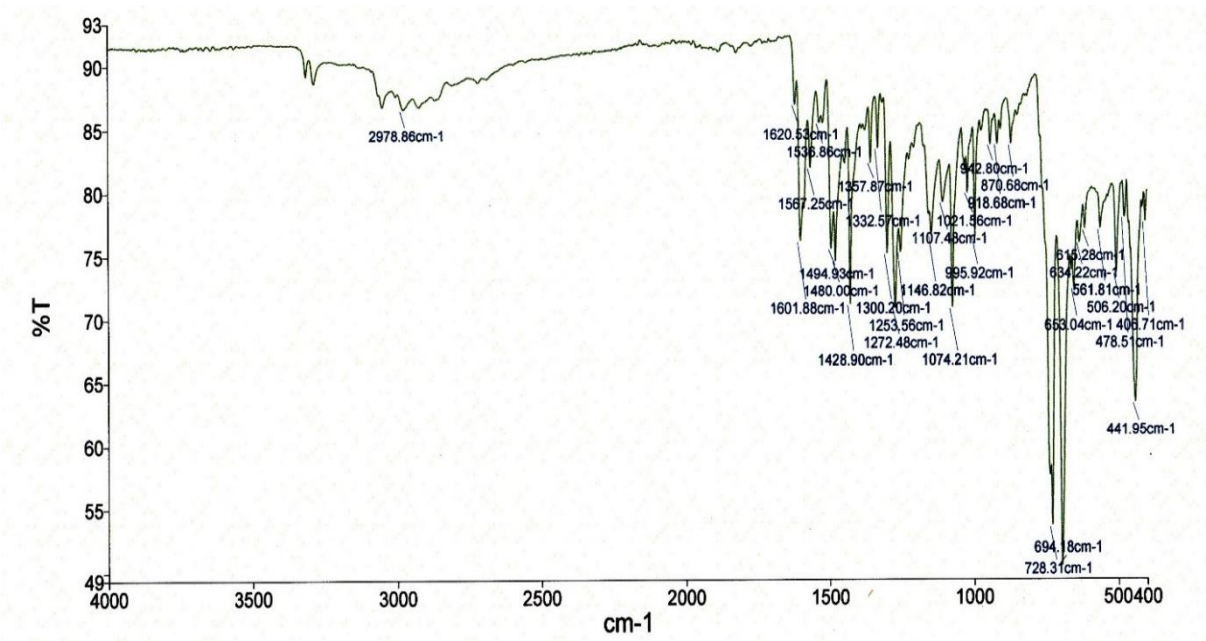


Figure S24. IR spectra of Metformin derivative Met6.

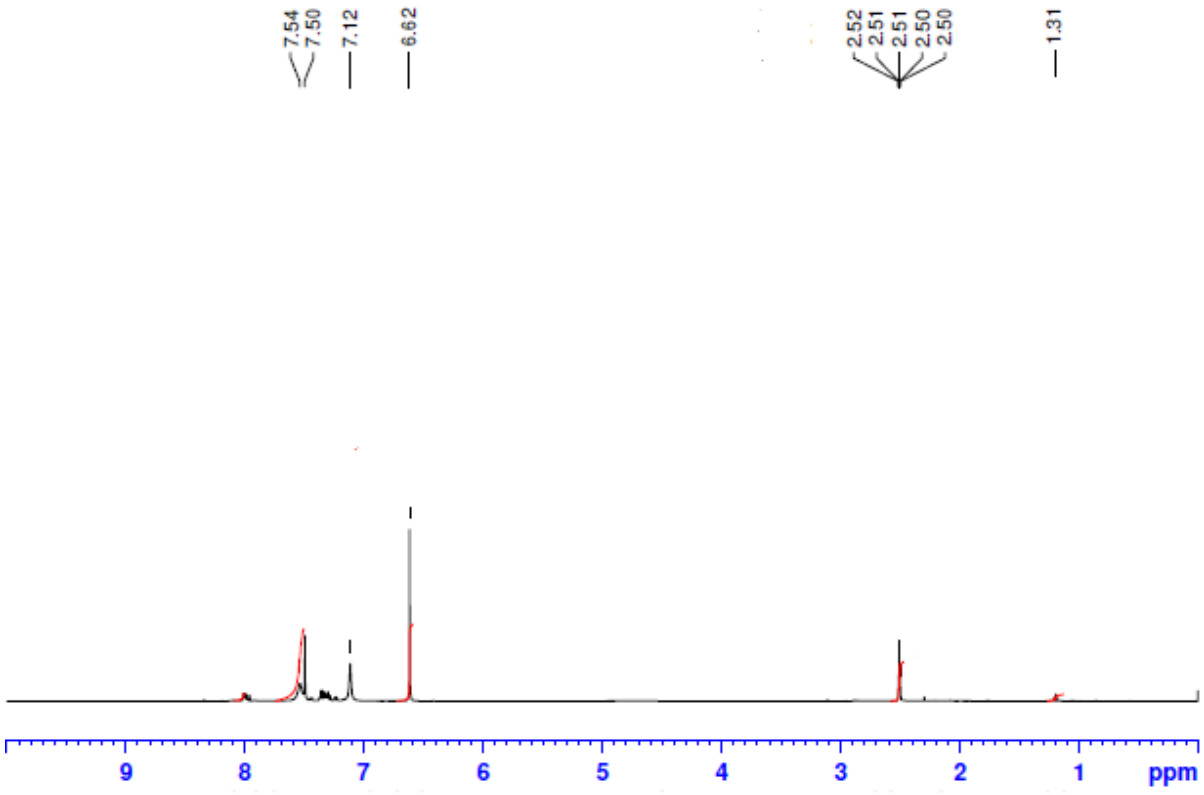


Figure S25. H^1 spectra of Metformin derivative Met6.

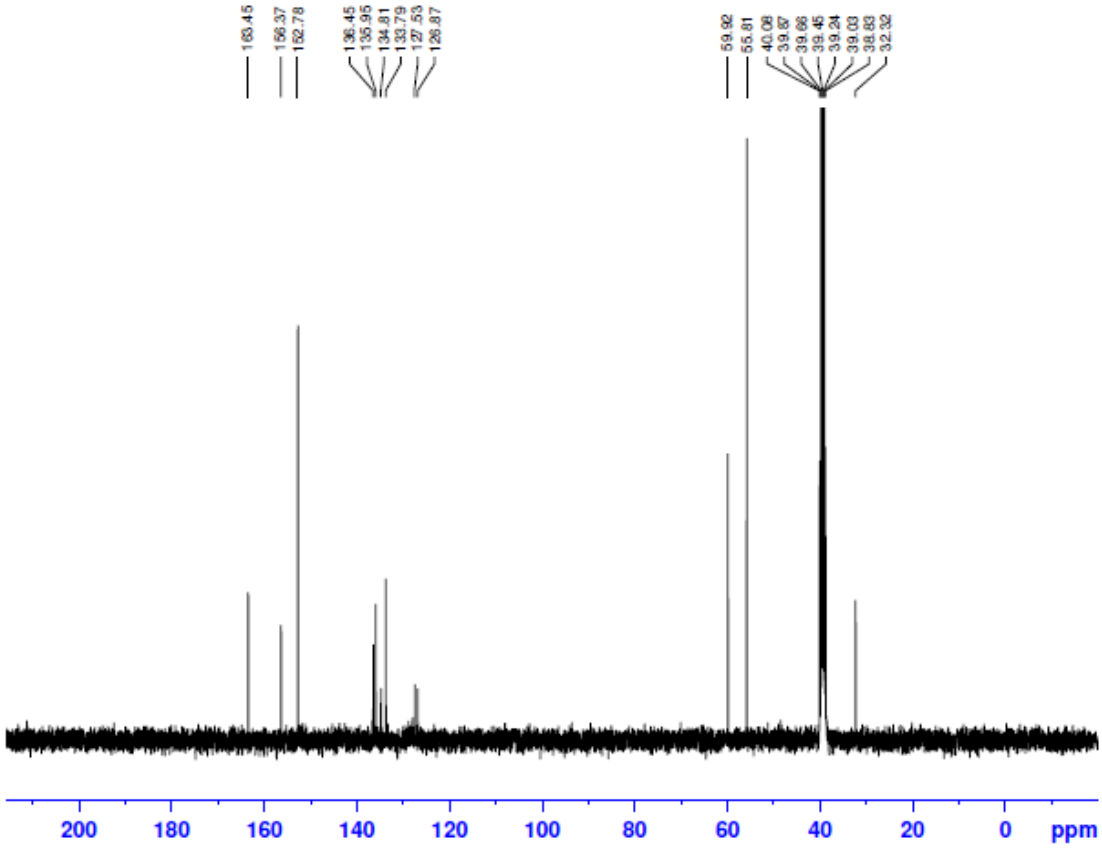


Figure S26. C^{13} spectra of Metformin derivative Met6.

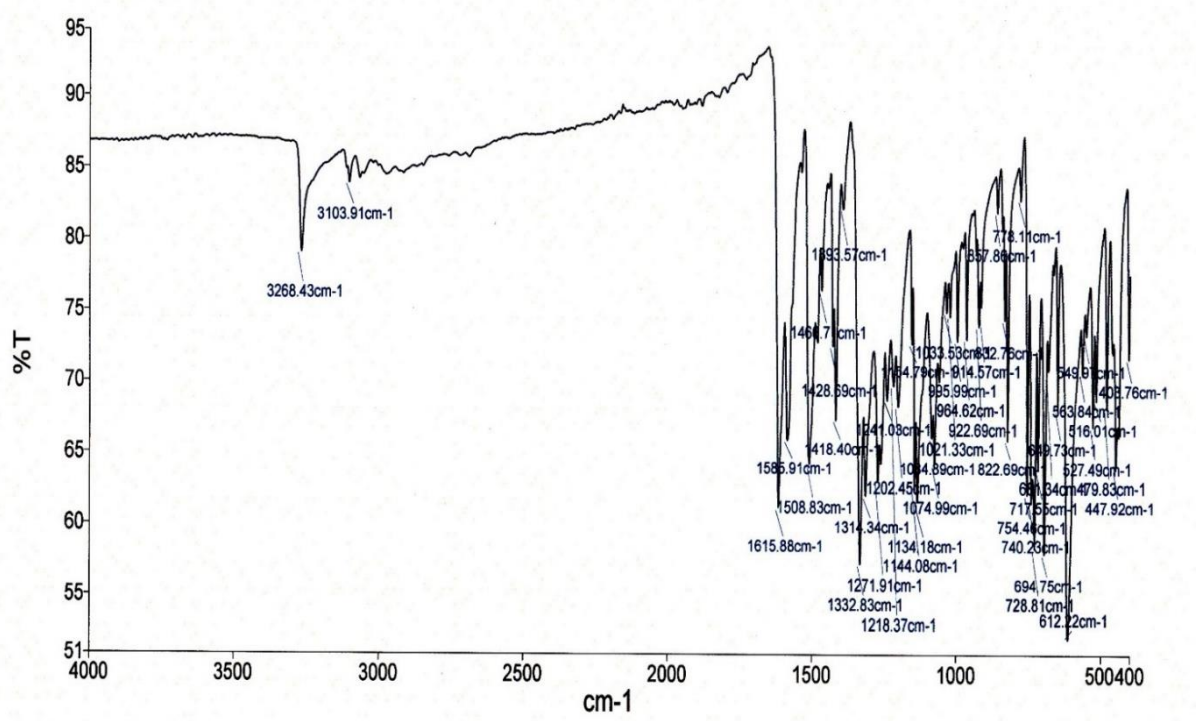


Figure S27. IR spectra of Metformin derivative Met7.

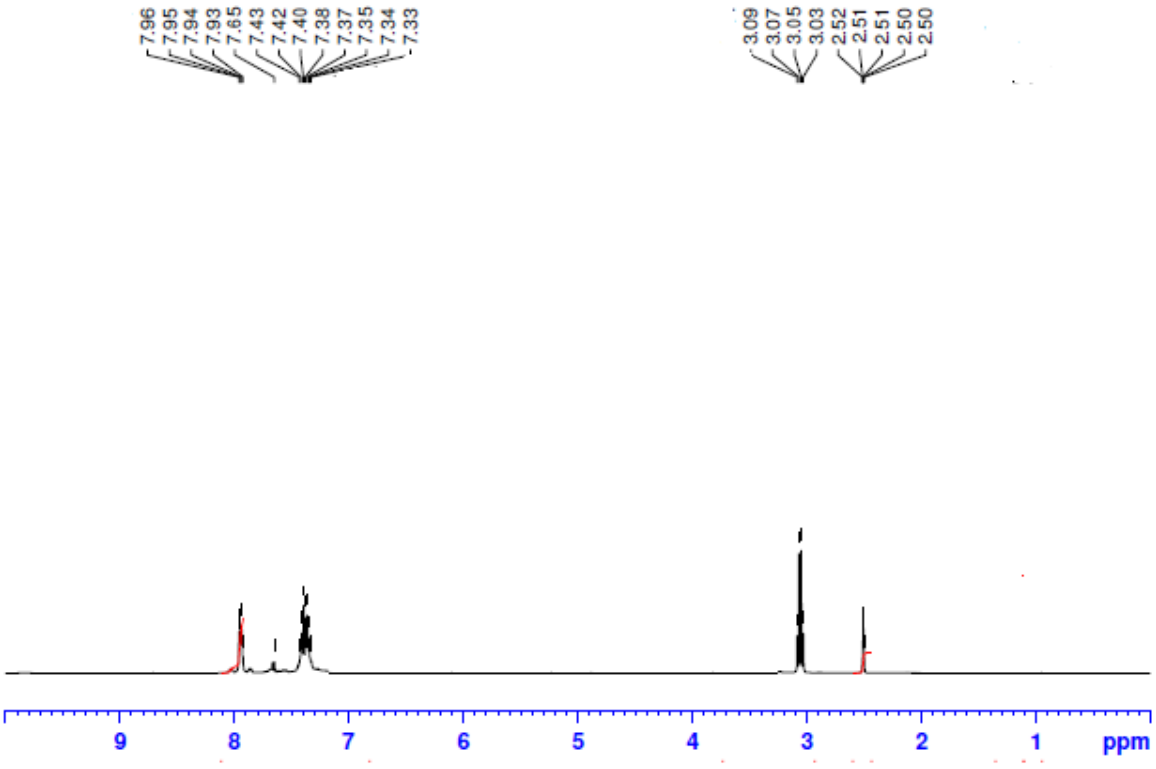


Figure S28. H[1] spectra of Metformin derivative Met7.

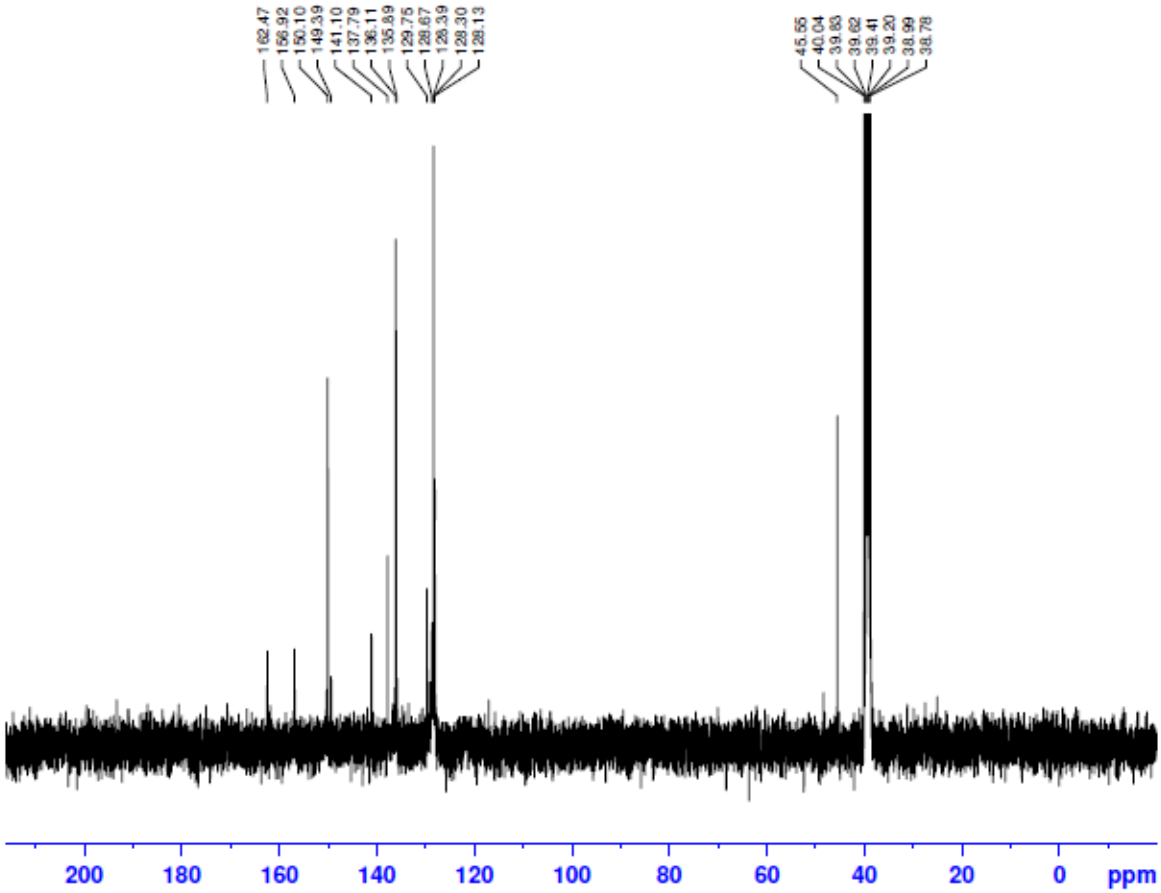


Figure S29. C^{13} spectra of Metformin derivative Met7.

Met 8;

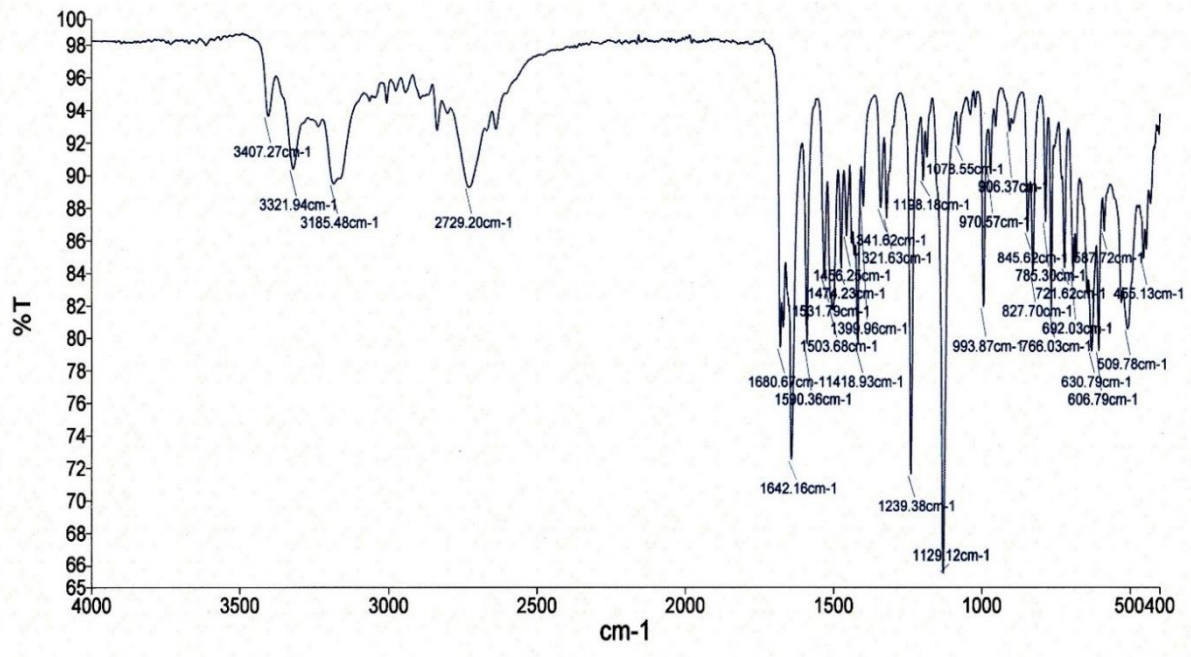


Figure S30. IR spectra of Metformin derivative Met8.

Met 9;

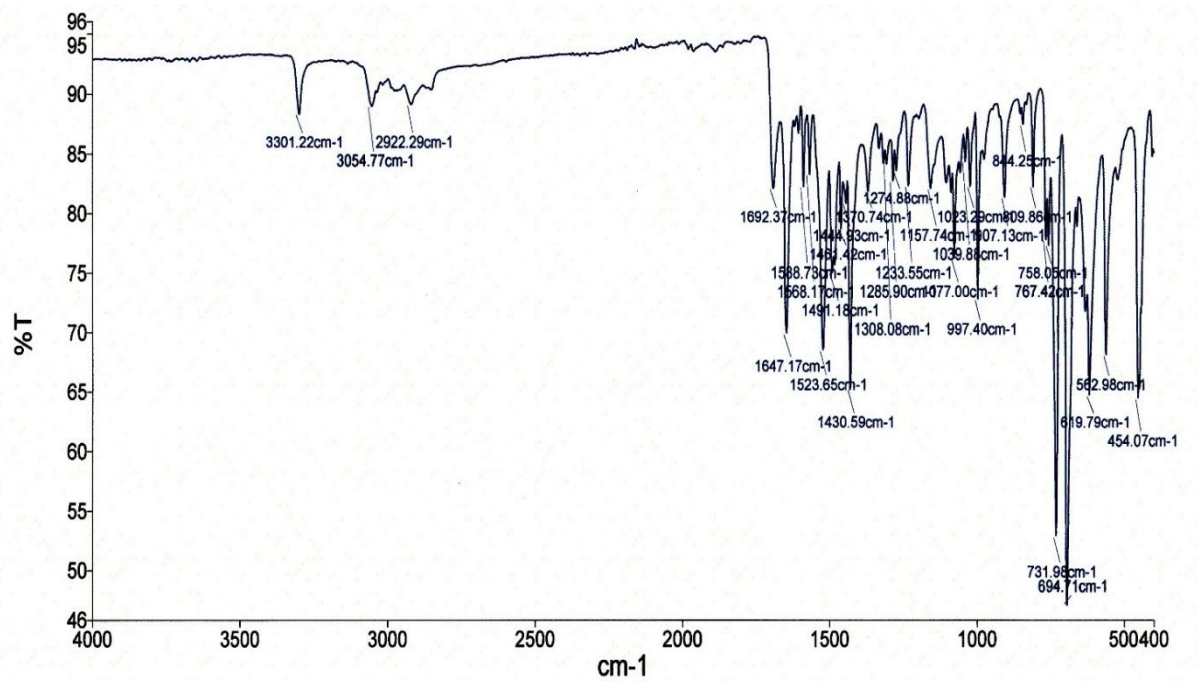


Figure S31. IR spectra of Metformin derivative Met9.