Supporting information

Sl. No.	Name	Brief caption
1	**Supplementary Table S1**	Composition for the components
2	**Supplementary Table S2**	Docking scores of the α1 adrenoreceptor antagonist (AAA) with the α1 adrenergic receptors from humans, mice, and *C. elegans*. BA: Binding affinity; DR: Docking rank.
3	**Supplementary Table S3**	Determination of toxicity of ASA, AAA and Ascorbic acidin *C. elegans*
4	**Supplementary Table S4**	Determination of *in vivo* optimum dose of commercial ASA, Ascorbic acid, and AAA against LC_{50} value of MTV.
5	**Supplementary Table S5**	Physical or behavioral changes in MTV-treated albino Wistar strain rat and their recovery by formulated drug 2 [ASA (187.5 µg), Ascorbic acid (0.1 µg), AAA (3 µM)]. The symptoms were noted 24 h post-injection of MTV.
6	**Supplementary Figure S1**	Homology modelled structures of the following proteins taken from SwissProt [Structure through AlphaFold]. Protein-ligand interactions of α1 adrenoreceptor antagonist (AAA) with α1 adrenergic receptor.
7	**Supplementary Figure S2**	The LC_{50} value of *C. elegans* N2 calculated after 24h treatment of scorpion venom (*M. tamulus* venom). The LC_{50} value calculated for Scorpion venom towards *C. elegans*, after 24 h incubation, was 125 µg/ml.

8	**Supplementary Figure S3**	Fluorescence image of confocal microscopy of *M. tamulus* venom induced ROS generation in *C. elegans* after 6h of *M. tamulus* venom (LC_{50} concentration) treatment and its neutralization by Prazosin, Silodosin and Terazosin. ROS level in positive control (CCCP1) *C. elegans* was considered as baseline (100%) and other values were compared with that.
9	**Supplementary Figure S4**	Fluorescence image of confocal microscopy of MTV-induced alteration of mitochondrial membrane potential and its neutralization by Prazosin, Silodosin and Terazosin. ROS level in positive control (CCCP1) *C. elegans* was considered as baseline (100%) and other values were compared with that.
10	**Supplementary Figure S5**	shows the DPPH free radical-scavenging activity of **(a)** the optimum dose of individual formulation components, their combinations, and different concentrations of formulations, **(b)** Individual components of the formulation and their combinations compared with formulation 2. Data represent mean ± SD of three determinations. Significance of difference, **p*≤0.05 as compared to formulation 2. There was no significant difference (p>0.05) between formulations 2 and 3.
11	**Supplementary Figure S6**	Histopathological analysis of the *M. tamulus* venom-induced Wistar rat tissues and their neutralisation by formulation 2. Light microscopic observation of a) Heart, b) Kidney, c) Liver, d) Lung, e) Testis and f) Ovary from control and treated groups, Bar-100µM. The black arrow indicates the morphological

		changes observed in MTV-induced rat tissue compared to the control
12	**Supplementary Figure S7**	Circulating levels of pro-inflammatory cytokines in the Swiss albino mice with and without *Mesobuthus tamulus* envenomation, MTV-treated plasma and control plasma, respectively. Significance of difference, **p*≤0.05 as compared to control

Supplementary Table S1. Composition of the components used for formulation

S. No.	**Component of the formulation**	**Solubility**
1	ASA (% venom specific antibodies: 6.29%)	Water/ 1xPBS
2	AAA (Prazosin-HCL)	Water/ 1XPBS and then heating at 50-60 °C for 3-5 min
3	Ascorbic acid	Water/ 1XPBS

Supplementary Table S2. Docking scores of the α1 adrenoreceptor antagonist (AAA) with the α1 adrenergic receptors from humans, mice, and *C. elegans*. BA: Binding affinity; DR: Docking rank.

Receptor	**Docking score with prazosin hydrochloride [PMCID: 68546]**				**Docking score with terazosin hydrochloride [PMCID: 68546]**				**Docking score with silodosin [PMCID: 68546]**			
	BA	**rmsd /ub**	**rmsd/lb**	**DR**	**BA**	**rmsd/ub**	**rmsd/lb**	**DR**	**BA**	**rmsd/ub**	**rmsd/lb**	**DR**
Alpha1A adrenergic receptor, (AAAR) (human)	-7.7	4.372	2.808	1	-6.8	27.117	24.472	5	-6.9	2.866	1.929	4
Alpha1B adrenergic receptor (ABAR) (human)	-6.4	30.045	26.824	7	-7.1	17.451	13.724	4	-7	33.115	29.702	3
Alpha1D adrenergic receptor (ADAR) (human)	-6.9	44.121	40.803	4	-6.5	41.723	37.361	6	-7.6	2.399	1.596	2
Alpha1A adrenergic receptor (AAAR) (mouse)	-6.7	18.454	16.899	5	-6.5	19.056	16.835	6	-6.7	60.691	57.074	6
Alpha1B adrenergic receptor (ABAR) (mouse)	-7.1	2.835	1.907	3	-7.3	17.909	17.004	3	-6.4	23.825	19.373	7
Alpha1D adrenergic receptor (ADAR) (mouse)	-7.3	27.734	25.635	2	-7.6	18.07	16.309	1	-7.7	37.322	31.764	1
SER6 receptor (*C. elegans*)	-6.6	8.822	4.309	6	-7.5	15.602	10.429	2	-6.8	43.083	40.303	5

Supplementary Table S3. Determination of toxicity of ASA, AAA and Ascorbic acid in *C. elegans.* Data represent mean ± SD of three determinations.

S. No.	**Components**	**Viability of *C. elegans* (%)**	
		0 h	**24 h**
1	Control	100.00 ± 5	97.20 ± 4.86
2	ASA (PSVPL)	100.00 ± 5	96.10 ± 4.81
3	ASA (HBC)	100.00 ± 5	95.92 ± 4.73
4	AAA (Prazosin)	100.00 ± 5	96.78 ± 4.80
5	AAA (Silodosin)	100.00 ± 5	97.13 ± 4.69
6	AAA (Terazosin)	100.00 ± 5	96.98 ± 4.84

Supplementary Table S4. Determination of *in vivo* optimum dose of commercial ASA, Ascorbic acid, and AAAs against LC_{50} of *M. tamulus* venom.

S. No.	Name of samples	Optimum dose
1	ASA (PSVPL and HBC)	1500 µg
2	Ascorbic acid	1 µg
3	AAAs: Prazosin, Terazosin Silodosin	 50 µM 50 µM 25 µM

Supplementary Table S5. Physical or behavioral changes in MTV-treated albino Wistar strain rat and their recovery by formulation 2 [ASA (187.5 µg), Ascorbic acid (0.1 µg), AAA (3 µM)]. The symptoms were noted 24 h post-injection of MTV.

S. No.	Pathophysiological symptoms post MTV-treatment	Treatment with the formulation 2
1	High urination	Recovered
2	Fast breathing	Recovered
3	Defecation	Recovered
4	Become more thirsty	Recovered
5	Weak grip strength	Recovered

Protein-ligand interactions:

Generation of the 3D structure of Prazosin Hydrochloride [PMCID: 68546]:

Canonical SMILES:
COC1=C(C=C2C(=C1)C(=NC(=N2)N3CCN(CC3)C(=O)C4=CC=CO4)N)OC.Cl

Molecular Formula:

C19H22ClN5O4

3D structure was generated using Corina Classic software.

Generation of the 3D structure of Terazosin hydrochloride [PMCID: 44383]:

Canonical SMILES:
COC1=C(C=C2C(=C1)C(=NC(=N2)N3CCN(CC3)C(=O)C4CCCO4)N)OC.Cl

Molecular Formula:

C19H26ClN5O4

3D structure was generated using Corina Classic software.

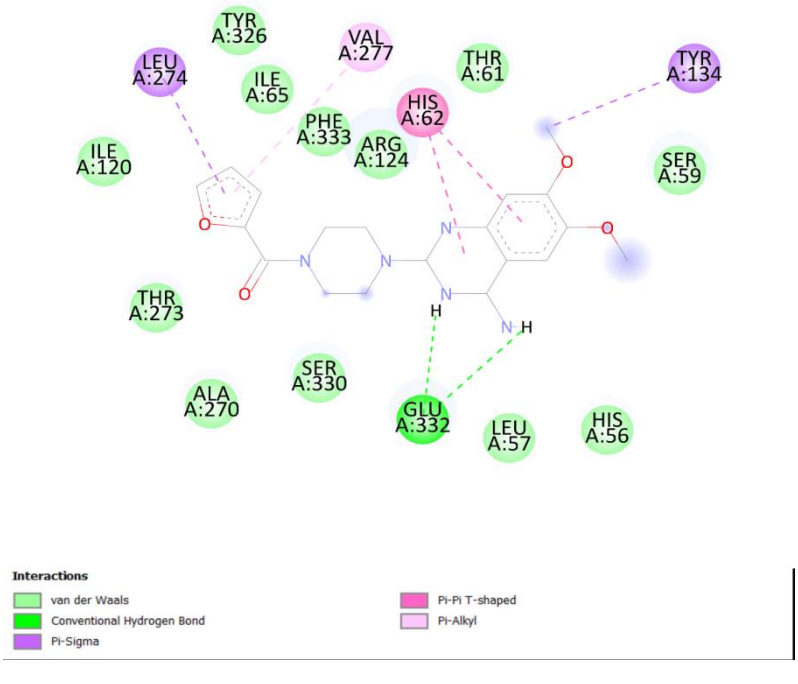
Generation of the 3D structure of Silodosin [PMCID: 5312125]:

Canonical SMILES:
CC(CC1=CC2=C(C(=C1)C(=O)N)N(CC2)CCCO)NCCOC3=CC=CC=C3OCC(F)(F)F

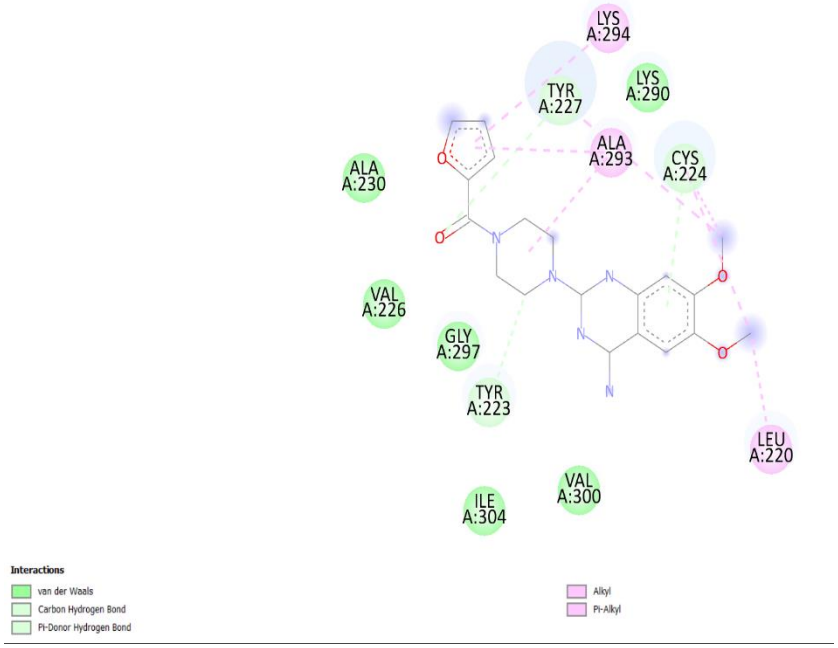
Molecular Formula:

C25H32F3N3O4

3D structure was generated using Corina Classic software.



1.a AAAR (human) + Prazosin-HCL [AlphaFold identifier of AAAR: AF-P35348-F1, SwissProt Accession No.: P35348]



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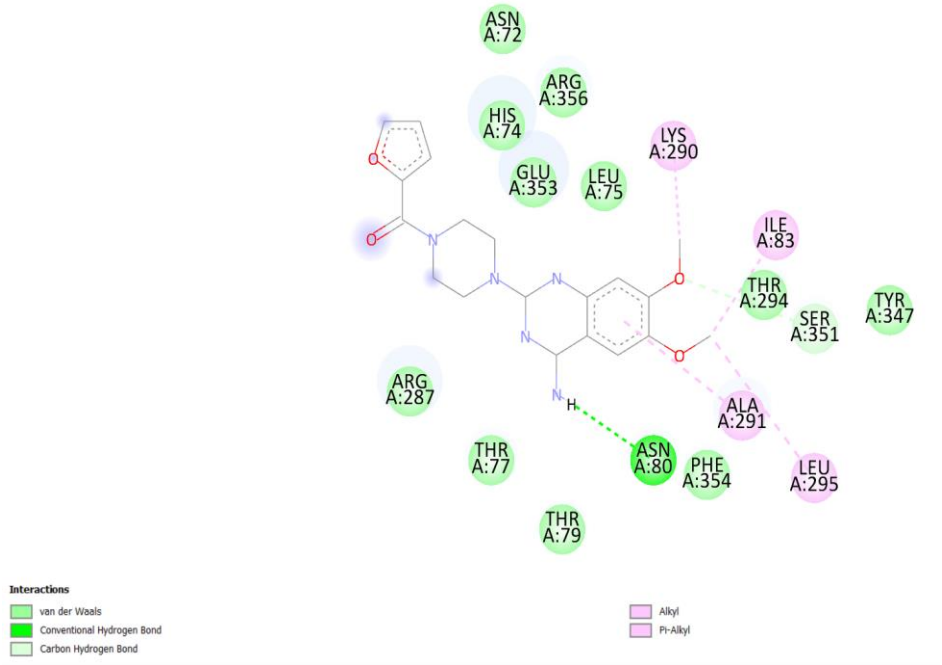

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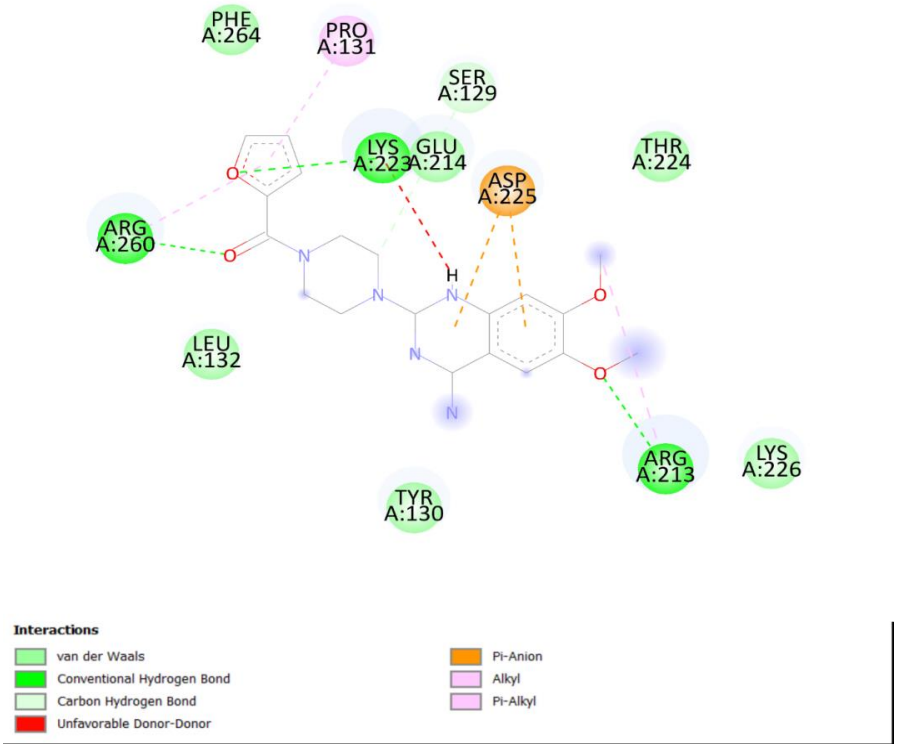
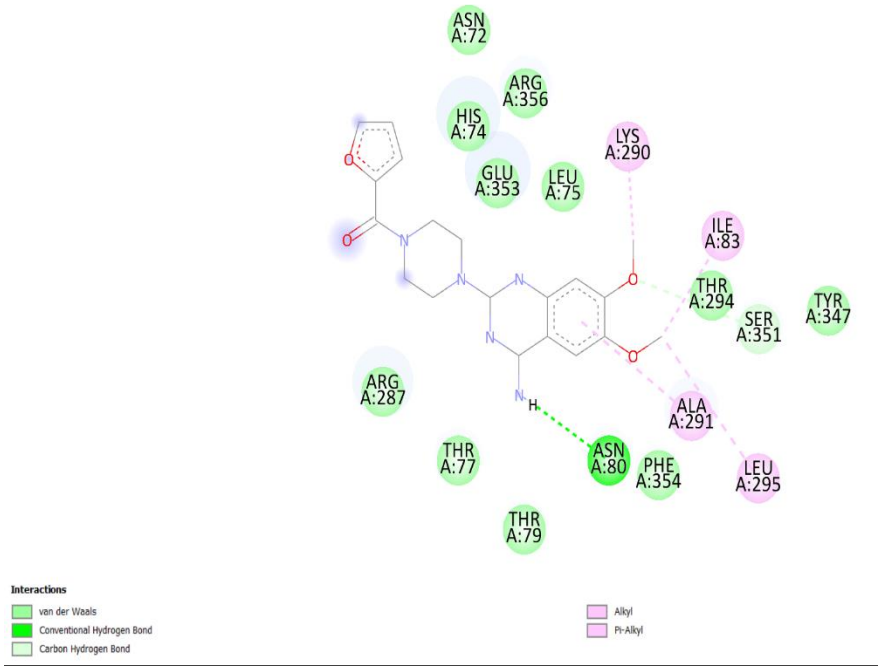


1.d AAAR (Mouse)+ Prazosin-HCL [AlphaFold identifier of AAAR: AF-P97718-F1, SwissProt Accession No.: P97718]



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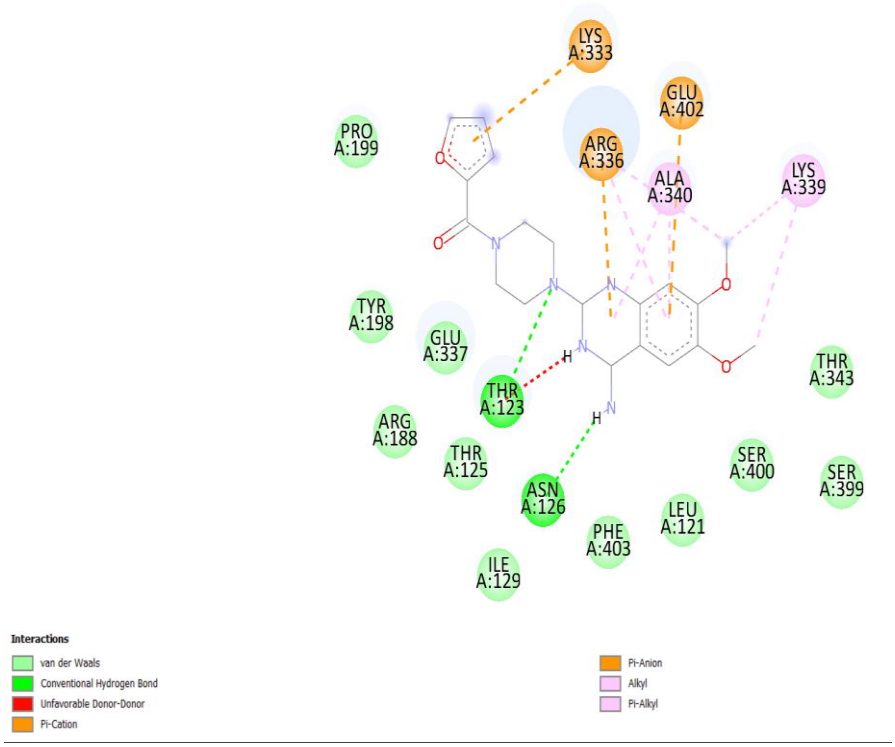
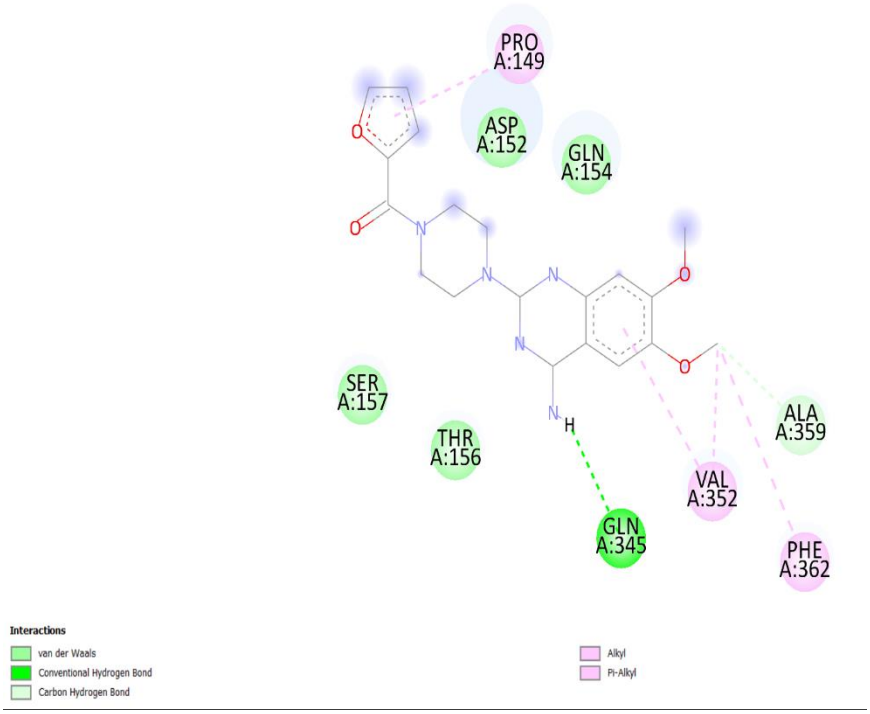
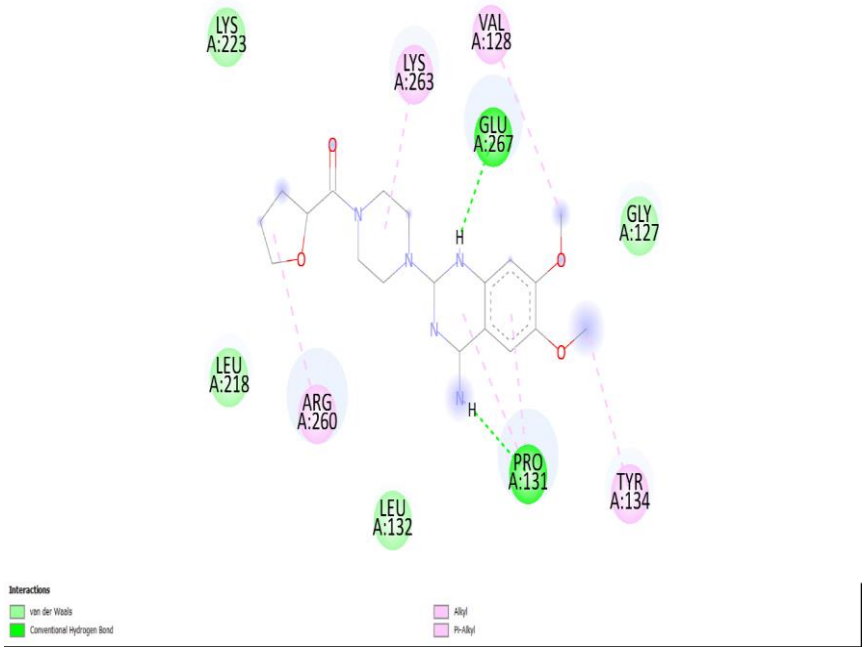


1.f ADAR (Mouse)+ Prazosin-HCL [AlphaFold identifier of ADAR: AF-P97714-F1, SwissProt Accession No.: P97714]



1.g SER6 receptor (*C. elegans*)+ Prazosin-HCL [AlphaFold identifier: AF-Q8MXS7-F1, SwissProt Accession No.: Q8MXS7]



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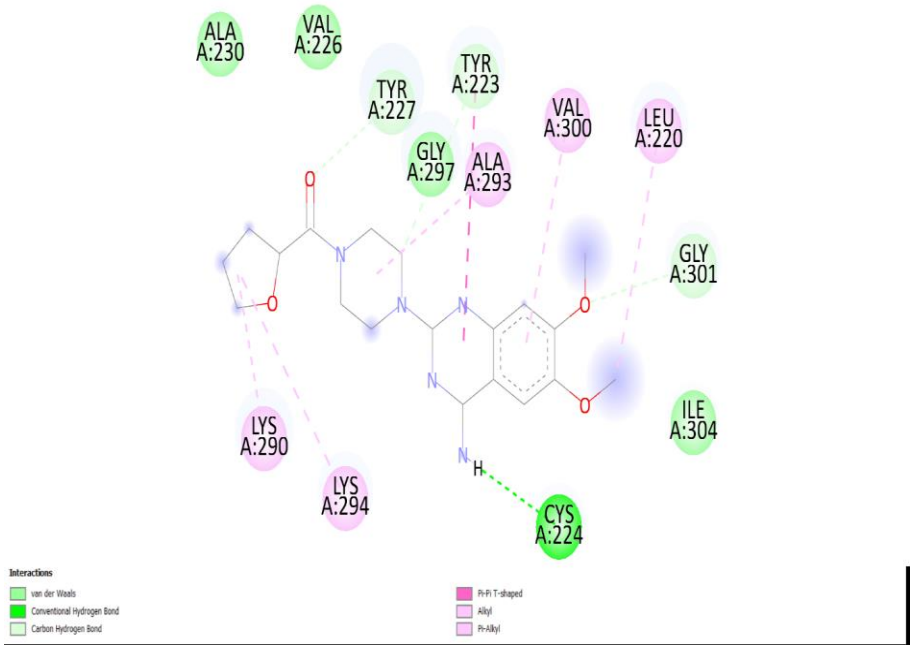

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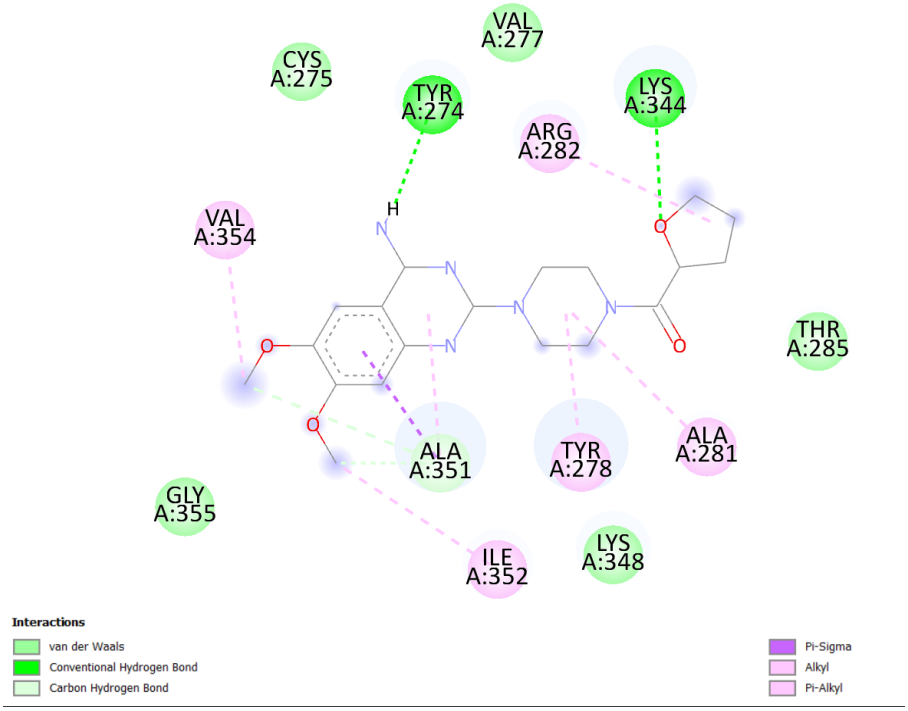

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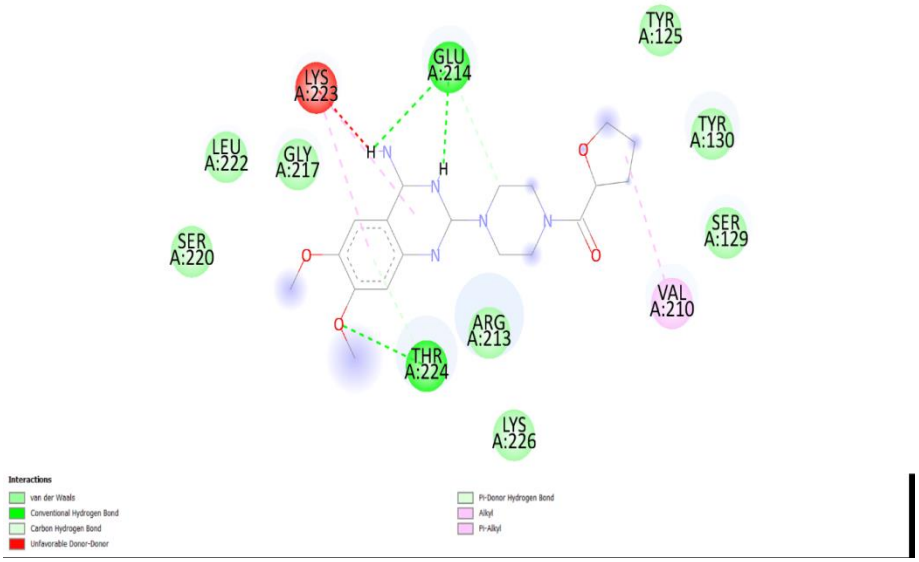
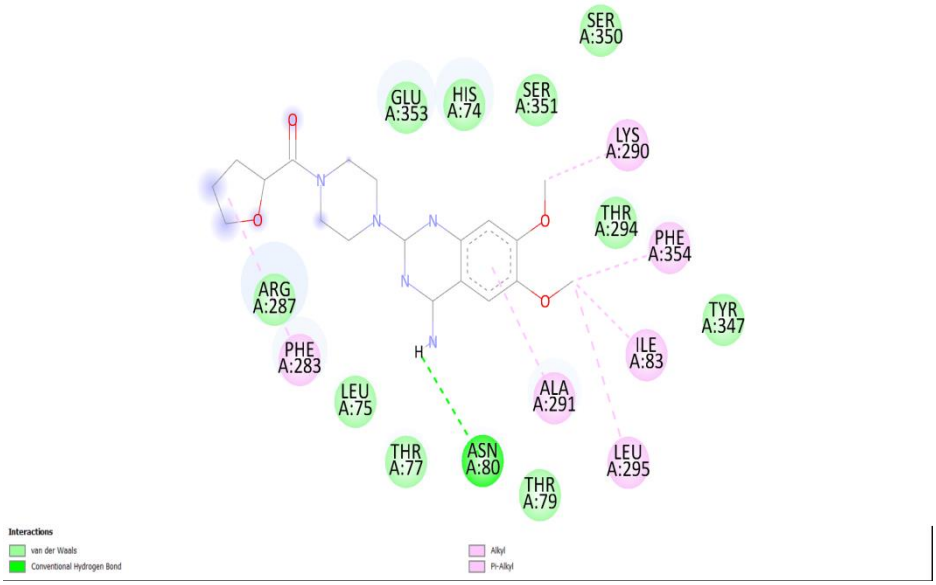
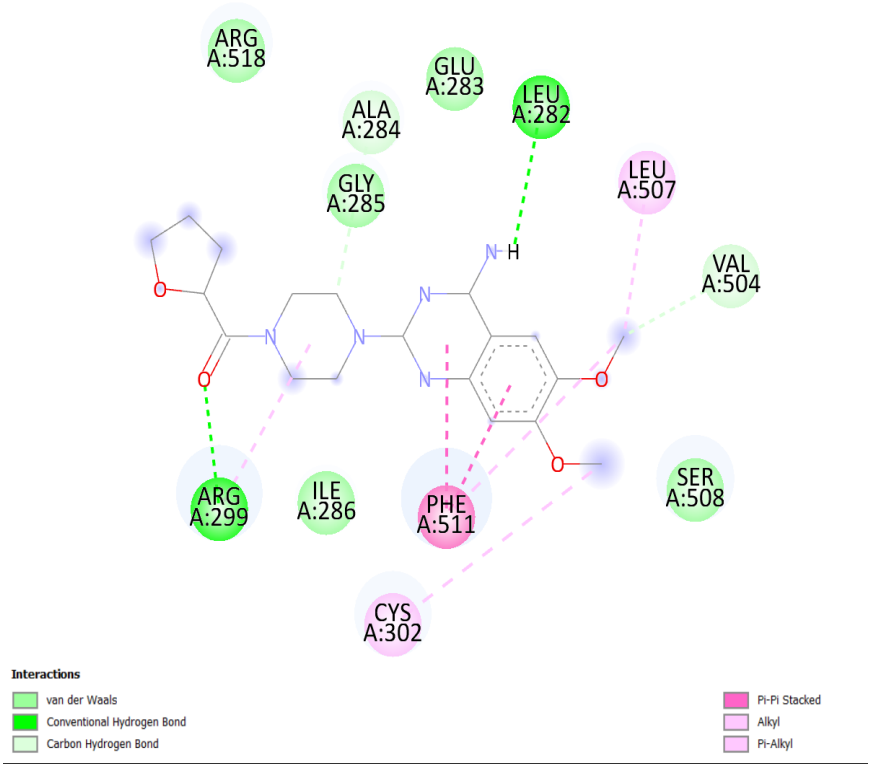


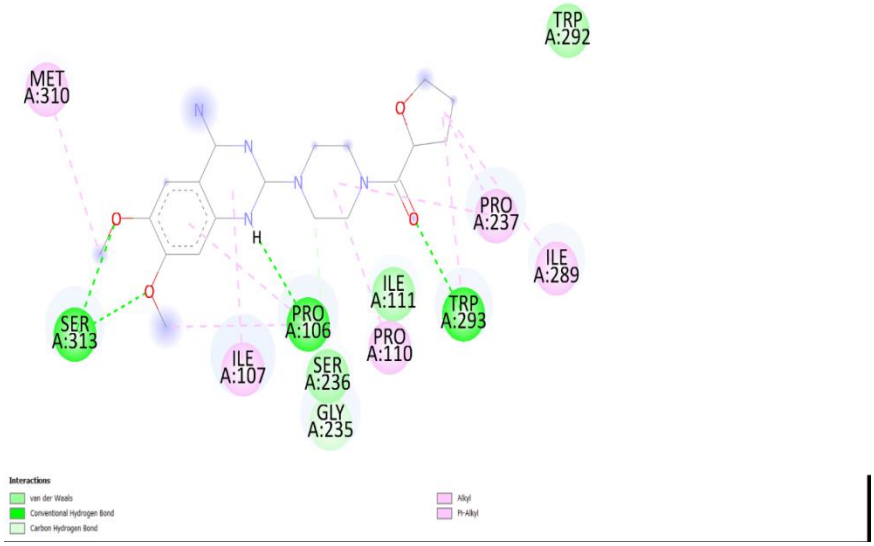
1.k AAAR (Mouse)+ Terazosin-HCL [AlphaFold identifier of AAAR: AF-P97718-F1, SwissProt Accession No.: P97718]



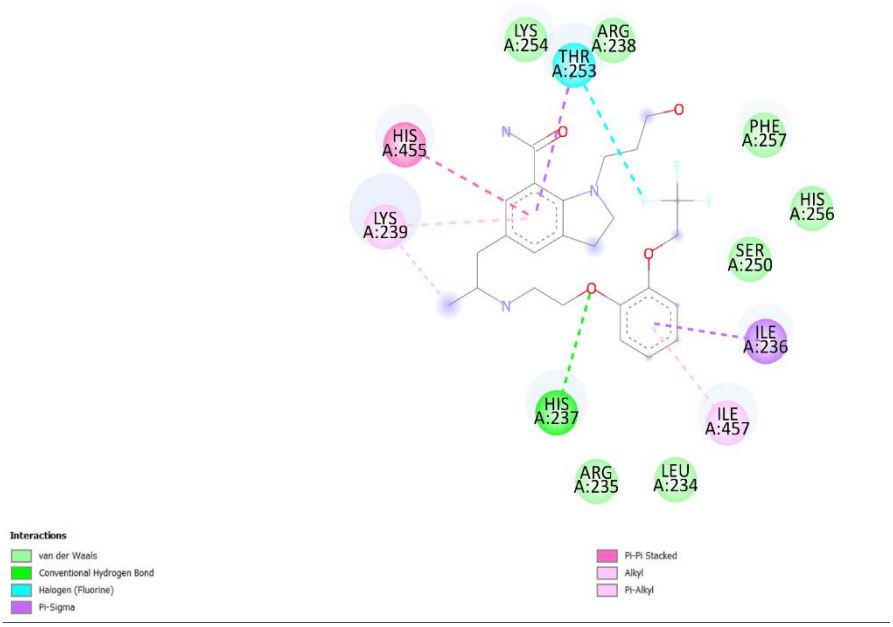
1.l ABAR (Mouse)+ Terazosin-HCL [AlphaFold identifier of ABAR: AF-P97717-F1, SwissProt Accession No.: P97717]



1.m ADAR (Mouse)+ Terazosin-HCL [AlphaFold identifier of ADAR: AF-P97714-F1, SwissProt Accession No.: P97714]



1.n SER6 receptor (*C. elegans*)+ Terazosin-HCL [AlphaFold identifier: AF-Q8MXS7-F1, SwissProt Accession No.: Q8MXS7]



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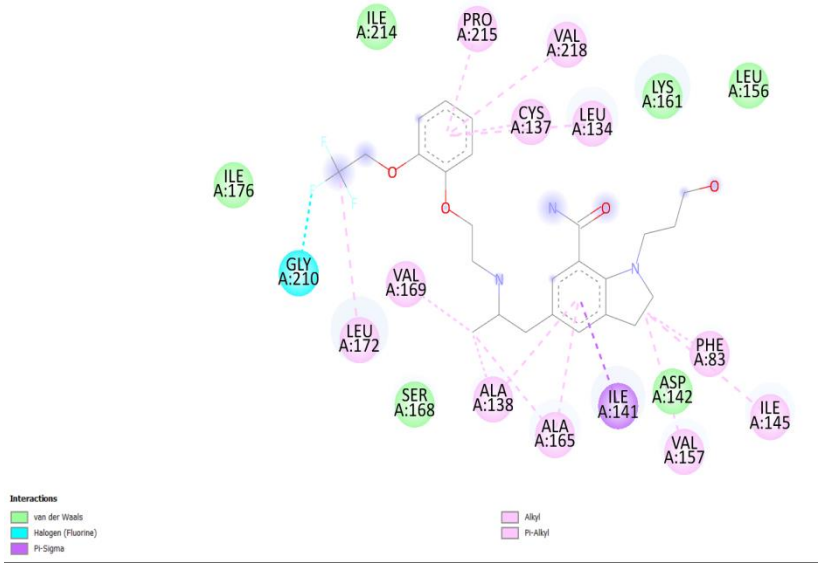
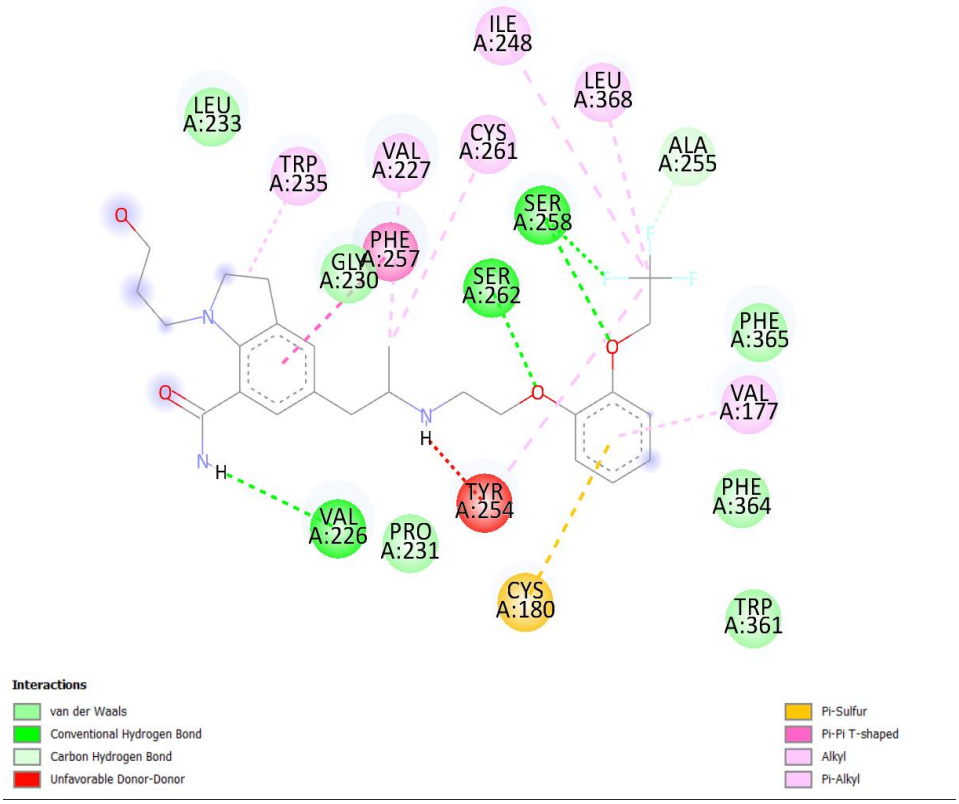
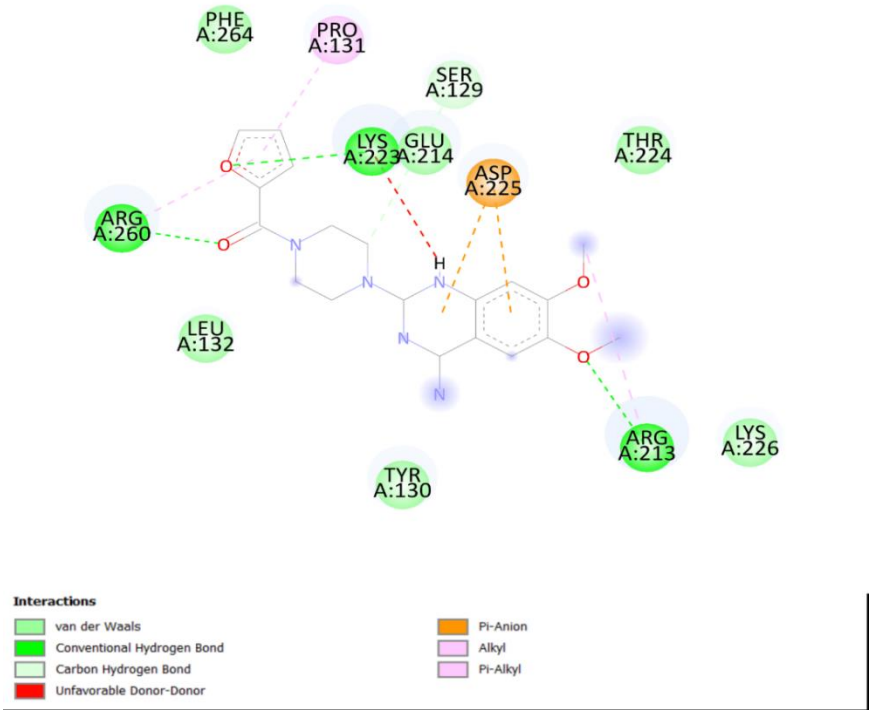


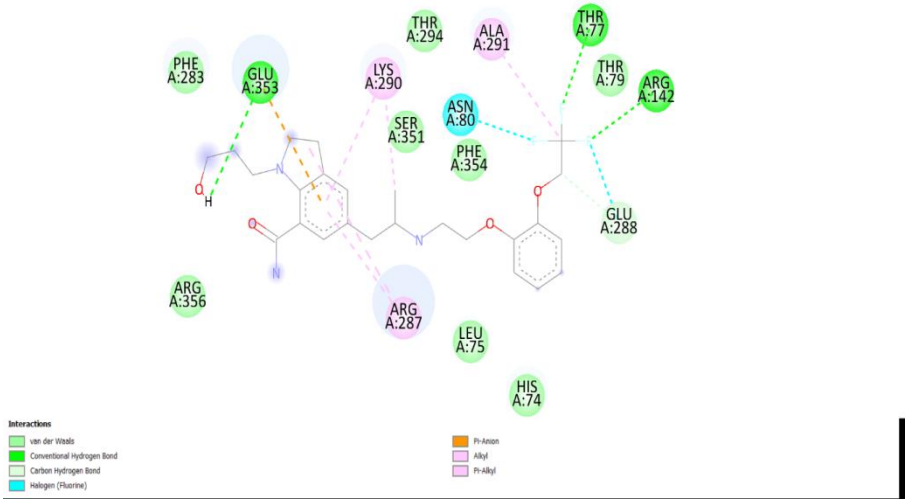
1.p ABAR (human)+ Silodosin [AlphaFold identifier of ABAR: AF-P35368-F1, SwissProt Accession No.: P35368]



1.q ADAR (human)+ Silodosin [AlphaFold identifier of ADAR: AF-P25100-F1, SwissProt Accession No.: P25100]



1.r AAAR (Mouse)+ Silodosin[AlphaFold identifier of AAAR: AF-P97718-F1, SwissProt Accession No.: P97718]



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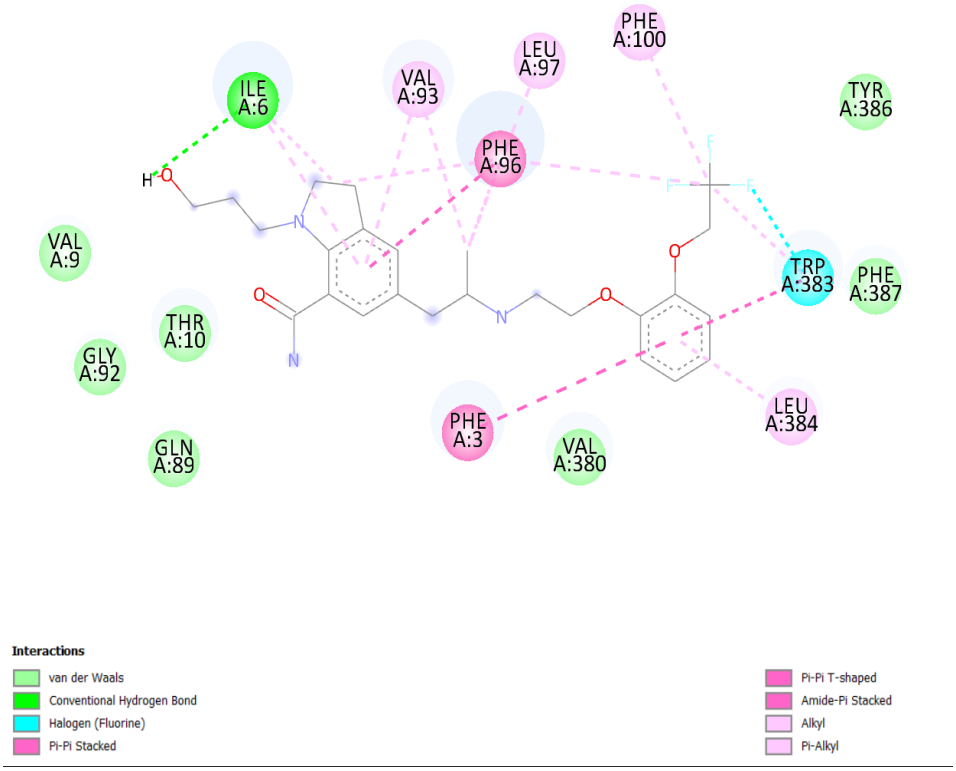
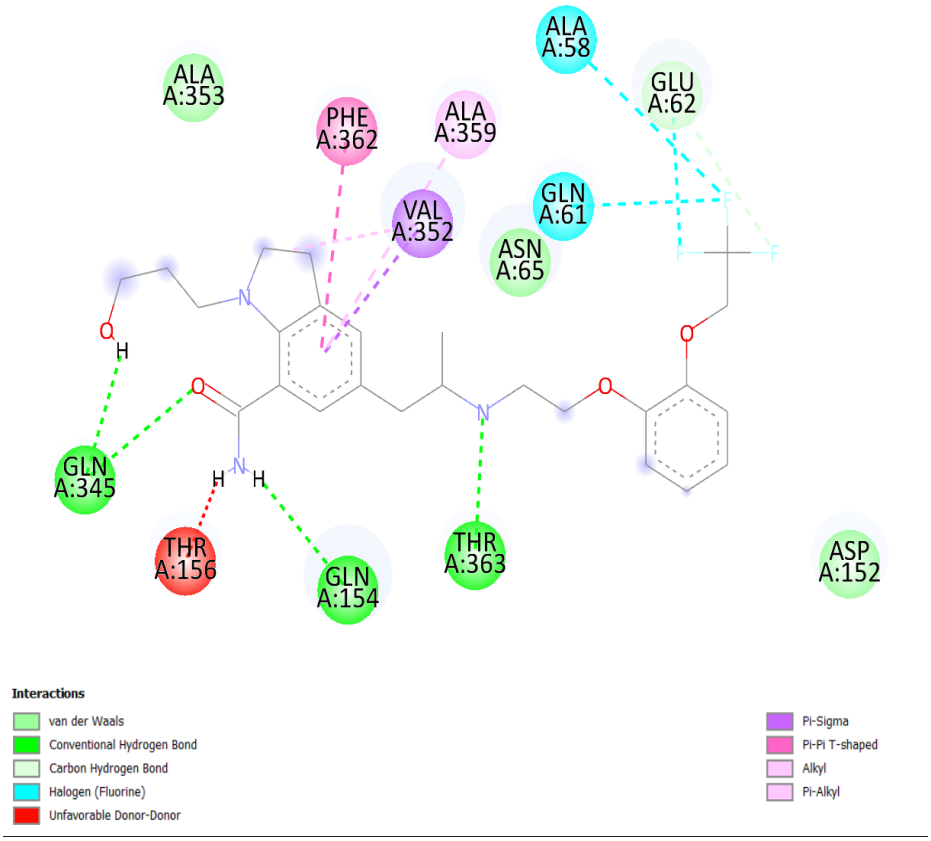
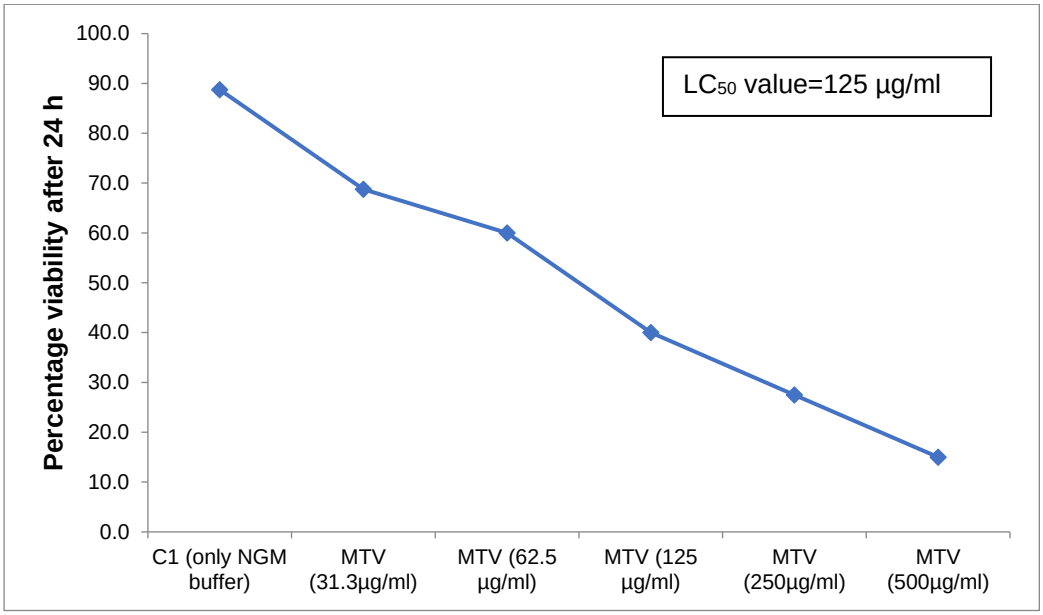


1.t ADAR (Mouse)+ Silodosin [AlphaFold identifier of ADAR: AF-P97714-F1, SwissProt Accession No.: P97714]

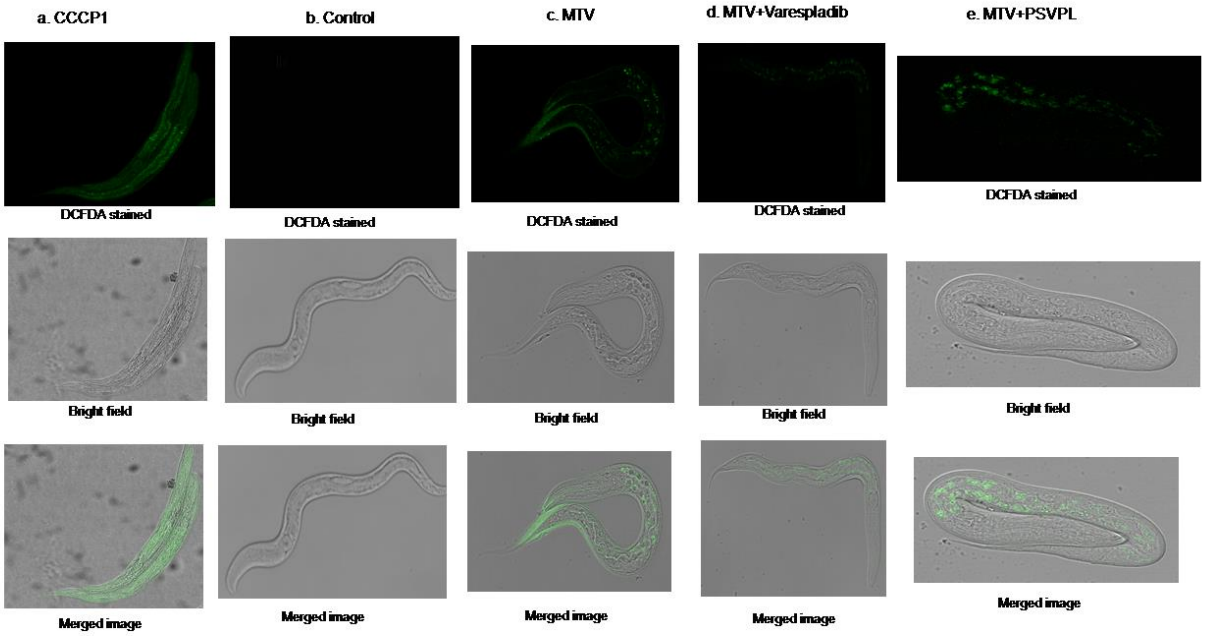


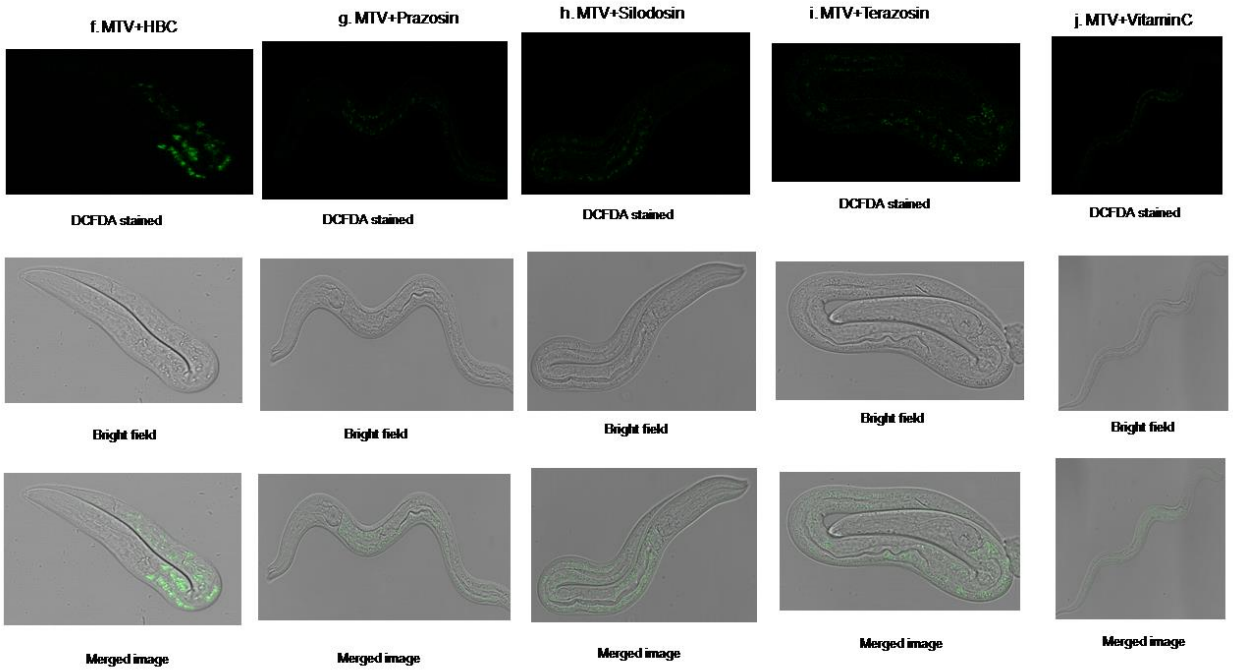
1.u SER6 receptor (*C. elegans*)+ Silodosin [AlphaFold identifier: AF-Q8MXS7-F1, SwissProt Accession No.: Q8MXS7]

Supplementary Figure S1. a–u.Homology modelled structures of the following proteins taken from SwissProt [Structure through AlphaFold]. Protein-ligand interactions of α1-adrenoreceptor antagonist (AAA) with α1-adrenergic receptor.

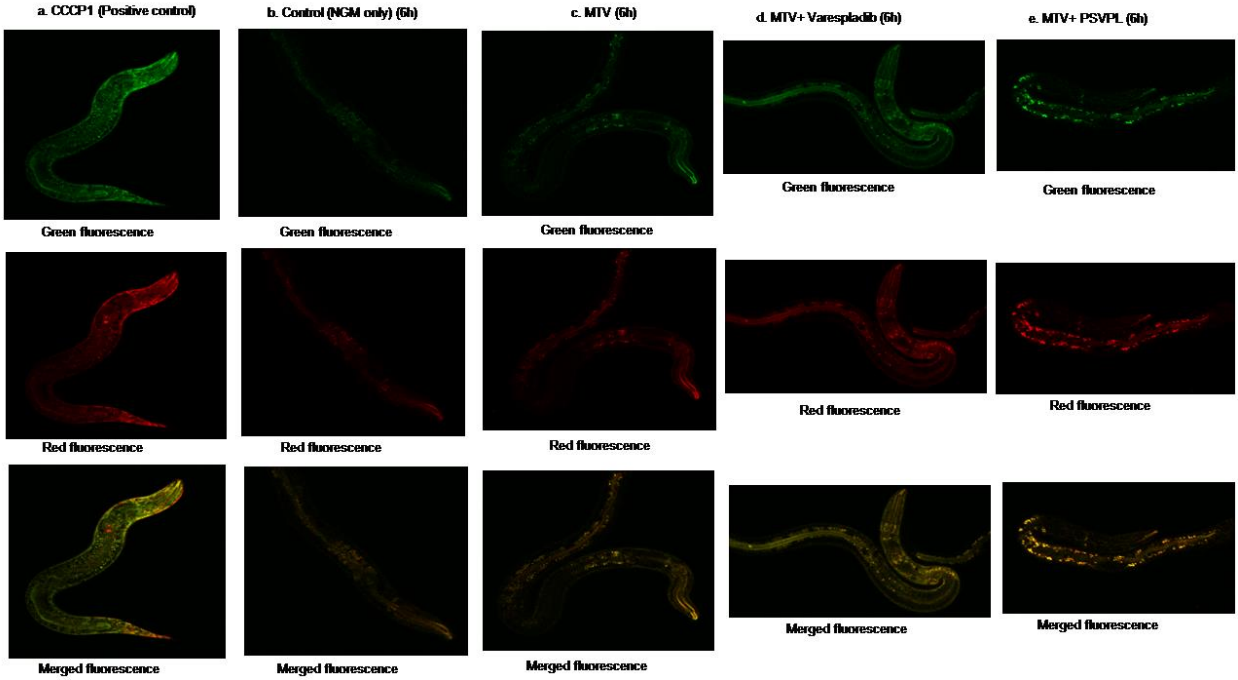


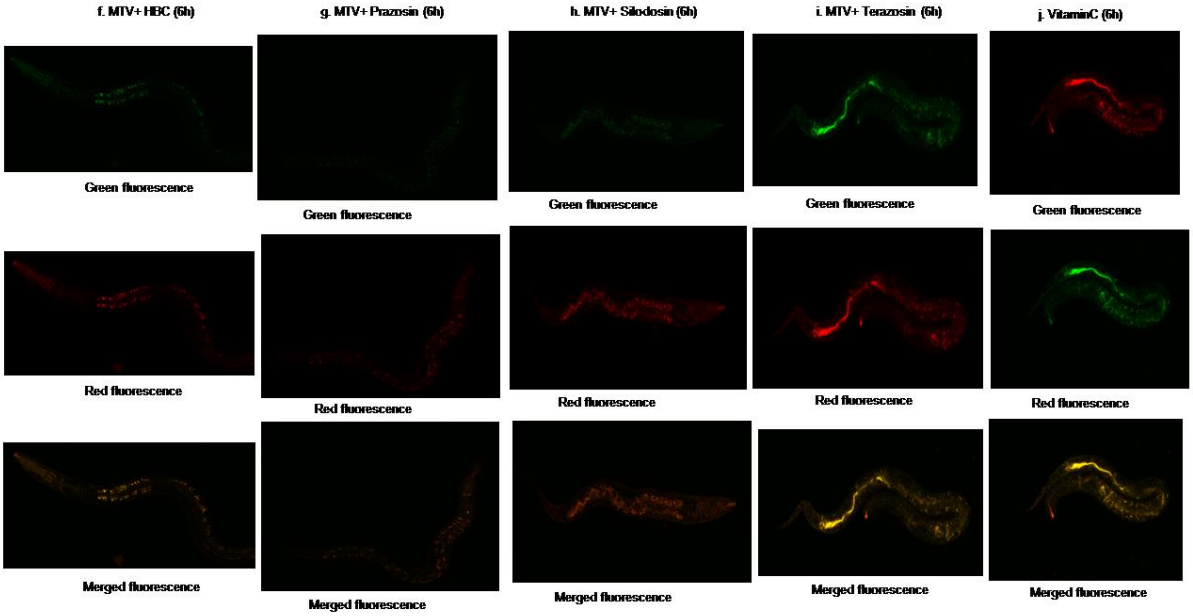
Supplementary Figure S2. The LC_{50} value of *C. elegans* N_2 calculated after 24 h treatment of *M. tamulus* venom (MTV). The LC_{50} value calculated for MTV towards *C. elegans*, after 24 h incubation, was 125 µg/ml.

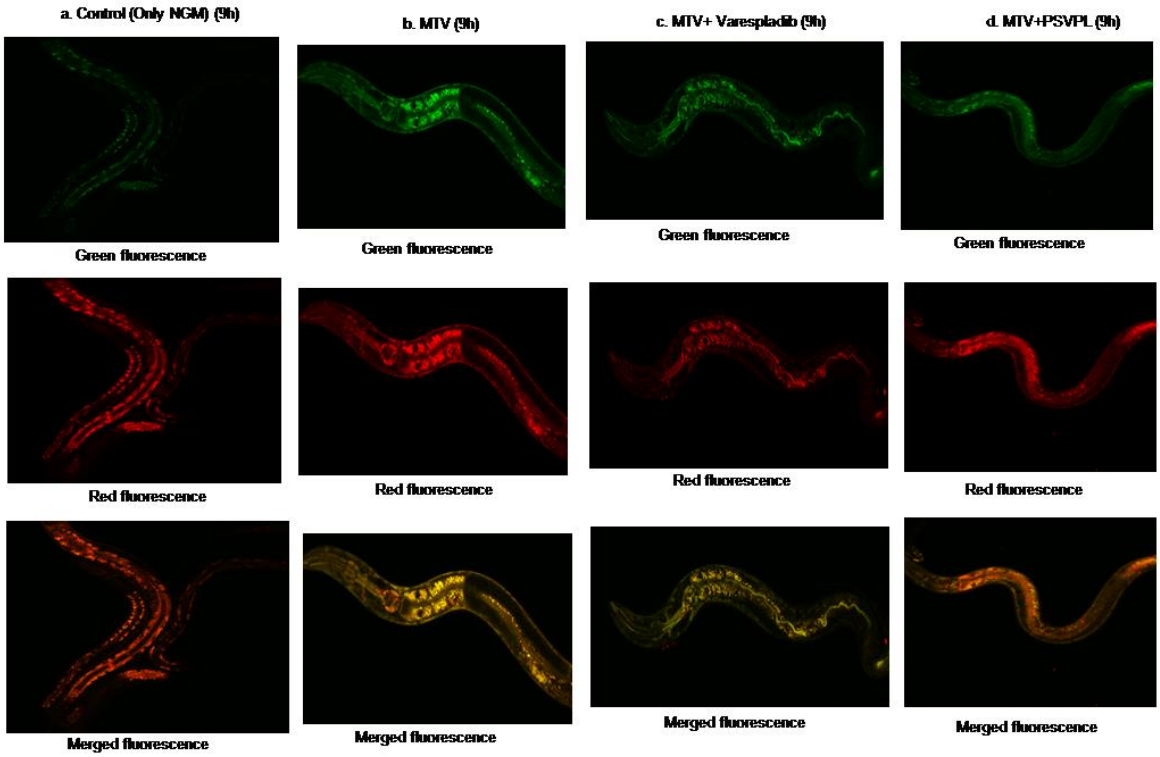


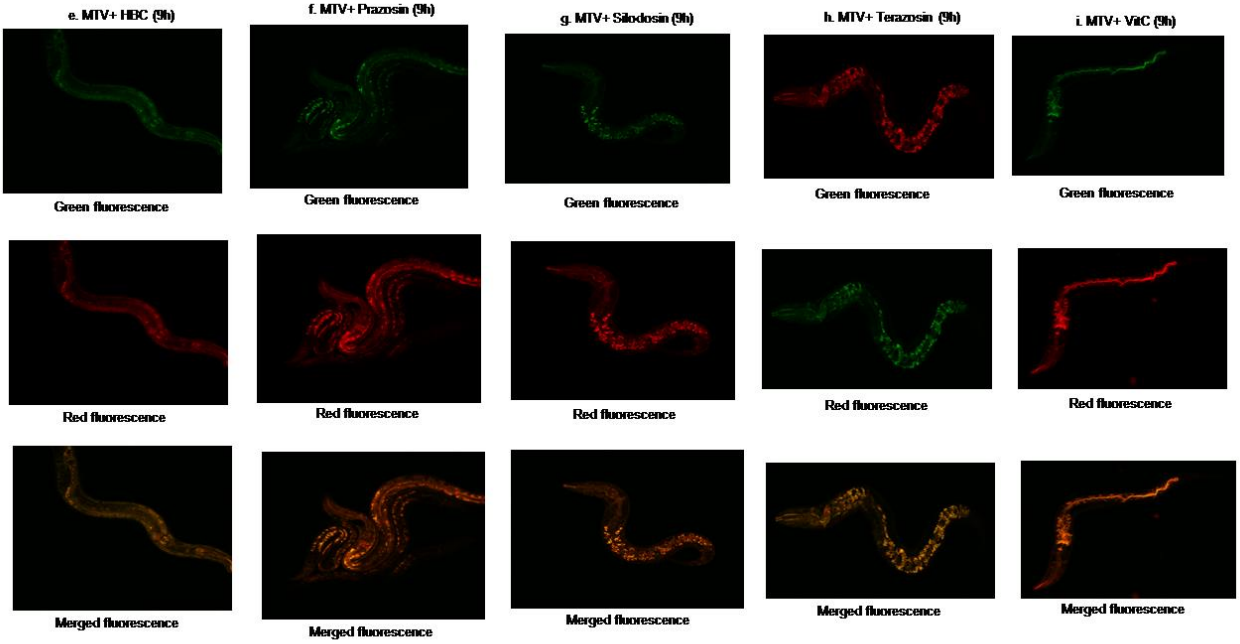


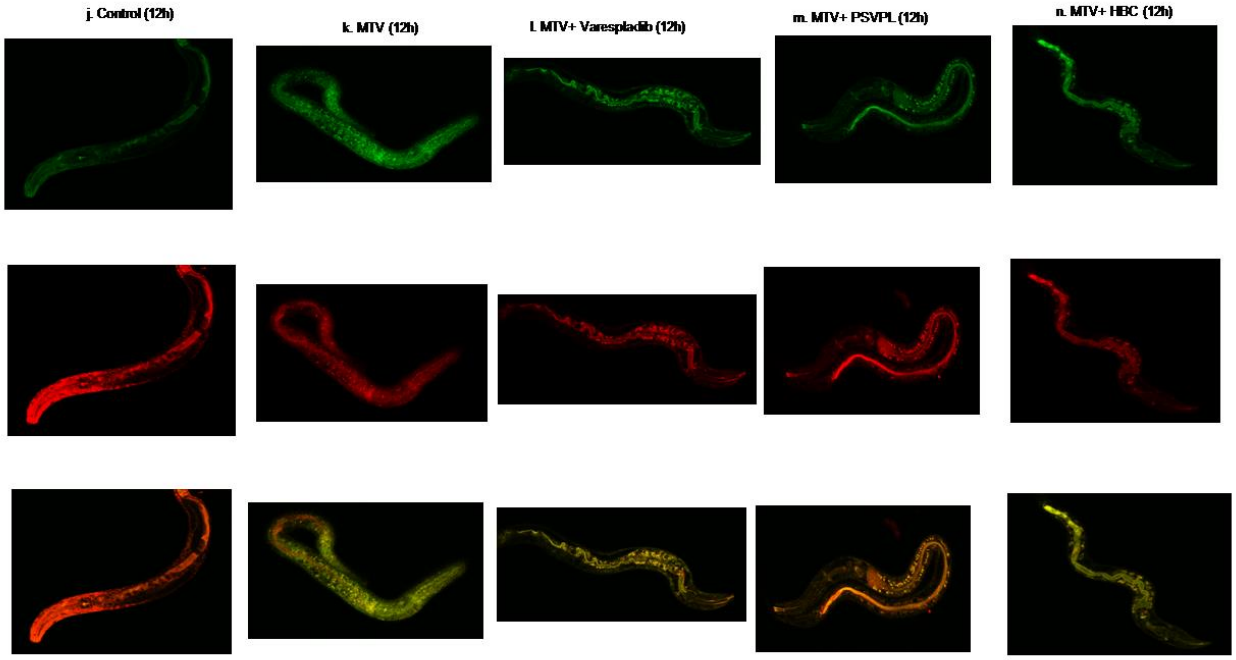
Supplementary Figure S3. Fluorescence image of confocal microscopy of *M. tamulus* venom induced ROS generation in *C. elegans* after 6h of *M. tamulus* venom (LC_{50} concentration) treatment and its neutralization by Prazosin, Silodosin and Terazosin. ROS level in positive control (CCCP1) *C. elegans* was considered as baseline (100%) and other values were compared with that.

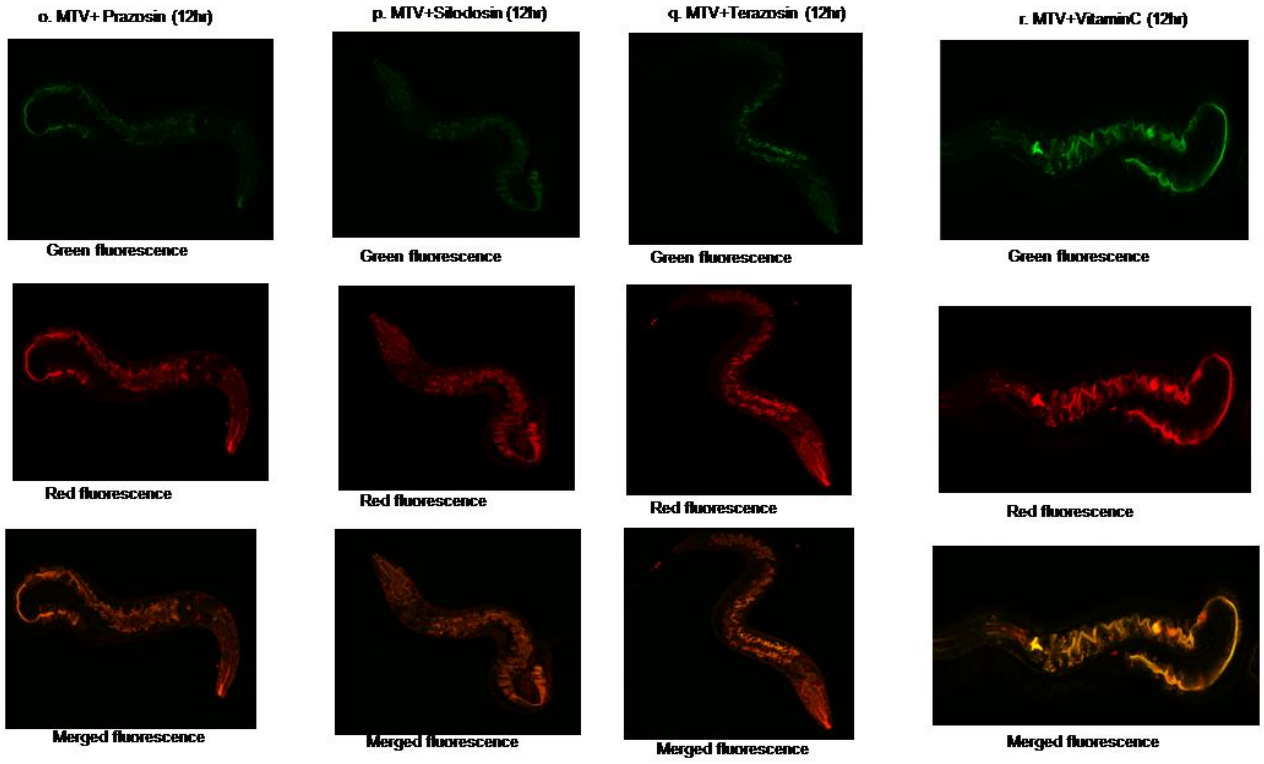



f. MTV+ HBC (6h)
g. MTV+ Prazosin (6h)
h. MTV+ Silodosin (6h)
i. MTV+ Terazosin (6h)
j. VitaminC (6h)
Green fluorescence
Green fluorescence
Green fluorescence
Green fluorescence
Green fluorescence
Red fluorescence
Red fluorescence
Red fluorescence
Red fluorescence
Red fluorescence
Merged fluorescence
Merged fluorescence
Merged fluorescence
Merged fluorescence
Merged fluorescence


a. Control (Only NGM) (9h)
b. MTV (9h)
c. MTV+ Varespladib (9h)
d. MTV+PSVPL (9h)
Green fluorescence
Green fluorescence
Green fluorescence
Green fluorescence
Red fluorescence
Red fluorescence
Red fluorescence
Red fluorescence
Merged fluorescence
Merged fluorescence
Merged fluorescence
Merged fluorescence

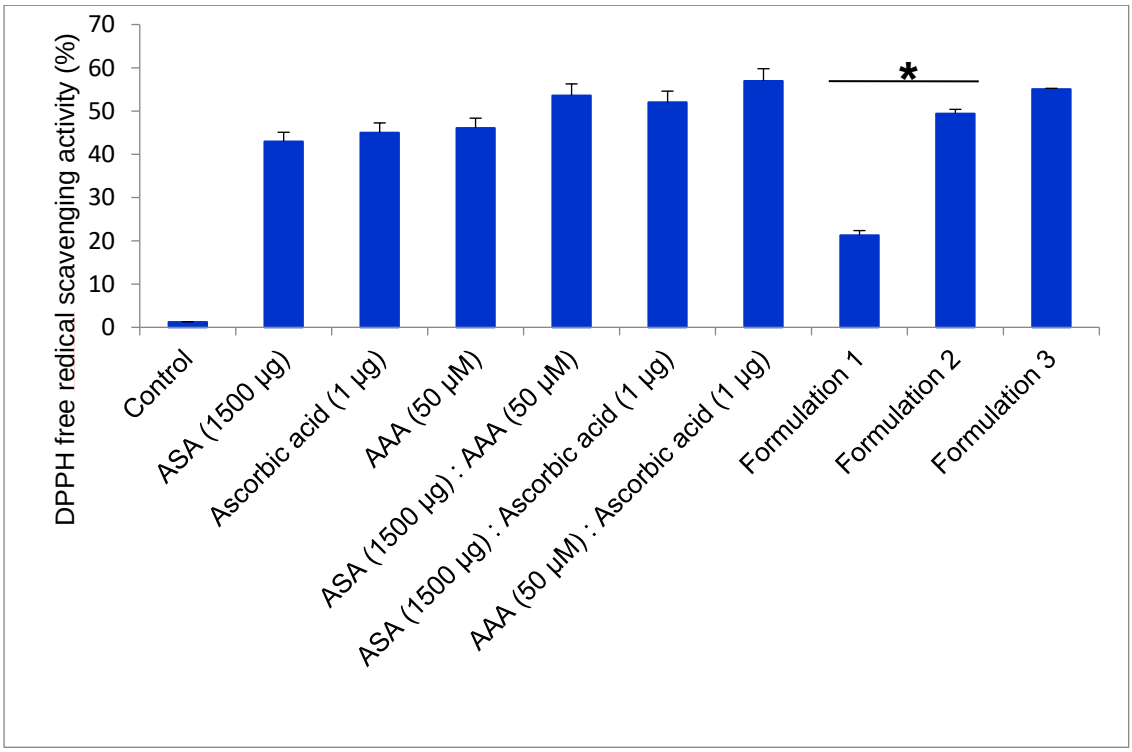

e. MTV+ HBC (9h)
f. MTV+ Prazosin (9h)
g. MTV+ Silodosin (9h)
h. MTV+ Terazosin (9h)
i. MTV+ VitC (9h)
Green fluorescence
Green fluorescence
Green fluorescence
Green fluorescence
Green fluorescence
Red fluorescence
Red fluorescence
Red fluorescence
Red fluorescence
Red fluorescence
Merged fluorescence
Merged fluorescence
Merged fluorescence
Merged fluorescence
Merged fluorescence


j. Control (12h)
k. MTV (12h)
l. MTV+ Varespladib (12h)
m. MTV+ PSVPL (12h)
n. MTV+ HBC (12h)

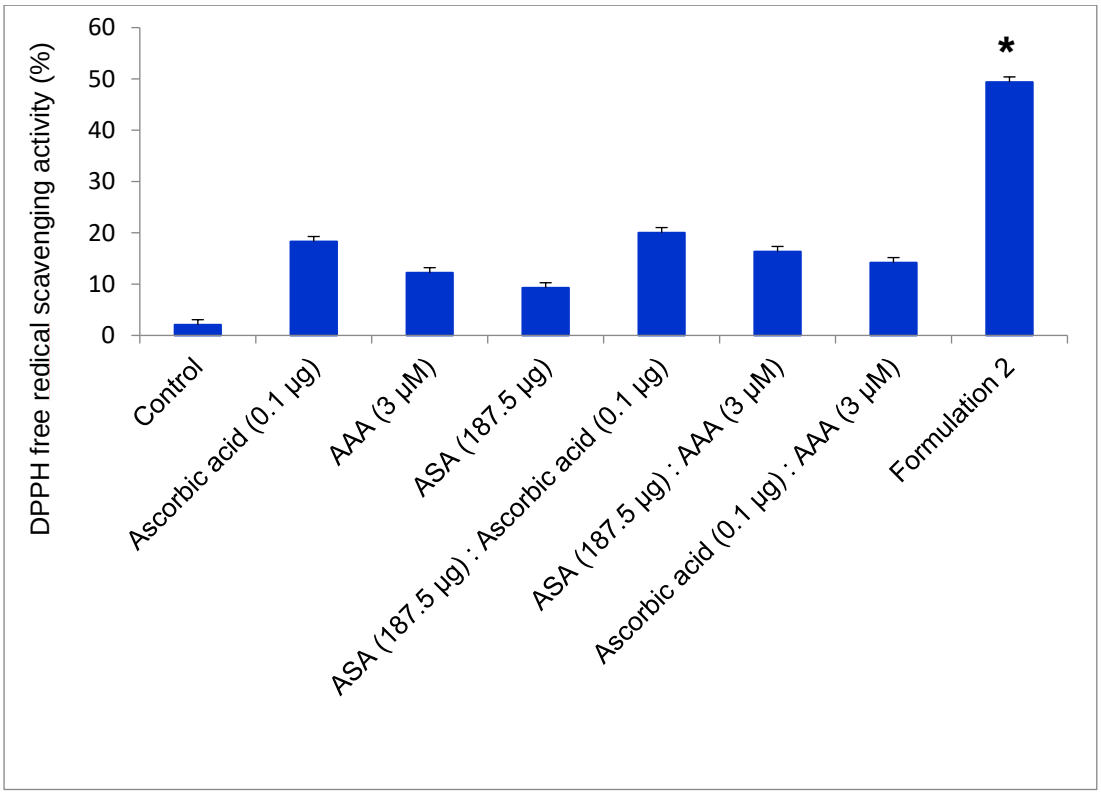


Supplementary Figure S4. Fluorescence image of confocal microscopy of MTV-induced alteration of mitochondrial membrane potential and its neutralization by Prazosin, Silodosin and Terazosin. ROS level in positive control (CCCP1) *C. elegans* was considered as baseline (100%) and other values were compared with that.

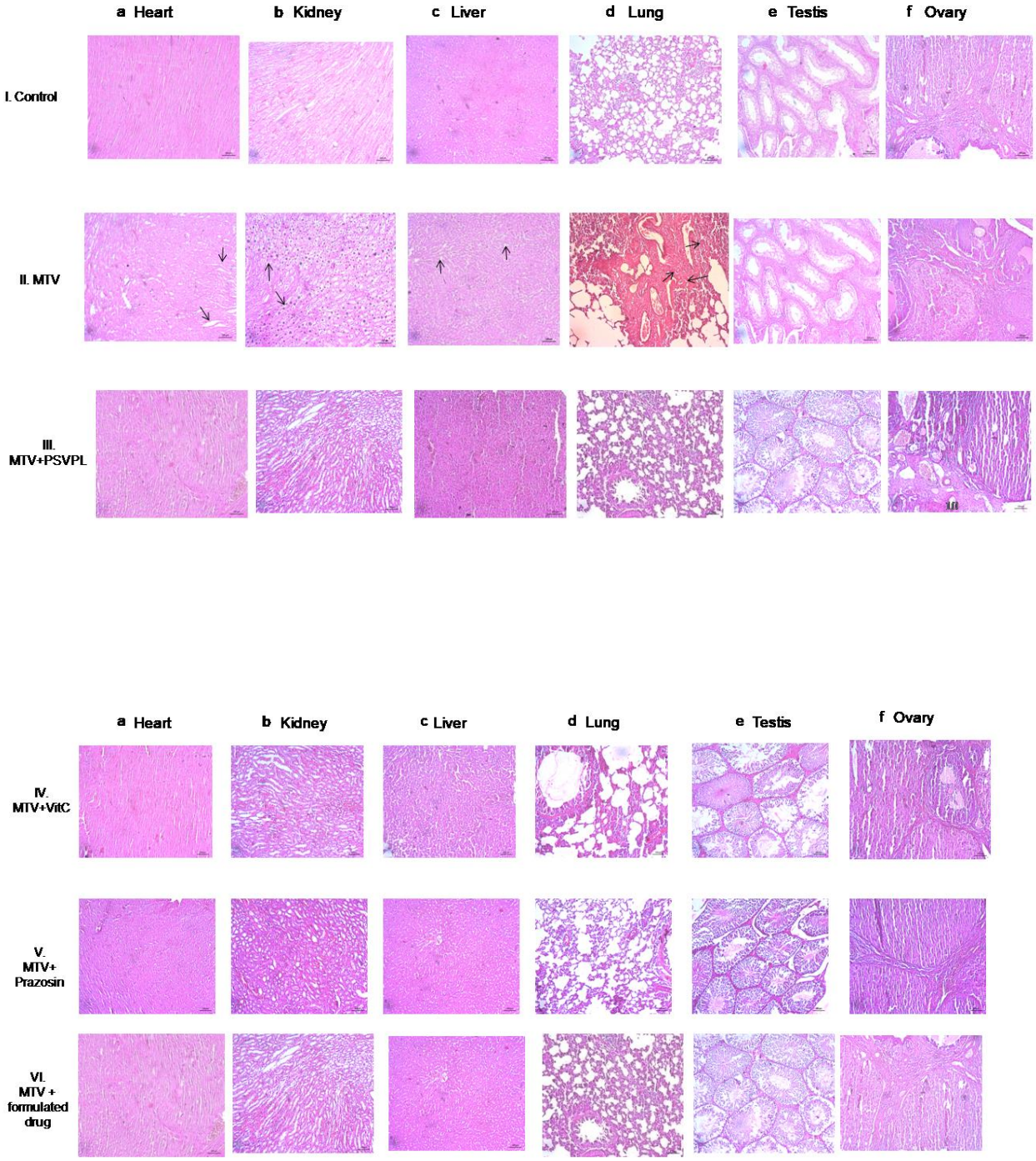
a



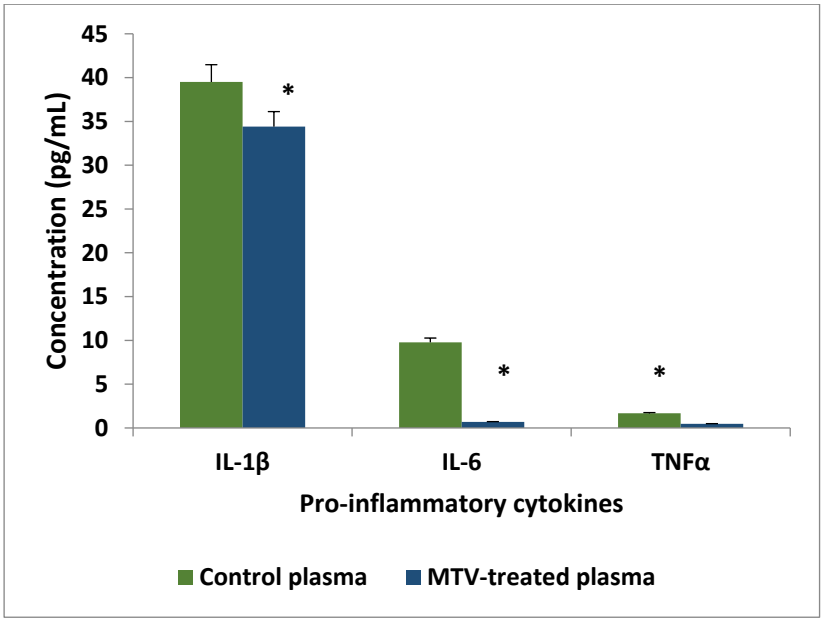
b



Supplementary Figure S5. shows the DPPH free radical-scavenging activity of **(a)** the optimum dose of individual formulation components, their combinations, and different concentrations of formulations, **(b)** Individual components of the formulation and their combinations compared with formulation 2. Data represent mean ± SD of three determinations. Significance of difference, *$p \leq 0.05$ as compared to formulation 2. There was no significant difference ($p > 0.05$) between formulations 2 and 3.



Supplementary Figure S6. Histopathological analysis of the *M. tamulus* venom-induced Wistar rat tissues and their neutralisation by formulation 2. Light microscopic observation of (a) Heart, (b) Kidney, (c) Liver, (d) Lung, (e) Testis and (f) Ovary from control and treated groups, Bar-100µM. The black arrow indicates the morphological changes observed in MTV-induced rat tissue compared to the control.



Supplementary Figure S7. Circulating levels of pro-inflammatory cytokines in the Swiss albino mice with and without *M. tamulus* envenomation, MTV-treated plasma and control plasma, respectively. Significance of difference, *$p \leq 0.05$ as compared to control