Electronic Supplementary Material (ESI) for RSC Advances.

Supplementary Table 1: Lipinski rule of 5 for predicting drug likeness properties of used nutraceuticals

Name of Agents	PubChem CID	Mass (g/mol)	H-Bond Donor	H-Bond Acceptor	cLogP	Molar Refractivity
DEC	3052	199.29	0	4	0.6956	57.386
Albandazole	2082	263.33	2	4	3.24	73.13
B-Carotene	5280489	536.9	0	0	12.605	181.39
Lycopene	4469	536.9	0	0	12.93	185.57
Ascorbic Acid	54670067	176	4	6	1.707	35.256
Naringin	442428	580.5	8	14	1.16	134.14
Zerumbone	5470187	218.339	0	1	4.21	69.29
Emodin	3220	270.24	3	5	1.88	69.48
Cirtic Acid	311	192.12	4	7	-1.24	37.09

Supplementary Table 2. Properties of selected nutraceutical components used in the docking analysis.

Parameters	Name of Drug/ Agent								
Absorption	DEC	Albandazole	β-Carotene	Lycopene	Ascorbic acid	Naringin	Zerumbone	Emodin	Citric Acid
Blood-Brain Barrier	BBB+	BBB+	BBB+	BBB+	BBB+	BBB-	BBB+	BBB+	BBB+
Human Intestinal Absorption	HIA+	HIA+	HIA+	HIA+	HIA+	HIA+	HIA+	HIA+	HIA+
Caco-2 Permeability	Caco2+	Caco2+	Caco2+	Caco2+	Caco2-	Caco2-	Caco2+	Caco2+	Caco2-
P-glycoprotein Substrate	Substrate Non Inhibitor	Substrate Non Inhibitor	Non-Substrate Inhibitor	Non Substrate Non Inhibitor	Non-Substrate Non Inhibitor	Substrate Non Inhibitor	Substrate Non Inhibitor	Substrate Non Inhibitor	Non-Substrate Non Inhibitor
hERG	Weak Inhibitor	Weak Inhibitor	Weak Inhibitor	Weak Inhibitor	Weak Inhibitor	Weak Inhibitor	Weak Inhibitor	Weak Inhibitor	Weak Inhibitor
AMES Toxicity	Non-AMES Toxic	Non-AMES Toxic	Non-AMES Toxic	Non-AMES Toxic	Non-AMES Toxic	AMES Toxic	Non-AMES Toxic	AMES Toxic	Non-AMES Toxic
Carcinogens	Non-Carcinogens	Non-Carcinogens	Non-Carcinogens	Non-Carcinogens	Non-Carcinogens	Non-Carcinogens	Non-Carcinogens	Non-Carcinogens	Non-Carcinogens
Acute Oral Toxicity	III	III	III	III	IV	III	III	III	III
Rat Acute Toxicity	2.2639 LD50, mol/Kg	2.075 LD50, mol/Kg	1.598 LD50, mol/Kg	1.5357 LD50, mol/Kg	1.3059 LD50, mol/Kg	2.2619 LD50, mol/Kg	1.8726 LD50, mol/Kg	2.5826 LD50, mol/Kg	1.778 LD50, mol/Kg

Supplementary Table 3: ENOLASE Docked complex showing interacting receptor residue, interacting residue common in active site and ligand and protein complex involved in H-bonding.

Receptor	**Drug Name** (PubChem CID)	**Interacting receptor residue**	**Interacting residue in active site**	**Ligand and Protein atom involved in H-bonding**
Enolase	DEC	GLY^{105}, ALA^{106}, SER^{107}, HIS^{225}, GLN^{233}, $GLU^{234,}$ GLU^{277}, GLU^{317}, ASP^{386} ASP^{387}, LYS^{411}, HIS^{439}, ARG^{440}, SER^{441}, LYS^{462}	NA	LYS^{411}:HZ2 - LIGAND:O1
	Albendazole	THR^{376}, VAL^{400}, LYS^{403}, CYS^{405}, ASN^{406}, ASN^{431}, GLY^{432}, TRP^{433}, ARG^{497}, LYS^{498}	ACTIVE SITE 1	LIGAND:H20 – GLY^{432}:O
	β- Carotene	THR^{246}, MET_{249}, LYS^{250}, SER^{253}, GLU^{254}, HIS^{257}, HIS^{258}, ASN^{261}, LEU^{479}, GLU^{482}, GLU^{483}, GLY^{486}	ACTIVE SITE 1	NA
	Lycopene	LYS^{229}, LYS^{266}, GLN^{285}, SER^{286}, LYS^{288}, GLU^{289}, ASN^{292}, SER^{295}, ASP^{296}, ILE^{298}, ALA^{299}, THR^{304}, ASP^{327}, ASN^{330}, LYS^{332}, SER^{333}, ASP^{334}	NA	NA
	Ascorbic acid	GLY^{105}, ALA^{106}, ASN^{218}, HIS^{225}, GLN^{233}, GLU^{234}, GLU^{277}, ASP^{312}, LYS^{411}, HIS^{439}, ARG^{440}, SER^{441}, LYS^{462}, ARG^{471}	ACTIVE SITE 2	GLN^{233}:HE22 – LIGAND:O3 LYS^{411}:HZ1 – LIGAND:O2 HIS^{439}:HE2 – LIGAND:O5 ARG^{440}:HE – LIGAND:O4 SER^{441}:H – LIGAND :O4 LIGAND:H18 – GLU^{234}:OE2
	Zerumbone	LYS^{229}, LEU^{230}, ALA^{231}, GLN^{285}, SER^{286}, ASN^{287}, LYS^{288}, LEU^{326}, ASP^{327}, ASP^{334}, GLN^{337}, LEU^{339}, LEU^{347}, PHE^{351}	ACTIVE SITE 2	NA
	Naringin	ASP^{80}, ARG^{82}, ASN^{84}, SER^{104}, GLY^{105}, ALA^{106}, SER^{107}, THR^{108}, GLY^{109}, VAL^{110}, GLU^{112}, ALA^{113}, LEU^{114} GLU^{115}, ARG^{117}, ASN^{119}, LYS^{127}, GLY^{442}	ACTIVE SITE 2	ARG^{82}:HH22 – LIGAND:O6 THR^{108}:H – LIGAND:O8 LIGAND:60 – SER^{107}:OG LIGAND:H73 – GLU^{112}:O
	Emodin	GLY^{105}, SER^{107}, THR^{108}, GLY^{109}, VAL^{110}, GLU^{112} ALA^{113}, LEU^{114}, GLU^{115}, ARG^{117}, ASN^{119}, LYS^{127}, ARG^{440}	ACTIVE SITE 2	NA
	Citric acid	GLY^{105}, ALA^{106}, SER^{107}, HIS225, GLN^{233}, GLN^{234}, GLU^{277}, $ASP^{312,}$ ASP^{361}, ASP^{386}, LYS^{411}, SER^{438}, HIS^{439}, ARG^{440}, SER^{441}	ACTIVE SITE 2	ALA^{106}:N – LIGAND:O5 LYS^{411}:NZ – LIGAND:O2 LIGAND:H19 – HIS^{439}:O LIGAND:H20 – ASP^{312}:OD2

Supplementary Table 4: ES-62 precursor showing interacting receptor residue, interacting residue common in active site and ligand and protein complex involved in H-bonding.

Receptor	**Drug Name** (PubChem CID)	**Interacting receptor residue**	**Interacting residue in active site**	**Ligand and Protein atom involved in H-bonding**
ES62 Precursor	DEC	LEU^{175}, ARG^{178}, ARG^{179}, THR^{209}, GLY^{210}, ALA^{211}, GLU^{328}, GLU^{329}, GLY331, TYR^{332}, GLN^{477} ASN^{479}, LYS^{481}	ACTIVE SITE 1 and ACTIVE SITE 3	GLY^{331}:H – LIGAND:O1
	Albendazole	LEU^{175}, ARG^{178}, ARG^{179}, THR^{209}, GLU^{328}, GLU^{329}, GLY^{331}, TYR^{332}, HIS^{433}, HIS^{434}, GLN^{477}, ASN^{479}, LYS^{481}	ACTIVE SITE 1	ARG^{178}:HH12 – LIGAND:O4 HIS^{433}:HE2 – LIGAND:O2
	β carotene	PRO^{104}, ASN^{105}, PRO^{107}, HIS^{108}, TRP^{109}, GLY^{132}, GLY^{133}, GLU^{212}, THR^{215}, TYR^{249}, GLN^{330}, HIS^{337}, ILE^{340}, THR^{341}, LYS343	ACTIVE SITE 1	NA
	Lycopene	TYR^{147}, ASP^{148}, ALA^{165}, GLN^{166}, THR^{167}, ALA^{169} GLY^{170}, LEU^{173}, TYR^{177}, GLU^{230}, TYR^{233}, ARG^{234}, GLY^{236}, LEU^{367}	ACTIVE SITE 2	NA
	Ascorbic acid	LEU^{175}, ARG^{178}, ARG^{179}, GLY^{208}, THR^{209}, TRP^{281}, GLU^{328}, GLU^{329}, TYR^{332}, HIS^{433}, HIS^{434}, ASN^{479}, LYS^{481}	ACTIVE SITE 1	ARG^{178}:HH12 – LIGAND:O5 ARG^{178}:HH22 – LIGAND:O3 TYR^{332}:HH – LIGAND:O4 HIS^{433}:HE2 – LIGAND:O5 LIGAND:H17 – GLU^{328}:OE1 LIGAND:H18 – GLU^{329}:OE2 LIGAND:H19 – ASN^{479}:OD1
	Zerumbone	PRO^{107}, HIS^{108}, TRP^{109}, GLY^{132}, GLY^{133}, THR^{215}, TYR^{249}, GLN^{330}	ACTIVE SITE 3	NA
	Naringin	LEU^{175}, ARG^{179}, LYS^{182}, THR^{209}, GLY^{210}, ALA^{211}, GLU^{212}, GLU^{328}, GLU^{329}, GLN^{330}, GLY^{331}, TYR^{332}, THR^{408}, LYS^{412}, PRO^{475}, GLN^{476}, GLN^{477}, ASN^{479}, LYS^{481}	ACTIVE SITE 2	GLY^{331}:H – LIGAND:O5 LIGAND:H60 – GLU^{328}:OE1 LIGAND:H62 – GLY^{210}:O
	Emodin	LEU^{175}, ARG^{179}, LYS^{182}, THR^{209}, GLY^{210}, ALA^{211}, GLU^{212}, GLU^{328} GLU^{329}, GLN^{330}, GLY^{331}, TYR^{332}, THR^{408}, LYS^{412}, PRO^{475}, GLN^{476}, GLN^{477}, ASN^{479}, LYS^{481}	ACTIVE SITE 1	ARG^{178}:HH11 – LIGAND:O3 GLY^{331}:H – LIGAND:O4
	Citric acid	TYR^{171}, TYR^{172}, THR^{174}, LEU^{175}, ARG^{178}, TYR^{429},	ACTIVE SITE 1	THR^{174}:OG1 – LIGAND:O4 THR^{174}:OG1 – LIGAND:O6

		HIS^{433}, ASN^{479}, LYS^{481}		ARG^{178}:NH1 – LIGAND:O7 TYR^{429}:OH – LIGAND:O2 LIGAND:H20 – THR^{174}:OG1

Supplementary Table 5: Serpin showing interacting receptor residue, interacting residue common in active site and ligand and protein complex involved in H-bonding

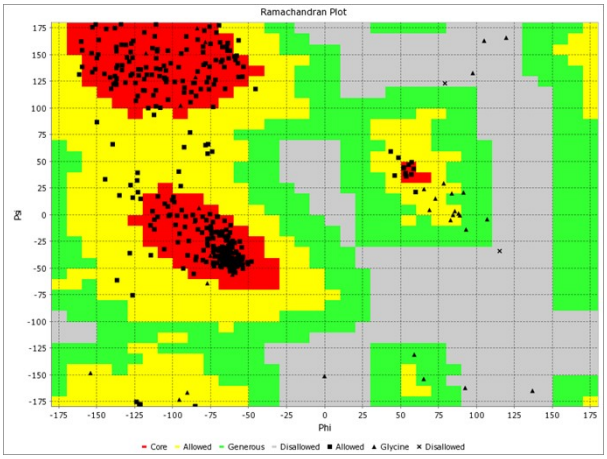
Receptor	**Drug Name** (PubChem CID)	**Interacting receptor residue**	**Interacting residue in active site**	**Ligand and Protein atom involved in H-bonding**
Serpin	DEC	ILE^{43,} GLN^{45}, LYS^{48}, SER^{49}, VAL^{50}, VAL^{51}, GLY^{295}, LYS^{296}, MET^{297}, ASP^{298}, GLU^{301}, THR^{302}, LYS^{305}	ACTIVE SITE 2	NA
	Albendazole	THR^{196}, GLN^{197}, ASP^{199}, ASN^{202}, LEU^{223}, GLN^{224}, SER^{225}, GLU^{226}, PHE^{227}, LEU^{240}, PRO^{241}, TYR^{242}, ILE^{243}, GLY^{244}, GLU^{245}	ACTIVE SITE 1	GLN^{224}:H – LIGAND:O2
	β carotene	PRO^{27}, TYR^{30}, ALA^{31}, ASN^{34}, ILE^{35}, ILE^{78}, PHE^{79}, GLY^{81}, GLY^{82}, ARG^{270}, LEU^{273}, SER^{274}, SER^{277}, ILE^{306}, GLY^{307}, LYS^{379}	ACTIVE SITE 1	NA
	Lycopene	GLY^{121}, PHE^{122}, SER^{123}, SER^{144}, GLU^{146}, GLN^{147}, SER^{148}, GLN^{149}, GLN^{150}, GLN^{153}, THR^{322}, ASN^{323}	NA	NA
	Ascorbic acid	LEU^{97}, ASP^{101}, ASN^{111}, ILE^{112}, ALA^{113}, ASN^{114}, ARG^{115}, GLY^{137} GLU^{138}, THR^{139}, LYS^{162}	ACTIVE SITE 1	ALA^{113}:H - LIGAND:O5 ARG^{115}:HE – LIGAND:O6 LIGAND:H17 – ASP^{101}:OD1 LIGAND:H17 – ASP^{101}:OD2 LIGAND:H19 – ASN^{111}:OD1 LIGAND:H20 – THR^{139}:OG1
	Zerumbone	TYR^{117}, HIS^{141}, SER^{142}, PHE^{143}, GLU^{154}, ASN^{157}, TRP^{158}, GLN^{161}	NA	NA
	Naringin	PHE^{12}, SER^{15}, ILE^{16}, VAL^{19}, ILE^{25}, HIS^{92}, LYS^{95}, LEU^{96}, VAL^{99}, ARG^{103}, GLY^{244}, GLU^{245}, GLU^{246}, GLN^{376}, ASN^{377}, LEU^{378}	ACTIVE SITE 1	ARG^{103}:HH12 – LIGAND:O1 ARG^{103}:HH12 – LIGAND:O4 ARG^{103}:HH22 – LIGAND:O4 ASN^{377}:HD22 – LIGAND:O7 LIGAND:H73 – HIS^{92}:O
	Emodin	ILE^{25}, LYS^{95}, LEU^{96}, VAL^{99}, ILE^{100}, ARG^{103}, GLU^{246}, VAL^{247}, GLN^{376}, ASN^{377}, LEU^{378}	ACTIVE SITE 1	ARG^{103}:HH22 – LIGAND:O2
	Citric acid	LEU^{96}, VAL^{99}, ILE^{100}, ARG^{103}, LEU^{110}, GLU2^{45},	ACTIVE SITE 3	LIGAND:H19 –GLU^{246}:O

		GLU^{246}, VAL^{247}, GLN^{276}, ASN^{277}, LUE2^{78}, THR^{380}		

Supplementary Table 6: Cystatin showing interacting receptor residue, interacting residue common in active site and ligand and protein complex involved in H-bonding

Receptor	Drug Name	Interacting receptor residue	Interacting residue in active site	Ligand and Protein atom involved in H-bonding
Cystatin	DEC	ILE^{5}, LEU^{8}, SER^{9}, LEU^{12}, SER^{15}, VAL^{70}, ALA^{71}, GLY^{72}, ILE^{73}, TRP^{114}, SER^{115}, ALA^{116}, GLN^{119}, THR^{121}, PHE^{122}, LYS^{123}	ACTIVE SITE 1	NA
	Albendazole	VAL^{10}, LEU^{11}, LEU^{12}, ILE^{13}, LYS^{16}, SER^{17}, PHE^{18}, ALA^{19}, ARG^{20}, GLU^{21}, ARG^{23}, LEU^{24}, ARG^{26}, GLN^{68}	NA	NA
	β carotene	LYS^{16}, ARG^{20}, GLU^{21}, ILE^{22}, TYR^{29}, ASP^{33}, GLU^{35}, ILE^{36}, THR^{67}, VAL^{69}, VAL^{70}, ALA^{71}, GLY^{72}, ILE^{73}, TYR^{75}, TRP^{118}	ACTIVE SITE 3	NA
	Lycopene	MET^{1}, PRO^{4}, LEU^{8}, GLN^{50}, THR^{51}, ARG^{52}, TYR^{53}, ARG^{54}, TYR^{57}, PRO^{105}, LYS^{107}, PHE^{109}, LYS^{123}, LEU^{126}, THR^{127}	ACTIVE SITE 1	NA
	Ascorbic acid	LEU^{11}, LEU^{12}, ILE^{13}, LYS^{16}, SER^{17}, PHE^{18}, ALA^{19}, ARG^{20}, GLU^{21}, ILE^{22}, ARG^{23}, LEU^{24}, VAL^{69}, VAL^{70}	NA	LEU^{24}:H - LIGAND:O6 LIGAND:H17 – SER^{17}:O LIGAND:H20 – ILE^{92}:O
	Zerumbone	ILE^{5}, LEU^{8}, SER^{9}, LEU^{12}, SER^{15}, LYS^{16}, VAL^{70} ALA^{71}, TRP^{114}, ALA^{116}, GLN^{119}, THR^{121}, LYS^{123}	ACTIVE SITE 1	NA
	Naringin	ILE^{5}, LEU^{8}, SER^{9}, LEU^{12}, SER^{15}, LYS^{16}, ARG^{20}, GLU^{21}, VAL^{70}, ALA^{71}, GLY^{72}, ILE^{73}, TRP^{114}, SER^{115}, ALA^{116}, GLN^{119}, THR^{121}, PHE^{122}, LYS^{123}	ACTIVE SITE 1	SER^{15}:HG – LIGAND:O12 ARG^{20}:HH21 – LIGAND:O5 LIGAND:H73 – TRP^{114}:O
	Emodin	LEU^{8}, SER^{9}, LEU^{12}, SER^{15}, LYS^{16}, VAL^{70}, ALA^{71}, GLY^{72}, ILE^{73}, LYS^{74}, TRP^{114}, SER^{115},	ACTIVE SITE 1	SER^{115}:H – LIGAND:O5 LIGAND:H30 – ILE^{73}:O

		ALA^{116}, GLN^{119}, THR^{121}		
	Citric acid	LEU^{11}, LEU^{12}, ILE^{13}, LYS^{16}, SER^{17}, PHE^{18}, ALA^{19}, GLU^{21}, ILE^{22}, ARG^{23}, LEU^{24}, VAL^{70}	ACTIVE SITE 1	LIGAND:H20 – SER^{17}:O LIGAND:H21 – GLU^{21}:OE1



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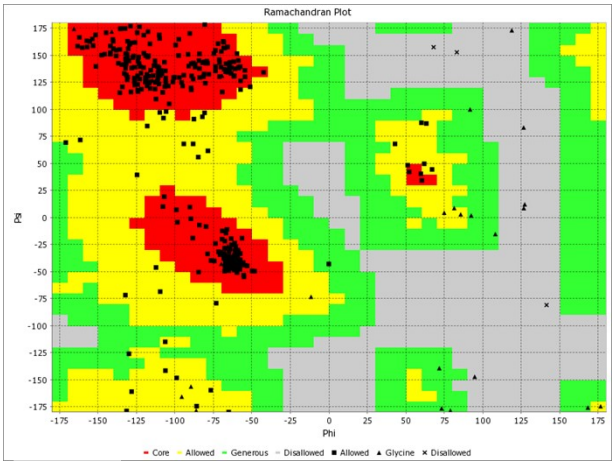

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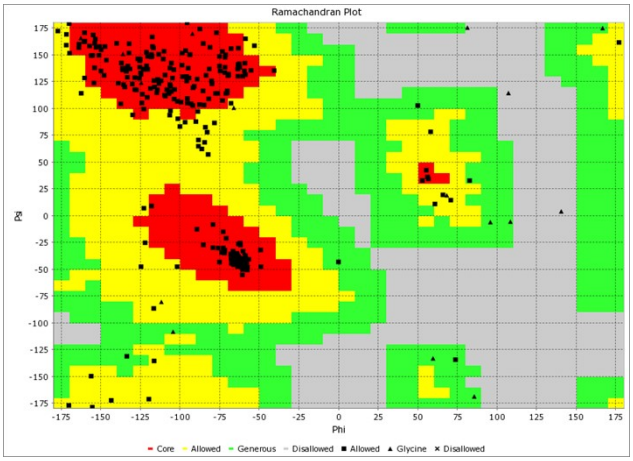

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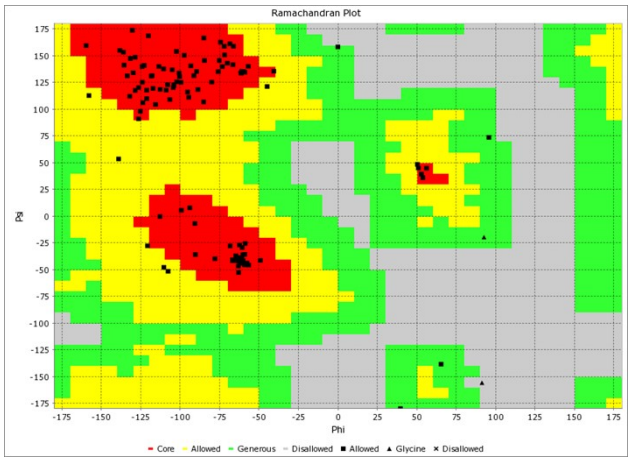
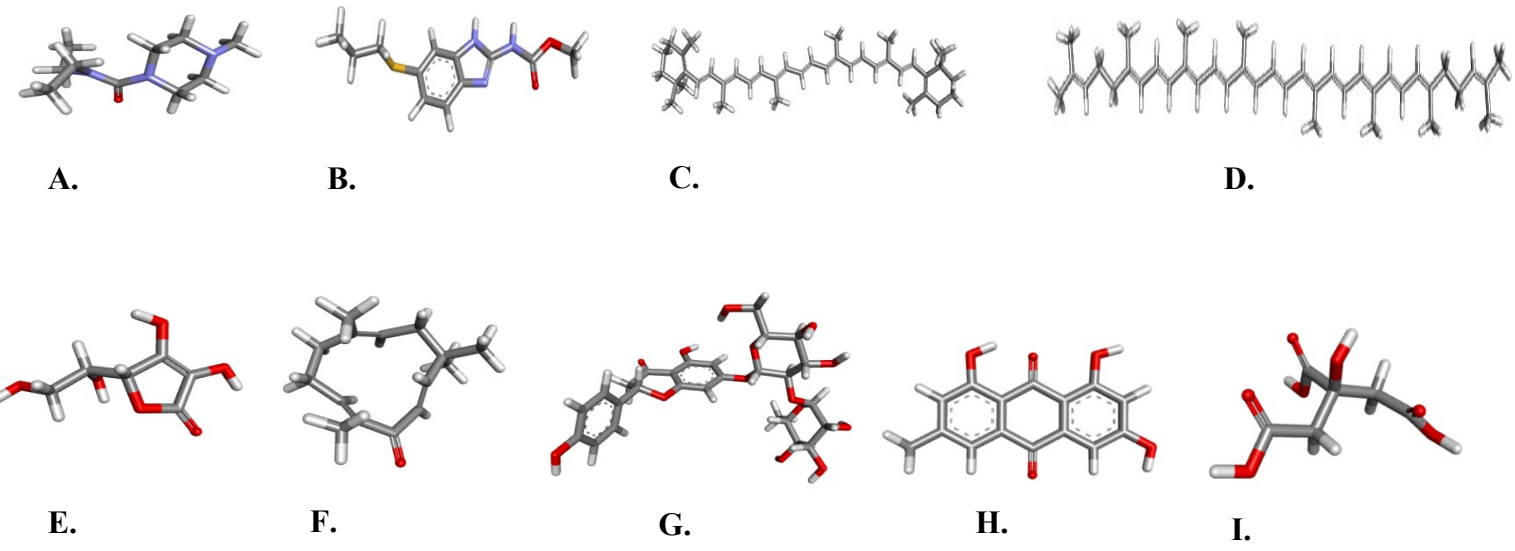
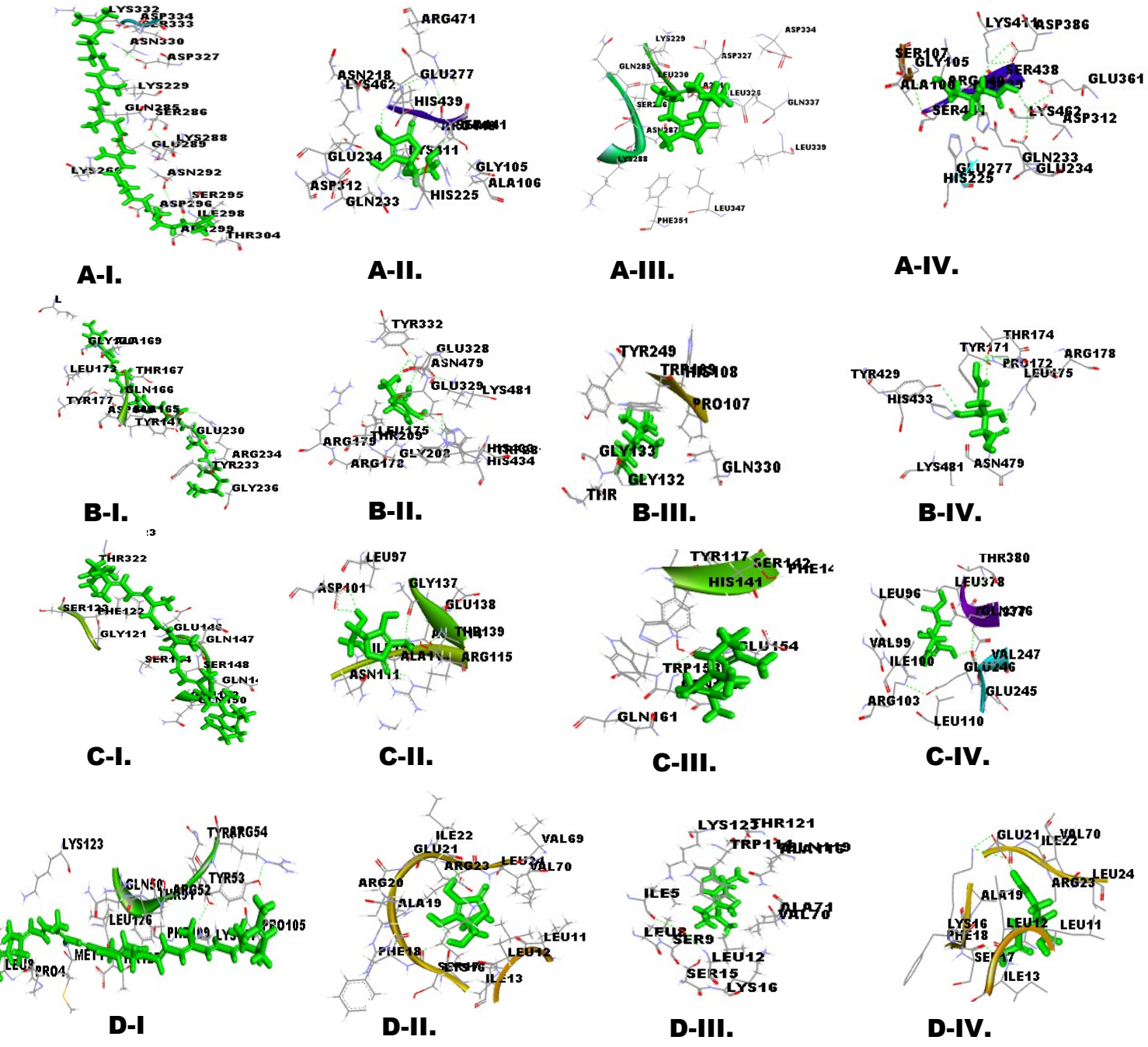


D.

Supplementary Figure 1. Ramachandran plot showing the distribution of the protein's main chain ϕ-Ψ torsion angles (black squares) relative to the "core" (red) and "allowed" (yellow) regions, with residues falling in the "generously allowed" (green) and "disallowed" region black crossed, A. Enolase, B. ES-62 Precursor, C. Serpin, D. Cystatin.



Supplementary Figure 2. Three dimensional structures of anti-filarial drugs and nutraceutical compounds A. DEC, B. Albendazole C. β-Carotene, D. Lycopene, E. Ascorbic acid, F. Naringin, G. Zerumbone, H. Emodin and I. Citric acid



Supplementary Figure 3. Three dimensional (3D) interactions of filarial immune-modulatory proteins with anti-filarial drugs and nutraceutical compounds docked complexes were visualized by discovery studio 3.5. The ligands were represented by stick model in green color whereas interacting residue were labeled in black color: (A) Enolase, and (B) ES-62 Precursor, (C) Serpin and (D) Cystatin and I-Lycopene, II- Ascorbic Acid, III- Zerumbone and IV- Citric Acid.