Supplementary tables

Table S1: Validation of the models modelled using Modeller and refined by ModRefiner

Target gene	ProSA (z-score)	ERRAT (overall quality factor)	WHATIF Ramachandran (Z-score)	Verify3D (residues having averaged 3D-1D score >= 0.2)	Anolea (e/kt)	ProCheck			QMEAN score
						Favored region	Allowed region	Outlier region	
CDC42	-6.92	73.7705	-0.375	85.86%	-1129	91.6%	8.4%	0%	-0.65
HOG1	-8.59	72.2857	-0.588	82.23%	-749	91.1%	6.9%	1%	-2.60

Table S2: Screening of lead molecules from natural sources by molecular weight and drug likeliness

Compounds	Source	PubChem ID	Molecular Weight (g/mol)	IUPAC Name	Drug likeliness				
					CMC Like Rule	Lead Like Rule	MDDR Like Rule	Rule of five	WDI Like Rule
1,3-Dihydroxy-2-methyl-6-methoxy-9,10 anthraquinone	*Cassia italica*	56600270	284.267	1,3-dihydroxy-6-methoxy-2-methylanthracene-9,10-dione	Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	In 90% cut-off
Alpha-	*Litsea*specie	7462	136.238	1-methyl-4-	Not	Violate	Mid-	Suitabl	In

terpiene	s			propan-2-ylcyclohexa-1,3-diene	Qualified	d	structure	e	90% cut-off
Apigenin	*Petroselinum crispum*	5280443	270.24	5,7-dihydroxy-2-(4-hydroxyphenyl) chromen-4-one	Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	In 90% cut-off
Apigenin	*Matricaria chamomilla*	5280443	270.24	5,7-dihydroxy-2-(4-hydroxyphenyl) chromen-4-one	Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	In 90% cut-off
Apritone	*Basidiomycetous yeasts*	6437428	220.356	2-[(2E)-3,7-dimethylocta-2,6-dienyl]cyclopentan-1-one	Qualified	Violated	Mid-structure	Suitable	Out of 90% cut-off
Aureomycin	*Streptomyces aureofaciens*	54675777	478.882	(4*S*,4*aS*,5*aS*,6*S*,12*aR*)-7-chloro-4-(dimethylamino)-1,6,10,11,12*a*-pentahydroxy-6-methyl-3,12-dioxo-4,4*a*,5,5*a*-tetrahydrotetracene-2-carboxamide	Not Qualified	Violated	Mid-structure	Suitable	Out of 90% cut-off

Azaphilone	*Pestalotiopsisfordon*	57384025	386.4	[(7R,8R,8aR)-7-hydroxy-7-methyl-6-oxo-3-[(E)-prop-1-enyl]-8,8a-dihydro-1H-isochromen-8-yl] 2,4-dihydroxy-6-methylbenzoate	Qualified	Violated	Mid-structure	Suitable	In 90% cut-off
Baicalein	*Scutellaria*species	5281605	270.24	5,6,7-trihydroxy-2-phenylchromen-4-one	Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	In 90% cut-off
Berberine	*Berberis*species, *Mahonia aquifolium*	2353	336.367	16,17-dimethoxy-5,7-dioxa-13-azoniapentacyclo[11.8.0.0.$0^{4,8}$.0]henicosa-1(13),2,4(8),9,14,16,18,20-octaene	Failed	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	Failed
Berberine	*Berberis vulgaris*	2353	336.367	16,17-dimethoxy-5,7-dioxa-13-azoniapentacyclo[11.8.0.$0^{2,10}$.$0^{4,8}$.$0^{15,20}$]henicosa-	Failed	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	Failed

				1(13),2,4(8),9,14,16,18,20-octaene					
Buddledin A	*Buddlejaglobosa*	5281514	276.376	[(1*R*,2*R*,4*E*,9*S*)-4,11,11-trimethyl-8-methylidene-3-oxo-2-bicyclo[7.2.0]undec-4-enyl] acetate	Qualified	Violated	Mid-structure	Suitable	In 90% cut-off
Buddledin B	*Buddlejaglobosa*	6443194	234.339	(1*R*,2*R*,4*Z*,9*S*)-2-hydroxy-4,11,11-trimethyl-8-methylidenebicyclo[7.2.0]undec-4-en-3-one	Qualified	Violated	Mid-structure	Suitable	In 90% cut-off
Buddlejone	*Buddlejaglobosa*	9972034	300.442	(4aS,10aS)-8-hydroxy-1,1,4a-trimethyl-7-propan-2-yl-3,4,10,10a-tetrahydro-2H-phenanthren-9-one	Qualified	Violated	Mid-structure	Suitable	In 90% cut-off
Caffeic acid phenethyl ester	*Apis mellifera*	5281787	284.311	2-phenylethyl (E)-3-(3,4-dihydroxyphenyl)prop-2-enoate	Qualified	Violated	Mid-structure	Suitable	In 90% cut-off
Capsaicin	*Capsicum* species	1548943	305.418	(E)-N-[(4-hydroxy-3-	Qualified	Violated	Mid-structur	Suitable	Out of

				methoxyphenyl) methyl]-8-methylnon-6-enamide			e		90% cut-off
Carvacol	*Cuminumcyminum, Thymus vulgaris*	10364	150.22	2-methyl-5-propan-2-ylphenol	Not Qualified	Violated	Mid-structure	Suitable	Out of 90% cut-off
Carvacrol	*Origanum vulgare*	10364	150.221	2-methyl-5-propan-2-ylphenol	Not Qualified	Violated	Mid-structure	Suitable	In 90% cut-off
Chlorogenic acid	*Calluna vulgaris*	1794427	354.311	(1S,3R,4R,5R)-3-[(E)-3-(3,4-dihydroxyphenyl)prop-2-enoyl]oxy-1,4,5-trihydroxycyclohexane-1-carboxylic acid	Not Qualified	Violated	Mid-structure	Suitable	In 90% cut-off
Chrysin	*Passiflora*species, *Oroxylumindicum*	5281607	254.241	5,7-dihydroxy-2-phenylchromen-4-one	Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	In 90% cut-off
Cianidanol	*Theobroma cacao*	9064	290.271	(2R,3S)-2-(3,4-dihydroxyphenyl)-3,4-dihydro-2H-chromene-	Qualified	Suitable if its binding affinity	Mid-structure	Suitable	In 90% cut-off

				3,5,7-triol		>0.1µM			
Cinnamaldehyde	*Cinnamomum verum*	637511	132.162	(E)-3-phenylprop-2-enal	Not Qualified	Suitable if its binding affinity >0.1µM	Non Drug like	Suitable	In 90% cut-off
Cinnamic acid	*Cinnamomum verum*	444539	148.16	(E)-3-phenylprop-2-enoic acid	Not Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	In 90% cut-off
Cinnamodial	*Cinnamosafragrans*	442354	308. 374	[(1R,4S,4aS,8aS)-3,4-diformyl-4-hydroxy-4a,8,8-trimethyl-5,6,7,8a-tetrahydro-1H-naphthalen-1-yl] acetate	Qualified	Suitable	Mid-structure	Suitable	In 90% cut-off
Cinnamosmolide	*Cinnamosafragrans*	12303262	308.374	[(5R,5aS,9aS,9bS)-9b-hydroxy-6,6,9a-trimethyl-3-oxo-1,5,5a,7,8,9-hexahydrobenzo[e][2]benzofuran-5-yl] acetate	Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	In 90% cut-off
Cocaine	*Erythroxylu*	446220	303.358	methyl	Not	Violate	Mid-	Suitabl	In

	*m*species			(1*R*,2*R*,3*S*,5*S*)-3-benzoyloxy-8-methyl-8-azabicyclo[3.2.1]octane-2-carboxylate	Qualified	d	structure	e	90% cut-off
Colchicine	*Colchicum autumnale*	6167	399	N-[(7S)-1,2,3,10-tetramethoxy-9-oxo-6,7-dihydro-5H-benzo[a]heptalen-7-yl]acetamide	Qualified	Violated	Mid-structure	Suitable	In 90% cut-off
Cudraflavanone B	*Cudraniacochinchinensis*	509244	356.374	2-(2,4-dihydroxyphenyl)-5,7-dihydroxy-6-(3-methylbut-2-enyl)-2,3-dihydrochromen-4-one	Qualified	Violated	Mid-structure	Suitable	In 90% cut-off
Cudraxanthone S	***Cudraniacochinchinensis***	**5495918**	**328.32**	**1,3,5,6-tetrahydroxy-2-(2-methylbut-3-en-2-yl)xanthen-9-one**	**Qualified**	**Suitable if its binding affinity >0.1µM**	**Mid-structure**	**Suitable**	**In 90% cut-off**
Deoxybuddlejone	*Buddlejaglobosa*	10334025	284.443	(4bS,8aS)-4b,8,8-trimethyl-2-	Qualified	Violated	Mid-structure	Suitable	Out of 90%

				propan-2-yl-6,7,8a,9-tetrahydro-5H-phenanthren-1-one					cut-off
Drimane	*Pleodendroncostaricense*	9548719	208.389	(1S,2S,4aS,8aR)-1,2,5,5,8a-pentamethyl-1,2,3,4,4a,6,7,8-octahydronaphthalene	Qualified	Violated	Mid-structure	Suitable	Out of 90% cut-off
Emerimidine A	*Emericellavariecolor*	53363661	209.201	4-hydroxy-5,6-dimethoxy-2,3-dihydroisoindol-1-one	Qualified	Violated	Mid-structure	Suitable	Out of 90% cut-off
Eugenol	*Syzgiumaromaticum, Myristicafragrans*	3314	164.204	2-methoxy-4-prop-2-enylphenol	Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	Out of 90% cut-off
Eugenol	*Elettariacardamomum*	3314	164.204	2-methoxy-4-prop-2-enylphenol	Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	Out of 90% cut-off
Ferulic acid	*Ferulafoetida*	445858	194.186	(E)-3-(4-hydroxy-3-methoxyphenyl) prop-2-enoic	Qualified	Suitable if its binding affinity	Mid-structure	Suitable	Out of 90% cut-

				acid		>0.1µM			off
Galangin	*Alpiniaofficinarum*	5281616	270.24	3,5,7-trihydroxy-2-phenylchromen-4-one	Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	In 90% cut-off
Genistein	*Genistatinctoria*	5280961	270.24	5,7-dihydroxy-3-(4-hydroxyphenyl) chromen-4-one	Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	In 90% cut-off
Gereniol	*Cymbopogon martini*	637566	154.253	(2E)-3,7-dimethylocta-2,6-dien-1-ol	Not Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	Out of 90% cut-off
Helenalin	*Arnica montana, Arnica chamissonis*	23205	262.305	(3*aR*,5*R*,5*aR*,8*aR*,9*S*,9*aS*)-9-hydroxy-5,8*a*-dimethyl-1-methylidene-3*a*,4,5,5*a*,9,9*a*-hexahydroazuleno[6,7-b]furan-2,8-dione	Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	In 90% cut-off
Hesperetin	*Cordia obliqua*	72281	302.282	(2*S*)-5,7-dihydroxy-2-(3-hydroxy-4-	Qualified	Suitable if its binding	Mid-structure	Suitable	In 90% cut-

				methoxyphenyl)-2,3-dihydrochromen-4-one		affinity >0.1µM			off
Hexanal	*Olea europaea*	6184	100.161	hexanal	Not Qualified	Suitable if its binding affinity >0.1µM	Non drug like	Suitable	In 90% cut-off
Honokiol	*Magnolia* species	72303	266.34	2-(4-hydroxy-3-prop-2-enylphenyl)-4-prop-2-enylphenol	Qualified	Violated	Mid-structure	Suitable	In 90% cut-off
Hydroxytyrosol	*Olea europaea*	82755	154.165	4-(2-hydroxyethyl)benzene-1,2-diol	Not Qualified	Violated	Non Drug like	Suitable	In 90% cut-off
Hyoscyamine	*Datura metel*	154417	289.37	[(1R,5S)-8-methyl-8-azabicyclo[3.2.1]octan-3-yl] (2S)-3-hydroxy-2-phenylpropanoate	Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	In 90% cut-off
Levomenol	*Matricaria chamomilla*	442343	222.0	(2S)-6-methyl-2-[(1S)-4-methylcyclohex-3-en-1-yl]hept-5-en-2-ol	Qualified	Violated	Mid-structure	Suitable	Out of 90% cut-off

Linalool	*Piper aduncum*	6549	154.253	3,7-dimethylocta-1,6-dien-3-ol	Not Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	Out of 90% cut-off
l-menthone	*Mentha piperita*	26447	154.253	(2*S*,5*R*)-5-methyl-2-propan-2-ylcyclohexan-1-one	Not Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	In 90% cut-off
Magnolol	*Magnolia* species	72300	266.34	2-(2-hydroxy-5-prop-2-enylphenyl)-4-prop-2-enylphenol	Qualified	Violated	Mid-structure	Suitable	In 90% cut-off
Manoalide	*Luffariellav ariabilis*	6437368	416.558	(2R)-2-hydroxy-3-[(2R,6R)-6-hydroxy-5-[(E)-4-methyl-6-(2,6,6-trimethylcyclohexen-1-yl)hex-3-enyl]-3,6-dihydro-2H-pyran-2-yl]-2H-furan-5-one	Not Qualified	Violated	Drug like	Suitable	Out of 90% cut-off
Masoprocol	*Larreatridentata*	71398	302.37	4-[(2*S*,3*R*)-4-(3,4-dihydroxyphenyl)-2,3-	Qualified	Violated	Mid-structure	Suitable	In 90% cut-off

				dimethylbutyl]benzene-1,2-diol					
Mescaline	*Lophophora williamsii*	4076	211.261	2-(3,4,5-trimethoxyphenyl)ethanamine	Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	Out of 90% cut-off
Motualevic acid F	*Siliquariaspongiasp*	25242627	421.173	2R)-3-[(1E)-13,13-dibromotrideca-1,12-dienyl]-2H-azirine-2-carboxylic acid	Not Qualified	Violated	Mid-structure	Suitable	Out of 90% cut-off
Nerolidiol	*Zingiberofficinale*	5284507	222.372	(6E)-3,7,11-trimethyldodeca-1,6,10-trien-3-ol	Qualified	Violated	Non Drug like	Suitable	Out of 90% cut-off
Omacetaxine	*Cephalotaxusharringtonii*	285033	545.629	1-*O*-[(2*S*,3*S*,6*R*)-4-methoxy-16,18-dioxa-10-azapentacyclo[11.7.0.0.0.0]icosa-1(20),4,13,15(19)-tetraen-3-yl] 4-*O*-methyl (2*R*)-2-hydroxy-2-(4-hydroxy-4-methylpentyl)bu	Not Qualified	Violated	Drug-like	Suitable	Out of 90% cut-off

				tanedioate					
Oroidin	*Agelas schmidti*	6312649	389.05	N-[(E)-3-(2-amino-1H-imidazol-5-yl)prop-2-enyl]-4,5-dibromo-1H-pyrrole-2-carboxamide	Qualified	Violated	Mid-structure	Suitable	Out of 90% cut-off
Pestafolide A	*Pestalotiopsisfordon*	24850054	282.336	(3S,6S,6'S,7R)-6,7-dihydroxy-6',7-dimethylspiro[1,4,5,6-tetrahydroisochromene-3,2'-oxane]-8-one	Qualified	Violated	Mid-structure	Suitable	In 90% cut-off
Petalostemumol	*Petalostemumpurpurem*	15232524	508.611	(2R,3R)-2-[3,4-dihydroxy-2,6-bis(3-methylbut-2-enyl)phenyl]-3,5,7-trihydroxy-8-(3-methylbut-2-enyl)-2,3-dihydrochromen-4-one	Not Qualified	Violated	Drug like	Violated	Out of 90% cut-off
Phloretin	*Prunus mandshurica*	4788	274.272	3-(4-hydroxyphenyl)-1-(2,4,6-trihydroxyphenyl)propan-1-one	Qualified	Suitable if its binding affinity >0.1µ	Mid-structure	Suitable	In 90% cut-off

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Phloretin	*Malus sylvestris*	4788	274.272	3-(4-hydroxyphenyl)-1-(2,4,6 trihydroxyphenyl)propan-1-one	Not Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	In 90% cut-off
Piperine	*Piper nigrum*	638024	285.343	(2*E*,4*E*)-5-(1,3-benzodioxol-5-yl)-1-piperidin-1-ylpenta-2,4-dien-1-one	Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	In 90% cut-off
Quercetin	*Capparisspinosa, Ceratonia siliqua*	528043	302.238	2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxychromen-4-one	Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	In 90% cut-off
Quercetin	*Brassica oleracea*	5280343	302.238	2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxychromen-4-one	Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	In 90% cut-off
Reserpine	*Rauvolfiaserpentina*	5770	608.688	methyl (1*R*,15*S*,17*R*,18*R*,19*S*,20*S*)-6,18-dimethoxy-17-(3,4,5-trimethoxybenz	Not Qualified	Violated	Drug-like	Suitable	Out of 90% cut-off

				oyl)oxy-1,3,11,12,14,15,16,17,18,19,20,21-dodecahydroyohimban-19-carboxylate					
Rhein	*Rheum* species, *Cassia reticulata*	10168	284.223	4,5-dihydroxy-9,10-dioxoanthracene-2-carboxylic acid	Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	In 90% cut-off
Rotiorinol C	*Chaetorium cupreum*	11703984	398.455	(9R,9aR)-3-acetyl-9-hydroxy-6-[(1E,3E,5S)-7-hydroxy-3,5-dimethylhepta-1,3-dienyl]-9a-methyl-9H-furo[3,2-g]isochromen-2-one	Qualified	Violated	Drug like	Suitable	In 90% cut-off
Rubrorotiorin	*Chaetorium cupreum*	12004205	414.882	6aS)-9-acetyl-5-chloro-3-[(1E,3E,5S)-3,5-dimethylhepta-1,3-dienyl]-6a-methylfuro[2,3-h]isochromene-	Qualified	Violated	Mid-structure	Suitable	In 90% cut-off

				6,8-dione					
Salicin	*Salix alba*	439503	286.289	(2R,3S,4S,5R,6S)-2-(hydroxymethyl)-6-[2-(hydroxymethyl)phenoxy]oxane-3,4,5-triol	Not Qualified	Violated	Mid-structure	Suitable	In 90% cut-off
Scutifoliamide A	*Piper scutifolium*	5320621	273.332	(2*E*,4*E*)-5-(1,3-benzodioxol-5-yl)-*N*-(2-methylpropyl)penta-2,4-dienamide	Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	Out of 90% cut-off
Scutifoliamide B	***Piper scutifolium***	**101838332**	**315.369**	**(2*E*,4*E*)-5-(1,3-benzodioxol-5-yl)-*N*-(2,2-dimethyl-3-oxobutyl)penta-2,4-dienamide**	**Qualified**	**Suitable if its binding affinity >0.1µM**	**Mid-structure**	**Suitable**	**Out of 90% cut-off**
Sordarin	*Sordariaara neosa*	100917394	492.609	(1R,2S,4R,5R,8R,9S)-9-formyl-5-methyl-13-propan-2-yl-2-[[(2R,3S,4S,5S,6R)-3,4,5-trihydroxy-5,6-dimethyloxan-2-yl]oxymethyl]tetracyclo[7.4.0.02,11.04,8]tridec	Not Qualified	Violated	Mid-structure	Suitable	In 90% cut-off

				-12-ene-1-carboxylic acid					
Tamaridone	*Terminalia catappa*	15345466	330.292	5,7-dihydroxy-2-(2-hydroxy-4-methoxyphenyl)-6-methoxychromen-4-one	Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	In 90% cut-off
Terpinen-4-ol	*JuniperusCommunis*	11230	154.253	4-methyl-1-propan-2-ylcyclohex-3-en-1-ol	Not Qualified	Suitable if its binding affinity >0.1µM	Mid-structure	Suitable	In 90% cut-off
Thymol	*Thymus vulgaris*	6898	150.22	2-chloro-6-methylphenol	Not Qualified	Violated	Mid-structure	Suitable	Out of 90% cut-off
Totarol	*Podacarpus nagi*	92783	286.459	(4bS,8aS)-4b,8,8-trimethyl-1-propan-2-yl-5,6,7,8a,9,10-hexahydrophenanthren-2-ol	Not Qualified	Violated	Mid-structure	Suitable	Out of 90% cut-off
Withaferin A	*Withaniasomniferum*	265237	470.606	(1S,2R,6S,7R,9R,11S,12S,15R,16S)-6-hydroxy-15-[(1S)-1-[(2R)-5-(hydroxymethyl	Not Qualified	Violated	Mid-structure	Suitable	Out of 90% cut-off

				)-4-methyl-6-oxo-2,3-dihydropyran-2-yl]ethyl]-2,16-dimethyl-8-oxapentacyclo[9.7.0.02,7.07,9.012,16]octadec-4-en-3-one					
β- sitosterol	*Pleodendroncostaricense*	222284	414.718	(3S,8S,9S,10R,13R,14S,17R)-17-[(2R,5R)-5-ethyl-6-methylheptan-2-yl]-10,13-dimethyl-2,3,4,7,8,9,11,12,14,15,16,17-dodecahydro-1H-cyclopenta[a]phenanthren-3-ol	Not Qualified	Violated	Drug like	Suitable	Out of 90% cut-off
δ-tocotrienol	*Pleodendroncostaricense*	5282350	396.615	(2R)-2,8-dimethyl-2-[(3E,7E)-4,8,12-trimethyltrideca-3,7,11-trienyl]-3,4-dihydrochromen-6-ol	Not Qualified	Violated	Mid-structure	Suitable	Out of 90% cut-off

Table S3: ADME tests was carried out for the lead compounds that qualified drug likeliness using PreADMET tool

Compounds	Blood Brain Barrier	CaCo-2 (nm/sec)	Human Intestinal Absorption (%)	Plasma Protein Binding (%)	Skin Permeability (cm/hour)
1,3-Dihydroxy-2-methyl-6-methoxy-9,10 anthraquinone	0.5921	21.111	92.817	92.6597	-3.5063
Apigenin	0.5651	10.5468	88.2283	97.2534	-4.1457
Apigenin	0.5611	10.5468	88.122	97.2534	-4.1457
Apritone	10.242	56.217	100	100	-0.8142
Azaphilone	0.2280	13.7151	89.223	82.5614	-3.1495
Baicalein	0.7708	1.2802	88.1054	98.9832	-4.1355
Bereberine	0.6931	55.5786	97.8846	58.5420	-4.3731
Buddledin A	0.8570	38.3918	98.2232	94.7561	-1.5493
Buddledin B	3.0719	26.1097	95.3083	92.7976	-1.2977
Buddlejone	6.6770	26.8354	95.6751	100	-1.8875
Caffeic acid phenethyl ester	1.2427	22.0658	93.0360	87.8756	-2.232
Capsaicin	4.0987	37.371	92.4846	92.8564	-1.8899
Chrysin	0.9325	2.4782	92.6439	95.0956	-3.3464
Cianidanol	0.3949	0.6569	66.7079	100	-4.2930
Cinnamodial	0.6724	21.2557	91.0823	79.3048	-2.9222
Cinnamosmolide	0.6891	21.072	92.9940	80.3581	-3.5947
Cocaine	0.0135	27.0183	98.2902	49.5809	-3.7082
Colchicine	0.0143	37.4451	96.902	65.422	-3.9639
Cudraflavanone B	1.8042	17.8119	85.0191	100	-3.1415
Cudraxanthone S	**0.1904**	**20.8695**	**81.0600**	**95.9378**	**-3.8074**
Emerimidine A	0.3796	19.5459	87.9189	54.1613	-4.5060
Eugenol	2.2554	46.8865	96.7744	100	-1.3109
Eugenol	2.2554	46.8865	96.7744	100	-1.3109
Ferulic acid	0.7584	21.1177	90.60	50.4142	-1.8720

Galangin	0.6713	3.7058	88.1226	88.1221	-4.1908
Genistein	0.1782	5.7471	88.1228	89.7381	-4.2201
Helenalin	0.5734	20.8664	94.6875	66.1637	-3.6910
Hesperetin	0.2227	7.0037	87.1929	96.7928	-4.1875
Honokiol	8.8512	26.5692	93.6476	100	-1.4144
Hyoscyamine	0.0508	28.2833	95.4038	35.2645	-3.6597
Levomenol	10.5531	51.1062	100	90.29	-0.7935
Magnolol	8.8187	27.8519	93.6473	100	-1.4193
Masoprocol	3.9349	15.8894	84.2771	100	-2.6101
Mescaline	0.7995	14.94	95.1730	27.8292	-2.4912
Omacetaxine	0.0166	26.1699	94.4875	47.4193	-2.7161
Pestafolide A	0.3797	0.7469	88.2453	50.3000	-4.7352
Phloretin	0.7380	18.1041	78.9809	100	-3.6207
Phloretin	0.738	18.1041	78.9809	100	-3.7207
Piperine	0.0503	52.383	98.1801	90.4489	-3.4147
Quercetin	0.1727	3.4129	63.4852	93.2361	-4.4334
Quercetin	0.1727	3.1429	63.485	93.2361	-4.4334
Reserpine	0.0984	45.5921	94.8014	78.5407	-4.2182
Rhein	0.4085	2.8446	82.9613	88.5191	-3.7464
Rotiorinol C	0.0410	21.5788	94.6939	71.6247	-3.2701
Rubrorotiorin	0.0354	26.993	97.8512	90.8407	-3.0360
Scutifoliamide A	0.5886	41.237	95.2669	86.6667	-3.0197
Scutifoliamide B	**0.0374**	**28.091**	**95.9735**	**84.7090**	**-2.8511**
Tamaridone	0.0737	15.7166	87.82	85.8158	-3.84
Terpinen-4-ol	5.5395	50.8078	100	100	-1.3052

Table S4: Toxicity tests were carried out for the lead compounds that qualified ADME test using PreADMET tool

Compounds	Ames test	Carcinogen test		hERG inhibition	Daphnia test	Fish toxicity		Algae test	TA100_10 RLI	TA100_ NA	TA1535_10 RLI	TA1535_ NA
		Mouse	Rat			Medaka	Minnow					

1,3-Dihydroxy-2-methyl-6-methoxy-9,10 anthraquinone	Non mutagen	negative	negative	Medium risk	0.0994	0.0164	0.0097	0.0358	Positive	Positive	Negative	Nsegative
Apigenin	Mutagen	Positive	Positive	Medium risk	0.1301	0.0280	0.0152	0.0527	Positive	Positive	Negative	Negative
Apigenin	Mutagen	Positive	Positive	Medium risk	0.1301	0.0280	0.0152	0.0527	Positive	Positive	Negative	Negative
Apritone	Non Mutagen	Negative	Positive	Low risk	0.0877	0.0098	0.0046	0.0137	Negative	Negative	Negative	Negative
Azaphilone	Non Mutagen	Positive	Negative	Medium risk	0.1124	0.0235	0.0436	0.0277	Negative	Negative	Negative	Negative
Buddledin A	Mutagen	Positive	Positive	Low risk	0.0881	0.0114	0.0029	0.0390	Negative	Negative	Negative	Negative
Buddledin B	Mutagen	Positive	Positive	Low risk	0.1664	0.0366	0.0072	0.0334	Negative	Negative	Positive	Negative
Buddlejone	Mutagen	Negative	Negative	Low risk	0.0208	0.0007	0.0011	0.0113	Negative	Negative	Positive	Negative
Caffeic acid phenethyl ester	Non Mutagen	Negative	Negative	Medium risk	0.0488	0.0041	0.0066	0.0204	Negative	Negative	Negative	Negative
Cinnamodial	Non Mutagen	Positive	Negative	Low risk	0.5312	0.3673	0.2466	0.1055	Negative	Negative	Negative	Negative
Cinnamosmolide	Non Mutagen	Positive	Negative	Low risk	0.4024	0.2130	0.1896	0.0681	Negative	Negative	Negative	Negative

Cocaine	Non-Mutagen	Negative	Positive	Mediumrisk	0.2431	0.085	0.1069	0.1007	Negative	Negative	Negative	Negative
Cudraflavanone	Non Mutagen	Negative	Negative	Medium risk	0.0207	0.0008	0.0010	0.0050	Negative	Negative	Negative	Negative
Cudraxanthone S	**Mutagen**	**Positive**	**Negative**	**Medium risk**	**0.0590**	**0.0067**	**0.0069**	**0.0290**	**Negative**	**Negative**	**Negative**	**Negative**
Ferulic acid	Mutagen	Negative	Negative	Low risk	3.9511	18.0919	16.1785	0.1383	Negative	Positive	Positive	Negative
Honokiol	Non-Mutagen	Positive	Negative	Lowrisk	0.0043	4.16E-05	4.37E-05	0.0162	Negative	Negative	Negative	Negative
Hyoscyamine	Non Mutagen	Positive	Positive	Medium risk	0.3701	0.1883	0.2765	0.0784	Negative	Negative	Negative	Negative
Levomenol	Non Mutagen	Negative	Negative	Low risk	0.0586	0.0045	0.0058	0.0114	Negative	Negative	Negative	Negative
Magnolol	Non-Mutagen	Positive	Negative	Low risk	0.0041	3.83E-05	4.30E-05	0.0166	Negative	Negative	Negative	Negative
Masoprocol	Non-Mutagen	Negative	Negative	Mediumrisk	0.0245	0.0010	0.0007	0.0049	Negative	Negative	Negative	Negative
Mescaline	Mutagen	Positive	Negative	Low risk	0.8078	0.7579	0.7036	0.0967	Negative	Negative	Positive	Negative
Omacetaxine	Non-Mutagen	Negative	Negative	Ambiguous	0.0826	0.0145	0.0399	0.0081	Negative	Negative	Negative	Negative
Pestafolide A	Mutagen	Negative	Negative	Low risk	2.0043	4.5512	2.6958	0.0899	Negative	Positive	Negative	Negative

Quercetin	Mutagen	Negative	Positive	Medium risk	0.2143	0.7788	0.0335	0.0378	Negative	Positive	Negative	Negative
Reserpine	Non-Mutagen	Negative	Positive	Mediumrisk	0.0079	0.0001	0.0007	0.0025	Negative	Negative	Negative	Negative
Rotiorinol C	Non Mutagen	Positive	Positive	Medium risk	0.2415	0.1052	0.3406	0.0424	Negative	Negative	Negative	Negative
Rubrorotiorin	Non Mutagen	Positive	Negative	Medium risk	0.0396	0.0034	0.0106	0.0191	Negative	Negative	Negative	Negative
Scutifoliamide A	Mutagen	Positive	Positive	Medium risk	0.1261	0.0239	0.0291	0.0378	Positive	Negative	Negative	Negative
Scutifoliamide B	**Non Mutagen**	**Positive**	**Negative**	**Medium risk**	**0.1787**	**0.0504**	**0.0720**	**0.0437**	**Negative**	**Negative**	**Negative**	**Negative**
Tamaridone	Non Mutagen	Positive	Positive	Medium risk	0.1207	0.0254	0.0181	0.0276	Negative	Negative	Negative	Negative