Heterocyclic Letters
Vol. 15| No.3|495-515|May-July|2025
ISSN : (print) 2231–3087 / (online) 2230-9632
CODEN: HLEEAI
http://heteroletters.org

ANALYSING ADME PROPERTIES OF USNIC ACID AND ITS ANALOGUES – IN SILICO STUDY

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ABSTRACT:
Usnic acid [UA] and its derivatives [UA1 to UA10] have been selected to virtually screen for drug properties using various cheminformatics tools such as Molsoft and Molinspiration. The molecules were further subjected to find the target by Swiss Target prediction to bind with enzymes. The results show that all the molecules have the positive value for nuclear receptor interaction.

KEYWORDS: Usnic acid, ADME properties, cheminformatics, Molsoft, Molinspiration and SwissADME.

INTRODUCTION:

Phytochemical constituents distributed in different parts of plants cause therapeutic effects on treatment of acute and chronic diseases. The identification of bioactive compounds in plants has led to the development of herbal medicines, dietary supplements and pharmaceutical drugs derived from natural sources [i]. Lichens are symbiotic organisms consisting of a fungus partner and a photosynthetic organism, either an alga or Cyanobacteria. These organisms have historically been used as a cure for human diseases, food, dyes, in the production of alcohol and in the perfume industry[ii]. Usnic acid is a phytochemical and a secondary metabolite isolated predominately from lichen species and has been shown to exhibit antiproliferative properties. However, its application is limited by poor drug-like properties and low specificity. Numerous studies have investigated the various biological activity exhibited by usnic Acid including antibacterial, antiviral and antiprotozoal activity[iii]. Usnic acid is being studied for medical applications, especially in cancer research[iv]. Several in vitro studies described the anti-inflammatory activity of usnic acid in an attempt to discover the potential mechanism at the cellular level[v]. In silico analysis of usnic acid and its analogues has been recently reported using SwissADME web tool[vi]. In this work, usnic Acid [UA] is the lead compound. Its structure is modified to get its derivatives [UA1 – UA10] and their drug properties are computationally studied using Molsoft[vii], Molinspiration[viii] and Swiss target prediction[ix-xi].

METHODOLOGY:

Softwares used for studying drug properties

Molsoft

Molsoft[vii] is a leading provider of tools, databases and consulting services in the area of structure prediction, structural proteomics, bioinformatics, cheminformatics, molecular visualization and animation, and rational drug design. Molsoft offers complete solutions customized for a biotechnology or pharmaceutical company in the areas of computational biology and chemistry.

Physicochemical properties:

- MolLogP (octanol/water partition coefficient)
- MolLogS (water solubility Log(Mol/L))
- MolPSA (Molecular Polar Surface Area (PSA) and Volume)
- PSA is defined as sum of surfaces of oxygens, nitrogens and attached hydrogens.

Drug-likeness score:

★ Predicts an overall drug-likeness score using and Molsoft's chemical fingerprints. The training set for this mode consisted of:

★ 5K of marketed drugs from WDI (positives)

★ 10K of carefully selected non-drug compounds. (negatives)

Molinspiration

Molinspiration[viii] offers a broad range of cheminformatics software tool supporting molecule manipulation and processing, including SMILES and SD file conversion, normalization of molecules, generation of tautomers, molecule fragmentation, calculation of various molecular properties needed in QSAR, molecular modelling and drug design, high quality molecule depiction, molecular database tools supporting substructure and similarity searches. It supports also fragment-based virtual screening, bioactivity prediction and data visualization. Molinspiration tools are written in Java, therefore can be used practically on any computer platform. Molinspiration interactive web services are available from now not only on desktop computers, but also on touch devices including iPhone, iPad and Android phones and tablets. A molecule structure 8 input to our property calculation and bioactivity prediction services is powered by the JSME molecule editor written in JavaScript. Also our Galaxy 3D molecule visualizer that allows interactive display of molecules in various modes and visualization of surface molecule lipophilicity potential and polar surface area is written in JavaScript.

Molinspiration Molecule Viewer

Molinspiration Molecule Viewer allows visualization of collection of molecules encoded as SMILES or SDF file. SMILES is automatically transformed into molecule 2D representation by depiction engine. Display of associated data, selection of molecules, built-in substructure search and export of selected molecules is supported.

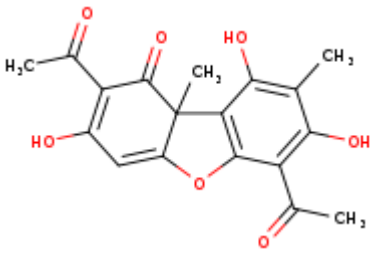
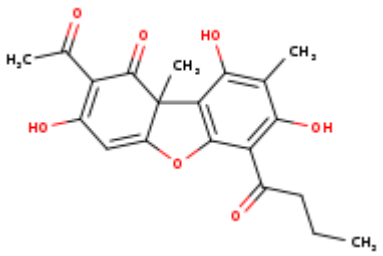
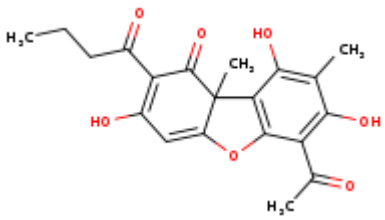
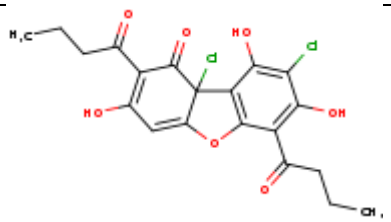
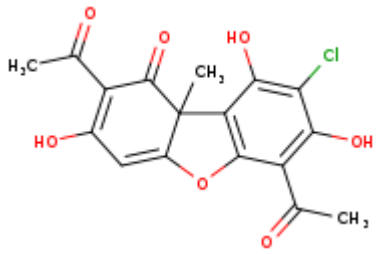
Swiss target prediction

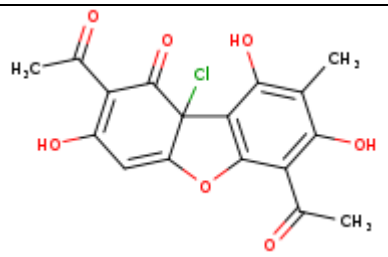
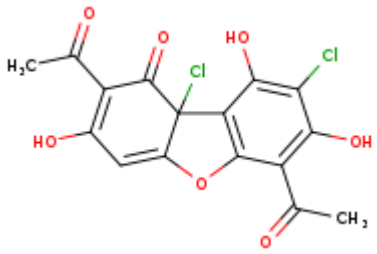
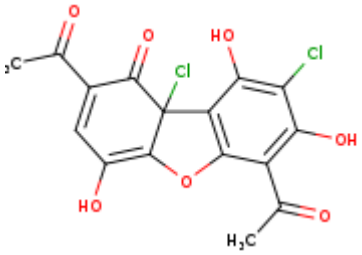
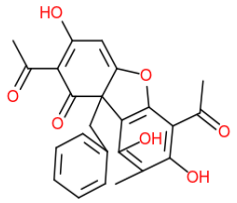
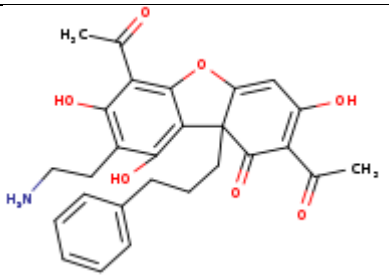
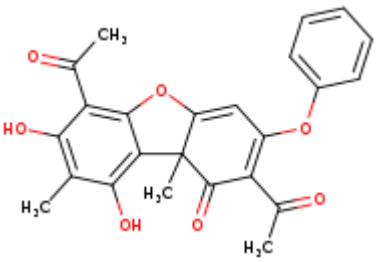
Swiss target prediction is a web interface designed by Swiss instituted of bioinformatics[ix]. It can predict the targets for any bioactive drug molecule. It enables us to select species like Homo sapiens, Mus musculus, Rattus. The input is provided has SMILES are through graphical interface proved by chemaxon. The list of targets and their details are available.

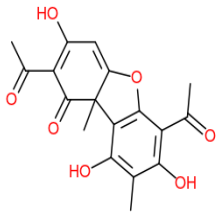
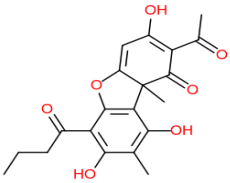
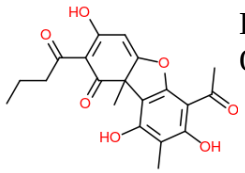
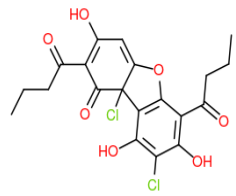
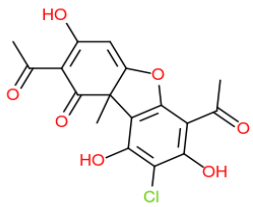
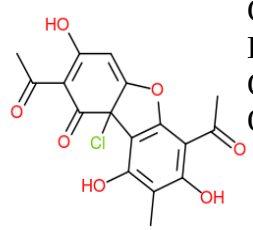
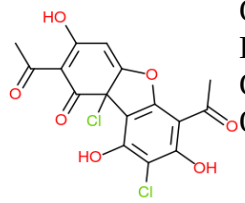
RESULTS AND DISCUSSION:

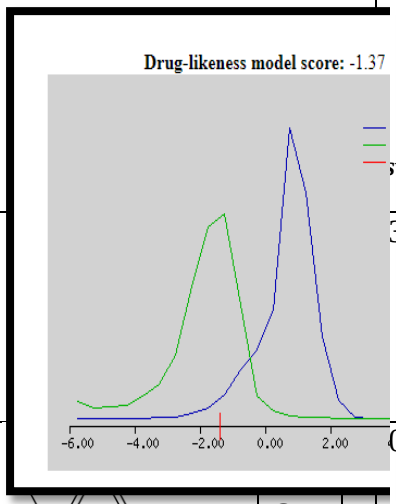
The molecule chosen for virtual screening and drug action studies are lichen class of phytochemical shown in Table 1.

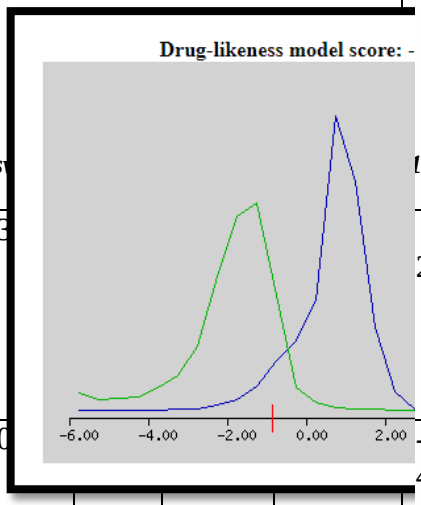
Table 1. Molecules selected for the work

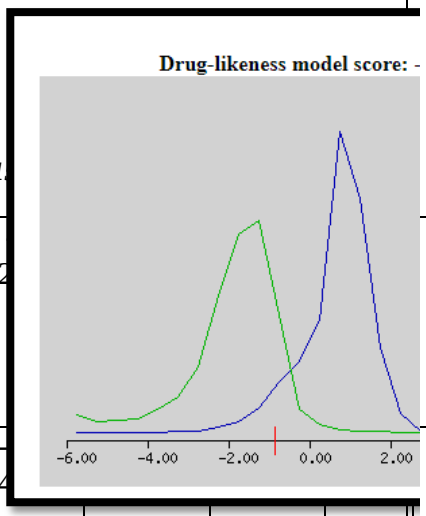
S. No.	IUPAC name	Structure	Label
1.	4,10-diacetyl-5,11,13-trihydroxy-2,12-dimethyl-8-oxatricyclo[7.4.0.0^{2,7}]trideca-1(9),4,6,10,12-pentaen-3-one (**Usnic acid**)		UA
2.	4-acetyl-10-butanoyl-5,11,13-trihydroxy-2,12-dimethyl-8-oxatricyclo[7.4.0.0^{2,7}]trideca-1(9),4,6,10,12-pentaen-3-one		UA1
3.	10-acetyl-4-butanoyl-5,11,13-trihydroxy-2,12-dimethyl-8-oxatricyclo[7.4.0.0^{2,7}]trideca-1(9),4,6,10,12-pentaen-3-one		UA2
4.	4,10-dibutanoyl-2,12-dichloro-5,11,13-trihydroxy-8-oxatricyclo[7.4.0.0^{2,7}]trideca-1(9),4,6,10,12-pentaen-3-one		UA3
5.	4,10-diacetyl-12-chloro-5,11,13-trihydroxy-2-methyl-8-oxatricyclo[7.4.0.0^{2,7}]trideca-1(9),4,6,10,12-pentaen-3-one		UA4

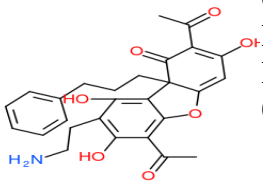
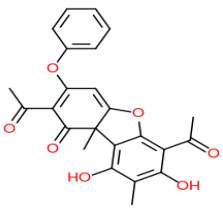
6.	4,10-diacetyl-2-chloro-5,11,13-trihydroxy-12-methyl-8-oxatricyclo[7.4.0.0^{2,7}]trideca-1(9),4,6,10,12-pentaen-3-one		UA5
7.	4,10-diacetyl-2,12-dichloro-5,11,13-trihydroxy-8-oxatricyclo[7.4.0.0^{2,7}]trideca-1(9),4,6,10,12-pentaen-3-one		UA6
8.	4,10-diacetyl-2,12-dichloro-6,11,13-trihydroxy-8-oxatricyclo[7.4.0.0^{2,7}]trideca-1(9),4,6,10,12-pentaen-3-one		UA7
9.	4,10-diacetyl-2-benzyl-5,11,13-trihydroxy-12-methyl-8-oxatricyclo[7.4.0.0^{2,7}]trideca-1(9),4,6,10,12-pentaen-3-one		UA8
10.	4,10-diacetyl-12-(2-aminoethyl)-5,11,13-trihydroxy-2-(3-phenylpropyl)-8-oxatricyclo[7.4.0.0^{2,7}]trideca-1(9),4,6,10,12-pentaen-3-one		UA9
11.	4,10-diacetyl-11,13-dihydroxy-2,12-dimethyl-5-phenoxy-8-oxatricyclo[7.4.0.0^{2,7}]trideca-1(13),4,6,9,11-pentaen-3-one		UA10

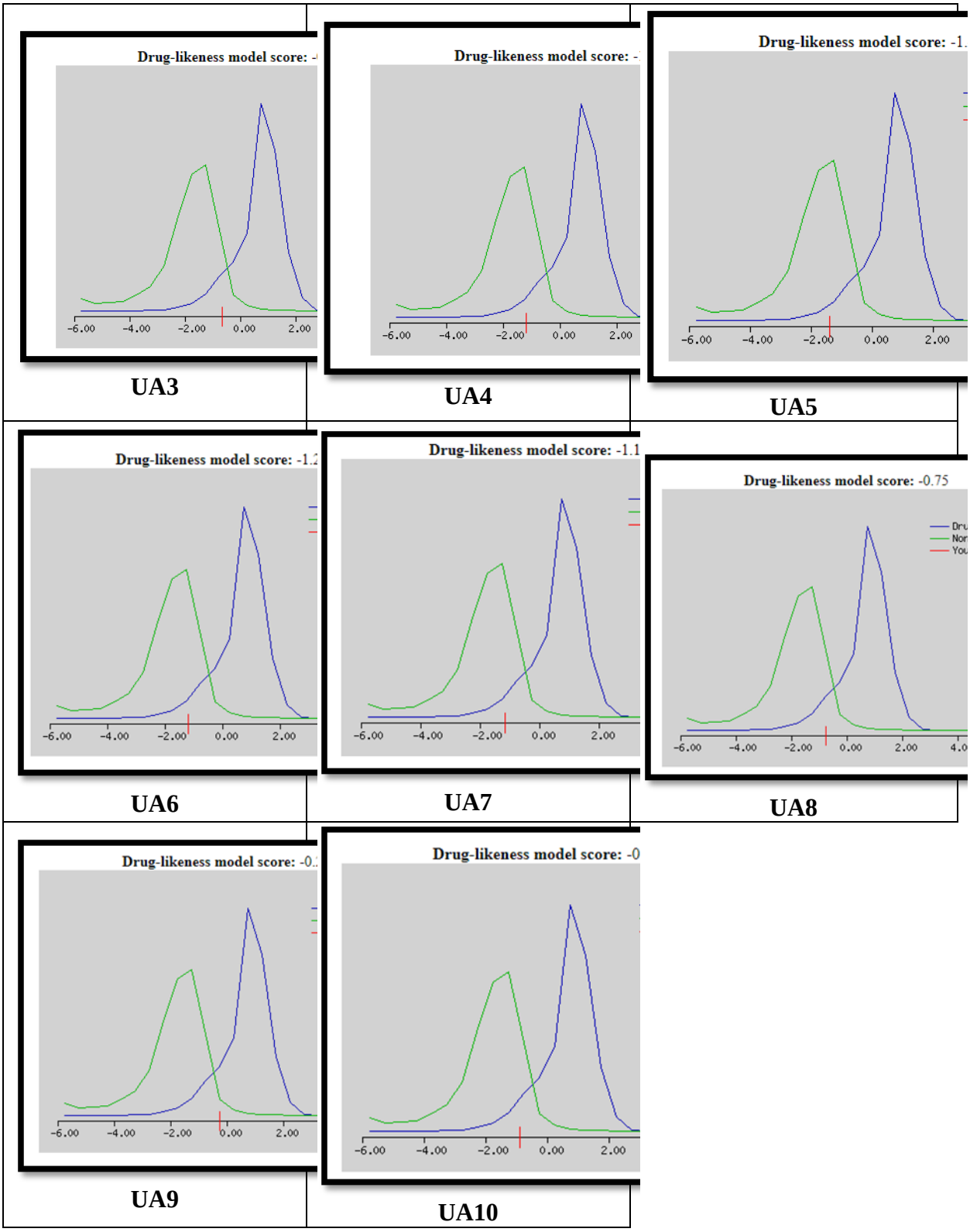
Properties	Structure	M. F.	M. W.	No. of HBA	No. of HBD	MolLogP	MolLogS	MolPSA	MolVol	Pks of most basic group	Pka of acidic group	BBB score	No. of Stereo centers
UA		$C_{18}H_{16}O_7$	344.09	7	3	3.33	-3.51	96.12 A^2	388.01 A^3	<0	7.77	2.40	1
UA1		$C_{20}H_{20}O_7$	372.12	7	3	4.22	-4.48	95.54 A^2	424.73 A^3	<0	7.77	2.34	1
UA2		$C_{20}H_{20}O_7$	372.12	7	3	4.42	-4.51	95.54 A^2	422.70 A^3	<0	7.77	2.34	1
UA3		$C_{20}H_{18}Cl_2O_7$	440.04	7	3	4.73	-4.85	94.96 A^2	450.88 A^3	<0	6.11	2.28	1
UA4		$C_{17}H_{13}ClO_7$	364.03	7	3	3.06	-3.24	96.12 A^2	381.70 A^3	<0	5.80	2.40	1
UA5		$C_{17}H_{13}ClO_7$	364.03	7	3	3.00	-3.31	96.12 A^2	385.78 A^3	<0	8.08	2.40	1
UA6		$C_{16}H_{10}Cl_2O_7$	383.98	7	3	2.74	-3.10	96.12 A^2	379.47 A^3	<0	6.11	2.40	**1**







UA7		3				2				6.11	2.42	1
UA8		O_7			**UA1**				**UA2**	6.98	2.36	**1**
UA9		$C_{27}H_{27}NO_7$	477.18	8	5	4.02	-4.38	117.00 A^2	521.97 A^3	9.40	7.46	2.38	**1**
UA10		$C_{24}H_{20}O_7$	420.12	7	2	5.09 (> 5)	-4.84	88.07 A^2	467.07 A^3	<0. / 7.77	<0. / 7.77	2.47	1



The above compounds were analyzed for various QSAR descriptors using the following softwares.

1. Molsoft
2. Molinspiration
3. Swiss target prediction

Results from Molsoft software

Table 2. Physicochemical properties from Molsoft

Figure 1. Drug-likeness score from Molsoft

Molsoft L.L.C- Molsoft is a foremost provider of tools, databases and consulting services in the field of structure prediction, structural proteomics, bioinformatics, cheminformatics, molecular visualization and animation, and rational drug design. MolSoft is building unique technologies for structure prediction that improves our understanding of the spatial organization of biological molecules and their interactions with each other, their biological substrates and drug-like molecules at the atomic level.

The Table 2 represents the data obtained from molsoft and the Figure 1 represents the druglikeness score graphically. Except UA9, other compounds show the number of HBA and HBD as in Swiss ADME software. Log P value of the compounds under study are in the range 2.52 to 4.73 and UA10 have the Log P value greater than 5 showing its poor drug property.

The Log P values obtained from Molsoft are not agreement with those values obtained from Swiss ADME[vi] but matches with the Log P values obtained from molinspiration.

Log S value represents aqueous solubility and for the molecules under study it is in the range -4.85 to – 2.88 which is greater than -6 shows that all the molecules have good drug dissolution.

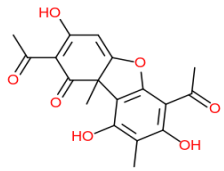
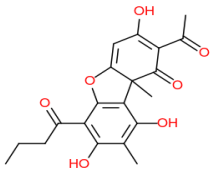
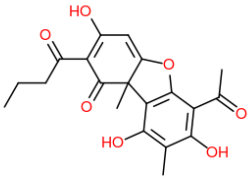
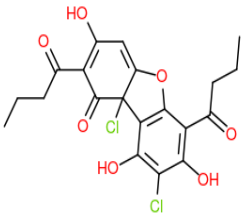
Molecular weight of all the ligands was found to be less than 500 and thus anticipating their easy transportation, absorption, and difusion.

Lesser the Pka value, more acidic is the acid. Among the molecules under study, UA 4 has the lowest Pka value of 5.80 showing that it is the most acidic compound.

From the figure 7, it is seen that all the compounds have negative druglikeness score indicating that they have to be optimized to act as drugs.

Molinspiration

Table 3. physicochemical properties from molinspiration

Name	Structure	Milogp	TPSA	MW	Nrotb	Volume
UA		3.75	104.06	358.39	4	321.35
UA1		2.65	121.13	372.37	4	323.53
UA2		3.98	121.13	441.26	6	351.09
UA3		1.82	121.13	364.74	2	286.90

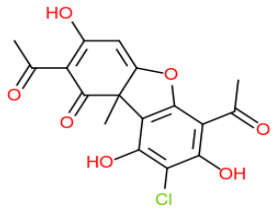
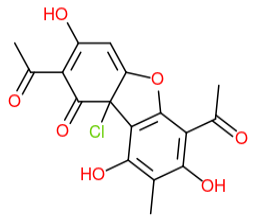
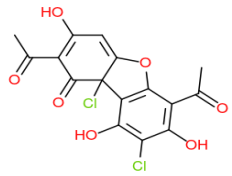
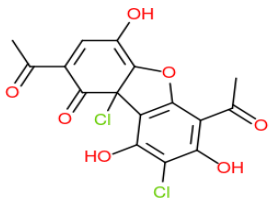
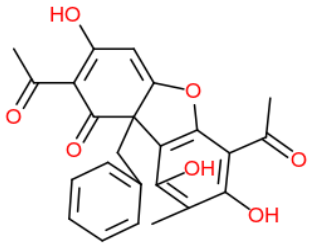
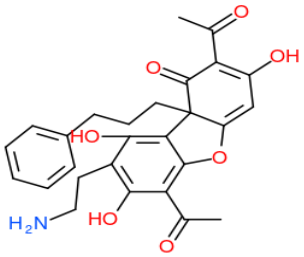
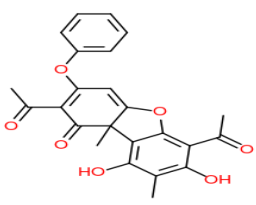
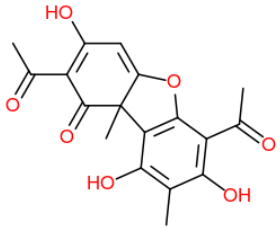
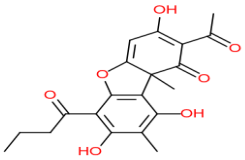
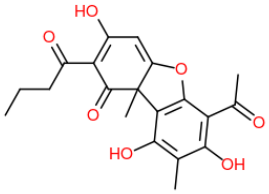
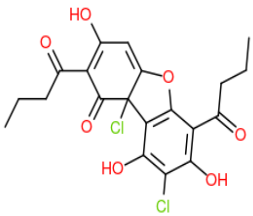
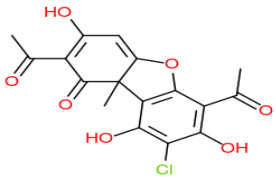
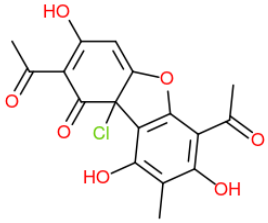
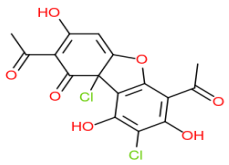
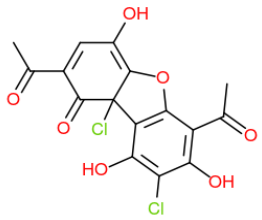
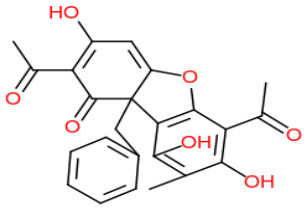
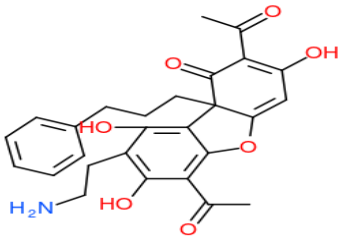
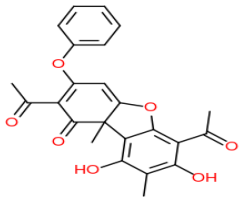
UA4		1.63	121.13	364.74	2	286.90
UA5		1.82	121.13	364.74	2	286.90
UA6		1.86	121.13	385.15	2	283.88
UA7		1.86	121.13	385.15	2	283.88
UA8		2.84	121.13	420.42	4	361.58
UA9		3.90	110.14	420.42	4	362.31
UA10		2.65	121.13	372.37	4	323.53

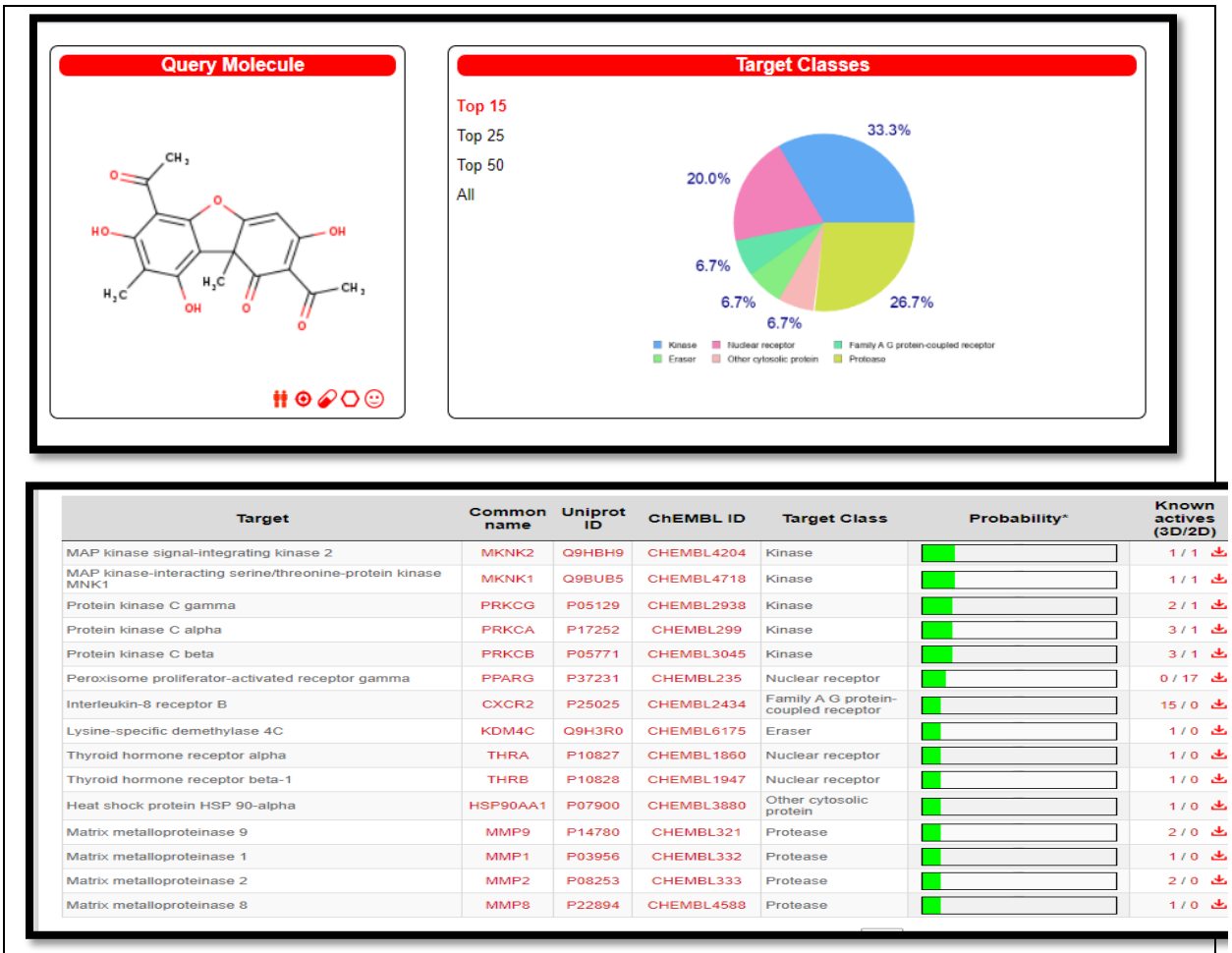
Table 4. Bioactivity properties from Molinspiration

Name	Structure	GPCR ligand	Ion channel	Kinase inhibitor	Nuclear receptor	Protease inhibitor	Enzyme inhibitor
UA		-0.16	-0.16	-0.26	0.84	-0.26	0.13
UA1		-0.26	-0.23	-0.29	1.02	-0.21	0.10
UA2		-0.30	-0.29	-0.39	0.42	-0.19	0.06
UA3		-0.34	-0.21	-0.01	1.02	-0.30	0.00
UA4		-0.41	-0.29	-0.41	0.48	-0.40	-0.01
UA5		-0.34	-0.21	-0.01	1.02	-0.30	0.00

UA6		-0.27	-0.25	-0.40	0.13	-0.35	-0.18
UA7		-0.27	-0.25	-0.40	0.13	-0.35	-0.18
UA8		-0.25	-0.17	-0.16	0.77	-0.26	0.07
UA9		-0.14	-0.14	-0.09	0.81	-0.23	0.10
UA10		-0.21	-0.16	-0.11	1.05	-0.26	0.17

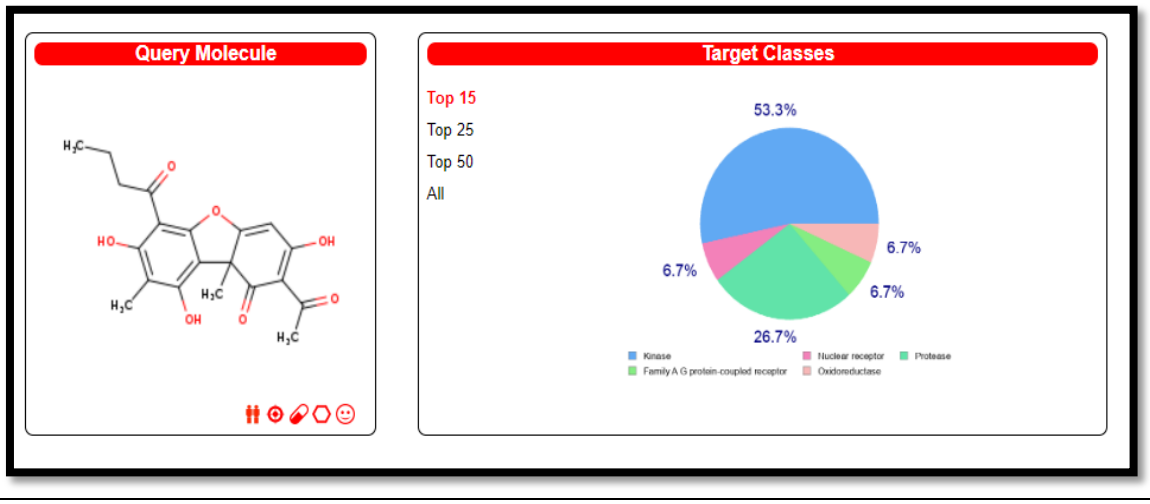
Except UA1, the TPSA values obtained in molinspiration (Table 3.) for the molecules under study matches with those obtained in SwissADME web tool [16]. The bioavailability score of these molecules indicates that they are bioactive by binding to enzyme in the form of inhibitor and have the values ranging from -0.18 to 0. 17 (Table 4.). It is to be noted that the maximum value showing that the molecule has maximum interaction. From the bioactivity score, it is seen that drug interacts with the target as a nuclear receptor. All the molecules have the positive value for nuclear receptor interaction which suggests that the molecule plays a role in gene formation which may have its effect in reproduction and anti-carcinogenic activity.

SWISS Target prediction



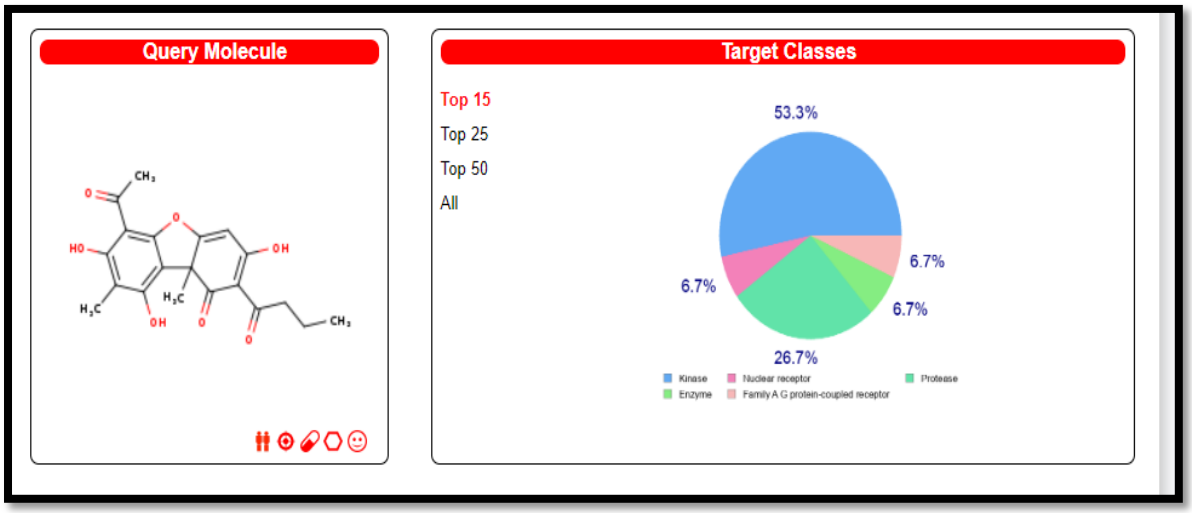
Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
MAP kinase signal-integrating kinase 2	MKNK2	Q9HBH9	CHEMBL4204	Kinase		1 / 1
MAP kinase-interacting serine/threonine-protein kinase MNK1	MKNK1	Q9BUB5	CHEMBL4718	Kinase		1 / 1
Protein kinase C gamma	PRKCG	P05129	CHEMBL2938	Kinase		2 / 1
Protein kinase C alpha	PRKCA	P17252	CHEMBL299	Kinase		3 / 1
Protein kinase C beta	PRKCB	P05771	CHEMBL3045	Kinase		3 / 1
Peroxisome proliferator-activated receptor gamma	PPARG	P37231	CHEMBL235	Nuclear receptor		0 / 17
Interleukin-8 receptor B	CXCR2	P25025	CHEMBL2434	Family A G protein-coupled receptor		15 / 0
Lysine-specific demethylase 4C	KDM4C	Q9H3R0	CHEMBL6175	Eraser		1 / 0
Thyroid hormone receptor alpha	THRA	P10827	CHEMBL1860	Nuclear receptor		1 / 0
Thyroid hormone receptor beta-1	THRB	P10828	CHEMBL1947	Nuclear receptor		1 / 0
Heat shock protein HSP 90-alpha	HSP90AA1	P07900	CHEMBL3880	Other cytosolic protein		1 / 0
Matrix metalloproteinase 9	MMP9	P14780	CHEMBL321	Protease		2 / 0
Matrix metalloproteinase 1	MMP1	P03956	CHEMBL332	Protease		1 / 0
Matrix metalloproteinase 2	MMP2	P08253	CHEMBL333	Protease		2 / 0
Matrix metalloproteinase 8	MMP8	P22894	CHEMBL4588	Protease		1 / 0

Figure 1. Swiss target prediction of UA



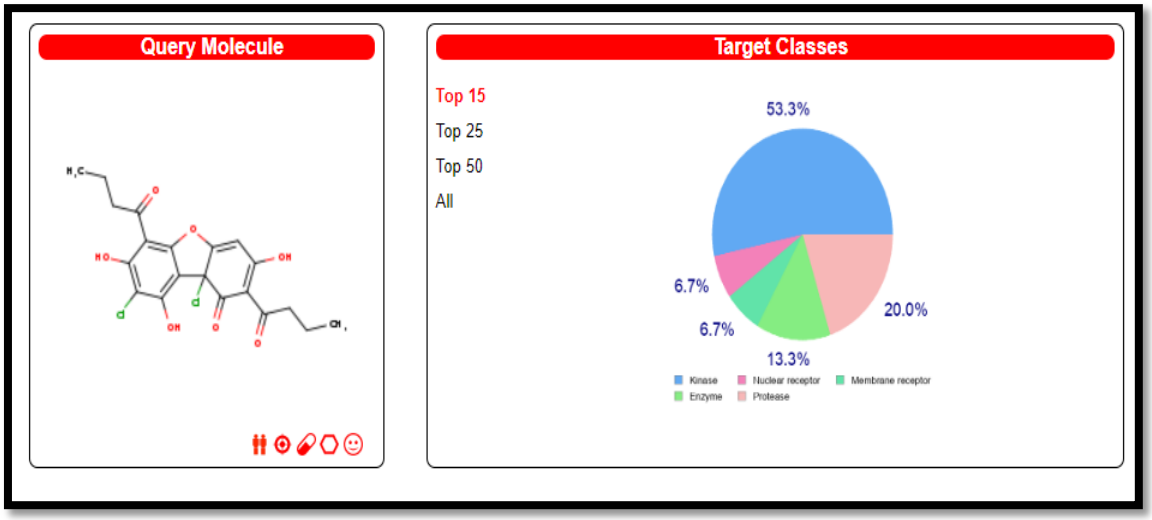
Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Protein kinase C gamma	PRKCG	P05129	CHEMBL2938	Kinase		15 / 1
Protein kinase C alpha	PRKCA	P17252	CHEMBL299	Kinase		17 / 1
Protein kinase C beta	PRKCB	P05771	CHEMBL3045	Kinase		18 / 1
Peroxisome proliferator-activated receptor gamma	PPARG	P37231	CHEMBL235	Nuclear receptor		0 / 17
MAP kinase signal-integrating kinase 2	MKNK2	Q9HBH9	CHEMBL4204	Kinase		1 / 1
MAP kinase-interacting serine/threonine-protein kinase MNK1	MKNK1	Q9BUB5	CHEMBL4718	Kinase		1 / 1
Matrix metalloproteinase 9	MMP9	P14780	CHEMBL321	Protease		2 / 0
Matrix metalloproteinase 1	MMP1	P03956	CHEMBL332	Protease		1 / 0
Matrix metalloproteinase 2	MMP2	P08253	CHEMBL333	Protease		3 / 0
Matrix metalloproteinase 8	MMP8	P22894	CHEMBL4588	Protease		1 / 0
Interleukin-8 receptor B	CXCR2	P25025	CHEMBL2434	Family A G protein-coupled receptor		28 / 0
Protein kinase C delta	PRKCD	Q05655	CHEMBL2996	Kinase		14 / 0
Protein kinase C epsilon	PRKCE	Q02156	CHEMBL3582	Kinase		16 / 0
Protein kinase C eta	PRKCH	P24723	CHEMBL3616	Kinase		13 / 0
Egl nine homolog 1	EGLN1	Q9GZT9	CHEMBL5697	Oxidoreductase		53 / 0

Figure 2. Swiss target prediction of UA1



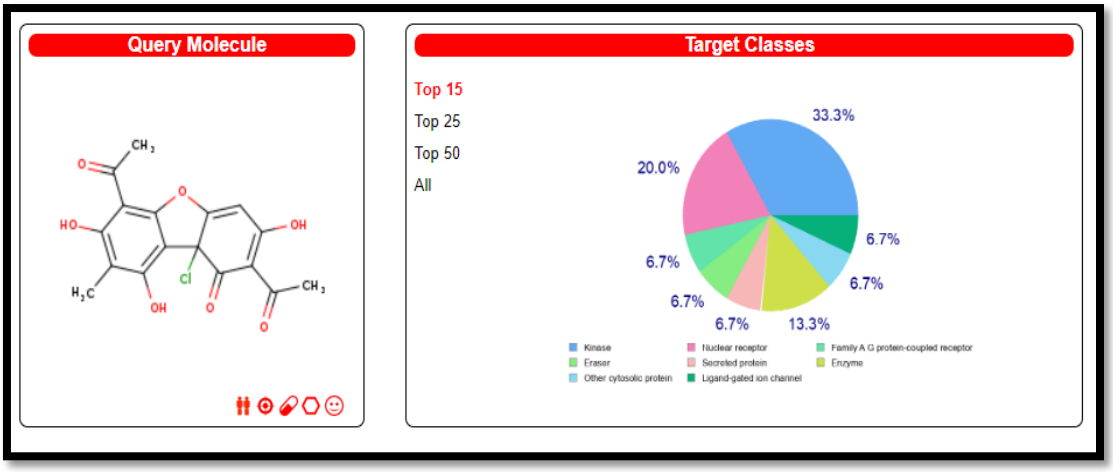
Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Kn act (3D
Protein kinase C gamma	PRKCG	P05129	CHEMBL2938	Kinase		16
Protein kinase C alpha	PRKCA	P17252	CHEMBL299	Kinase		19
Protein kinase C beta	PRKCB	P05771	CHEMBL3045	Kinase		20
Peroxisome proliferator-activated receptor gamma	PPARG	P37231	CHEMBL235	Nuclear receptor		0 /
MAP kinase signal-integrating kinase 2	MKNK2	Q9HBH9	CHEMBL4204	Kinase		1
MAP kinase-interacting serine/threonine-protein kinase MNK1	MKNK1	Q9BUB5	CHEMBL4718	Kinase		1
Matrix metalloproteinase 9	MMP9	P14780	CHEMBL321	Protease		2
Matrix metalloproteinase 1	MMP1	P03956	CHEMBL332	Protease		1
Matrix metalloproteinase 2	MMP2	P08253	CHEMBL333	Protease		3
Matrix metalloproteinase 8	MMP8	P22894	CHEMBL4588	Protease		1
PI3-kinase p110-alpha subunit	PIK3CA	P42336	CHEMBL4005	Enzyme		7
Interleukin-8 receptor B	CXCR2	P25025	CHEMBL2434	Family A G protein-coupled receptor		27
Protein kinase C delta	PRKCD	Q05655	CHEMBL2996	Kinase		15
Protein kinase C epsilon	PRKCE	Q02156	CHEMBL3582	Kinase		18
Protein kinase C eta	PRKCH	P24723	CHEMBL3616	Kinase		15

Figure 3. Swiss target prediction of UA2



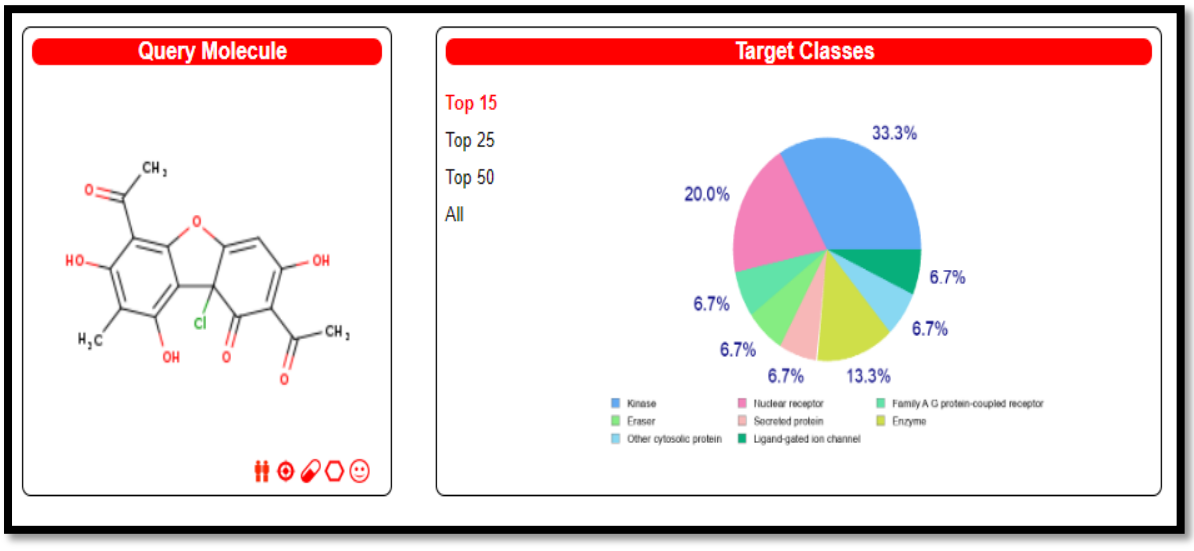
Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Protein kinase C gamma	PRKCG	P05129	CHEMBL2938	Kinase		16 / 1
Protein kinase C alpha	PRKCA	P17252	CHEMBL299	Kinase		19 / 1
Protein kinase C beta	PRKCB	P05771	CHEMBL3045	Kinase		20 / 1
Peroxisome proliferator-activated receptor gamma	PPARG	P37231	CHEMBL235	Nuclear receptor		0 / 17
MAP kinase signal-integrating kinase 2	MKNK2	Q9HBH9	CHEMBL4204	Kinase		1 / 1
MAP kinase-interacting serine/threonine-protein kinase MNK1	MKNK1	Q9BUB5	CHEMBL4718	Kinase		1 / 1
Matrix metalloproteinase 9	MMP9	P14780	CHEMBL321	Protease		2 / 0
Matrix metalloproteinase 1	MMP1	P03956	CHEMBL332	Protease		1 / 0
Matrix metalloproteinase 2	MMP2	P08253	CHEMBL333	Protease		3 / 0
Matrix metalloproteinase 8	MMP8	P22894	CHEMBL4588	Protease		1 / 0
PI3-kinase p110-alpha subunit	PIK3CA	P42336	CHEMBL4005	Enzyme		7 / 0
Interleukin-8 receptor B	CXCR2	P25025	CHEMBL2434	Family A G protein-coupled receptor		27 / 0
Protein kinase C delta	PRKCD	Q05655	CHEMBL2996	Kinase		15 / 0
Protein kinase C epsilon	PRKCE	Q02156	CHEMBL3582	Kinase		18 / 0
Protein kinase C eta	PRKCH	P24723	CHEMBL3616	Kinase		15 / 0

Figure 4. Swiss target prediction of UA3



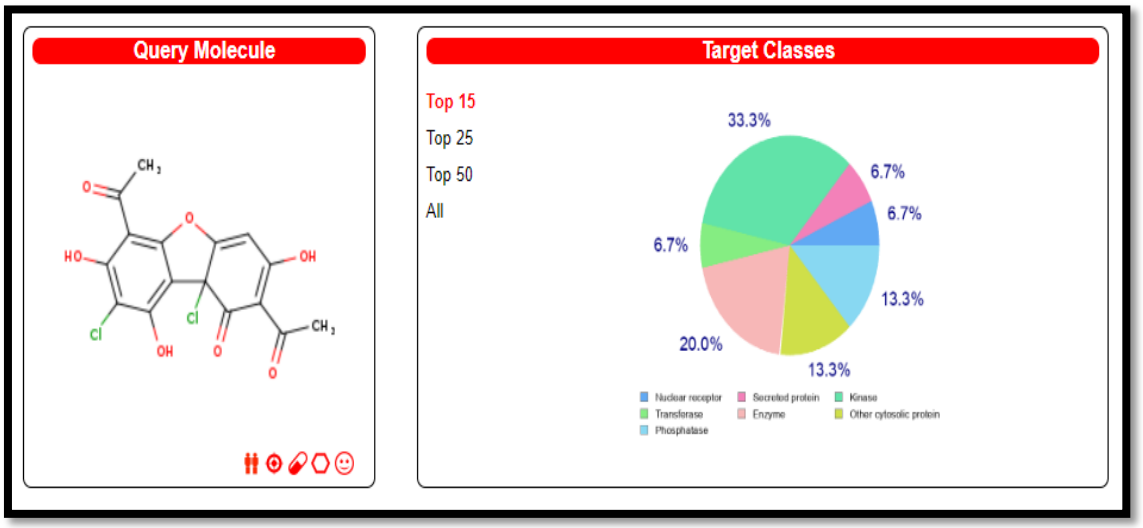
Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
MAP kinase signal-integrating kinase 2	MKNK2	Q9HBH9	CHEMBL4204	Kinase		1 / 1
MAP kinase-interacting serine/threonine-protein kinase MNK1	MKNK1	Q9BUB5	CHEMBL4718	Kinase		1 / 1
Peroxisome proliferator-activated receptor gamma	PPARG	P37231	CHEMBL235	Nuclear receptor		0 / 15
Protein kinase C gamma	PRKCG	P05129	CHEMBL2938	Kinase		1 / 1
Protein kinase C alpha	PRKCA	P17252	CHEMBL299	Kinase		1 / 1
Protein kinase C beta	PRKCB	P05771	CHEMBL3045	Kinase		1 / 1
Insulin-like growth factor binding protein 3	IGFBP3	P17936	CHEMBL3997	Secreted protein		3 / 0
Lysine-specific demethylase 4C	KDM4C	Q9H3R0	CHEMBL6175	Eraser		1 / 0
Estradiol 17-beta-dehydrogenase 2	HSD17B2	P37059	CHEMBL2789	Enzyme		4 / 0
Estradiol 17-beta-dehydrogenase 1	HSD17B1	P14061	CHEMBL3181	Enzyme		4 / 0
Interleukin-8 receptor B	CXCR2	P25025	CHEMBL2434	Family A G protein-coupled receptor		8 / 0
Thyroid hormone receptor alpha	THRA	P10827	CHEMBL1860	Nuclear receptor		1 / 0
Thyroid hormone receptor beta-1	THRB	P10828	CHEMBL1947	Nuclear receptor		1 / 0
Heat shock protein HSP 90-alpha	HSP90AA1	P07900	CHEMBL3880	Other cytosolic protein		1 / 0
Catechol O-methyltransferase	COMT	P21964	CHEMBL2023	Transferase		15 / 0

Figure 5. Swiss target prediction of UA4



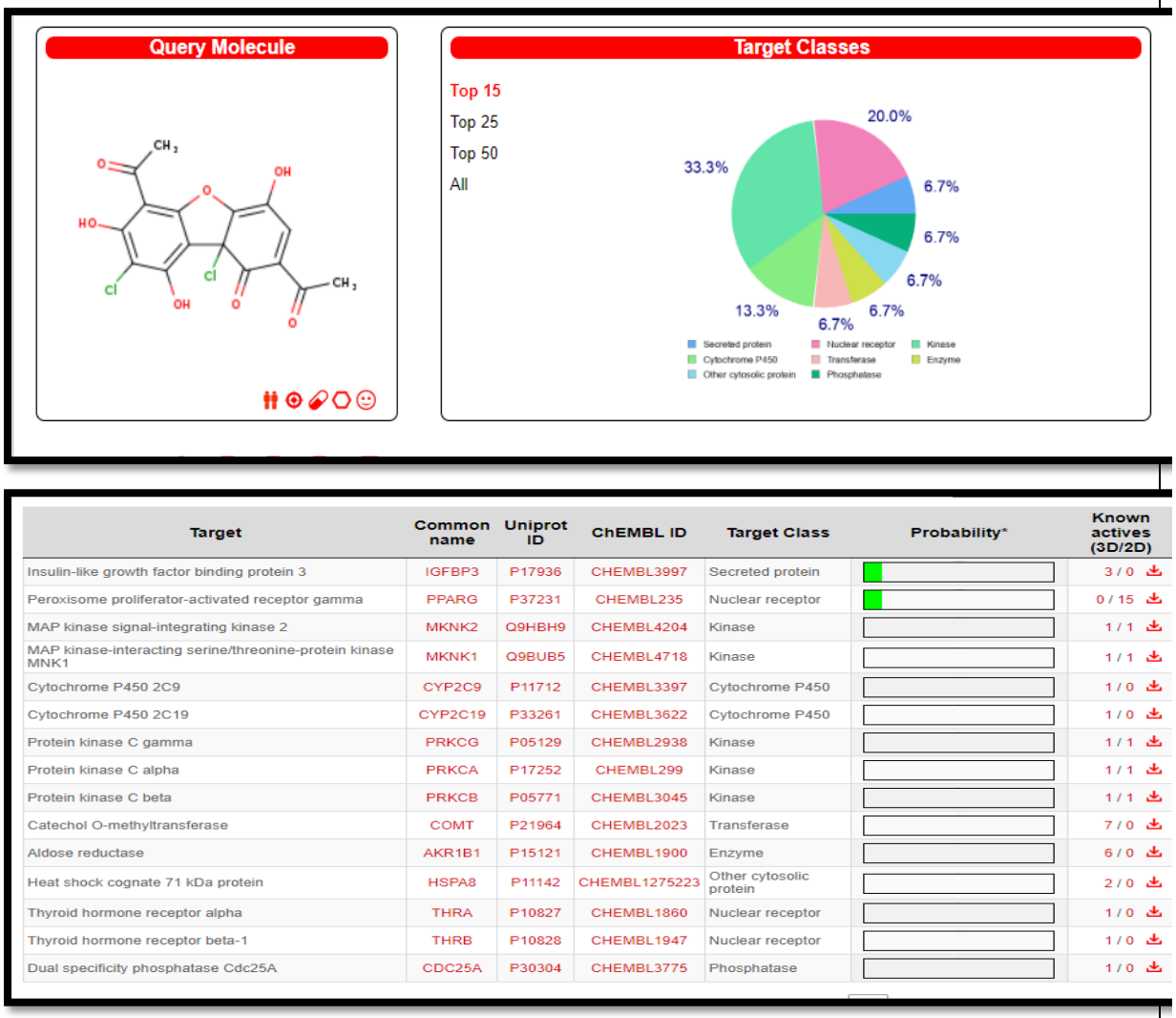
Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
MAP kinase signal-integrating kinase 2	MKNK2	Q9HBH9	CHEMBL4204	Kinase		1 / 1
MAP kinase-interacting serine/threonine-protein kinase MNK1	MKNK1	Q9BUB5	CHEMBL4718	Kinase		1 / 1
Protein kinase C gamma	PRKCG	P05129	CHEMBL2938	Kinase		1 / 1
Protein kinase C alpha	PRKCA	P17252	CHEMBL299	Kinase		2 / 1
Protein kinase C beta	PRKCB	P05771	CHEMBL3045	Kinase		2 / 1
Peroxisome proliferator-activated receptor gamma	PPARG	P37231	CHEMBL235	Nuclear receptor		0 / 15
Interleukin-8 receptor B	CXCR2	P25025	CHEMBL2434	Family A G protein-coupled receptor		11 / 0
Lysine-specific demethylase 4C	KDM4C	Q9H3R0	CHEMBL6175	Eraser		1 / 0
Insulin-like growth factor binding protein 3	IGFBP3	P17936	CHEMBL3997	Secreted protein		3 / 0
Flap endonuclease 1	FEN1	P39748	CHEMBL5027	Enzyme		2 / 0
Heat shock protein HSP 90-alpha	HSP90AA1	P07900	CHEMBL3880	Other cytosolic protein		1 / 0
Thyroid hormone receptor alpha	THRA	P10827	CHEMBL1860	Nuclear receptor		1 / 0
Thyroid hormone receptor beta-1	THRB	P10828	CHEMBL1947	Nuclear receptor		1 / 0
P2X purinoceptor 3	P2RX3	P56373	CHEMBL2998	Ligand-gated ion channel		4 / 0
Peptidyl-prolyl cis-trans isomerase NIMA-interacting 1	PIN1	Q13526	CHEMBL2288	Enzyme		2 / 0

Figure 6. Swiss target prediction of UA5



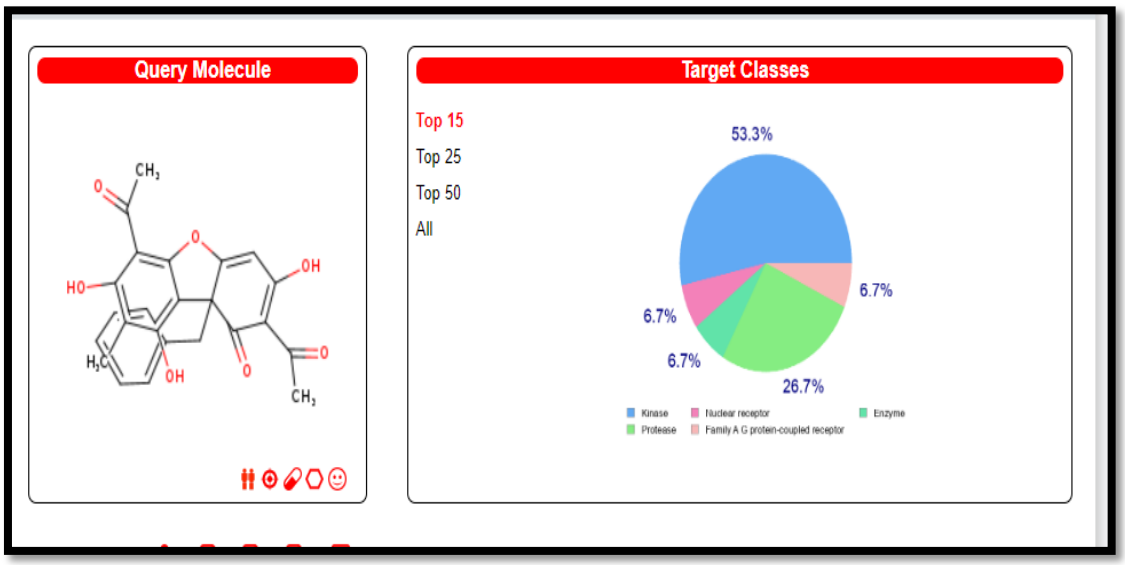
Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Peroxisome proliferator-activated receptor gamma	PPARG	P37231	CHEMBL235	Nuclear receptor		0 / 15
Insulin-like growth factor binding protein 3	IGFBP3	P17936	CHEMBL3997	Secreted protein		3 / 0
MAP kinase signal-integrating kinase 2	MKNK2	Q9HBH9	CHEMBL4204	Kinase		1 / 1
MAP kinase-interacting serine/threonine-protein kinase MNK1	MKNK1	Q9BUB5	CHEMBL4718	Kinase		1 / 1
Protein kinase C gamma	PRKCG	P05129	CHEMBL2938	Kinase		1 / 1
Protein kinase C alpha	PRKCA	P17252	CHEMBL299	Kinase		1 / 1
Protein kinase C beta	PRKCB	P05771	CHEMBL3045	Kinase		1 / 1
Catechol O-methyltransferase	COMT	P21964	CHEMBL2023	Transferase		9 / 0
Estradiol 17-beta-dehydrogenase 2	HSD17B2	P37059	CHEMBL2789	Enzyme		3 / 0
Estradiol 17-beta-dehydrogenase 1	HSD17B1	P14061	CHEMBL3181	Enzyme		3 / 0
Flap endonuclease 1	FEN1	P39748	CHEMBL5027	Enzyme		1 / 0
Heat shock cognate 71 kDa protein	HSPA8	P11142	CHEMBL1275223	Other cytosolic protein		2 / 0
Dual specificity phosphatase Cdc25A	CDC25A	P30304	CHEMBL3775	Phosphatase		1 / 0
Dual specificity phosphatase Cdc25B	CDC25B	P30305	CHEMBL4804	Phosphatase		1 / 0
Heat shock 70 kDa protein 1	HSPA1A	P0DMV8	CHEMBL5460	Other cytosolic protein		2 / 0

Figure 7. Swiss target prediction of UA6



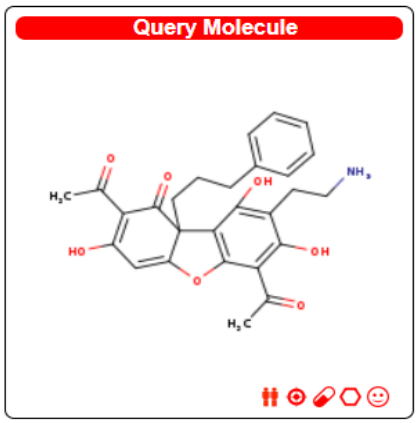
Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Insulin-like growth factor binding protein 3	IGFBP3	P17936	CHEMBL3997	Secreted protein		3 / 0
Peroxisome proliferator-activated receptor gamma	PPARG	P37231	CHEMBL235	Nuclear receptor		0 / 15
MAP kinase signal-integrating kinase 2	MKNK2	Q9HBH9	CHEMBL4204	Kinase		1 / 1
MAP kinase-interacting serine/threonine-protein kinase MNK1	MKNK1	Q9BUB5	CHEMBL4718	Kinase		1 / 1
Cytochrome P450 2C9	CYP2C9	P11712	CHEMBL3397	Cytochrome P450		1 / 0
Cytochrome P450 2C19	CYP2C19	P33261	CHEMBL3622	Cytochrome P450		1 / 0
Protein kinase C gamma	PRKCG	P05129	CHEMBL2938	Kinase		1 / 1
Protein kinase C alpha	PRKCA	P17252	CHEMBL299	Kinase		1 / 1
Protein kinase C beta	PRKCB	P05771	CHEMBL3045	Kinase		1 / 1
Catechol O-methyltransferase	COMT	P21964	CHEMBL2023	Transferase		7 / 0
Aldose reductase	AKR1B1	P15121	CHEMBL1900	Enzyme		6 / 0
Heat shock cognate 71 kDa protein	HSPA8	P11142	CHEMBL1275223	Other cytosolic protein		2 / 0
Thyroid hormone receptor alpha	THRA	P10827	CHEMBL1860	Nuclear receptor		1 / 0
Thyroid hormone receptor beta-1	THRB	P10828	CHEMBL1947	Nuclear receptor		1 / 0
Dual specificity phosphatase Cdc25A	CDC25A	P30304	CHEMBL3775	Phosphatase		1 / 0

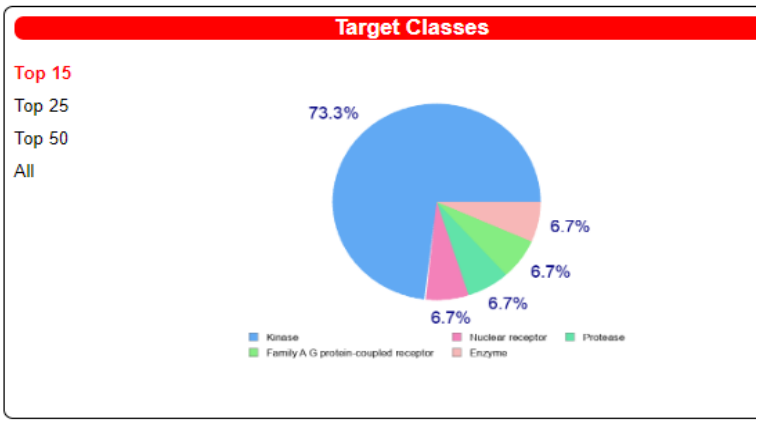
Figure 8. Swiss target prediction of UA7



Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Protein kinase C gamma	PRKCG	P05129	CHEMBL2938	Kinase		27 / 1
Protein kinase C alpha	PRKCA	P17252	CHEMBL299	Kinase		30 / 1
Protein kinase C beta	PRKCB	P05771	CHEMBL3045	Kinase		30 / 1
MAP kinase signal-integrating kinase 2	MKNK2	Q9HBH9	CHEMBL4204	Kinase		0 / 1
MAP kinase-interacting serine/threonine-protein kinase MNK1	MKNK1	Q9BUB5	CHEMBL4718	Kinase		0 / 1
Peroxisome proliferator-activated receptor gamma	PPARG	P37231	CHEMBL235	Nuclear receptor		0 / 17
Protein kinase C delta	PRKCD	Q05655	CHEMBL2996	Kinase		27 / 0
Protein kinase C epsilon	PRKCE	Q02156	CHEMBL3582	Kinase		29 / 0
Protein kinase C eta	PRKCH	P24723	CHEMBL3616	Kinase		26 / 0
PI3-kinase p110-alpha subunit	PIK3CA	P42336	CHEMBL4005	Enzyme		6 / 0
Matrix metalloproteinase 9	MMP9	P14780	CHEMBL321	Protease		2 / 0
Matrix metalloproteinase 1	MMP1	P03956	CHEMBL332	Protease		1 / 0
Matrix metalloproteinase 2	MMP2	P08253	CHEMBL333	Protease		3 / 0
Matrix metalloproteinase 8	MMP8	P22894	CHEMBL4588	Protease		1 / 0
Interleukin-8 receptor B	CXCR2	P25025	CHEMBL2434	Family A G protein-coupled receptor		24 / 0

Figure 9. Swiss target prediction of UA8

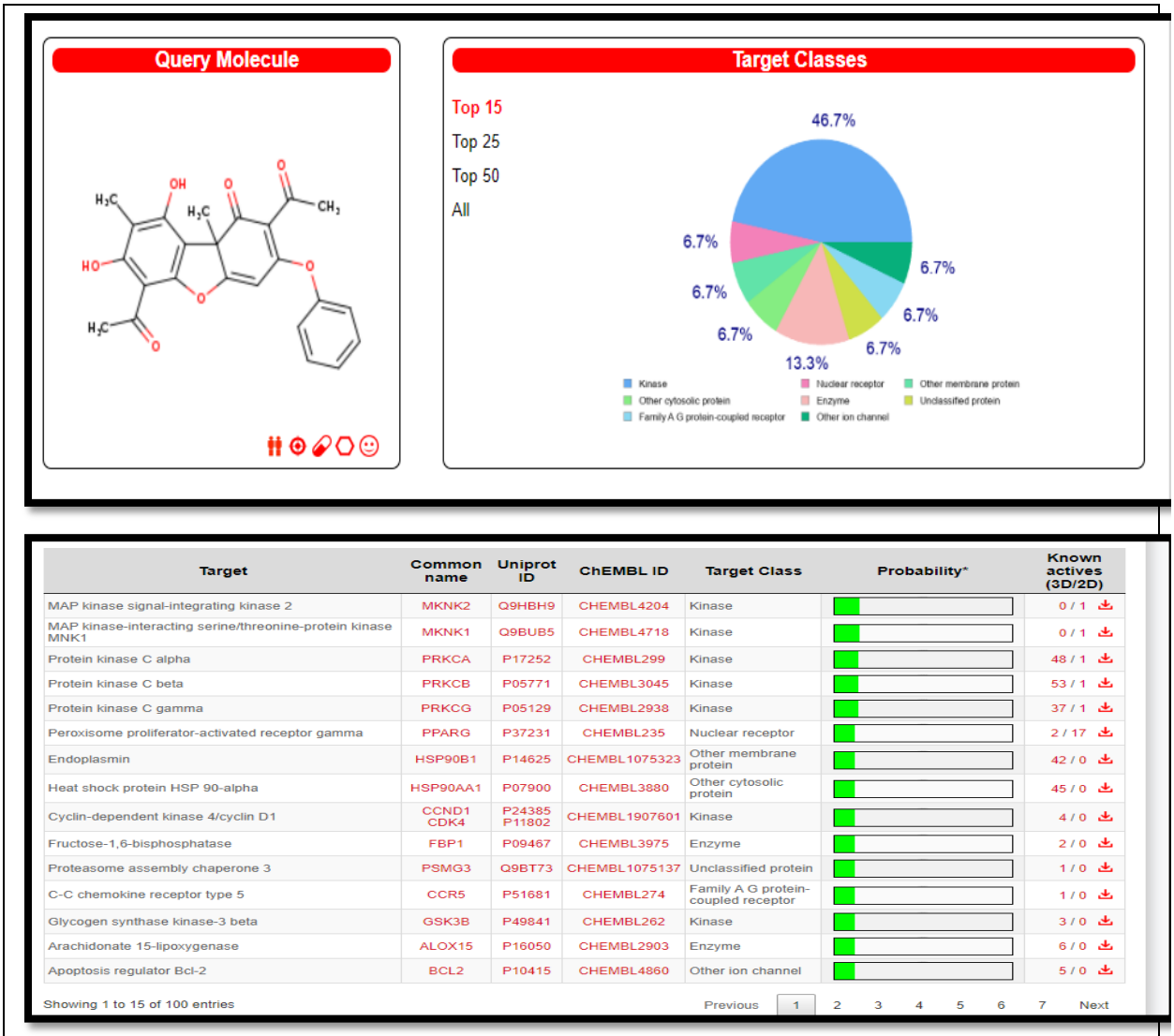




Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Protein kinase C gamma	PRKCG	P05129	CHEMBL2938	Kinase		72 / 1
Protein kinase C alpha	PRKCA	P17252	CHEMBL299	Kinase		83 / 1
Protein kinase C beta	PRKCB	P05771	CHEMBL3045	Kinase		91 / 1
MAP kinase signal-integrating kinase 2	MKNK2	Q9HBH9	CHEMBL4204	Kinase		0 / 1
MAP kinase-interacting serine/threonine-protein kinase MNK1	MKNK1	Q9BUB5	CHEMBL4718	Kinase		0 / 1
Peroxisome proliferator-activated receptor gamma	PPARG	P37231	CHEMBL235	Nuclear receptor		0 / 17
Protein kinase C delta	PRKCD	Q05655	CHEMBL2996	Kinase		79 / 0
Protein kinase C (PKC)	PRKCZ	Q05513	CHEMBL3438	Kinase		12 / 0
Protein kinase C epsilon	PRKCE	Q02156	CHEMBL3582	Kinase		80 / 0
Protein kinase C eta	PRKCH	P24723	CHEMBL3616	Kinase		74 / 0
Thrombin and coagulation factor X	F10	P00742	CHEMBL244	Protease		38 / 0
cAMP-dependent protein kinase alpha-catalytic subunit	PRKACA	P17612	CHEMBL4101	Kinase		20 / 0
Interleukin-8 receptor B	CXCR2	P25025	CHEMBL2434	Family A G protein-coupled receptor		13 / 0
Aldose reductase *(by homology)*	AKR1B1	P15121	CHEMBL1900	Enzyme		6 / 0
Serine/threonine-protein kinase AKT	AKT1	P31749	CHEMBL4282	Kinase		3 / 0

Showing 1 to 15 of 100 entries Previous 1 2 3 4 5 6 7 Ne

Figure 10. Swiss target prediction of UA9



Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
MAP kinase signal-integrating kinase 2	MKNK2	Q9HBH9	CHEMBL4204	Kinase		0 / 1
MAP kinase-interacting serine/threonine-protein kinase MNK1	MKNK1	Q9BUB5	CHEMBL4718	Kinase		0 / 1
Protein kinase C alpha	PRKCA	P17252	CHEMBL299	Kinase		48 / 1
Protein kinase C beta	PRKCB	P05771	CHEMBL3045	Kinase		53 / 1
Protein kinase C gamma	PRKCG	P05129	CHEMBL2938	Kinase		37 / 1
Peroxisome proliferator-activated receptor gamma	PPARG	P37231	CHEMBL235	Nuclear receptor		2 / 17
Endoplasmin	HSP90B1	P14625	CHEMBL1075323	Other membrane protein		42 / 0
Heat shock protein HSP 90-alpha	HSP90AA1	P07900	CHEMBL3880	Other cytosolic protein		45 / 0
Cyclin-dependent kinase 4/cyclin D1	CCND1 CDK4	P24385 P11802	CHEMBL1907601	Kinase		4 / 0
Fructose-1,6-bisphosphatase	FBP1	P09467	CHEMBL3975	Enzyme		2 / 0
Proteasome assembly chaperone 3	PSMG3	Q9BT73	CHEMBL1075137	Unclassified protein		1 / 0
C-C chemokine receptor type 5	CCR5	P51681	CHEMBL274	Family A G protein-coupled receptor		1 / 0
Glycogen synthase kinase-3 beta	GSK3B	P49841	CHEMBL262	Kinase		3 / 0
Arachidonate 15-lipoxygenase	ALOX15	P16050	CHEMBL2903	Enzyme		6 / 0
Apoptosis regulator Bcl-2	BCL2	P10415	CHEMBL4860	Other ion channel		5 / 0

Showing 1 to 15 of 100 entries Previous 1 2 3 4 5 6 7 Next

Figure 11. Swiss target prediction of UA10

Analysis of Swiss target prediction

All the studied molecules (Figure 1-11.), except UA6 and UA7, show effective binding for the enzyme kinase that catalyzes the transfer of phosphate groups from high-energy, phosphate-donating molecules to specific substrates. UA6 has high binding percentage for the enzyme nuclear receptor which directly regulate transcription of genes that control a wide variety of biological processes, including cell proliferation, development, metabolism, and reproduction. UA7 has high binding percentage for the enzymes secreted protein and nuclear receptor.

CONCLUSION:

All the selected compounds, except UA9, exhibit high GI absorption, indicating their potential for usage as oral medications. Not every chemical has BBB penetration. They cannot therefore be used for illnesses relating to the brain. The log P value for molecules UA1, UA2, UA3, UA8, UA9, and UA10 is larger than 2, indicating that they are unable to reach the central nervous system. The remaining compounds, with the exception of UA6 and

UA7, exhibit efficient binding for the kinase enzyme, which catalyzes the transfer of phosphate groups from high-energy, phosphate-donating molecules to particular substrates. The nuclear receptor enzyme, which directly controls the transcription of genes that govern a wide range of biological activities, including cell proliferation, development, metabolism, and reproduction, is bound by UA6 with a high percentage. UA7 binds to nuclear receptors and secreted proteins with a high proportion. The fact that all of the compounds have positive nuclear receptor interaction values indicates that they play a part in gene creation, which may have an impact on reproduction and anti-carcinogenic properties.

REFERENCES:

i. Liu R. H.; Potential synergy of phytochemicals in cancer prevention: mechanism of action; J. Nutri, 2004, **134**, 12.
ii. Marijana K.; Branislav; Ranković; Tatjana S.; Perica V. and Nedeljko M.; Biological activities and chemical composition of lichens from Serbia; Excli. J., 2014, **13**, 1226.
iii. Ingólfsdóttir K.; Usnic acid; Phytochemistry, 2002, **61**, 7, 729.
iv. Wojciech P.; Irma P.; Marta G.; Paweł P.; Karolina, G., and Agnieszka, G., Inflammation and Natural Products; Life; 2023, **13**, 1046.
v. https://www.acs.org/molecule-of-the-week/archive/u/usnic-acid.html
vi. Olimathi A.; Akilandeswari L. and Kalpana P.; Medicinal Properties of Usnic Acid and Its Analogues - A SwissADME Study; IJCRT; 2025, **13** (3), 654.
vii. https://www.molsoft.com/about.html
viii. www.molinspiration.com
ix. Daina A.; Michielin O. and Zoete V.; SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules; Sci. Rep. 2017, **7**, 42717.
x. http://www.swissadme.ch/
xi. http://www.swisstargetprediction.ch

Received on April 9, 2025