Rheum rhaponticum and Rheum rhabarbarum Extracts As Modulators of Endothelial Cell Inflammatory Response

Oleksandra Liudvytska [1,*], Michał B. Ponczek [1], Oskar Ciesielski [2,3], Justyna Krzyżanowska-Kowalczyk [4], Mariusz Kowalczyk [4], Aneta Balcerczyk [2] and Joanna Kolodziejczyk-Czepas [1]

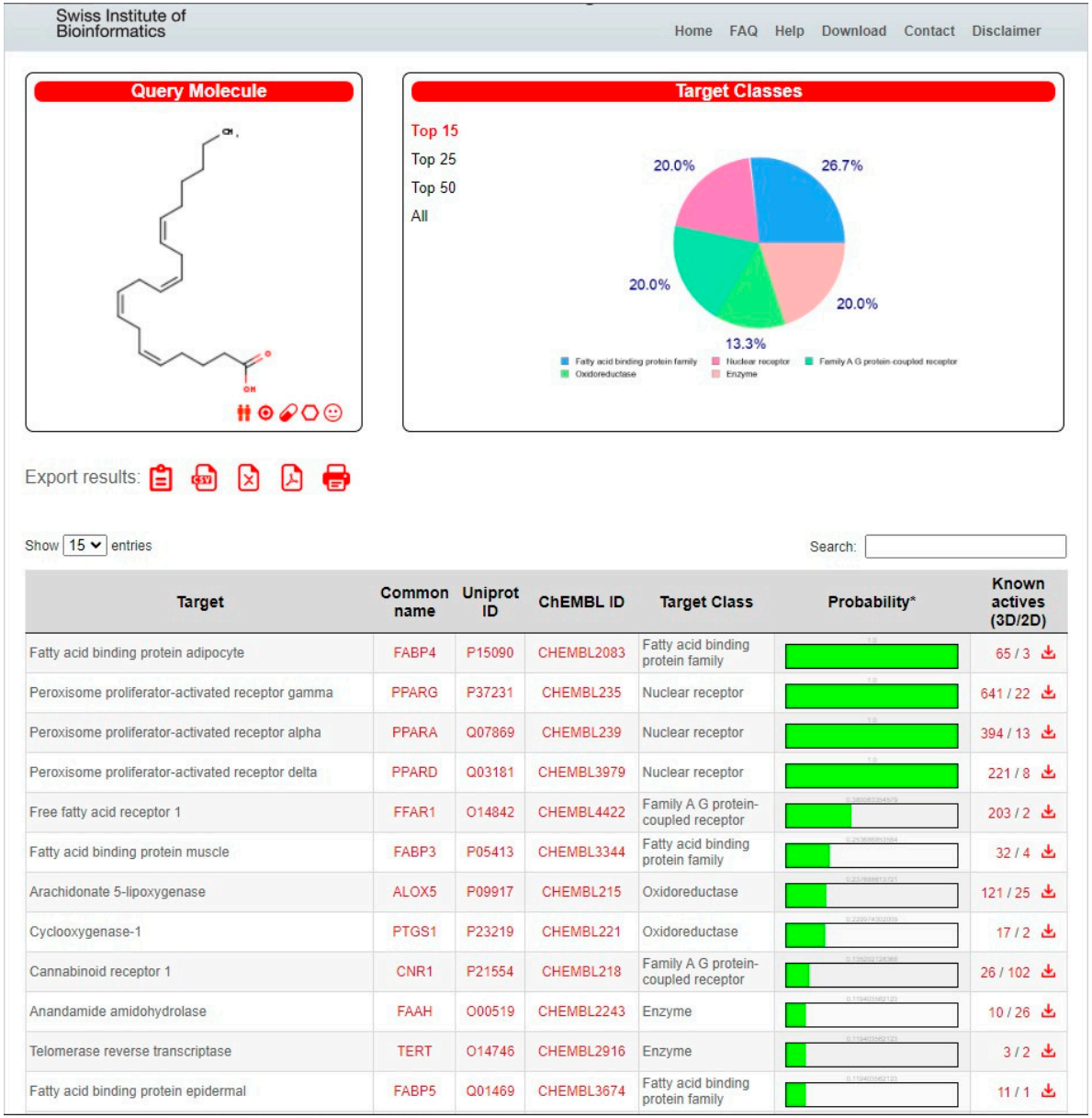
[1] Department of General Biochemistry, Faculty of Biology and Environmental Protection, University of Lodz, 90-236 Lodz, Poland

[2] Department of Sociobiology and Epigenetics, Faculty of Biology and Environmental Protection, University of Lodz, 90-236 Lodz, Poland

[3] The Bio-Med-Chem Doctoral School, University of Lodz and Lodz Institutes of the Polish Academy of Sciences, University of Lodz, Banacha 12/16, 90-237, Lodz, Poland

[4] Department of Biochemistry and Crop Quality, Institute of Soil Science and Plant Cultivation, State Research Institute, Czartoryskich 8, 24-100 Puławy, Poland

***** Correspondence: oleksandra.liudvytska@biol.uni.lodz.pl; Tel.: +48-42-635-44-84



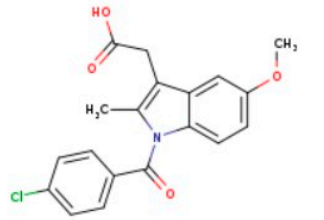
arachidonic acid (substrate for both enzymes)

SIB Swiss Institute of Bioinformatics

SwissTargetPrediction

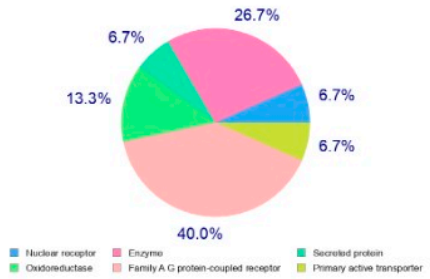
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Query Molecule



Target Classes

Top 15
Top 25
Top 50
All

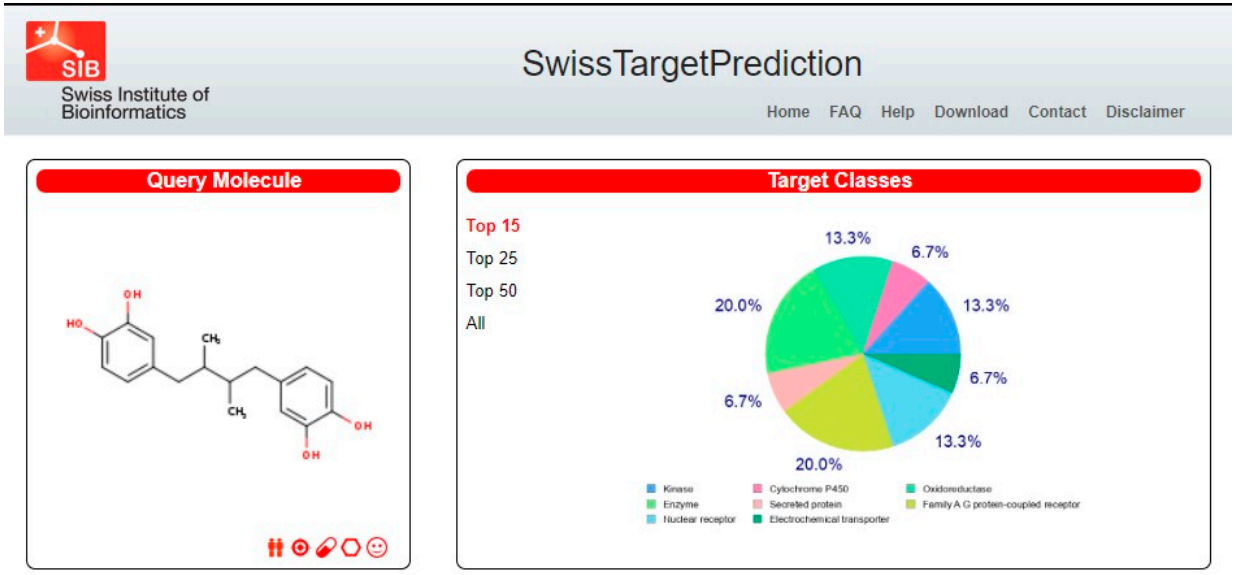


Export results:

Show 15 entries Search:

Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Androgen Receptor	AR	P10275	CHEMBL1871	Nuclear receptor		6 / 4
Aldose reductase	AKR1B1	P15121	CHEMBL1900	Enzyme		395 / 12
Interleukin-8	CXCL8	P10145	CHEMBL2157	Secreted protein		12 / 1
Cyclooxygenase-1	PTGS1	P23219	CHEMBL221	Oxidoreductase		59 / 32
Cyclooxygenase-2	PTGS2	P35354	CHEMBL230	Oxidoreductase		155 / 179
Aldo-keto-reductase family 1 member C3	AKR1C3	P42330	CHEMBL4681	Enzyme		172 / 55
G protein-coupled receptor 44	PTGDR2	Q9Y5Y4	CHEMBL5071	Family A G protein-coupled receptor		1115 / 341
Nitric oxide synthase, inducible *(by homology)*	NOS2	P35228	CHEMBL4481	Enzyme		2 / 1
P-glycoprotein 1	ABCB1	P08183	CHEMBL4302	Primary active transporter		1 / 20
Prostanoid DP receptor	PTGDR	Q13258	CHEMBL4427	Family A G protein-coupled receptor		148 / 90

Indomethacin (COX-2 inhibitor)



Export results:

Show 15 entries Search:

Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Insulin-like growth factor I receptor	IGF1R	P08069	CHEMBL1957	Kinase		23 / 14
Cytochrome P450 19A1	CYP19A1	P11511	CHEMBL1978	Cytochrome P450		43 / 47
Arachidonate 5-lipoxygenase	ALOX5	P09917	CHEMBL215	Oxidoreductase		31 / 18
Arachidonate 15-lipoxygenase	ALOX15	P16050	CHEMBL2903	Enzyme		27 / 17
Transthyretin	TTR	P02766	CHEMBL3194	Secreted protein		2 / 2
Arachidonate 12-lipoxygenase	ALOX12	P18054	CHEMBL3687	Enzyme		10 / 9
Leukotriene B4 receptor 1	LTB4R	Q15722	CHEMBL3911	Family A G protein-coupled receptor		3 / 1
Cyclooxygenase-2	PTGS2	P35354	CHEMBL230	Oxidoreductase		31 / 10
Estrogen receptor alpha	ESR1	P03372	CHEMBL206	Nuclear receptor		360 / 92

NDGA (COX-2 and 5-LOX inhibitor)

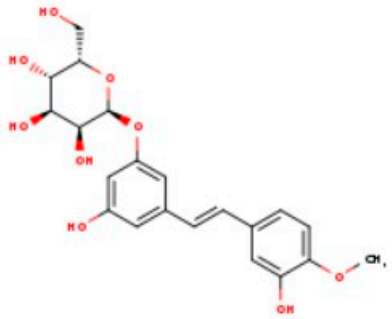
SwissDrugDesign | SwissDock SwissParam SwissSidechain SwissBioisostere **SwissTargetPrediction** SwissADME SwissSimilarity | About us

SIB Swiss Institute of Bioinformatics

SwissTargetPrediction

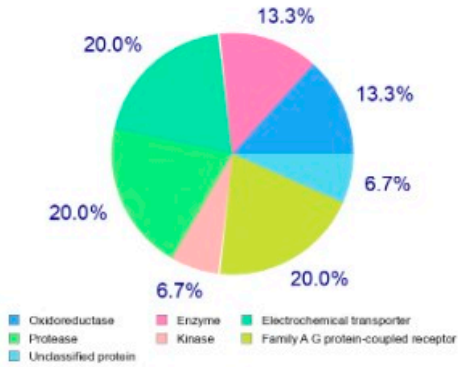
Home FAQ Help Download Contact Disclaimer

Query Molecule



Target Classes

Top 15
Top 25
Top 50
All



Export results:

Show 15 entries

Search: oxy

Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Cyclooxygenase-1	PTGS1	P23219	CHEMBL221	Oxidoreductase		0 / 3
Cyclooxygenase-2	PTGS2	P35354	CHEMBL230	Oxidoreductase		5 / 2
Hydroxycarboxylic acid receptor 2	HCAR2	Q8TDS4	CHEMBL3785	Family A G protein-coupled receptor		45 / 0

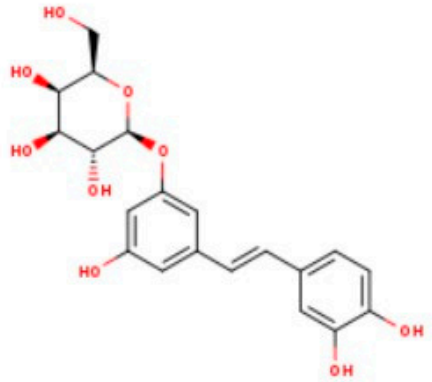
rhaponticin
(rhapontin)

Swiss Institute of Bioinformatics

SwissTargetPrediction

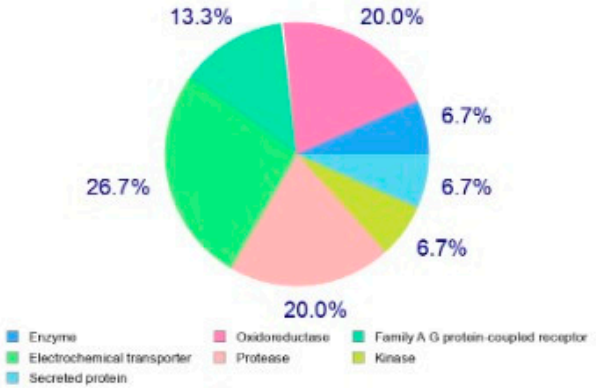
Home FAQ Help Download Contact Disclaimer

Query Molecule



Target Classes

Top 15
Top 25
Top 50
All



astringin

Export results:

Show 15 entries

Search: oxygen

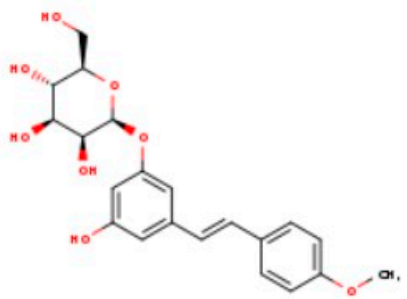
Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Cyclooxygenase-2	PTGS2	P35354	CHEMBL230	Oxidoreductase		2 / 3
Cyclooxygenase-1	PTGS1	P23219	CHEMBL221	Oxidoreductase		1 / 3

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SwissTargetPrediction

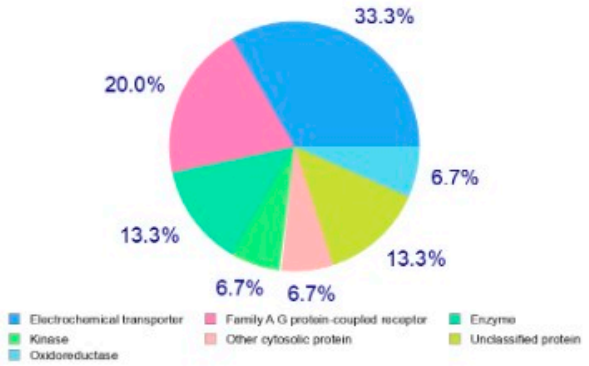
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Query Molecule



Target Classes

Top 15
Top 25
Top 50
All



deoxyrhaponticin

Export results:

Show 15 entries

Search: oxy

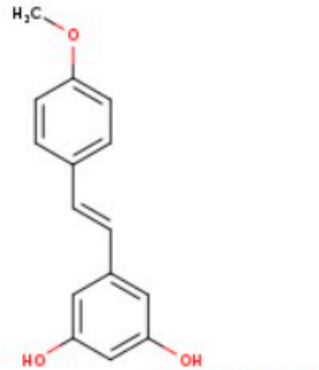
Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Cyclooxygenase-1	PTGS1	P23219	CHEMBL221	Oxidoreductase		0 / 4
Cyclooxygenase-2	PTGS2	P35354	CHEMBL230	Oxidoreductase		1 / 3
Hydroxycarboxylic acid receptor 2	HCAR2	Q8TDS4	CHEMBL3785	Family A G protein-coupled receptor		20 / 0

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SwissTargetPrediction

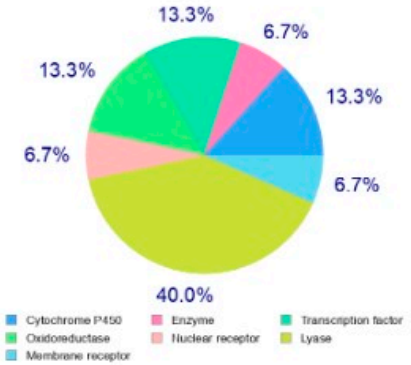
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Query Molecule



Target Classes

Top 15
Top 25
Top 50
All



deoxyrhapontigenin

Export results:

Show 15 entries

Search: oxy

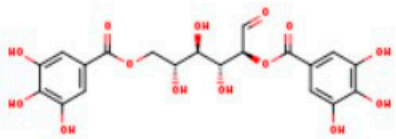
Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Cyclooxygenase-1	PTGS1	P23219	CHEMBL221	Oxidoreductase		20 / 29
Cyclooxygenase-2	PTGS2	P35354	CHEMBL230	Oxidoreductase		33 / 42
Arachidonate 5-lipoxygenase	ALOX5	P09917	CHEMBL215	Oxidoreductase		83 / 23
11-beta-hydroxysteroid dehydrogenase 1	HSD11B1	P28845	CHEMBL4235	Enzyme		23 / 3

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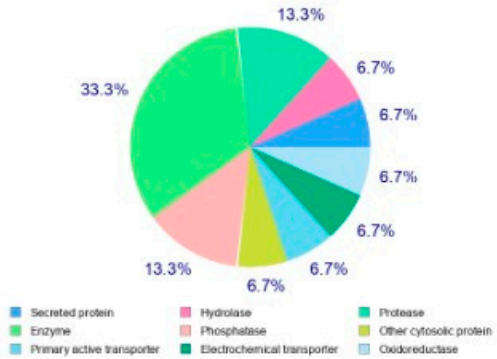
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Query Molecule



Target Classes

Top 15
Top 25
Top 50
All



digalloyl glucoside

Export results:

Show 15 entries

Search: oxy

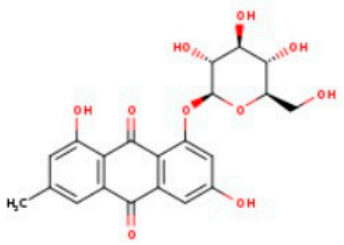
Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Squalene monooxygenase *(by homology)*	SQLE	Q14534	CHEMBL3592	Enzyme		0 / 23
Arachidonate 5-lipoxygenase	ALOX5	P09917	CHEMBL215	Oxidoreductase		0 / 5
Hydroxycarboxylic acid receptor 2	HCAR2	Q8TDS4	CHEMBL3785	Family A G protein-coupled receptor		3 / 0
Cyclooxygenase-2	PTGS2	P35354	CHEMBL230	Oxidoreductase		0 / 5

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SwissTargetPrediction

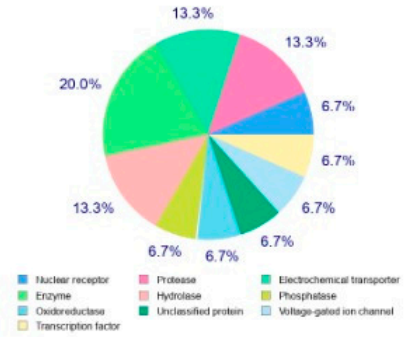
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Query Molecule



Target Classes

Top 15
Top 25
Top 50
All



emodin 8-O-glucoside

Export results:

Show 15 entries

Search: oxy

Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Cyclooxygenase-1 *(by homology)*	Ptgs1	P22437	CHEMBL2649	Enzyme		0 / 2
Cyclooxygenase-2 *(by homology)*	Ptgs2	Q05769	CHEMBL4321	Oxidoreductase		1 / 1

Showing 1 to 2 of 2 entries (filtered from 52 total entries)

Previous 1 Next

*Probability for the query molecule - assumed as bioactive - to have this protein as target.

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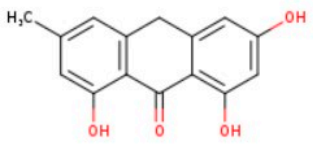
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SwissTargetPrediction

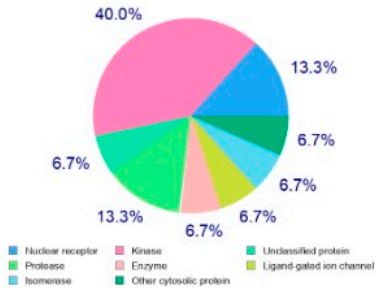
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Query Molecule



Target Classes

Top 15
Top 25
Top 50
All



Export results:

Show 15 entries

Search: oxy

Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
11-beta-hydroxysteroid dehydrogenase 1	Hsd11b1	P50172	CHEMBL3910	Enzyme		12 / 0
Palmitoleoyl-protein carboxylesterase NOTUM *(by homology)*	Notum	Q8R116	CHEMBL3758064	Hydrolase		1 / 0
Arachidonate 5-lipoxygenase-activating protein *(by homology)*	Alox5ap	P30355	CHEMBL3414408	Other cytosolic protein		5 / 0
Hydroxycarboxylic acid receptor 2 *(by homology)*	Hcar2	Q9EP66	CHEMBL4420	Family A G protein-coupled receptor		2 / 0

Showing 1 to 4 of 4 entries (filtered from 100 total entries)

Previous 1 Next

*Probability for the query molecule - assumed as bioactive - to have this protein as target.

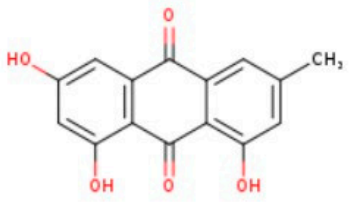
emodin anthrone

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SwissTargetPrediction

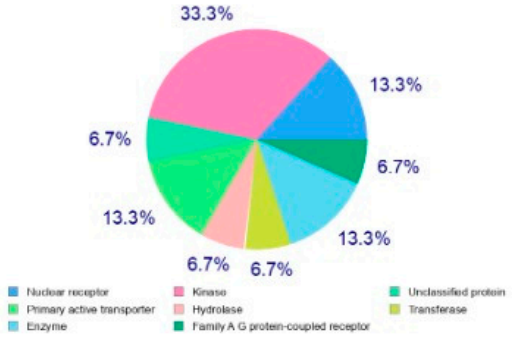
Home FAQ Help Download Contact Disclaimer

Query Molecule



Target Classes

Top 15
Top 25
Top 50
All



Export results:

emodin anthrone

Show 15 entries

Search: oxy

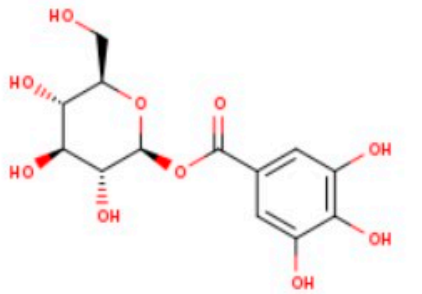
Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Cyclooxygenase-2 *(by homology)*	Ptgs2	Q05769	CHEMBL4321	Oxidoreductase		2 / 4
Cyclooxygenase-1 *(by homology)*	Ptgs1	P22437	CHEMBL2649	Enzyme		0 / 3
Arachidonate 5-lipoxygenase *(by homology)*	Alox5	P48999	CHEMBL5211	Oxidoreductase		4 / 5
Indoleamine 2,3-dioxygenase 1 *(by homology)*	Ido1	P28776	CHEMBL1075294	Enzyme		0 / 1
Arachidonate 12-lipoxygenase	Alox12	P39655	CHEMBL3225	Enzyme		9 / 3
Carboxylesterase 2 *(by homology)*	Ces2c	Q91WG0	CHEMBL2217	Enzyme		1 / 1

SwissTargetPrediction

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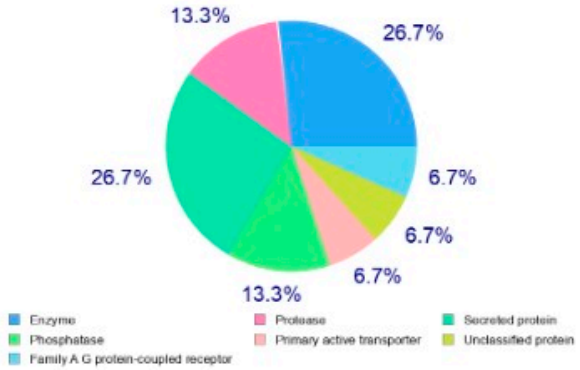
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Query Molecule



Target Classes

Top 15
Top 25
Top 50
All



glucagallin

Export results:

Show 15 entries

Search: oxygen

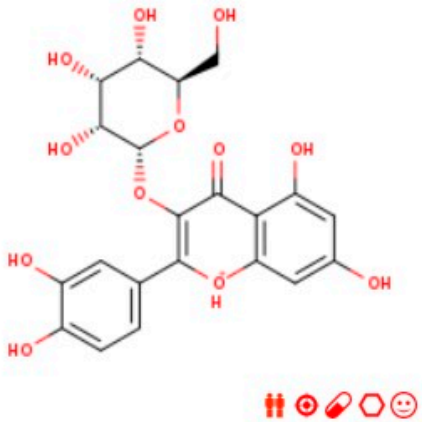
Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Squalene monooxygenase *(by homology)*	SQLE	Q14534	CHEMBL3592	Enzyme		0 / 23
Indoleamine 2,3-dioxygenase	IDO1	P14902	CHEMBL4685	Enzyme		1 / 0
Arachidonate 12-lipoxygenase	ALOX12	P18054	CHEMBL3687	Enzyme		1 / 0

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SwissTargetPrediction

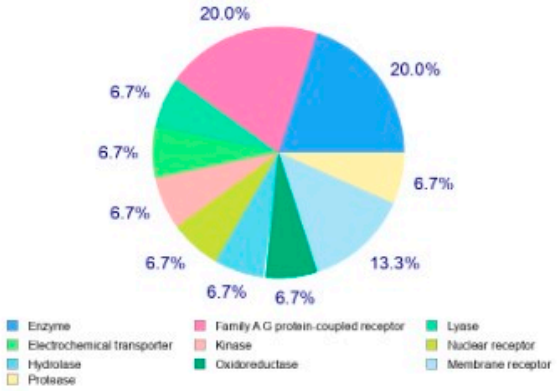
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Query Molecule



Target Classes

Top 15
Top 25
Top 50
All



Isoquercitrin

Export results:

Show 15 entries

Search: oxy

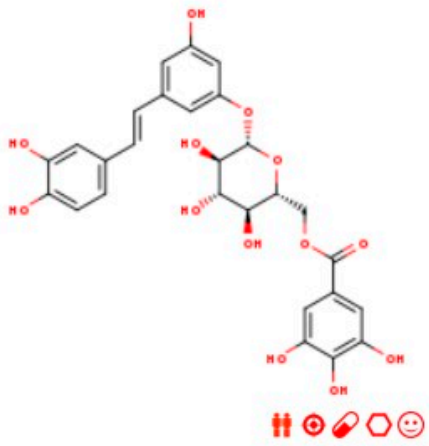
Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Squalene monooxygenase *(by homology)*	SQLE	Q14534	CHEMBL3592	Enzyme		2 / 0
Cyclooxygenase-1	PTGS1	P23219	CHEMBL221	Oxidoreductase		0 / 2
Cyclooxygenase-2	PTGS2	P35354	CHEMBL230	Oxidoreductase		1 / 1

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SwissTargetPrediction

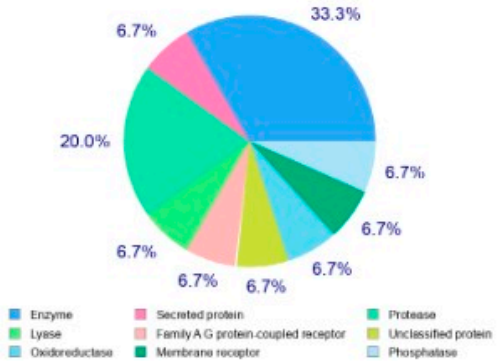
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Query Molecule



Target Classes

Top 15
Top 25
Top 50
All



rhapontigenin-galloyl-glucopyranoside

Export results:

Show 15 entries

Search: oxy

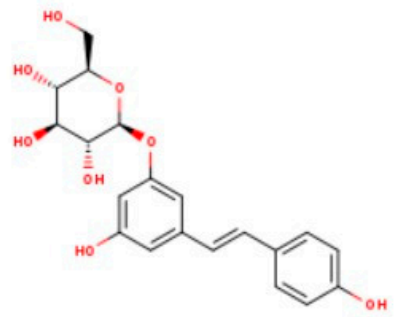
Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Squalene monooxygenase *(by homology)*	SQLE	Q14534	CHEMBL3592	Enzyme		0 / 14
Cyclooxygenase-1	PTGS1	P23219	CHEMBL221	Oxidoreductase		1 / 2
Cyclooxygenase-2	PTGS2	P35354	CHEMBL230	Oxidoreductase		2 / 5

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SwissTargetPrediction

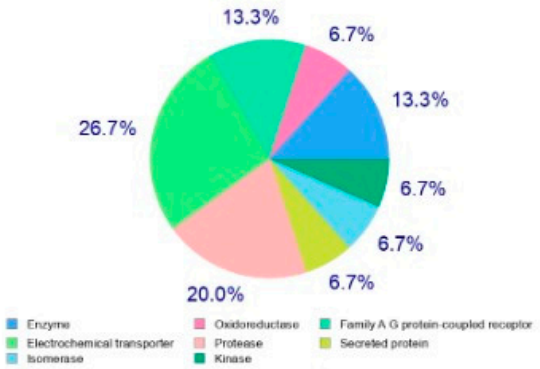
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Query Molecule



Target Classes

Top 15
Top 25
Top 50
All



piceid

Export results:

Show 15 entries

Search: oxy

Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Hydroxycarboxylic acid receptor 2	HCAR2	Q8TDS4	CHEMBL3785	Family A G protein-coupled receptor		41 / 0
Cyclooxygenase-2	PTGS2	P35354	CHEMBL230	Oxidoreductase		2 / 3
Glutamate carboxypeptidase II	FOLH1	Q04609	CHEMBL1892	Protease		4 / 0
Cyclooxygenase-1	PTGS1	P23219	CHEMBL221	Oxidoreductase		1 / 3

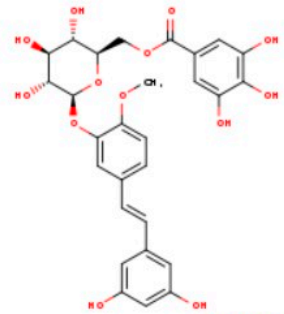
SwissDrugDesign | SwissDock SwissParam SwissSidechain SwissBioisostere **SwissTargetPrediction** SwissADME SwissSimilarity | About us

Swiss Institute of Bioinformatics

SwissTargetPrediction

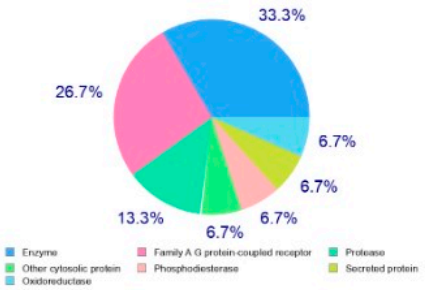
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Query Molecule



Target Classes

Top 15
Top 25
Top 50
All



rhapontigenin-galloyl-glucopyranoside

Export results:

Show 15 entries

Search: oxy

Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Squalene monooxygenase *(by homology)*	SQLE	Q14534	CHEMBL3592	Enzyme		0 / 14
Hydroxycarboxylic acid receptor 2	HCAR2	Q8TDS4	CHEMBL3785	Family A G protein-coupled receptor		62 / 0
Cyclooxygenase-2	PTGS2	P35354	CHEMBL230	Oxidoreductase		7 / 9

Showing 1 to 3 of 3 entries (filtered from 100 total entries)

Previous 1 Next

*Probability for the query molecule - assumed as bioactive - to have this protein as target.

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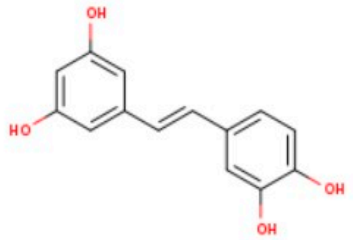
SwissDrugDesign | SwissDock SwissParam SwissSidechain SwissBioisostere **SwissTargetPrediction** SwissADME SwissSimilarity | About us

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SwissTargetPrediction

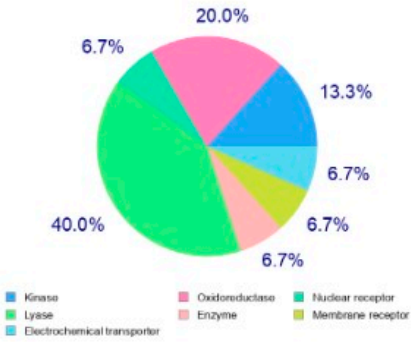
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Query Molecule



Target Classes

Top 15
Top 25
Top 50
All



rhapontigenin

Export results:

Show 15 entries

Search: oxy

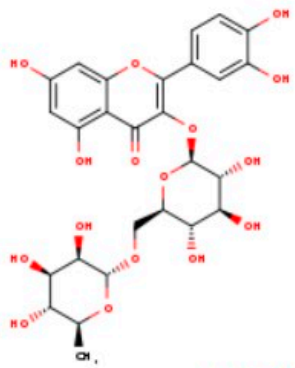
Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Cyclooxygenase-1	PTGS1	P23219	CHEMBL221	Oxidoreductase		9 / 24
Cyclooxygenase-2	PTGS2	P35354	CHEMBL230	Oxidoreductase		10 / 21
Arachidonate 5-lipoxygenase	ALOX5	P09917	CHEMBL215	Oxidoreductase		3 / 19
Arachidonate 15-lipoxygenase	ALOX15	P16050	CHEMBL2903	Enzyme		14 / 0
17-beta-hydroxysteroid dehydrogenase 14	HSD17B14	Q9BPX1	CHEMBL3712868	Enzyme		1 / 0

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SwissTargetPrediction

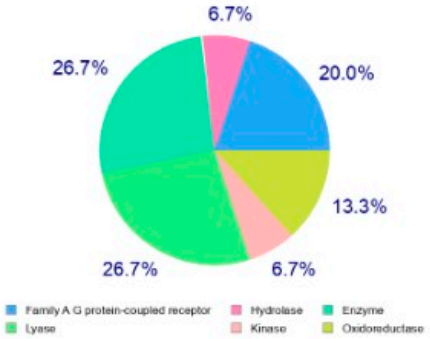
Home FAQ Help Download Contact Disclaimer

Query Molecule



Target Classes

Top 15
Top 25
Top 50
All



rutin

Export results:

Show 15 entries

Search: oxy

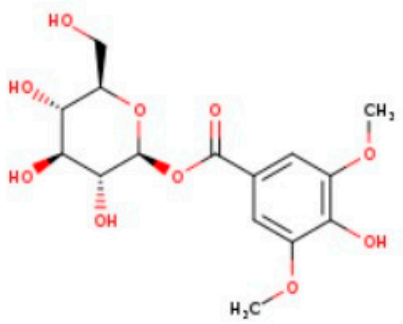
Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Cyclooxygenase-2	PTGS2	P35354	CHEMBL230	Oxidoreductase		1 / 4
Arachidonate 5-lipoxygenase	ALOX5	P09917	CHEMBL215	Oxidoreductase		0 / 45
Squalene monooxygenase *(by homology)*	SQLE	Q14534	CHEMBL3592	Enzyme		2 / 0
Arachidonate 15-lipoxygenase	ALOX15	P16050	CHEMBL2903	Enzyme		0 / 3
Arachidonate 12-lipoxygenase	ALOX12	P18054	CHEMBL3687	Enzyme		0 / 2

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SwissTargetPrediction

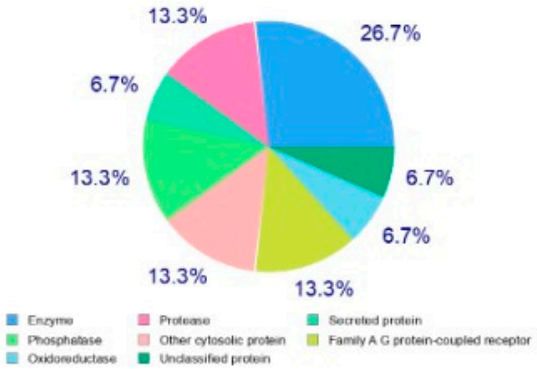
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Query Molecule



Target Classes

Top 15
Top 25
Top 50
All



syringoyl 1-*O*-glucopyranoside

Export results:

Show 15 entries

Search: oxy

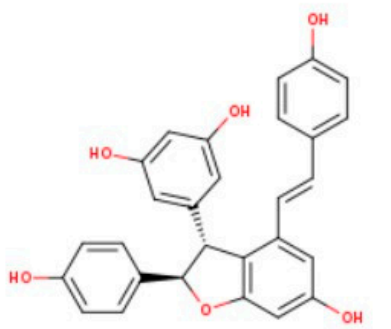
Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Squalene monooxygenase *(by homology)*	SQLE	Q14534	CHEMBL3592	Enzyme		0 / 21
Arachidonate 12-lipoxygenase	ALOX12	P18054	CHEMBL3687	Enzyme		1 / 0
Glutamate carboxypeptidase II	FOLH1	Q04609	CHEMBL1892	Protease		15 / 0

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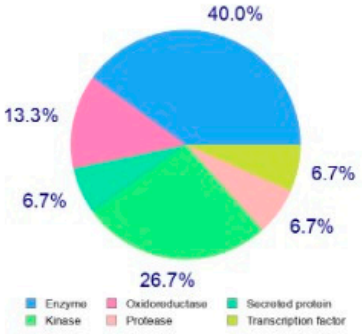
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Query Molecule



Target Classes

Top 15
Top 25
Top 50
All



viniferin (resveratrol-dehydrodimer)

Export results:

Show 15 entries

Search: oxy

Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Cyclooxygenase-1	PTGS1	P23219	CHEMBL221	Oxidoreductase		6 / 6
Cyclooxygenase-2	PTGS2	P35354	CHEMBL230	Oxidoreductase		7 / 6
Ubiquitin carboxyl-terminal hydrolase 4	USP4	Q13107	CHEMBL2406900	Enzyme		1 / 0
Ubiquitin carboxyl-terminal hydrolase 5	USP5	P45974	CHEMBL6158	Protease		1 / 0
11-beta-hydroxysteroid dehydrogenase 1	HSD11B1	P28845	CHEMBL4235	Enzyme		7 / 0

Figure S5. The estimation of the most probable macromolecular targets of rhubarb compounds. According to the tool description “The prediction is founded on a combination of 2D and 3D similarity with a library of 370000 known actives on more than 3000 proteins from three different species”. The webtool (http://www.swisstargetprediction.ch/ accessed on 15 October 2022) is described in the article: SwissTargetPrediction: updated data and new features for efficient prediction of protein targets of small molecules, Daina A., Michielin O., Zoete V. Nucleic Acids Res. 2019;47(W1):W357-W364. doi: 10.1093/nar/gkz382. (2019).