

SwissADME

By:

Mustafa Mahir Allawi

PhD. Candidate / pharmaceutical chemistry

SwissADME

- SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules.
- The ADME studies results for new synthesized analogues reported by Swiss ADME server to demonstrate which is the safer and potent drug candidate(s), for excluding the tested compounds that may fail in the next stages of the drug development because of the uncomplimentary ADME results.

SwissDrugDesign toolbar

Molecular sketcher:
draw, edit, import,
open molecular
structures from file

Transfer sketched
structure to
SMILES list (active
only if the sketcher is
not empty)

The screenshot shows the SwissADME web application interface. At the top, there is a navigation menu with links for 'SwissDrugDesign', 'SwissADME', and 'About Us'. The main header features the SIB logo and the text 'SwissADME' with links for 'Home', 'FAQ', 'Help', and 'Disclaimer'. Below the header, a text box provides information about the website's capabilities and references to scientific articles. The central part of the interface is divided into two main sections: a molecular sketcher on the left and a SMILES list on the right. The sketcher contains a chemical structure of a complex molecule and a toolbar with various editing tools. A red double arrow icon is positioned between the sketcher and the SMILES list, indicating the transfer of the sketched structure. The SMILES list contains three entries, each with a SMILES string and a name: 'Isosartan', 'Naproxen', and 'Sumatriptan'. At the bottom of the SMILES list, there are buttons for 'Fill with an example', 'Clear', and 'Run'. The footer of the page includes the SIB logo and the text 'Swiss Institute of Bioinformatics - © 2014'.

SwissADME
toolbar: Home,
FAQ, Help and
Disclaimer

SMILES list:
one molecule per
line and (optional)
name separated by
space

Run calculations
(active only if the list is
not empty)

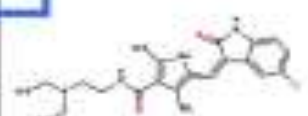
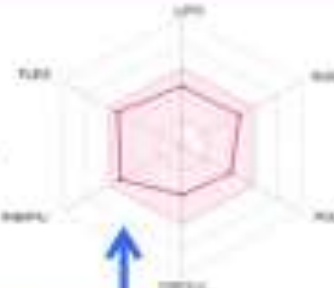
SwissADME submission page

- The actual input is a list of SMILES, which contains one molecule per line with an optional name separated by a space. Molecules can be directly pasted or typed in SMILES format, or inserted through the molecular sketcher. The latter enables importing from databases, opening a local file or drawing a 2D chemical structure to be transferred to the list by clicking on the double-arrow button. When the list of molecules is ready to be submitted, the user can start the calculations by clicking on the “Run” button.

SWISSADME

www.swissadme.ch/index.php

Sunitinib

SMILES: O=Cc1cc2c(c1)ccc3c2c(c1)C(=O)C1=CC=CC=C1F3

Physicochemical Properties

Formula	C22H27F4O2
Molecular weight	395.47 g/mol
Num. heavy atoms	29
Num. atom. heavy atoms	11
Fraction Csp3	0.36
Num. rotatable bonds	8
Num. H-bond acceptors	4
Num. H-bond donors	3
Molar Refractivity	116.31
TPSA	77.23 Å²

LogP values

Log P _{ow} (LOOP)	3.00
Log P _{ow} (XLOOP)	2.80
Log P _{ow} (MLOOP)	3.07
Log P _{ow} (MLLOOP)	3.86
Log P _{ow} (SLICCS-IT)	4.77
Consensus Log P _{ow}	3.21

Water Solubility

Log S (EOL)	-3.72
Solubility	7.59e-02 mg/ml; 1.30e-04 mol/l
Class	Soluble
Log S (AI)	-3.39
Solubility	4.39e-02 mg/ml; 1.25e-04 mol/l
Class	Soluble
Log S (SLICCS-IT)	-7.36
Solubility	1.76e-05 mg/ml; 4.43e-08 mol/l
Class	Poorly soluble

Pharmacokinetics

Oral absorption	High
BBB permeant	Yes
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	Yes
CYP2C9 inhibitor	No
CYP2D6 inhibitor	Yes
CYP3A4 inhibitor	Yes
Log K _p (skin permeation)	-6.86 cm/s

Druglikeness

Lipinski	Yes: 0 violation
Grease	Yes
Veber	Yes
Egan	Yes
Mungge	Yes
Bioavailability Score	0.55

Medicinal Chemistry

PAINS	0 alert
Brink	1 alert: michael_acceptor_1
Leadlikeness	No: 2 violations: MW=350, Rotors=7
Synthetic accessibility	3.58

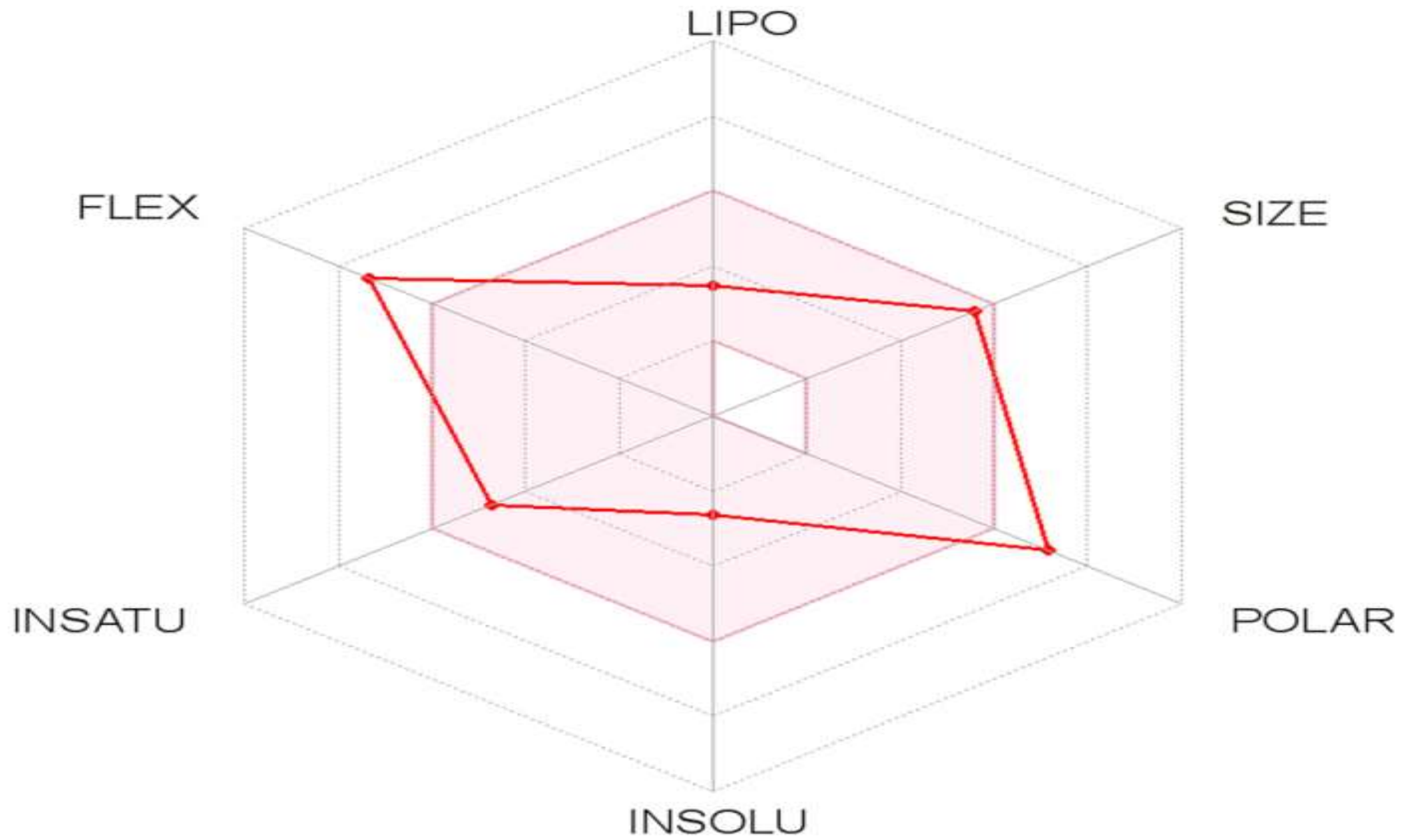
Molecule name or identifier

Submit this molecule to other SwissDrugDesign tools

Bioavailability Radar

Contextual Help

Scroll to the top of the page

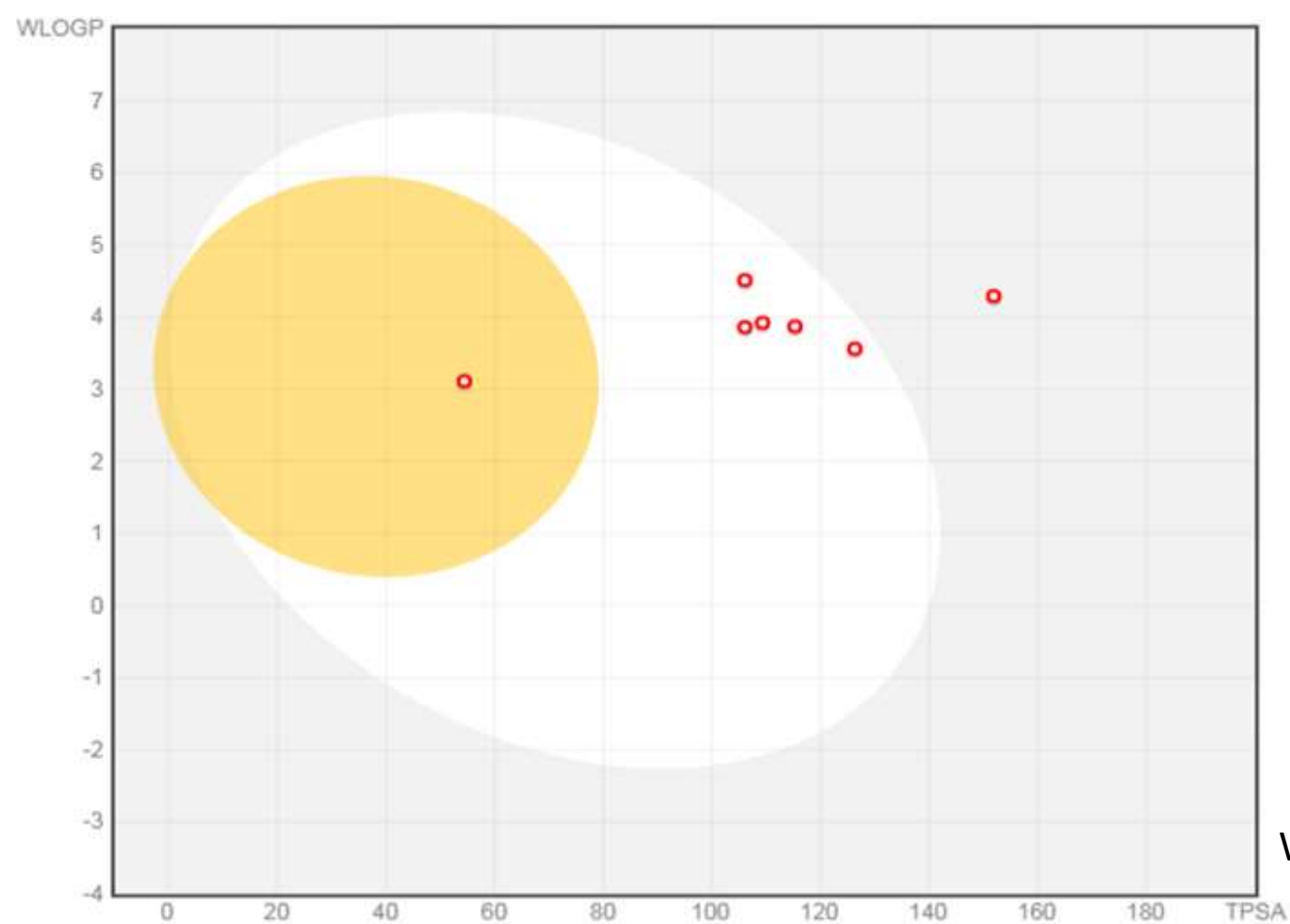


Ideal parameters

- Lipinski rule related to the oral administration of the drugs that should have ≤ 5 hydrogen bonds donor, ≤ 10 hydrogen bond acceptor, $\text{LogP} \leq 5$ and molecular weight (M.Wt.) ≤ 500 to be given orally.
- The topological polar surface area (TPSA) was calculated, because it consider as a very important characteristic that was associated with the bioavailability of the drugs. As a result, the passively absorbing molecules within a TPSA $>140 \text{ \AA}^2$ are considered to have lower oral bioavailability
- Fingerprints of molecular drug-likeness structure keys such as LogP and Log S.

Ideal parameters

- Statistical performance of SVM classification models for substrate or inhibitor of pharmacokinetics-relevant protein, P-gp and CYP.
- The BOILED-Egg: allows for intuitive evaluation of passive gastrointestinal absorption (HIA) and brain penetration (BBB) in function of the position of the molecules.



Actions

Show Molecules Name

Legends

BBB
 HIA
 PGP+
 PGP-

Remarks

None

BOILED EGG – for ketoprofen and final compounds.
 Yellow ovule (yolk): are molecule predicted to passively permeate through blood-brain barriers.
 White ovule (white): are molecule predicted to passively absorbed by the GIT.
 PGP+: Blue dots are for molecules predicted to be effluxed from the CNS by the P-glycoprotein.
 PGP-: Red dots are for molecules predicted not to be effluxed from the CNS by the P-glycoprotein.

References

- Christopher A. Lipinski. Rule of five in 2015 and beyond: Target and ligand structural limitations, ligand chemistry structure and drug discovery project decisions. *Advanced Drug Delivery Reviews*. Accepted 27 April 2016.
- Palm K, Stenberg P, Luthman K, Artursson P. Polar molecular surface properties predict the intestinal absorption of drugs in humans. *Pharmaceutical research*. 1997 May 1;14(5):568-71.
- Daina A, Michielin O, Zoete V. SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. *Sci Rep*. 2017 Mar 3;7:42717. doi: 10.1038/srep42717. PMID: 28256516; PMCID: PMC5335600

Thank you