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DESIGN AND COMPUTATIONAL STUDY ON 4, 4(3-SUBSTITUE PHENYL) ACRYLOYL) BENZYLIDENE) 2-METHYLOXAZOL-5-(4H)ONE DERIVATIVES

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Accredited by NAAC A^+ DUPADU, KURNOOL- 518218, AP. MAY-2025

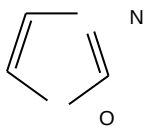
ABSTRACT: The present study involves Design and Computational study of 4,4(3-substituted phenyl) acryloyl)benzylidene)2-methyloxazol-5-(4H)one derivative. Computational studies were done by using online software tools like Molinspiration, Swiss ADME, Swiss Target Prediction, and molecular docking to evaluate pharmacokinetic properties, drug- likeness, bioactivity scores, and binding affinity to potential therapeutic targets. All the designed compounds satisfied Lipinski's rule of five, suggesting good oral bioavailability and favourable drug like lines behaviour. Molecular docking score indicated that the compounds exhibited strong binding affinity with targets such as the neuropeptide Y receptor and serine/threonine-protein kinase RAF. Among the series, compounds 1 and 3 showed potential activity against the glucagon receptor. These findings indicate the promising potential of oxazole derivatives in future drug development, especially in oncology and infectious disease treatment

KEYWORDS; Oxazole, Molinspiration, Swiss ADME, Swiss Target Prediction, and Molecular docking

INTRODUCTION

Oxazole:

Oxazole is a finve-membered heterocyclic aromatic compound consisting of three carbon atoms, one nitrogen atom, and one oxygen atom. Its molecular formula is C_3H_3NO, and it has a planar ring structure. The nitrogen and oxygen atoms are positioned at the 1 and 3 positions, respectively, making it a 1,3-oxazole compound. (1)



Structure and Properties:

Chemical formula: C_3H_3NO Molar mass: 69.06 g/mol

Aromaticity: Oxazole is aromatic due to the delocalization of electrons across the ring.

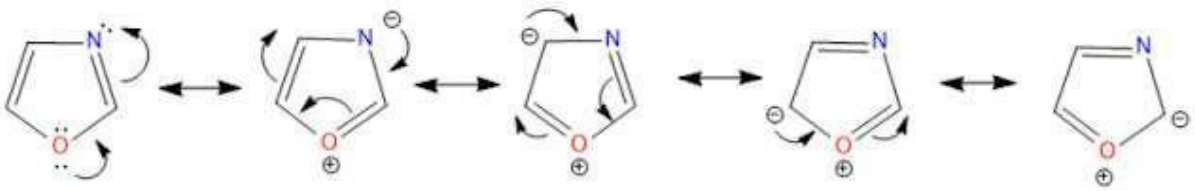
Physical properties: It is a colourless, volatile liquid with a characteristic odour. It is slightly soluble in water but soluble in organic solvents.

Oxazole is known for its diverse biological activities

1. Antibacterial Activity
2. Antifungal Activity
3. Anticancer Activity
4. Anti-inflammatory Activity
5. Antiviral Activity
6. Antioxidant Activity
7. Antidiabetic Activity
8. CNS Activity (Neuroprotective and Anticonvulsant)

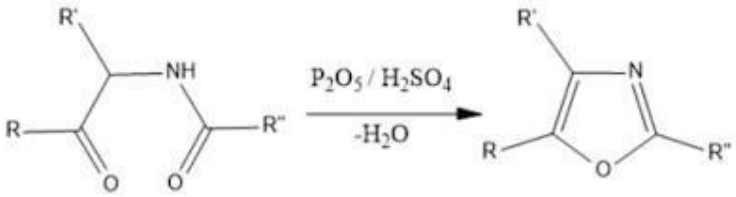
CHEMISTRY:

Resonance Structure:



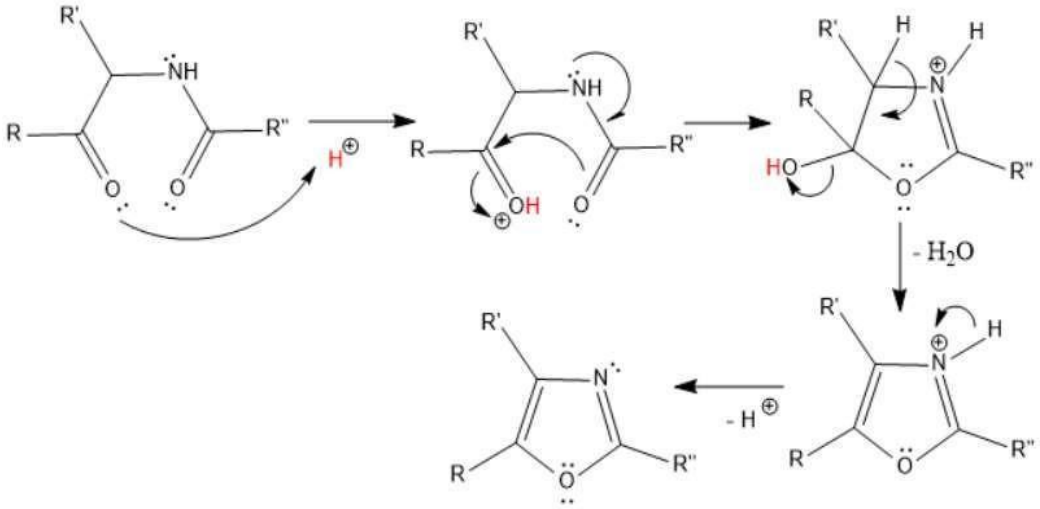
Robinson-Gabriel synthesis:

It is the most method for synthesis of oxazole's. It involves an α-acylamino ketone which undergoes cyclisation and dehydration in the presence of phosphorus pentoxide or strong mineral acid. This method is especially applicable for synthesis 2,5-diaryl oxazole's.



α-acylamino ketone

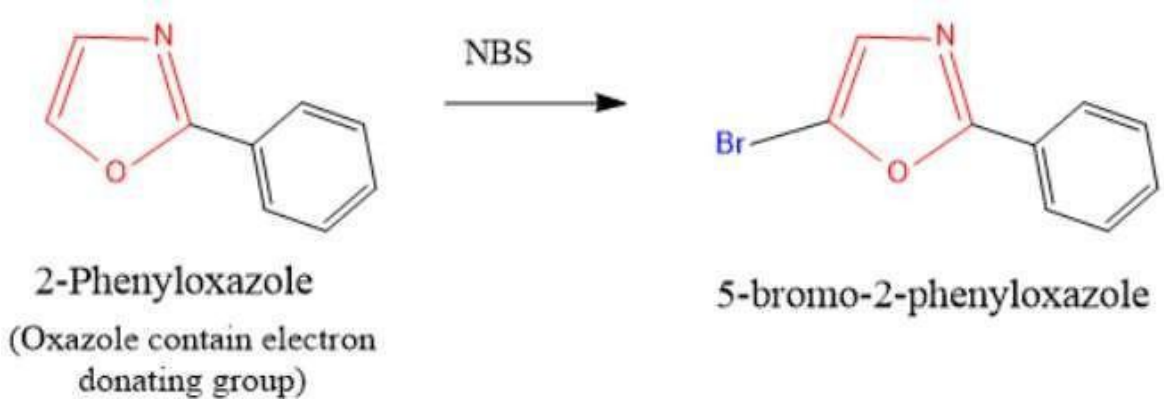
Synthesis:



Electrophilic substitution reactions:

Oxazole less reactive for electrophilic substitution reactions because of highly electronegative oxygen present in the ring, it makes deactivates the ring and not available for electrophilic substitution reactions. However, if ring activated by electron-donating groups electrophilic substitution reactions are possible at 5th position.

1. Halogenation:

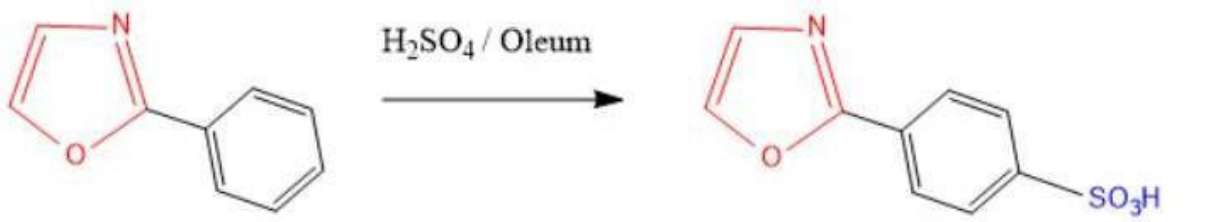


2-Phenyloxazole
(Oxazole contain electron donating group)

5-bromo-2-phenyloxazole

2. Nitration: Nitration and Sulphonation reactions are more difficult on oxazole ring.

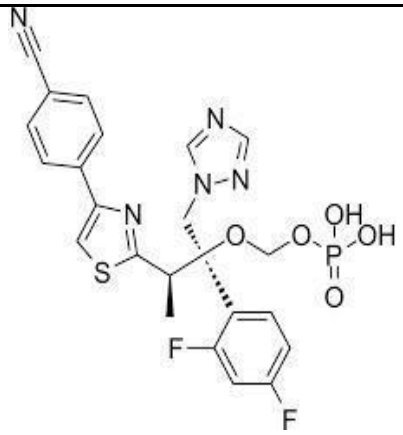
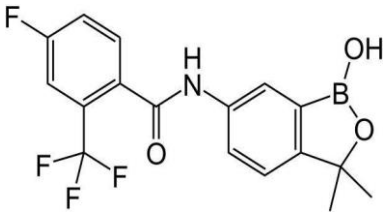
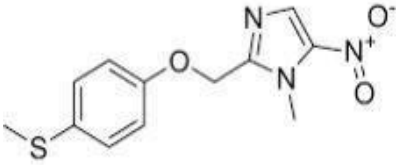
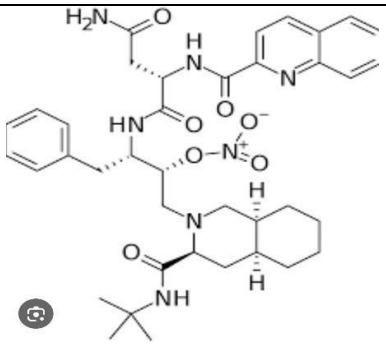
3. Sulphonation:



4-(oxazol-2-yl)-benzene-1-sulphonic acid

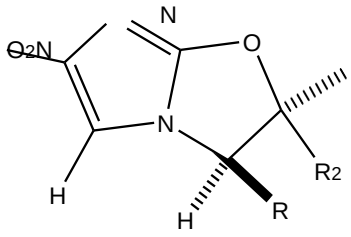
TABLE :1

Marketed Drugs containing Oxazole moiety:

Marketed Drugs	Structure	Therapeutic use
Fosravuconazole		Used for the treatment of fungal infection (2)
Acoziborole		Used for treatment of human African trypanosomiasis (sleeping sickness) (3)
Fexinidazole		Used for treatment of Oral treatment for both stages of African trypanosomiasis
OX 1001		Used for Treatment of various cancers

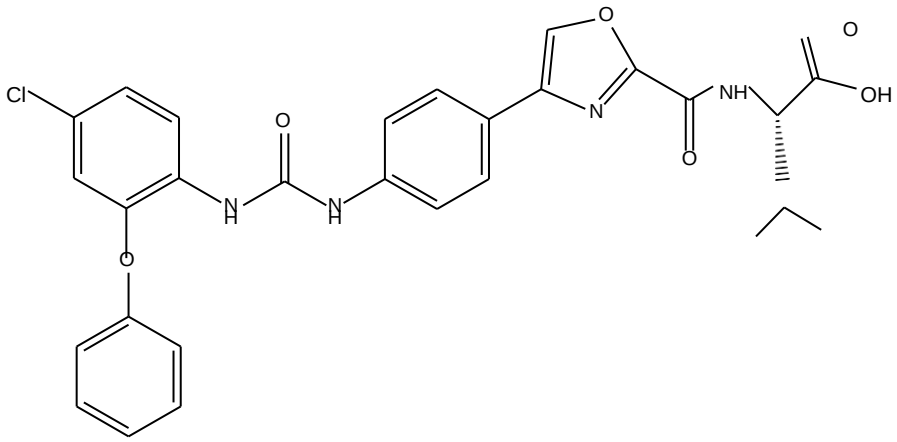
1.ANTI TUBERCULAR ACTIVITY:

Nagarajan *et al.* reported the synthesis of 2,3- dihydro -6-nitroimide(2,1-b) oxazole's derivatives, among the synthesized derivatives, two compounds exhibited excellent antimycobacterial activity both *in vivo &in vitro* which are compared with standard drugs like isoniazid & ethambutol. Tuberculosis is chronic communicable disease caused by *Mycobacterium tuberculosis* spread from one person to another through air. (4)



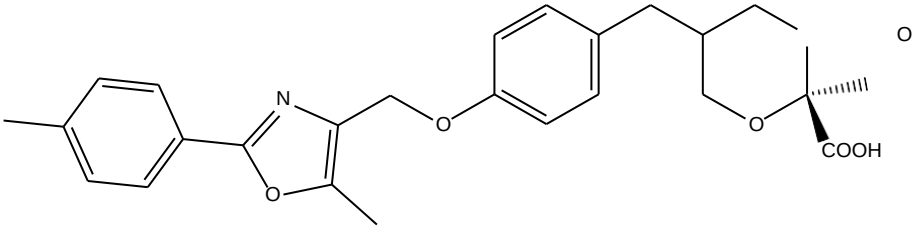
2. ANTI OBESITY ACTIVITY:

Griebenow *et.al* prepared a range of novel squalene synthase inhibitors and evaluated for lipid lowering activity. squalene synthase is an enzyme which involved in one of the steps of cholesterol of biosynthesis. This below compound was found to be more potent compared with standard drug.



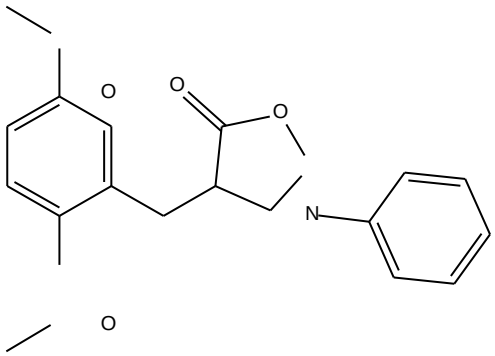
3. ANTI-DIABETIC ACTIVITY:

Pingali *et al.* synthesized 1,3 – dioxane carboxylic acid derivatives and evaluated for *in vitro* PPAR agonistic potential *& in vivo* sugar lowering & lipid lowering efficacy in animal models using rosiglitazone & tesaglitazar as standard compounds. p-methylphenyl group (a phenyl ring substituted with a methyl group at the para-position) Connected to a 1,3-dioxane ring (a six-membered ring with two oxygen atoms at positions 1 and 3) The dioxane ring is substituted at the 5-position with a long alkyl chain leading to a chiral centre with a carboxylic acid group (COOH) attached. (2R)-2-[4-(4- Methylphenyl)-1,3-dioxan-5-yl] pentatonic acid was found to be most active (EC_{50} =0.0015 um) (6)



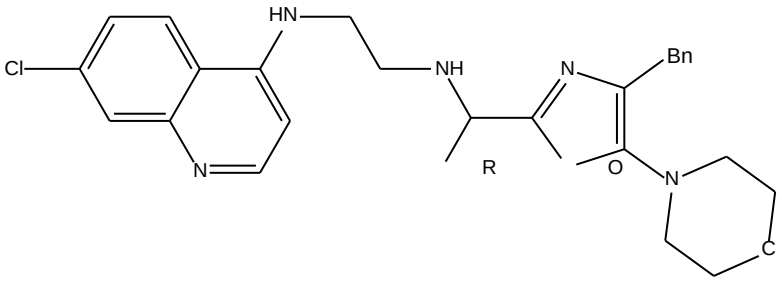
4. ANTI OXIDANT ACTIVITY:

Parveen *et, al.* synthesised several 4- arylidene -2-phenyl 5(4 H)-azlactones &evaluated for antioxidant activity which revealed that 4-arylidene-2-phenyl-5(4H)-oxazolone derivative was found to more potent. (7)



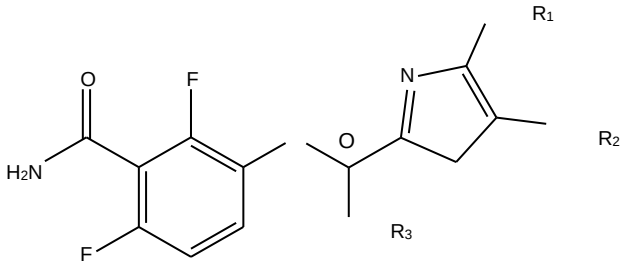
5. ANTI MALARIAL ACTIVITY:

Musonda *et.al* synthesized a novel series of 4- amino quinoline containing 2,4,5- trisubstituted amino oxazole's against *P. Falciparum* parasite *in vitro*. Among the derivatives N-{2-[(6-Chloropyridin-3-yl) amino] ethyl}-N'-[2-benzyl-6- (piperidin-1-yl) pyrimidin-4-yl] urea significantly more potent than the standard drug chloroquine were identified. (8)



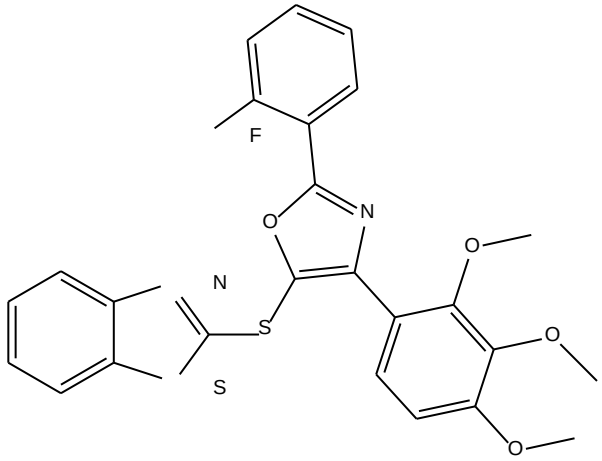
6.ANTI-BACTERIAL ACTIVITY:

Stokes *et.al.* designed a series of oxazole benzamide derivatives. The synthesized compounds had potent anti- staphylococcal activity &inhibited the cytokinesis of clinically significant bacterial pathogen *Staphylococcus aureus*. The study has provided small molecule inhibitors of Fts z with enhanced *invitro* & *in vivo* antibacterial efficacy. (9)



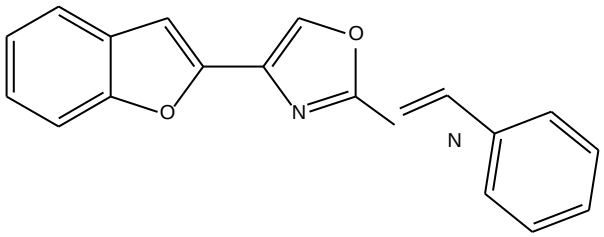
7.ANTI CANCER ACTIVITY:

Liu *et al.* synthesized various trisubstituted oxazole derivatives and evaluated for antitumour activity against two cancer cell, PC-3 and A431 using 5- fluorouracil as reference. (10)



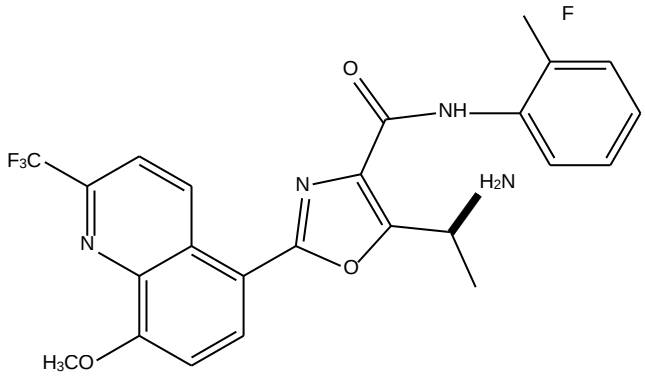
8.ANTI MICROBIAL ACTIVITY:

Kamble *et al.* synthesized various oxazole-2-amines and its analogues were evaluated for their antibacterial activity using amoxicillin as standard drug. The compounds (E)-4- (Benzofuran-2-yl)-N- benzylidene oxazole was found to be more potent (11)



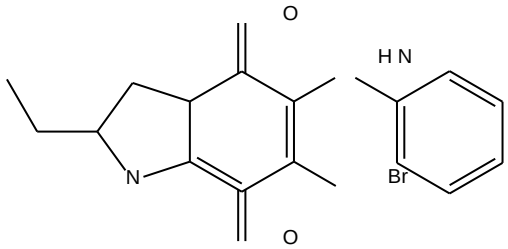
9. ANTI INFLAMMATORY ACTIVITY:

Kuang *et.al* synthesized a series of oxazole derivatives. Among them potent carboxamides, the N-benzyl carboxamides was found to exhibit good selectivity for phosphodiesterase 4 over phosphodiesterase 10& phosphodiesterase.



10. ANTI FUNGAL ACTIVITY:

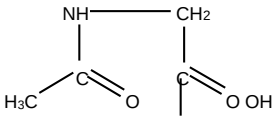
Ryu *et.al* synthesized a series of benzo oxazole's & evaluated for antifungal activity using 5- fluor cytosine as a reference drug.



AIM & OBJECTIVES

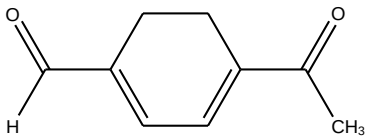
From the review of literature various biological activities were reported on oxazolone derivatives.
The main objective of the present work is to evaluate *in silico* properties of 4,4(3-substituted phenyl)acryloyl)benzylidene)2-methyloxazol-5-(4H)one derivative by using different online software tools like

1. Molinspiration
2. Swiss ADME
3. Molecular docking
4. Swiss target prediction
5. Auto Dock vina

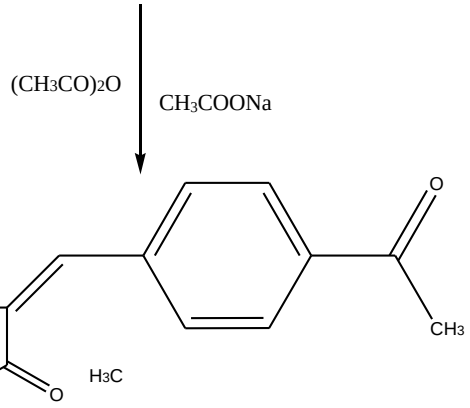


Acetyl glycine

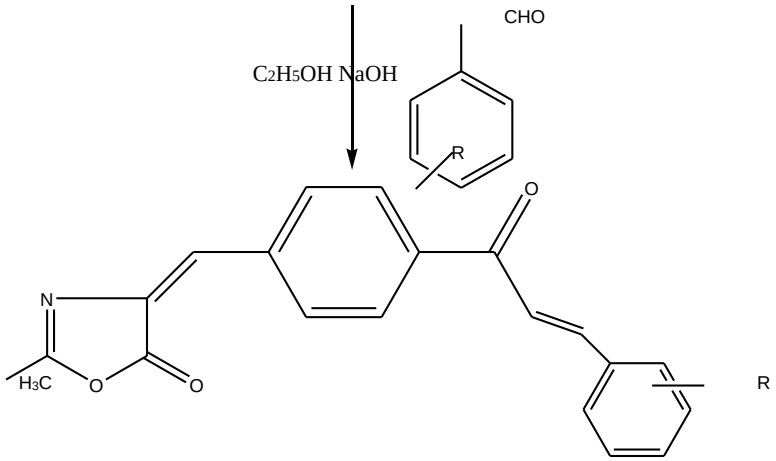
+



4- Acetyl benzaldehyde



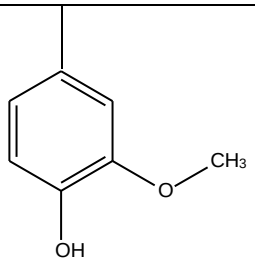
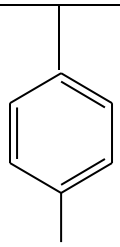
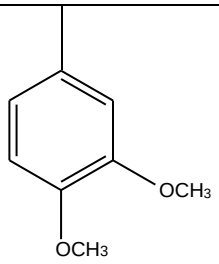
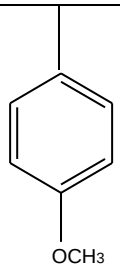
4-(4-Acetylbenzylidene)-2- methyloxazol-5(4H)- one

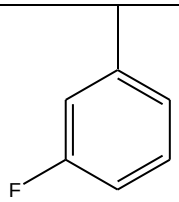


4,4(3- substituted phenyl)acryloyl)benzylidene) 2-methyl oxazol-5-(4H)on

TABLE :2

PHYSICAL DATA OF 4,4(3-SUBSTITUTED PHENYL)ACRYLOYL)BENZYLIDENE)2-METHYLOXAZOL-5-(4H)ONE DERIVATIVE

COMPOUND	R	Molecular formula	Molecular weight
1.		C21H17NO5	363.36g/mol
2.		C20H15NO4	333.34g/mol
3.		C20H14FNO3	335.33g/mol
4.		C21H17NO4	347.36g/mol

5.		C22H19NO5	377.392g/mol

1. MOLINSPIRATION:

Molinspiration is an independent research organization focused on development and application of modern chem informatics techniques, especially in connection with the internet. Molinspiration offers broad range of chem. informatics software tools supporting molecule manipulation and processing, including SMILES and SD file conversion, normalization of molecules, generation of tautomer's, molecule fragmentation, calculation of various molecular properties needed in QSAR, molecular modelling and drug design, high quality molecule depiction, molecular data base tools supporting substructure search or similarity and pharmacophore similarity search.

Molinspiration tools are therefore platform independent and may be run on any PC, Mac, UNIX or LINUX machine. The software is distributed in a form of toolkits, which may be used as stand- alone computational engines, used top over web-based tools, or easily incorporated into larger in-house Java applications.

Molinspiration mi screen engine allows fast prediction of biological activity- virtual screening of large collections of molecules and selection of molecules with the highest probability to show biological activity. The screening is based on identification of fragments or substructure features typical for the active molecules. The Molinspiration virtual screening is fast and therefore allows processing of very large molecular libraries.
Validation tests performed by our company, as well as results of our customers on various target classes show 10 to 20-fold increase in hit rate in comparison with random selection of molecules for screening.

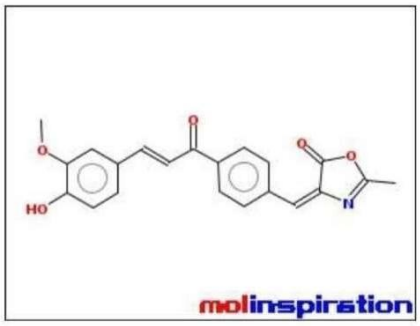
To run a virtual screening, three steps need to be performed:

1. Generation of fragments from a training set containing active and inactive molecules.
2. Development of a bioactivity model from fragment files generated in step 1 Actual virtual screening by using the model generated in step. (12)

COMPOUND:1

molinspiration Calculation of Molecular Properties

miSMILES: COc3cc(C=CC(=O)c2ccc(C=c1nc(C)oc1=O)cc2)ccc3O



Molinspiration property engine v2022.08

miLogP	2.83
TPSA	89.64
natoms	27
MW	363.37
nON	6
nOHNH	1
nviolations	0
nrotb	5
volume	319.78

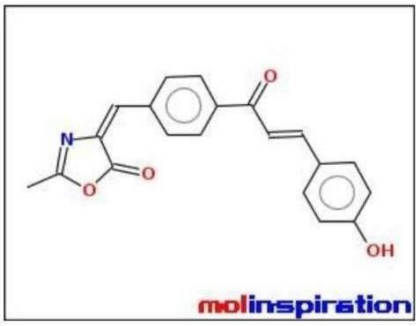
Get data as text (for copy / paste).

Get 3D geometry BETA

COMPOUND: 2

molinspiration Calculation of Molecular Properties

miSMILES: Cc3nc(=Cc2ccc(C(=O)C=Cc1ccc(O)cc1)cc2)c(=O)o3



Molinspiration property engine v2022.08

miLogP	3.01
TPSA	80.40
natoms	25
MW	333.34
nON	5
nOHNH	1
nviolations	0
nrotb	4
volume	294.24

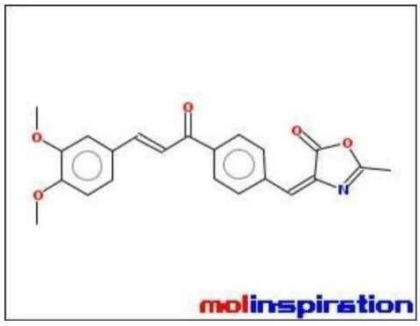
Get data as text (for copy / paste).

Get 3D geometry BETA

COMPOUND:3

molinspiration Calculation of Molecular Properties

miSMILES: COc3ccc(C=CC(=O)c2ccc(C=c1nc(C)oc1=O)cc2)cc3OC



Molinspiration property engine v2022.08

miLogP	3.14
TPSA	78.64
natoms	28
MW	377.40
nON	6
nOHNH	0
nviolations	0
nrotb	6
volume	337.31

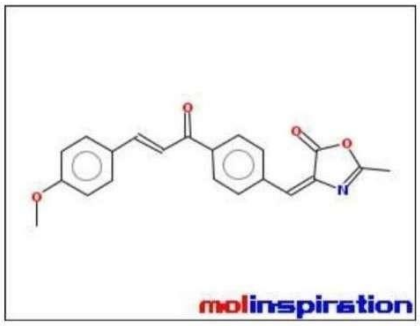
Get data as text (for copy / paste).

Get 3D geometry BETA

COMPOUND: 4

molinspiration Calculation of Molecular Properties

miSMILES: COc3ccc(C=CC(=O)c2ccc(C=c1nc(C)oc1=O)cc2)cc3



Molinspiration property engine v2022.08

miLogP	3.55
TPSA	69.41
natoms	26
MW	347.37
nON	5
nOHNH	0
nviolations	0
nrotb	5
volume	311.76

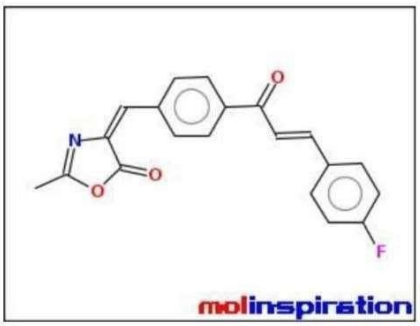
Get data as text (for copy / paste).

Get 3D geometry BETA

COMPOUND :5

molinspiration Calculation of Molecular Properties

miSMILES: Cc3nc(=Cc2ccc(C(=O)C=Cc1ccc(F)cc1)cc2)c(=O)o3



Molinspiration property engine v2022.08

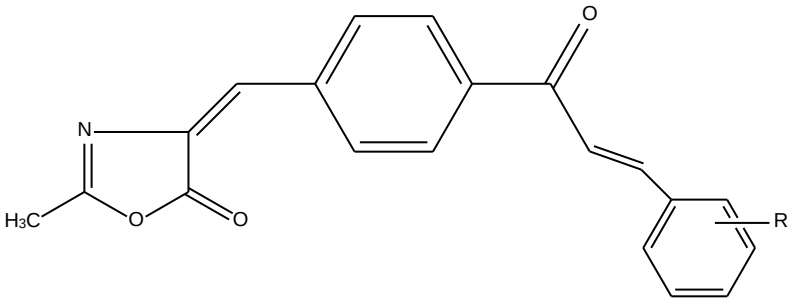
miLogP	3.65
TPSA	60.17
natoms	25
MW	335.33
nON	4
nOHNH	0
nviolations	0
nrotb	4
volume	291.15

Get data as text (for copy / paste).

Get 3D geometry BETA

TABLE :3

MOLECULAR PROPERTIES OF 4,4(3-SUBSTITUTED PHENYL)ACRYLOYL)BENZYLIDENE)2-METHYLOXAZOL-5-(4H)ONE DERIVATIVES



COMPOUND	Mi LogP	TPSA	N Atom	NON	NOH NH	N-Violations	N-Rotb	Volume	MW
1.	2.83	89.64	27	6	1	0	5	319.78	363.37
2.	3.01	80.40	25	5	1	0	4	294.24	333.34
3.	3.14	78.64	28	6	0	0	6	337.31	377.40
4.	3.55	69.41	26	5	0	0	5	311.76	347.3
5.	3.65	60.17	25	4	0	0	4	291.15	335.33

2. Swiss ADME:

A large variety of *in silico* methods share the objective of predicting ADME parameters from molecular structure. Noteworthy, the pioneer work of Lipinski et al. Examined orally active compounds to define physicochemical ranges for high probability to be an oral drug. This so-called Rule-of-five delineated the relationship between pharmacokinetic and physicochemical parameters. Whereas physicochemical parameters give a global description of the structure, molecules can be directly described by substructure searches. In turn, these ADME parameters can be evaluated separately by dedicated methods. It has been demonstrated that early estimation of ADME in the discovery phase reduces drastically the fraction of pharmacokinetics-related failure in the clinical phases. Computer models have been fostered as a valid alternative to experimental procedures for prediction of ADME, especially at initial steps, when investigated chemical structures are numerous but the availability of compounds is scarce.

A large variety of in silico methods share the objective of predicting ADME parameters from molecular structure. Noteworthy, the pioneer work of Lipinski et al. Examined orally active compounds to define physicochemical ranges for high probability to be an oral drug. This so- called Rule-of-five delineated the relationship between pharmacokinetic and physicochemical parameters. Whereas physicochemical parameters give a global description of the structure, molecules can be directly described by substructure searches. These techniques are at the root of Structural Alert, the PAINS or the Lilly Med Chem filters applied to cleanse chemical libraries from compounds most likely unstable, reactive, toxic, or prone to interfere with biological assays because unspecific frequent hitters, dyes or aggregators.

A) Chemical Structure and Bioavailability Radar:

The first section, including two-dimensional chemical structure and canonical SMILES, is located below the title. It shows on which chemical form the predictions were calculated. Moreover, our Bioavailability Radar is displayed for a rapid appraisal of drug-likeness. Six physicochemical properties are considered: lipophilicity, size.

INSILICO EVALUTION

Polarity, solubility, flexibility and saturation. A physicochemical range on each axis was defined by descriptors adapted and depicted as a pink area in which the radar plot of the molecule has to fall entirely to be considered drug-like. Leaving the mouse over the radar gives further information about the descriptors.

B) Physicochemical Properties:

Simple molecular and physicochemical descriptors like molecular weight (MW), molecular refractivity (MR), count of specific atom types and polar surface area (PSA) are compiled in this section. The values are computed with Open Babel, version 2.3.0.

The PSA is calculated using the fragmental technique called topological polar surface area (TPSA), considering sulphur and phosphorus as polar atoms. This has proven a useful descriptor in many models and rules to quickly estimate some ADME properties, especially with regards to biological barrier crossing such as absorption and brain access.

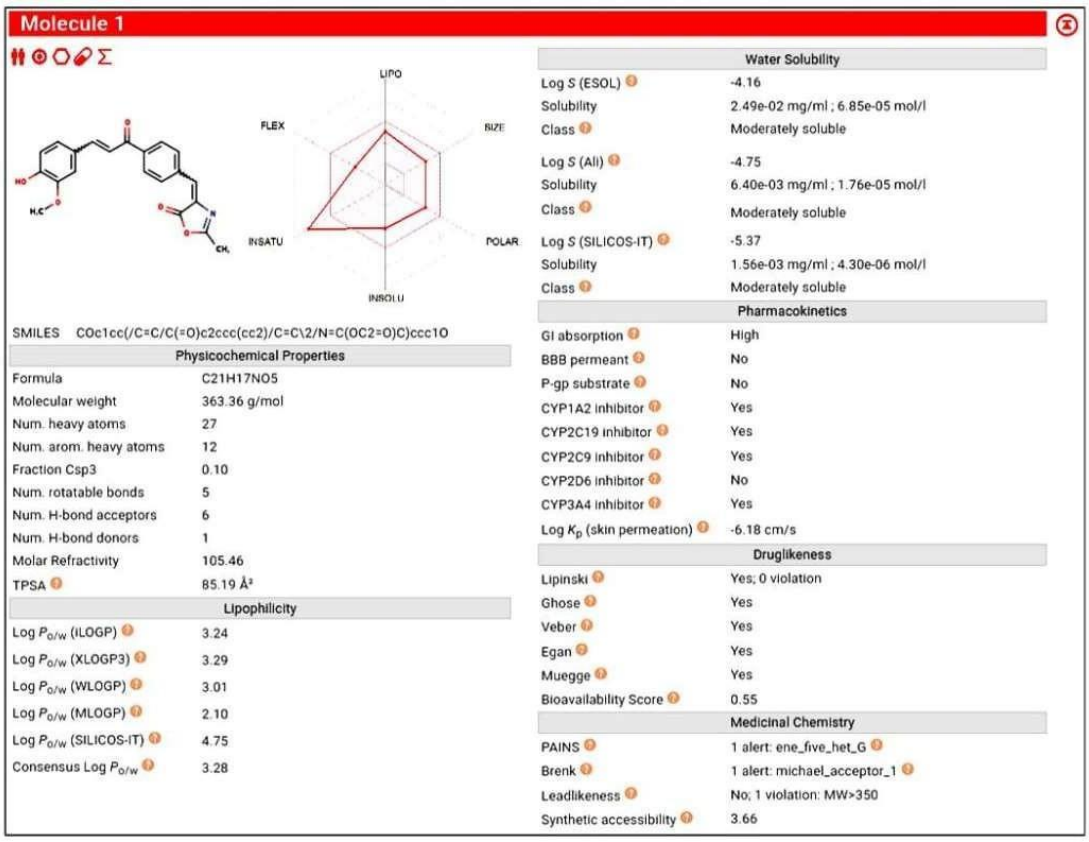
C) Lipophilicity:

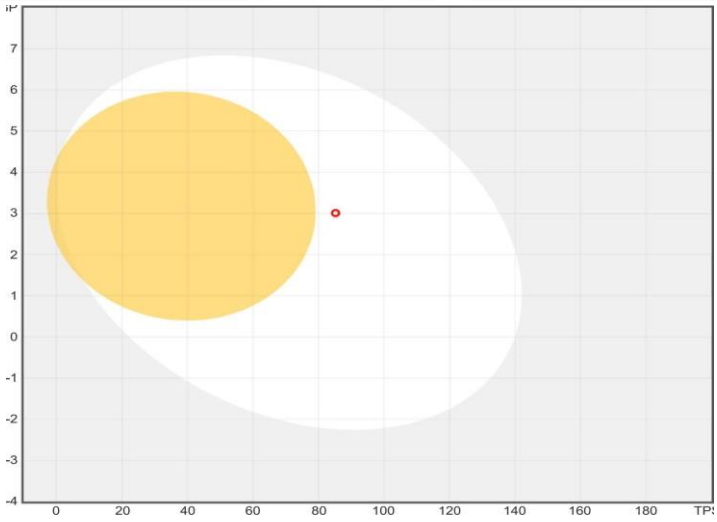
The partition coefficient between n-octanol and water is the classical descriptor for Lipophilicity. It has a dedicated section in Swiss ADME due to the critical importance of this physicochemical property for pharmacokinetics drug discovery. Many computational methods for log P o/w estimation were developed with diverse performance on various chemical sets. Common practice is to use multiple predictors either to select the most accurate methods for a given chemical series or to generate consensus estimation.

D) Water Solubility:

Having a soluble molecule greatly facilitates many drug development activities, primarily the ease of handling and formulation. Moreover, for discovery projects targeting oral administration, solubility is one major property influencing absorption. As well, a drug meant for parenteral usage has to be highly soluble in water to deliver a sufficient quantity of active ingredient in the small volume of such pharmaceutical dosage. Two topological methods to predict Water Solubility are included in Swiss ADME.

COMPOUND – 1


Molecule 1
LIPO
FLEX
SIZE
INSATU
POLAR
INSOLU
SMILES COc1cc(/C=C/C(=O)c2ccc(cc2)/C=C\2/N=C(OC2=O)C)ccc1O
Physicochemical Properties
Formula C21H17NO5
Molecular weight 363.36 g/mol
Num. heavy atoms 27
Num. arom. heavy atoms 12
Fraction Csp3 0.10
Num. rotatable bonds 5
Num. H-bond acceptors 6
Num. H-bond donors 1
Molar Refractivity 105.46
TPSA 85.19 Å²
Lipophilicity
Log Po/w (iLOGP) 3.24
Log Po/w (XLOGP3) 3.29
Log Po/w (WLOGP) 3.01
Log Po/w (MLOGP) 2.10
Log Po/w (SILICOS-IT) 4.75
Consensus Log Po/w 3.28
Water Solubility
Log S (ESOL) -4.16
Solubility 2.49e-02 mg/ml ; 6.85e-05 mol/l
Class Moderately soluble
Log S (Ali) -4.75
Solubility 6.40e-03 mg/ml ; 1.76e-05 mol/l
Class Moderately soluble
Log S (SILICOS-IT) -5.37
Solubility 1.56e-03 mg/ml ; 4.30e-06 mol/l
Class Moderately soluble
Pharmacokinetics
GI absorption High
BBB permeant No
P-gp substrate No
CYP1A2 inhibitor Yes
CYP2C19 inhibitor Yes
CYP2C9 inhibitor Yes
CYP2D6 inhibitor No
CYP3A4 inhibitor Yes
Log Kp (skin permeation) -6.18 cm/s
Druglikeness
Lipinski Yes; 0 violation
Ghose Yes
Veber Yes
Egan Yes
Muegge Yes
Bioavailability Score 0.55
Medicinal Chemistry
PAINS 1 alert: ene_five_het_G
Brenk 1 alert: michael_acceptor_1
Leadlikeness No; 1 violation: MW>350
Synthetic accessibility 3.66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80
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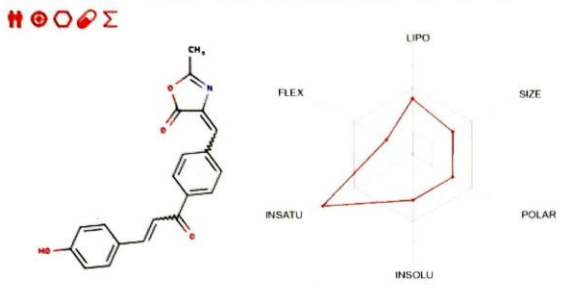
140
160
180

COMPOUND -2



SMILES O=C(c1ccc(cc1)/C=C/1\N=C(OC1=O)C)/C=C/c1ccc(cc1)O

Physicochemical Properties	
Formula	C20H15NO4
Molecular weight	333.34 g/mol
Num. heavy atoms	25
Num. arom. heavy atoms	12
Fraction Csp3	0.05
Num. rotatable bonds	4
Num. H-bond acceptors	5
Num. H-bond donors	1
Molar Refractivity	98.97
TPSA	75.96 Å²

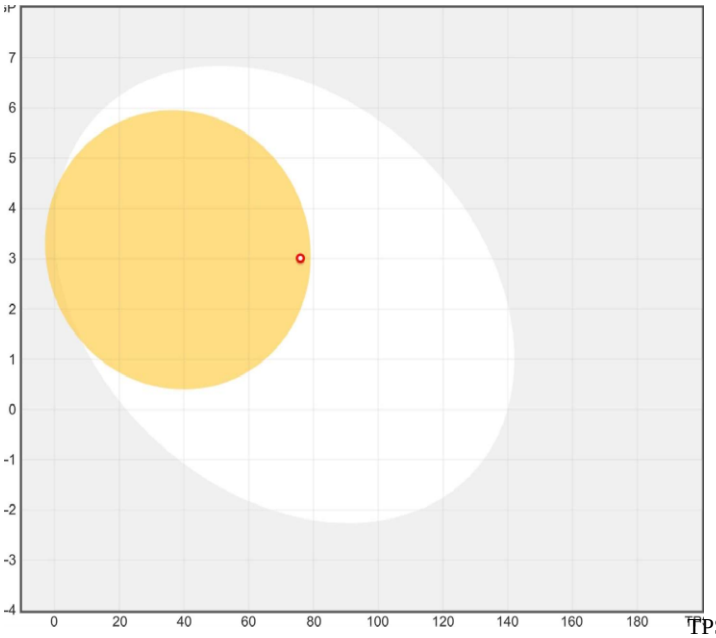
Lipophilicity	
Log $P_{o/w}$ (iLOGP)	2.76
Log $P_{o/w}$ (XLOGP3)	3.32
Log $P_{o/w}$ (WLOGP)	3.01
Log $P_{o/w}$ (MLOGP)	2.42
Log $P_{o/w}$ (SILICOS-IT)	4.69
Consensus Log $P_{o/w}$	3.24

Water Solubility	
Log S (ESOL)	-4.09
Solubility	2.71e-02 mg/ml ; 8.14e-05 mol/l
Class	Moderately soluble
Log S (Ali)	-4.59
Solubility	8.54e-03 mg/ml ; 2.56e-05 mol/l
Class	Moderately soluble
Log S (SILICOS-IT)	-5.26
Solubility	1.84e-03 mg/ml ; 5.51e-06 mol/l
Class	Moderately soluble

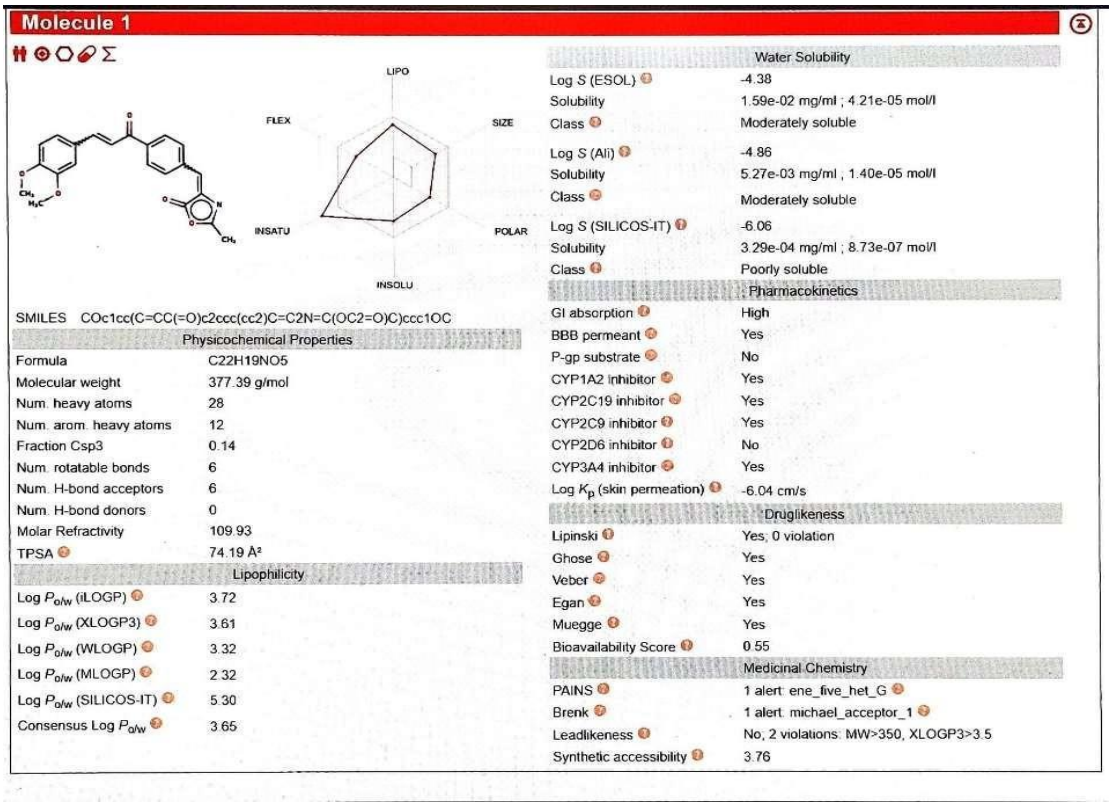
Pharmacokinetics	
GI absorption	High
BBB permeant	Yes
P-gp substrate	No
CYP1A2 inhibitor	Yes
CYP2C19 inhibitor	Yes
CYP2C9 inhibitor	Yes
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-5.98 cm/s

Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

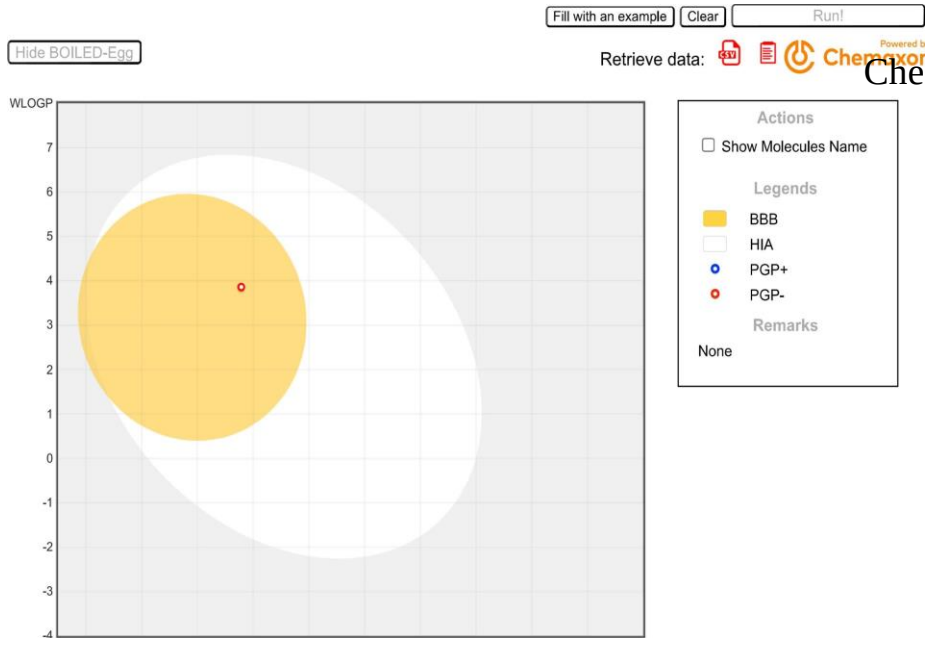
Medicinal Chemistry	
PAINS	1 alert: ene_five_het_G
Brenk	1 alert: michael_acceptor_1
Leadlikeness	Yes
Synthetic accessibility	3.55



COMPOUND – 3


Molecule 1
LIPO
FLEX
SIZE
INSATU
POLAR
INSOLU
SMILES COc1cc(C=CC(=O)c2ccc(cc2)C=C2N=C(OC2=O)C)ccc1OC
Physicochemical Properties
Formula C22H19NO5
Molecular weight 377.39 g/mol
Num. heavy atoms 28
Num. arom. heavy atoms 12
Fraction Csp3 0.14
Num. rotatable bonds 6
Num. H-bond acceptors 6
Num. H-bond donors 0
Molar Refractivity 109.93
TPSA 74.19 Å²
Lipophilicity
Log Po/w (iLOGP) 3.72
Log Po/w (XLOGP3) 3.61
Log Po/w (WLOGP) 3.32
Log Po/w (MLOGP) 2.32
Log Po/w (SILICOS-IT) 5.30
Consensus Log Po/w 3.65
Water Solubility
Log S (ESOL) -4.38
Solubility 1.59e-02 mg/ml ; 4.21e-05 mol/l
Class Moderately soluble
Log S (Ali) -4.86
Solubility 5.27e-03 mg/ml ; 1.40e-05 mol/l
Class Moderately soluble
Log S (SILICOS-IT) -6.06
Solubility 3.29e-04 mg/ml ; 8.73e-07 mol/l
Class Poorly soluble
Pharmacokinetics
GI absorption High
BBB permeant Yes
P-gp substrate No
CYP1A2 inhibitor Yes
CYP2C19 inhibitor Yes
CYP2C9 inhibitor Yes
CYP2D6 inhibitor No
CYP3A4 inhibitor Yes
Log Kp (skin permeation) -6.04 cm/s
Druglikeness
Lipinski Yes; 0 violation
Ghose Yes
Veber Yes
Egan Yes
Muegge Yes
Bioavailability Score 0.55
Medicinal Chemistry
PAINS 1 alert: ene_five_het_G
Brenk 1 alert: michael_acceptor_1
Leadlikeness No; 2 violations: MW>350, XLOGP3>3.5
Synthetic accessibility 3.76

b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PGP+
PGP-
Remarks
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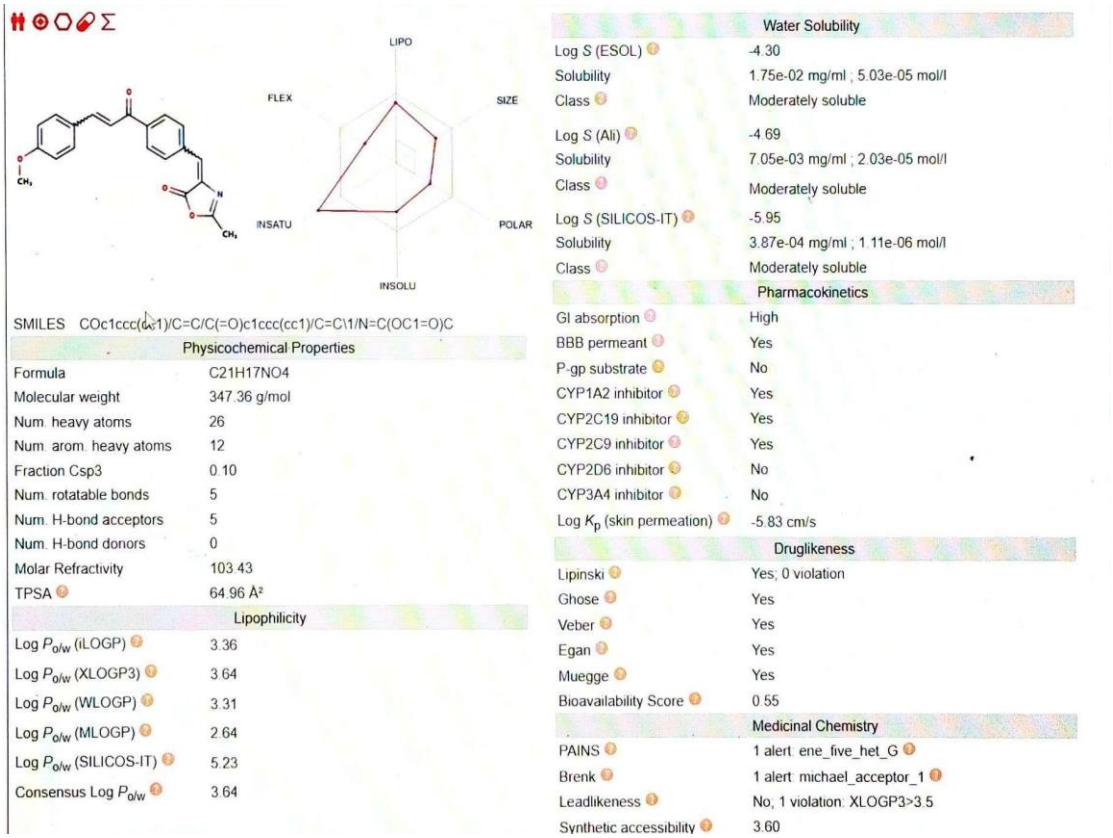
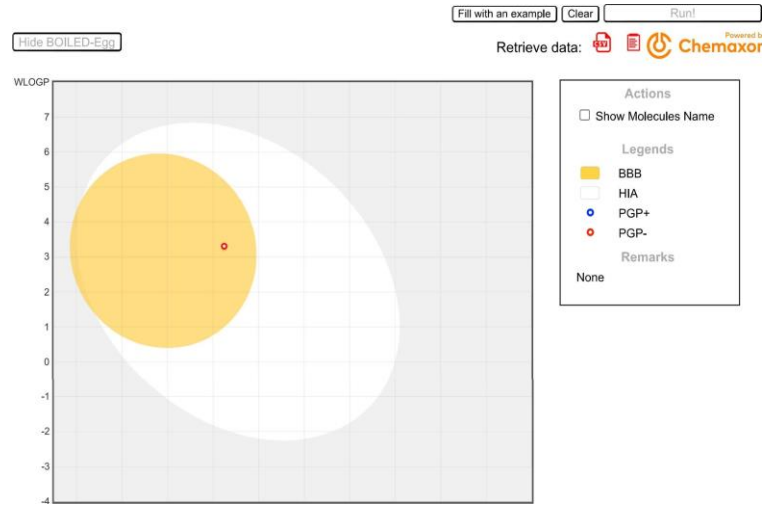
COMPOUND :4


LIPO
FLEX
SIZE
INSATU
POLAR
INSOLU
SMILES COc1ccc(cc1)/C=C/C(=O)c1ccc(cc1)/C=C\1/N=C(OC1=O)C
Physicochemical Properties
Formula C21H17NO4
Molecular weight 347.36 g/mol
Num. heavy atoms 26
Num. arom. heavy atoms 12
Fraction Csp3 0.10
Num. rotatable bonds 5
Num. H-bond acceptors 5
Num. H-bond donors 0
Molar Refractivity 103.43
TPSA 64.96 Å²
Lipophilicity
Log Po/w (iLOGP) 3.36
Log Po/w (XLOGP3) 3.64
Log Po/w (WLOGP) 3.31
Log Po/w (MLOGP) 2.64
Log Po/w (SILICOS-IT) 5.23
Consensus Log Po/w 3.64
Water Solubility
Log S (ESOL) -4.30
Solubility 1.75e-02 mg/ml ; 5.03e-05 mol/l
Class Moderately soluble
Log S (Ali) -4.69
Solubility 7.05e-03 mg/ml ; 2.03e-05 mol/l
Class Moderately soluble
Log S (SILICOS-IT) -5.95
Solubility 3.87e-04 mg/ml ; 1.11e-06 mol/l
Class Moderately soluble
Pharmacokinetics
GI absorption High
BBB permeant Yes
P-gp substrate No
CYP1A2 inhibitor Yes
CYP2C19 inhibitor Yes
CYP2C9 inhibitor Yes
CYP2D6 inhibitor No
CYP3A4 inhibitor No
Log Kp (skin permeation) -5.83 cm/s
Druglikeness
Lipinski Yes; 0 violation
Ghose Yes
Veber Yes
Egan Yes
Muegge Yes
Bioavailability Score 0.55
Medicinal Chemistry
PAINS 1 alert: ene_five_het_G
Brenk 1 alert: michael_acceptor_1
Leadlikeness No; 1 violation: XLOGP3>3.5
Synthetic accessibility 3.60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PGP+
PGP-
Remarks
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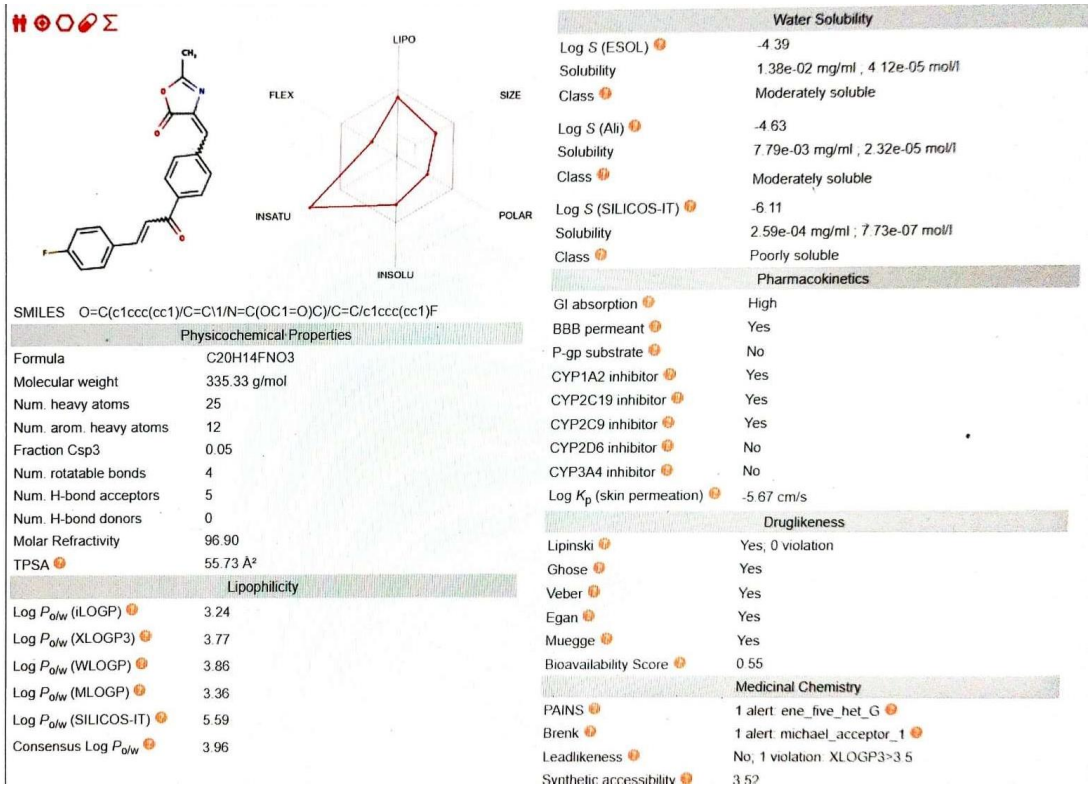
COMPOUND :5



Physicochemical Properties	
Formula	C20H14FNO3
Molecular weight	335.33 g/mol
Num. heavy atoms	25
Num. arom. heavy atoms	12
Fraction Csp3	0.05
Num. rotatable bonds	4
Num. H-bond acceptors	5
Num. H-bond donors	0
Molar Refractivity	96.90
TPSA	55.73 Å²
Lipophilicity	
Log $P_{o/w}$ (iLOGP)	3.24
Log $P_{o/w}$ (XLOGP3)	3.77
Log $P_{o/w}$ (WLOGP)	3.86
Log $P_{o/w}$ (MLOGP)	3.36
Log $P_{o/w}$ (SILICOS-IT)	5.59
Consensus Log $P_{o/w}$	3.96

Water Solubility	
Log *S* (ESOL)	-4.39
Solubility	1.38e-02 mg/ml ; 4.12e-05 mol/l
Class	Moderately soluble
Log *S* (Ali)	-4.63
Solubility	7.79e-03 mg/ml ; 2.32e-05 mol/l
Class	Moderately soluble
Log *S* (SILICOS-IT)	-6.11
Solubility	2.59e-04 mg/ml ; 7.73e-07 mol/l
Class	Poorly soluble
Pharmacokinetics	
GI absorption	High
BBB permeant	Yes
P-gp substrate	No
CYP1A2 inhibitor	Yes
CYP2C19 inhibitor	Yes
CYP2C9 inhibitor	Yes
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-5.67 cm/s
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55
Medicinal Chemistry	
PAINS	1 alert: ene_five_het_G
Brenk	1 alert: michael_acceptor_1
Leadlikeness	No; 1 violation: XLOGP3>3.5
Synthetic accessibility	3.52

b

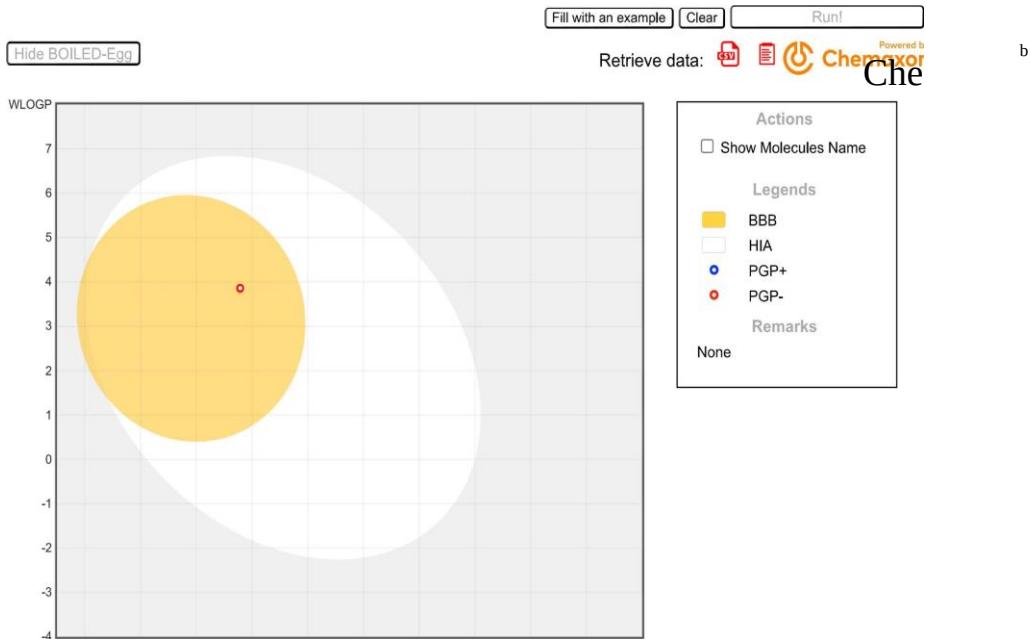


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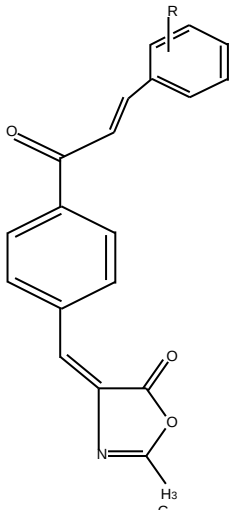
TABLE :4



Pharmaco kinetics	DRUG LINE SS	YES	YES	YES	YES	YES
	BBB	NO	YES	YES	YES	YES
	GI ABSORPTION	HIGH	HIGH	HIGH	HIGH	HIGH
	TSPA	85.19	75.96	55.73	64.96	74.19
Physio chemical properties	MOL REFRA	105.46	98.97	96.90	103.43	109.93
	NH-d	1	1	0	0	0
	NH-a	6	5	5	5	6
	N-RB	5	4	4	5	6
	NO AROM-HEAVY ATOMS	12	12	12	12	12
	NO HEAVY ATOMS	27	25	25	26	28
Compound		1	2	3	4	5

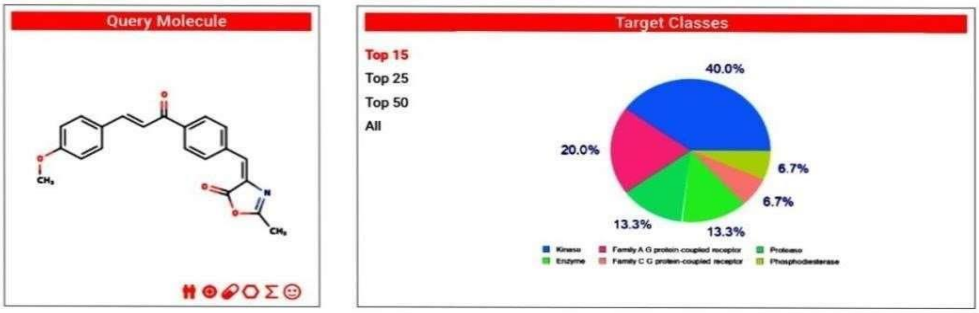
Dept. of. Pharmaceutical Chemistry Dr. I

Swiss target prediction has been primarily developed for identifying targets of molecules known to be bioactive. Swiss target prediction will suggest some target, based on the assumption that if the molecule is active, it will likely bind to some protein. For molecules with unknown bio activity this assumption is not valid perse and the molecule may not bind to any protein, in which case all predicted targets are false-positive .In particular, inactive compounds can sometimes exhibit good similarity with active molecules if they have been obtained by modifying an active compound at some key position that was crucial for its interactions .This is a known limitation of ligand based approaches when applied to any kind of compounds and therefore target predictions should be interpreted with care in the absence of Indication of bioactivity.

Swiss Target Prediction is a web-based tool, on-line since 2014, to perform ligand- based target prediction for any bioactive small molecule. The user-friendly graphical interface shields non-experts from methodological pitfalls and specialists from tedious technical efforts. This allows anyone to achieve reverse screening towards previously carefully prepared chemical libraries.

The Swiss Target Prediction model was trained by fitting a multiple logistic regression on various size related subsets of known actives in order to weight 2D and 3D similarity parameters in a so-called Combined-Score. A Combined Score higher than 0.5 predicts that the molecules are likely to share a common protein target. In reverse screening, the Combined-Score allows to calculate for any query molecule, assumed as bioactive, the probability to target a given protein. As 2D and 3D description of molecules are complementary, this Dual scoring ligand-based reverse screening showed high performance in predicting macromolecular targets in various test sets.

COMPOUND-1



Export results:

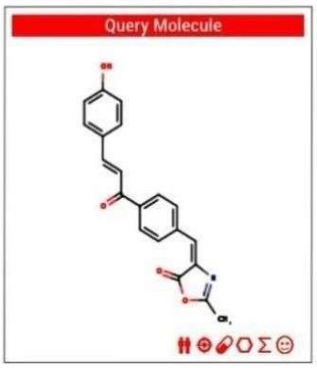
Show 15 entries Search:

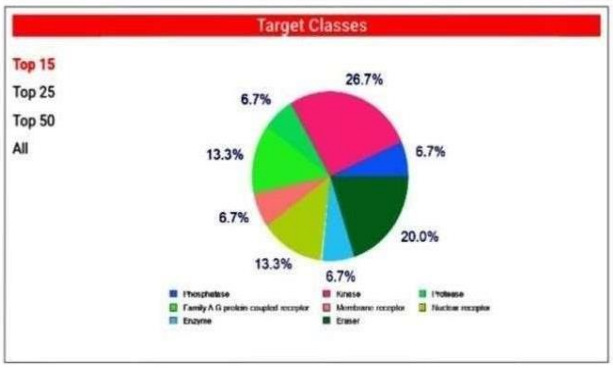
Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Casein kinase II alpha	CSNK2A1	P68400	CHEMBL3629	Kinase		24 / 0
Casein kinase II alpha (prime)	CSNK2A2	P19784	CHEMBL4070	Kinase		8 / 0
Muscarinic acetylcholine receptor M1	CHRM1	P11229	CHEMBL216	Family A G protein-coupled receptor		59 / 0
ALK tyrosine kinase receptor	ALK	Q9UM73	CHEMBL4247	Kinase		94 / 0
MAP kinase p38 alpha	MAPK14	Q16539	CHEMBL260	Kinase		742 / 0
ADAM17	ADAM17	P78536	CHEMBL3706	Protease		263 / 0
Complement factor D	CFD	P00746	CHEMBL2176771	Protease		292 / 0
MAP kinase ERK2	MAPK1	P28482	CHEMBL4040	Kinase		502 / 0
Orexin receptor 2	HCRTR2	O43614	CHEMBL4792	Family A G protein-coupled receptor		237 / 0
Orexin receptor 1	HCRTR1	O43613	CHEMBL5113	Family A G protein-coupled receptor		212 / 0
Anandamide amidohydrolase	FAAH	O00519	CHEMBL2243	Enzyme		244 / 0
Monoglyceride lipase	MGLL	Q99685	CHEMBL4191	Enzyme		53 / 0
Metabotropic glutamate receptor 5 *(by homology)*	GRM5	P41594	CHEMBL3227	Family C G protein-coupled receptor		197 / 0
Phosphodiesterase 10A *(by homology)*	PDE10A	Q9Y233	CHEMBL4409	Phosphodiesterase		666 / 0
MAP kinase-activated protein kinase 2	MAPKAPK2	P49137	CHEMBL2208	Kinase		92 / 0

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

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

COMPOUND-2





Export results:

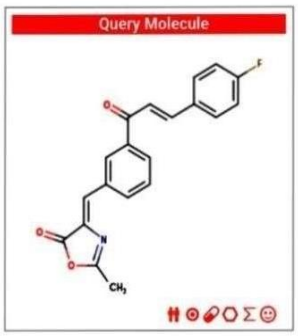
Show 15 entries Search:

Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Protein-tyrosine phosphatase 1B	PTPN1	P18031	CHEMBL335	Phosphatase		44 / 0
Cyclin-dependent kinase 5/CDK5 activator 1	CDK5R1 CDK5	Q15078 Q00535	CHEMBL1907600	Kinase		59 / 0
Dual-specificity tyrosine-phosphorylation regulated kinase 1A *(by homology)*	DYRK1A	Q13627	CHEMBL2292	Kinase		35 / 0
Beta-secretase 1	BACE1	P56817	CHEMBL4822	Protease		187 / 0
Pyruvate dehydrogenase kinase isoform 1	PDK1	Q15118	CHEMBL4766	Kinase		250 / 0
Dopamine D1 receptor	DRD1	P21728	CHEMBL2056	Family A G protein-coupled receptor		95 / 0
Dopamine D3 receptor	DRD3	P35462	CHEMBL234	Family A G protein-coupled receptor		813 / 0
Sigma opioid receptor	SIGMAR1	Q99720	CHEMBL287	Membrane receptor		314 / 0
MAP kinase-activated protein kinase 2	MAPKAPK2	P49137	CHEMBL2208	Kinase		54 / 0
Estrogen receptor alpha	ESR1	P03372	CHEMBL206	Nuclear receptor		107 / 0
Estrogen receptor beta	ESR2	Q92731	CHEMBL242	Nuclear receptor		90 / 0
Macrophage migration inhibitory factor	MIF	P14174	CHEMBL2085	Enzyme		16 / 0
Histone deacetylase 1	HDAC1	Q13547	CHEMBL325	Eraser		511 / 0
Histone deacetylase 6	HDAC6	Q9UBN7	CHEMBL1865	Eraser		336 / 0
Histone deacetylase 8	HDAC8	Q9BY41	CHEMBL3192	Eraser		272 / 0

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

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

COMPOUND -3



Export results:

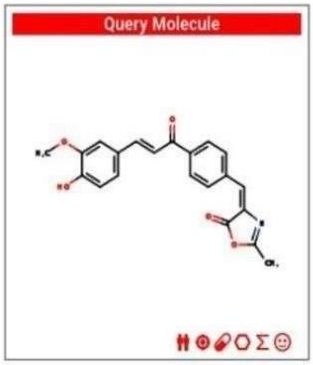
Show 15 entries Search:

Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Neuropeptide Y receptor type 5	NPY5R	Q15761	CHEMBL4561	Family A G protein-coupled receptor		519 / 0
P2X purinoceptor 7	P2RX7	Q99572	CHEMBL4805	Ligand-gated ion channel		621 / 0
Cannabinoid receptor 1	CNR1	P21554	CHEMBL218	Family A G protein-coupled receptor		1779 / 0
Cannabinoid receptor 2	CNR2	P34972	CHEMBL253	Family A G protein-coupled receptor		1444 / 0
Cathepsin S	CTSS	P25774	CHEMBL2954	Protease		400 / 0
Prolyl endopeptidase	PREP	P48147	CHEMBL3202	Protease		138 / 0
Chymase	CMA1	P23946	CHEMBL4068	Protease		100 / 0
Fibroblast activation protein alpha *(by homology)*	FAP	Q12884	CHEMBL4683	Protease		75 / 0
Receptor protein-tyrosine kinase erbB-2	ERBB2	P04626	CHEMBL1824	Kinase		239 / 0
Tyrosine-protein kinase BRK	PTK6	Q13882	CHEMBL4601	Kinase		22 / 0
Calpain 1	CAPN1	P07384	CHEMBL3891	Protease		185 / 0
Nerve growth factor receptor Trk-A	NTRK1	P04629	CHEMBL2815	Kinase		350 / 0
Ketohexokinase	KHK	P50053	CHEMBL1275212	Enzyme		9 / 0
Glycine transporter 1	SLC6A9	P48067	CHEMBL2337	Electrochemical transporter		155 / 0
Glycine transporter 2	SLC6A5	Q9Y345	CHEMBL3060	Electrochemical transporter		7 / 0

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

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

COMPOUND- 4



Export results:

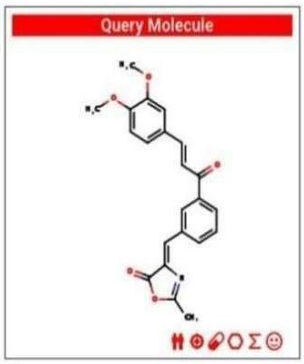
Show 15 entries Search:

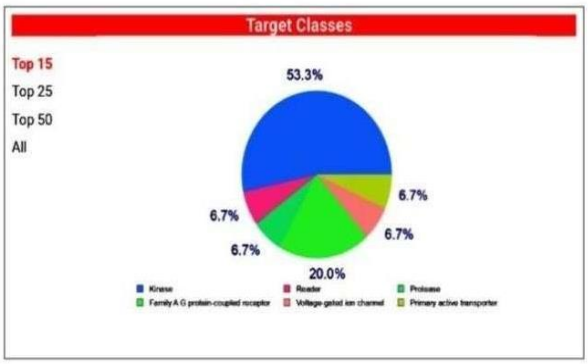
Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
ALK tyrosine kinase receptor	ALK	Q9UM73	CHEMBL4247	Kinase		60 / 0
Protein-tyrosine phosphatase 1B	PTPN1	P18031	CHEMBL335	Phosphatase		44 / 0
Histone deacetylase 1	HDAC1	Q13547	CHEMBL325	Eraser		400 / 0
Vanilloid receptor	TRPV1	Q8NER1	CHEMBL4794	Voltage-gated ion channel		166 / 0
Histone deacetylase 6	HDAC6	Q9UBN7	CHEMBL1865	Eraser		191 / 0
Histone deacetylase 8	HDAC8	Q9BY41	CHEMBL3192	Eraser		143 / 0
Poly [ADP-ribose] polymerase-1	PARP1	P09874	CHEMBL3105	Enzyme		349 / 0
Beta-secretase 1	BACE1	P56817	CHEMBL4822	Protease		190 / 0
Dopamine D1 receptor	DRD1	P21728	CHEMBL2056	Family A G protein-coupled receptor		50 / 0
Dopamine D2 receptor	DRD2	P14416	CHEMBL217	Family A G protein-coupled receptor		1281 / 0
Dopamine D3 receptor	DRD3	P35462	CHEMBL234	Family A G protein-coupled receptor		531 / 0
Sigma opioid receptor	SIGMAR1	Q99720	CHEMBL287	Membrane receptor		215 / 0
Cyclin-dependent kinase 2	CDK2	P24941	CHEMBL301	Kinase		136 / 0
Cyclin-dependent kinase 4	CDK4	P11802	CHEMBL331	Kinase		49 / 0
Estradiol 17-beta-dehydrogenase 2	HSD17B2	P37059	CHEMBL2789	Enzyme		71 / 0

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

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

COMPOUND - 5





Export results:

Show 15 entries Search:

Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Nerve growth factor receptor Trk-A	NTRK1	P04629	CHEMBL2815	Kinase		485 / 0
Bromodomain-containing protein 4	BRD4	O60885	CHEMBL1163125	Reader		252 / 0
Glycogen synthase kinase-3 beta	GSK3B	P49841	CHEMBL262	Kinase		661 / 0
MAP kinase ERK1	MAPK3	P27361	CHEMBL3385	Kinase		64 / 0
MAP kinase ERK2	MAPK1	P28482	CHEMBL4040	Kinase		623 / 0
Cathepsin K	CTSK	P43235	CHEMBL268	Protease		459 / 0
Epidermal growth factor receptor erbB1	EGFR	P00533	CHEMBL203	Kinase		1084 / 0
Serine/threonine-protein kinase PIM1	PIM1	P11309	CHEMBL2147	Kinase		227 / 0
Serine/threonine-protein kinase PIM2	PIM2	Q9P1W9	CHEMBL4523	Kinase		134 / 0
Orexin receptor 2	HCRTR2	O43614	CHEMBL4792	Family A G protein-coupled receptor		934 / 0
Orexin receptor 1	HCRTR1	O43613	CHEMBL5113	Family A G protein-coupled receptor		822 / 0
Transient receptor potential cation channel subfamily A member 1	TRPA1	O75762	CHEMBL6007	Voltage-gated ion channel		34 / 0
Multidrug resistance-associated protein 1	ABCC1	P33527	CHEMBL3004	Primary active transporter		28 / 0
Tyrosine-protein kinase SYK	SYK	P43405	CHEMBL2599	Kinase		619 / 0
Neuropeptide Y receptor type 5	NPY5R	Q15761	CHEMBL4561	Family A G protein-coupled receptor		432 / 0

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

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

AUTO DOCK VINA:

Auto Dock Vina- Auto Dock Vina is a freely available software. It provides a platform for the interaction of target protein with the ligand. The target protein was loaded on graphical windows of Auto Dock Vina and the target protein in .pdb format was prepared for docking by deleting water molecules, adding hydrogen polar atoms and by adding Kollman charges to the protein molecule and finally protein was saved in. pdbqt format. Ligand molecule was imported in .pdb format and was converted to. pdbqt format. After that grid box was selected for the region to be docked. Using command prompt Auto Dock Vina was executed and results were analysed.

Methodology:

A. Selection of Target Protein:

The structure of protein molecule of cyclooxygenase -2 (prostaglandin synthase-2) complexed with a selective inhibitor (1cx2) (pdb id: sc-558) which is an anti- inflammatory and was downloaded from Protein Data Bank (PDB). The structure of protein molecule was retrieved in .pdb format.

B. Ligand Preparation:

The ligands were downloaded in 3D structure in .sdf format. The downloaded structures of ligands were converted into .pdb format through online SMILES Translator. The converted files were downloaded in .pdb format. These .pdb files were used to run different tools and software's.

C. Preparation of protein molecule:

The protein preparation was done through Biovia Discovery Studio Visualizer. This software prepares the protein molecule for the docking studies. Analysis of the protein molecule was done to know the different properties. The protein was loaded in .pdb format and its hierarchy was analysed by selecting water molecules and ligands. The ligand attached molecules were deleted from the protein molecule and all the water molecules were also deleted. The crystal structure of protein was further saved in .pdb file.

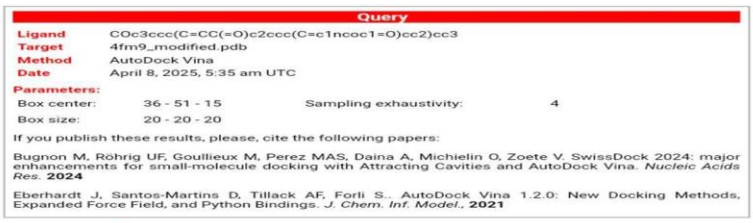
D. Screening of ligands:

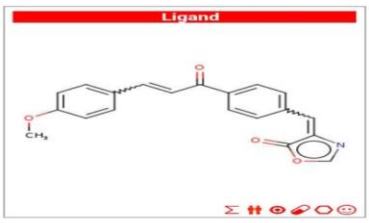
The screenings of ligands were done through PyRx software. PyRx is a freely available software for virtual screening of ligands based on their binding energies. Ligands which were found to be having minimum binding energy were screened for the drug likeliness property analysis. PyRx runs on. pdbqt format. The procedure of PyRx starts with loading of protein molecule, which was first converted from .pdb to. Pdbqt format and then ligands were imported from the specific folder in .sdf format. The energy of ligands was minimized followed by the conversion of .sdf file to. Pdbqt file. Docking was performed between protein target and ligand molecule, and according to minimum binding energy ligands were screened.

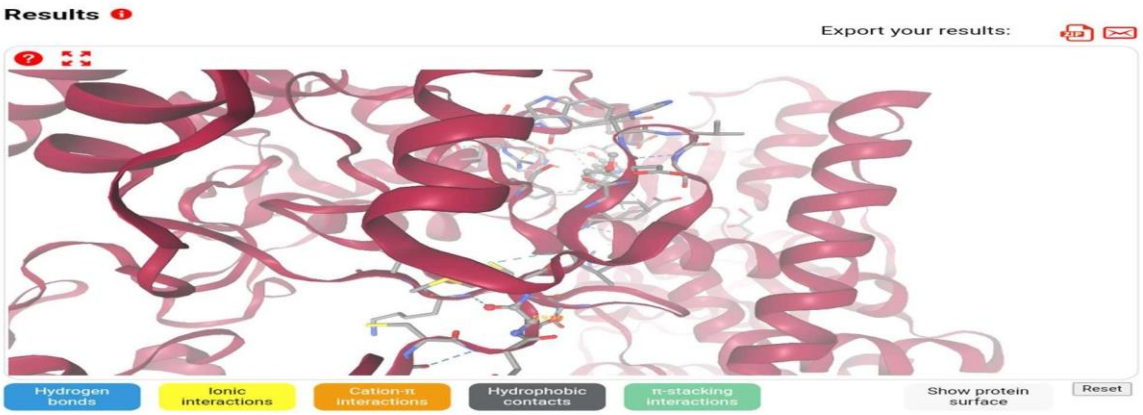
E. Final docking through Auto Dock Vina and Biovia Discovery Studio Client 2020:

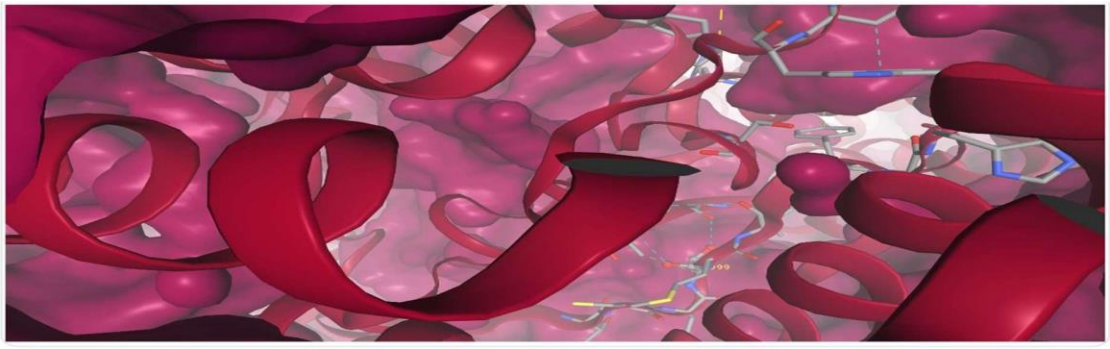
The screened ligands were selected for final docking through Auto Dock Vina and Biovia Discovery Studio Client 2020.

COMPOUND- 1









Model	Calculated affinity (kcal/mol)
1	-7.462
2	-7.317
3	-7.145
4	-6.872
5	-6.457
6	-6.375
7	-4.898

COMPOUND:2

Query

Ligand	Cc3nc(=Cc2ccc(C(=O)C=Cc1ccc(O)cc1)cc2)c(=O)o3
Target	4fm9_modified.pdb
Method	AutoDock Vina
Date	March 27, 2025, 6:44 am UTC

Parameters:

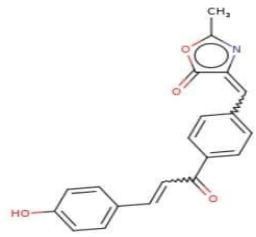
Box center:	36 - 51 - 15	Sampling exhaustivity:	4
Box size:	20 - 20 - 20		

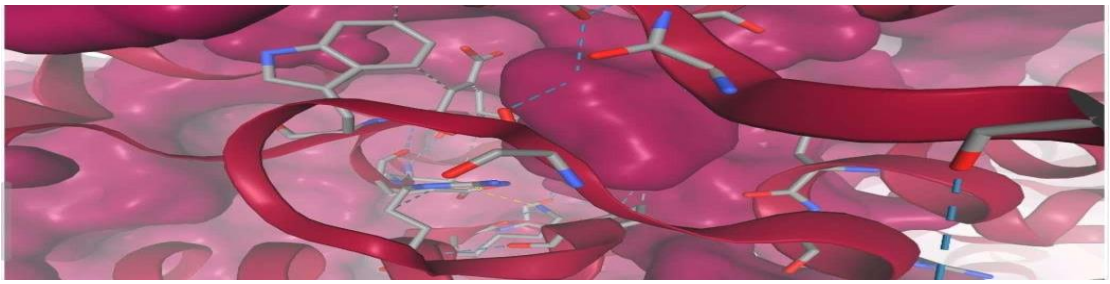
If you publish these results, please, cite the following papers:

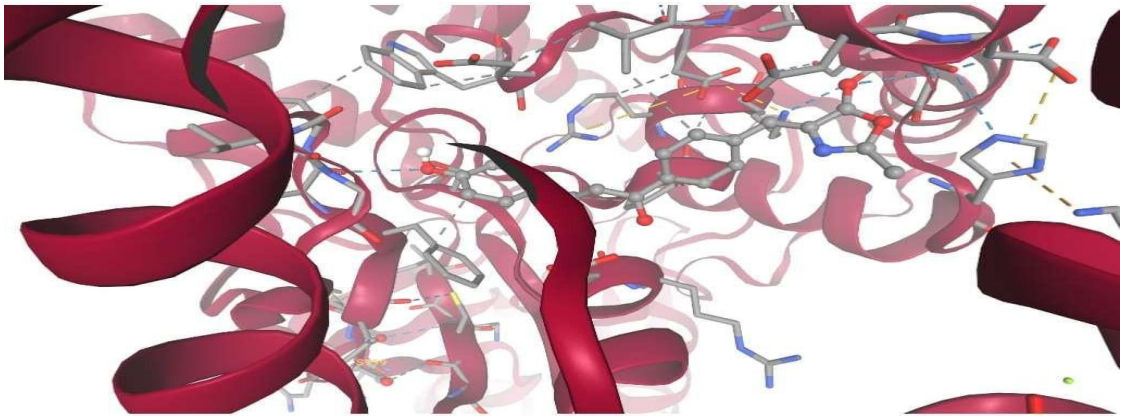
Bugnon M, Röhrig UF, Goullieux M, Perez MAS, Daina A, Michielin O, Zoete V. SwissDock 2024: major enhancements for small-molecule docking with Attracting Cavities and AutoDock Vina. *Nucleic Acids Res.* **2024**

Eberhardt J, Santos-Martins D, Tillack AF, Forli S., AutoDock Vina 1.2.0: New Docking Methods, Expanded Force Field, and Python Bindings. *J. Chem. Inf. Model.*, **2021**

Ligand

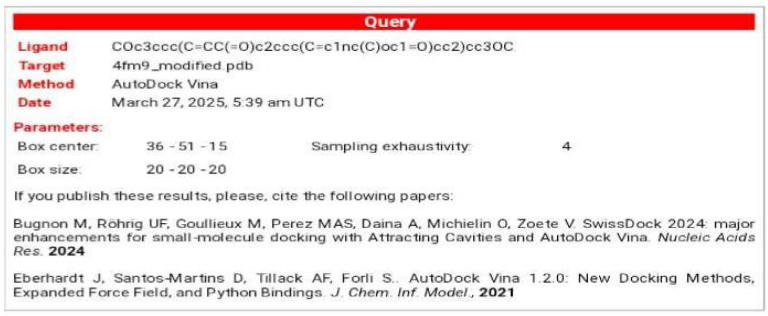


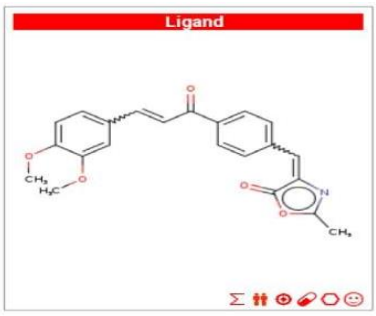


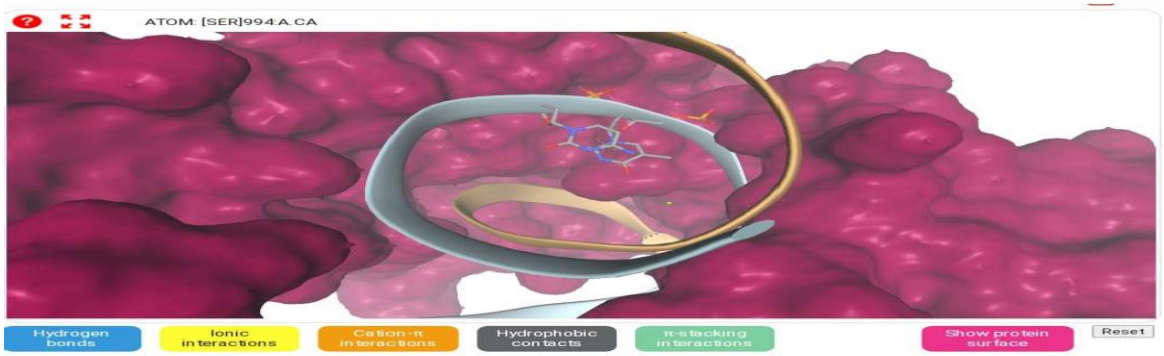


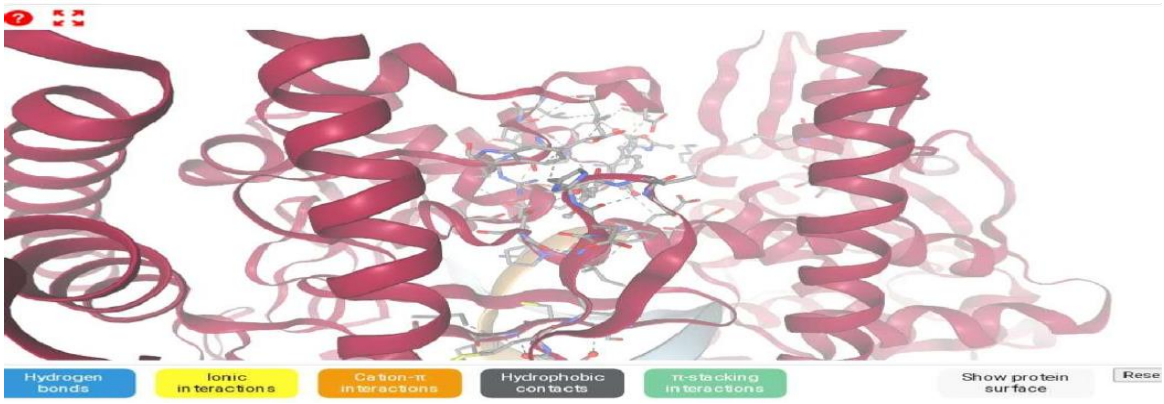
Model	Calculated affinity (kcal/mol)
1	-8.155
2	-7.986
3	-7.957
4	-7.796
5	-7.639
6	-7.374
7	-7.074
8	-6.579
9	-6.394
10	-6.347
11	-5.925
12	-5.601
13	-5.437

COMPOUND – 3









Model	Calculated affinity (kcal/mol)
1	-7.526
2	-7.401
3	-7.376
4	-6.556
5	-5.972
6	-5.499

COMPOUND: 4

Query

Ligand	COc3cc(C=CC(=O)c2ccc(C=c1nc(C)oc1=O)cc2)ccc3O
Target	4fm9_modified.pdb
Method	AutoDock Vina
Date	March 27, 2025, 6:33 am UTC

Parameters:

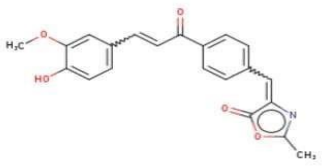
Box center:	36 - 51 - 15	Sampling exhaustivity:	4
Box size:	20 - 20 - 20		

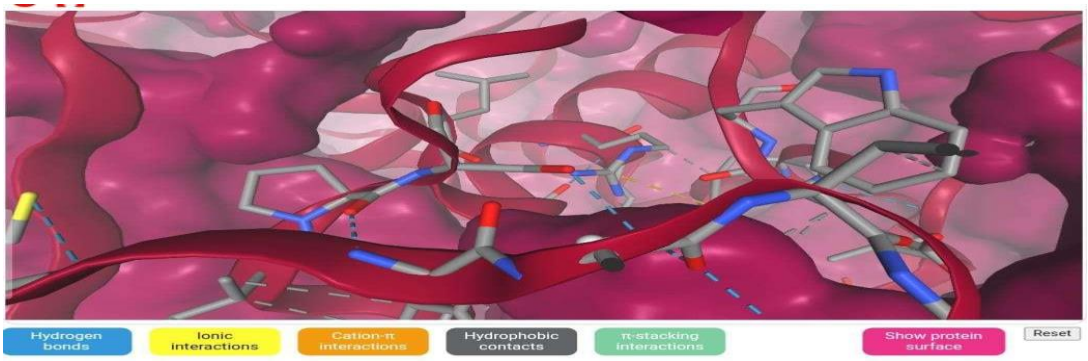
If you publish these results, please, cite the following papers:

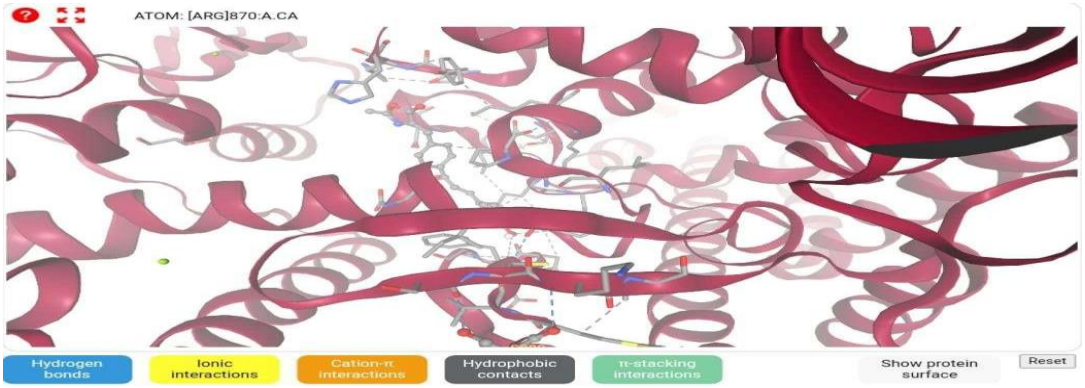
Bugnon M, Röhrig UF, Goullieux M, Perez MAS, Daina A, Michielin O, Zoete V. SwissDock 2024: major enhancements for small-molecule docking with Attracting Cavities and AutoDock Vina. *Nucleic Acids Res.* **2024**

Eberhardt J, Santos-Martins D, Tillack AF, Forli S.. AutoDock Vina 1.2.0: New Docking Methods, Expanded Force Field, and Python Bindings. *J. Chem. Inf. Model.*, **2021**

Ligand







Model	Calculated affinity (kcal/mol)
1	-8.035
2	-7.892
3	-7.892
4	-7.848
5	-7.120
6	-6.863
7	-6.800
8	-6.338
9	-6.245
10	-6.039
11	-5.796
12	-5.626
13	-5.310

COMPOUND :5

Query

Ligand	Cc3nc(=Cc2ccc(C(=O)C=Cc1ccc(F)cc1)cc2)c(=O)o3
Target	4fm9_modified.pdb
Method	AutoDock Vina
Date	March 27, 2025, 6:47 am UTC

Parameters:

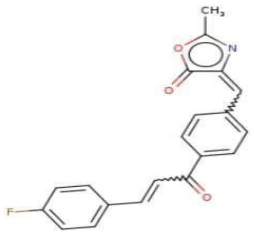
Box center:	36 - 51 - 15	Sampling exhaustivity:	4
Box size:	20 - 20 - 20		

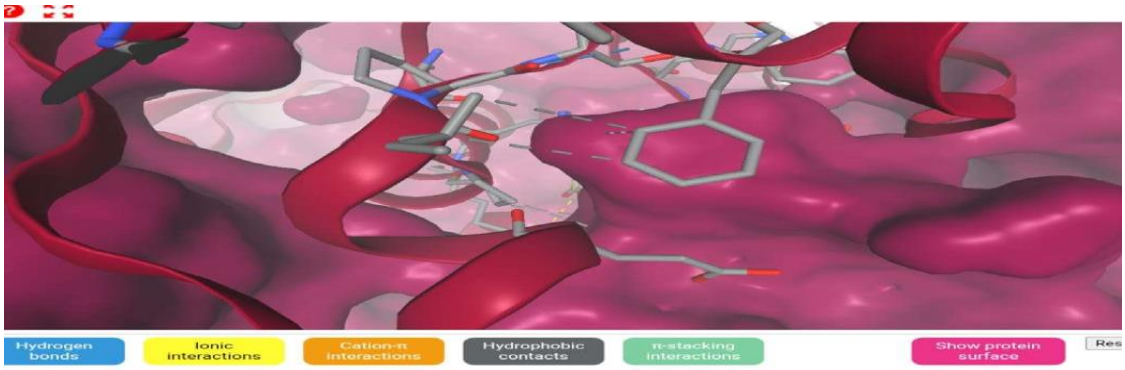
If you publish these results, please, cite the following papers:

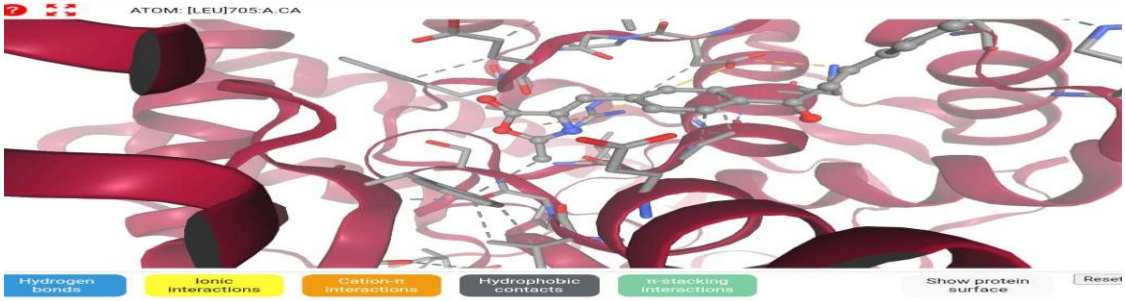
Bugnon M, Röhrig UF, Goullieux M, Perez MAS, Daina A, Michielin O, Zoete V. SwissDock 2024: major enhancements for small-molecule docking with Attracting Cavities and AutoDock Vina. *Nucleic Acids Res.* **2024**

Eberhardt J, Santos-Martins D, Tillack AF, Forli S.. AutoDock Vina 1.2.0: New Docking Methods, Expanded Force Field, and Python Bindings. *J. Chem. Inf. Model.*, **2021**

Ligand



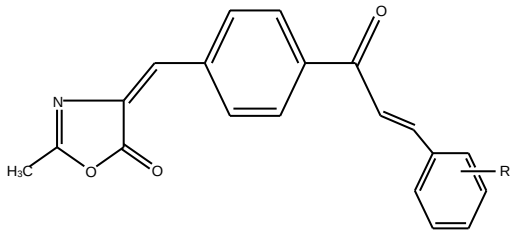




Model	Calculated affinity (kcal/mol)
1	-8.195
2	-8.155
3	-7.938
4	-7.923
5	-7.758
6	-7.709
7	-7.559
8	-7.402
9	-7.191
10	-6.939
11	-6.781
12	-6.615
13	-6.223
14	-5.807

TABLE:5

MOLECULAR DOCKING OF 4,4(3-SUBSTITUTED PHENYL)ACRYLOYL)BENZYLIDENE)2-METHYLOXAZOL- 5-(4H)ONE DERIVATIVE USING AUTO DOCK VINA



COMPOUND	Calculated affinity(kcal/mol)
1	-7.467
2	-8.155
3	-7.526
4	-8.035
5	-8.195

RESULTS AND DISCUSSION

The 4,4(3-substitutedphenyl)acryloyl)benzylidene)2-methyloxazol-5-4h)one derivative were evaluated for *in-silico* properties by using online software programmes like Molinspiration, Swiss ADME, Swiss Target Prediction, and Molecular Docking which are helpful to predict molecular properties and drug likeness. The results depicted that all the designed analogues satisfied and obey Lipinski five rule. The analogues have molecular weight less than 500g/mol and they log P value are less than 5 hence the derivatives showed well *in vivo* drug absorption and permeation. *Insilco* ADME prediction clearly showed that the designed analogues penetrate the blood brain barrier to the Negi able extent only. Hence the compound possesses drug likeliness properties. Based on the Lipinski rule molecular weight, hydrogen donor/and acceptor and non-rotational bonds of the designed motifs produced their affordable result towards their molecular properties. The polar surface area was also showed significant value, which is accountable for their oral bioavailability. Transport characteristics of molecules like BBB penetration and intestinal absorption were determined from molecular volume. In QSAR studies volume is used to denote the relationship between molecular properties and biological activities. Docking tools are designed to predict the binding of small molecules with known target proteins. The active sites of the target protein, the binding energies of the small molecules are determined based on their binding mechanism. Bio viva discovery studio visualizers are used to visualize the ligand position in the enzyme binding site. This tool is very useful to study the binding nature which is useful for development of potential drug molecules. Molecular docking score indicated that the compounds exhibited strong binding affinity with targets such as the neuropeptide Y receptor and serine/threonine-protein kinase RAF. Among the series, compounds 1 and 3 showed potential activity against the glucagon receptor. All the results were tabulated, and it was observed that compounds obeyed the Lipinski rule of five and were found to be active. Overall, para-substitution on the aromatic ring enhanced the compounds Physico chemical properties, underlining its importance in drug design. These derivatives show promising therapeutic potential, particularly for anti-cancer, anti- inflammatory, antimicrobial activities.

CONCLUSION:

A series of 4,4(3-substitutedphenyl)acryloyl)benzylidene)2-methyloxazol-5-4h)one derivative were designed and evaluated for *in silico* properties. Among the series the para-substituted derivatives exhibited superior efficacy. The in-silico evaluation revealed that all five compounds adhered to Lipinski's rule of five, indicating favourable pharmacokinetic properties and good oral absorption potential. Molecular docking studies showed strong binding interactions, particularly for compound 1, which exhibited the highest binding affinity with target proteins such as neuropeptide Y receptor and serine/threonine-protein kinase RAF. Additionally, compounds 2 and 3 showed notable affinity toward the glucagon receptor, suggesting potential in antidiabetic therapy. These findings collectively highlight the multifunctional biological significance of oxazole derivatives, reinforcing their value in medicinal chemistry. They serve as promising leads for further development in treating cancer, microbial infections, inflammation, and metabolic disorders.

BIBLIOGRAPHY:

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