Búsqueda computacional de moléculas contra la enfermedad de Alzheimer

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Máster en Bioinformática y Bioestadística

Bioinformática Farmacéutica

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FICHA DEL TRABAJO FINAL

Título del trabajo:	*Búsqueda computacional de moléculas contra la enfermedad de Alzheimer.*
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Palabras clave	*Alzheimer, molécula, cribado virtual*

Resumen del Trabajo (máximo 250 palabras): *Con la finalidad, contexto de aplicación, metodología, resultados i conclusiones del trabajo.*

Este trabajo se ha desarrollado con la finalidad de realizar un estudio que refleje el proceso bioinformático en la búsqueda de nuevos fármacos o "drug-discovery".

La enfermedad escogida para el estudio es el Alzheimer, una enfermedad compleja que actualmente no tiene cura y que dado su impacto en la sociedad es objeto de numerosos esfuerzos para encontrar un tratamiento eficaz.

La primera parte del estudio es la búsqueda y la elección de dianas contra las que pueda actuar pequeñas moléculas con finalidad terapéutica. Se ha aplicado el lenguaje R para obtener información de las bases de datos de genes relacionados con enfermedades DisGenet y Uniprot.

Posteriormente las dianas se han escogido en base a su relevancia en la enfermedad en la bibliografía disponible. Se han obtenido sus estructuras en la base de datos de estructuras de proteínas RSCB-PDB y algunas a través de su secuencia utilizando el servidor Phyre2 que proporciona la estructura por homología.

Las dianas escogidas han sido: dominio E1 de la proteína precursora amiloide, proteína amiloide de suero A1 , proteína Kinasa-1 con afinidad por microtúbulos, Preselinina-1 dominio CTF y RAMP3.

A continuación se ha realizado un cribado virtual (virtual sceening) con el servidor MTiOpenScreen para obtener las moléculas con posibilidad de actuar como fámacos.

Finalmente en base a las propiedades fisicoquímicas aportadas en los resultados del cribado y las propiedades ADMET obtenidas del servidor pkCSM

se han elegido seis moléculas con un posible potencial farmacológico:

2-[[4-benzyl-5-(4-fluorophenyl)-1,2,4-triazol-3-yl]sulfanyl]-1-(2,3-dihydroindol-1-yl)propan-1-one,4-[(E)-2-[5-chloro-2-(3,4-dichlorophenyl)phenyl]ethenyl]benzoic acid, benzene-1,2,4,5-tetrathiolate, (1S)-1-(2-cyclohexylsulfanylcyclopentyl)-N-diphenylphosphanyl-N-methylethanamine, 2-(6-chloro-3-oxo-4H-1,4-benzothiazin-2-yl)-N-(3-piperidin-1-ylpropyl)acetamide, 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-piperidin-1-ylpyrazole-3-carboxamide;metanol.

Abstract (in English, 250 words or less):

This work has been developed with the purpose of carrying out a study that reflects the bioinformatic process to find out new drugs or drug- discovery.

The disease chosen for the study is Alzheimer's disease, a complex disease that currently has no cure, due to its impact on society is the subject of numerous efforts to find an effective treatment.

The first part of the study is the search and choice of targets against which small molecules could be use to therapeutic purposes. The R language has been applied to acquire information from DisGenet and Uniprot databases of genes related to diseases.

Subsequently, the targets have been chosen based on their relevance to the disease in the available literature. Its structures has been obtained in the RSCB-PDB database of protein structure, and some of them through its sequence applying the Phyre2 server by homology.

The targets chosen were: E1 domain of the amyloid precursor protein, serum amyloid protein A1, protein kinase-1 with affinity for microtubules, Preselinin-1 domain CTF and RAMP3.

Next, a virtual screening was performed with the MTiOpenScreen server to obtain the molecules with the possibility of being used as drugs.

Finally, based on the physicochemical properties provided in the screening results and the ADMET properties obtained from the pkCSM server, six molecules with a possible pharmacological potential have been chosen:
2-[[4-benzyl-5-(4-fluorophenyl)-1,2,4-triazol-3-yl]sulfanyl]-1-(2,3-dihydroindol-1-yl)propan-1-one, 4 - [(E) -2- [5-chloro-2- (3,4-dichlorophenyl) phenyl] ethenyl] benzoic acid, benzene-1,2,4,5-tetrathiolate, (1S) -1- (2-cyclohexylsulfanylcyclopentyl) -N-diphenylphosphanyl-N-methylethanamine, 2-(6-chloro-3-oxo-4H-1,4-benzothiazin-2-yl) -N- (3-piperidin-1-ylpropyl) acetamide, 5- (4-chlorophenyl) -1- (2,4-dichlorophenyl) -N-piperidin-1-ylpyrazole-3-carboxamide; methanol.

Contenido

1. Introducción

1.1 Contexto y justificación del Trabajo

He elegido la enfermedad de Alzheimer como temática del trabajo fin de máster por su gran influencia en la sociedad. Actualmente la padecen más de 25 millones de personas en el mundo y debido al envejecimiento de la población en países occidentales su prevalencia va en aumento, incluso en países en vías de desarrollo como China, India o Latinoamérica.

La demencia puede ser de dos tipos enfermedad de Alzheimer (AD) y la demencia vascular (VaD), tienen influencia una sobre la otra y viceversa, es un tema de debate científico. No obstante el Alzheimer tiene una prevalencia del 60% y la demencia vascular un 20% sobre el total de pacientes[1].

En las figuras siguientes se muestre la previsión de la prevalencia de la demencia en el mundo y su distribución por regiones.

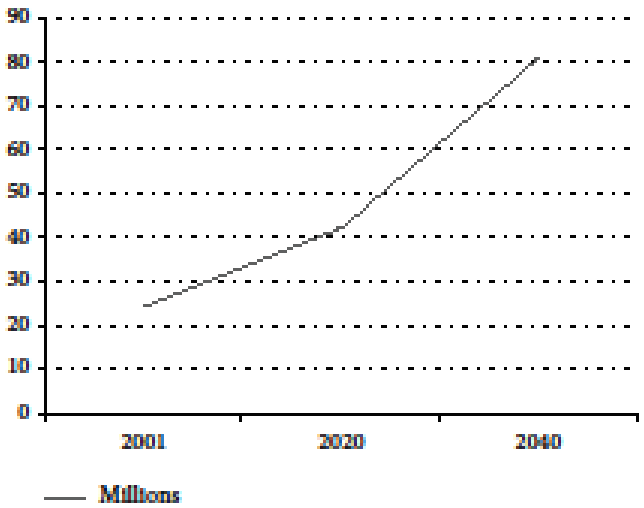

FIGURE 1: Estimate of numbers of people living with dementia worldwide. Based on raw data from Ferri et al., 2005 [4, page 2114].

Figura 1 Estimación de número de personas con demencia

[1] Bibliografía 2

TABLE 1: Worldwide estimate for the absolute number of cases of dementia according to the Delphi Consensus Study.

	Absolute number of people over 60 years old who have dementia (millions)		
	2001	2020	2040
Western Europe	4.9	6.9	9.9
Eastern Europe low adult mortality	1.0	1.6	2.8
Eastern Europe high adult mortality	1.8	2.3	3.2
North America	3.4	5.1	9.2
Latin America	1.8	4.1	9.1
North Africa and Middle Eastern Crescent	1.0	1.9	4.7
Developed Western Pacific	1.5	2.9	4.3
China and the developing Western Pacific	6.0	11.7	26.1
Indonesia, Thailand, and Sri Lanka	0.6	1.3	2.7
India and South Asia	1.8	3.6	7.5
Africa	0.5	0.9	1.6
Total	24.3	42.3	81.1

Created from raw data provided by Ferri et al., 2005 [4, Page 2115].

Figura 2. Estimación del número de personas con demencia por regiones

Es una enfermedad compleja en donde intervienen muchos factores tanto a nivel molecular como psicofisiológico. En la actualidad se están realizando grandes esfuerzos para encontrar un tratamiento adecuado que permita si no curarla completamente disminuir su efecto, aumentando la calidad de quienes la padecen.

El funcionamiento del cerebro y del sistema nervioso va a ser crucial para el desarrollo de la humanidad, ya que la esperanza de vida aumenta[2], también hay que aumentar su calidad a nivel cognitivo.

[2] Bibliografía 7

Cuadro 1. Esperanza de vida al nacer en hombres y mujeres en 2012 en los 10 países con mayores cifras

Hombres			Mujeres		
Orden	País	Esperanza de vida	Orden	País	Esperanza de vida
1	Islandia	81,2	1	Japón	87,0
2	Suiza	80,7	2	España	85,1
3	Australia	80,5	3	Suiza	85,1
4	Israel	80,2	4	Singapur	85,1
5	Singapur	80,2	5	Italia	85,0
6	Nueva Zelandia	80,2	6	Francia	84,9
7	Italia	80,2	7	Australia	84,6
8	Japón	80,0	8	República de Corea	84,6
9	Suecia	80,0	9	Luxemburgo	84,1
10	Luxemburgo	79,7	10	Portugal	84,0

Los países con menos de 250 000 habitantes se han omitido debido a la incertidumbre de las estimaciones de la esperanza de vida.

Figura 3. Esperanza de vida por regiones y sexo

1.2 Objetivos del Trabajo

1.2.1 Objetivos generales:

Objetivo 1: Encontrar dianas, al menos 3, de las posibles moléculas terapéuticas entre las proteínas que intervienen en el desarrollo de la enfermedad.

Objetivo 2: Encontrar varias moléculas, al menos 3, con posible efecto terapéutico conjunto de entre todas las posibles.

1.2.2 Objetivos específicos

Objetivo específico 1: búsqueda de dianas terapéuticas en base a su implicación en el desarrollo de la enfermedad utilizando bibliografía.

Objetivo específico 2: búsqueda de dianas terapéuticas en base a su diferente expresión en el desarrollo de la enfermedad.

Objetivos específico 3: elección de las moléculas contra las dianas previamente estudiadas.

Objetivo específico 4: comprobación de la viabilidad a nivel fisiológico de las moléculas elegidas.

Objetivo específico 5: presentar los resultados de al menos 3 moléculas conjuntas con potencial terapéutico y su posible efecto real.

1.3 Enfoque y método seguido

He usado herramientas bioinformáticas para la consecución de los objetivos del trabajo. La mayor parte de estas herramientas son propias de la bioinformàtica farmacéutica, tanto la búsqueda y elección de dianas como la capacidad de moléculas ligando de acoplarse a las proteínas diana y la predicción de las propiedades ADMET (propiedades farmacocinéticas) han sido siguiendo el estado del arte en este ámbito.

1.4 Planificación del Trabajo

- PROPUESTA DEL TRABAJO PEC 0

Búsqueda bibliográfica sobre la enfermedad de Alzheimer. Desarrollo de la enfermedad, proteínas implicadas.

- PLAN DE TRABAJO. PEC 1
- FASE 1. DESARROLLO DEL TRABAJO. PEC 2

Búsqueda en base de datos de proteínas implicadas en el desarrollo del Alzheimer. Uso de Script en R.

Búsqueda de genes diferecialmente expresado en el Alzheimer. Gene Expression Omnibus.

Búsqueda de las estructuras 3D de las proteínas encontradas en RSCBPDB.

Búsqueda alternativa de estructuras proteicas por homología en Swissdock y phyre2 . Elección de dianas se realizara en base a todas las búsquedas anteriores.

- FASE 2. DESARROLLO DEL TRABAJO. PEC 3

Virtual screening usando Drugbank. Automatización del proceso usando MTiOpenScren, mcule, swissDock.

Análisis de resultados y elección de moléculas, 10 por cada target.

HITO 2

Comprobación de pasar la barrera hematoencefálica de las moléculas. pkCSM.

Elección de moléculas en base a su toxicidad. Vega.

Comprobar si las moléculas elegidas pueden funcionar en otras enfermedades Parkinson o Ataxia.

HITO 3

- REDACCION DE LA MEMORIA. PEC 4.
- PREPARACIÓN DE LA PRESENTACION. PEC 5a
- DEFENSA PUBLICA. PEC 5b

CALENDARIO DEL TRABAJO FIN DE MASTER
PROPUESTA DEL TRABAJO
Busqueda bibliográfica sobre la enfermedad de Alzheimer. Desarrollo de la enfermedad, proteínas implicadas.
PLAN DEL TRABAJO FIN DE MASTER
FASE 1. DESARROLLO DEL TRABAJO
Busqueda en base de datos de proteinas implicadas en el desarrollo del Alzheimer. Uso de Script en R.
Búsqueda de genes diferecialmente expresado en el Alzheimer.Gene Expression Omnibus.
Búsqueda de las estructuras 3D de las proteínas encontradas en RSCPDB.
Búsqueda alternativa de estructuras proteicas por homología en Swissdockn y phyre2 . Elección de dianas en base a las búsquedas anteriores.
HITO 1
PEC 2
FASE 2. DESARROLLO DEL TRABAJO
Virtual screening usando Drugbank. Automatización del proceso usando MitopenScren, mcule, swissDock.
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Comprobación de pasar la barrera hematoencefálica de las moléculas. pkCSM.
Elección de móleculas en base a su toxicidad. Vega.
Comprobar si las moleculas elegidas pueden funcionar en otras enfermedades Parkinson o Ataxia.
HITO 3
PEC 3
REDACCION DE LA MEMORIA
PREPARACIÓN DE LA PRESENTACION
DEFENSA PUBLICA

Figura 4. Calendario de desarrollo del trabajo

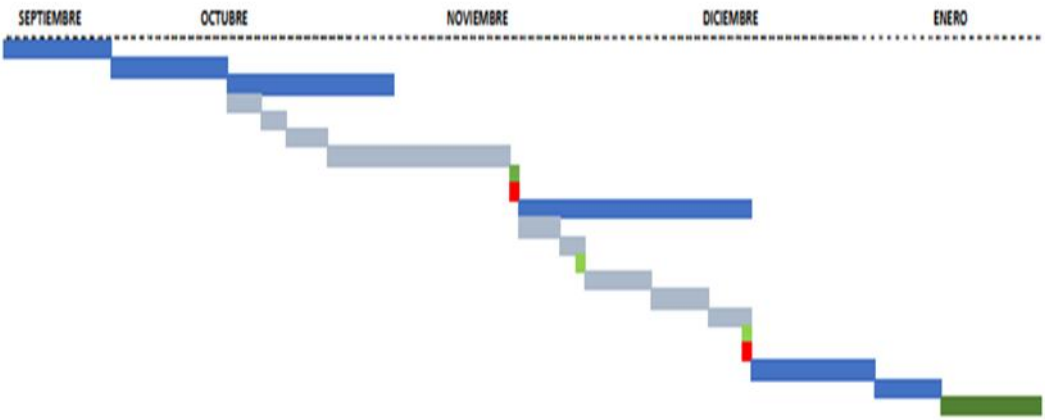

Figura 5. Diagrama de Gant.

1.5 Breve sumario de productos obtenidos

5.1 Memoria final

5.2 Presentación virtual

1.6 Breve descripción de los otros capítulos de la memoria

2.Metodología: en este apartado se describen las aplicaciones y webserver utilizados para realizar el Trabajo.

3.Resultados: se analizan los resultados obtenidos del Trabajo.
4.Conclusiones.
5.Glosario
6.Bibliografía
7.Anexos

2. Metodología

2.1 Búsqueda bibliográfica sobre la enfermedad de Alzheimer

En el inicio del Trabajo se realiza una primer acercamiento a la enfermedad de Alzheimer. A través de varios artículos se investiga sobre su desarrollo y evolución.

Asimismo se investiga sobre las principales proteínas y genes implicados y los fármacos descubiertos en la actualidad[3].

2.2 Búsqueda de dianas

Se utiliza el paquete RCurl y UniProt.ws (de Bioconductor) de R.
RCurl se usa para la búsqueda automatizada en la base de datos de DisGeNet (http://www.disgenet.org/web/DisGeNET/menu) de los genes implicados en la enfermedad de Alzheimer.

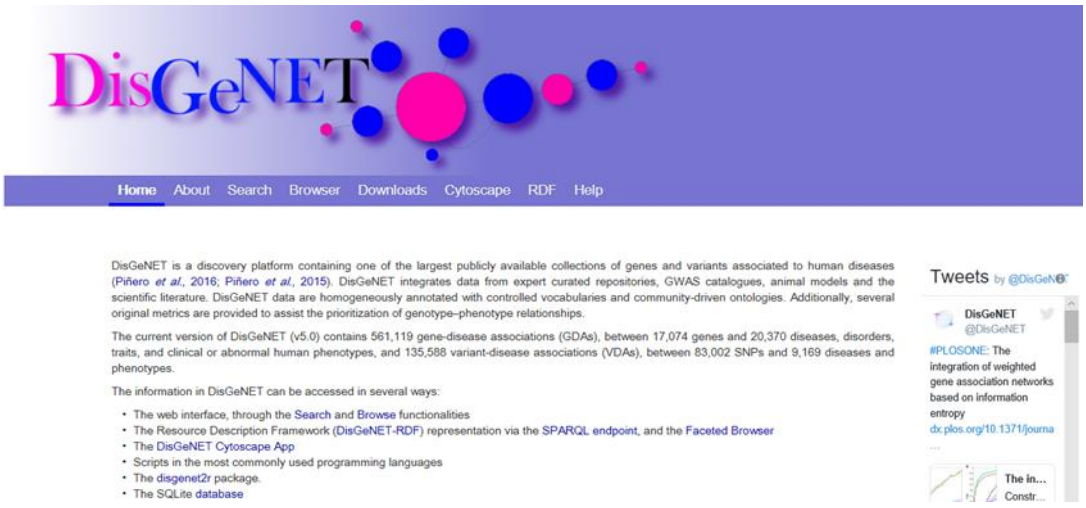

Figura 6: DisGeNET es una plataforma que contiene una de las mayores colecciones de genes y variantes asociadas a enfermedades humanas disponibles. Integra los datos de los depósitos expertos seleccionados, los catálogos GWAS, los modelos animales y la literatura científica.

Se aplica el código de R cargando el paquete RCurl y se conecta, con una serie de parámetros, con la base de datos de DisGeNet para el Alzheimer.

[3] Bibliografía 1,3,4,5,6

Una vez obtenida la tabla de los genes implicados se escogen cinco proteínas (dominios de proteínas en algun caso) que por la bibliografia investigada son importantes en el desarrollo de la enfermedad[4].

Para obtener los codigos PDB de dichas dianas se utiliza UniProt.ws del paquete Bioconductor de R. Posteriormente se descargan las estructuras de la pàgina RCSBPDB(http://www.rcsb.org/pdb/home/home.do).
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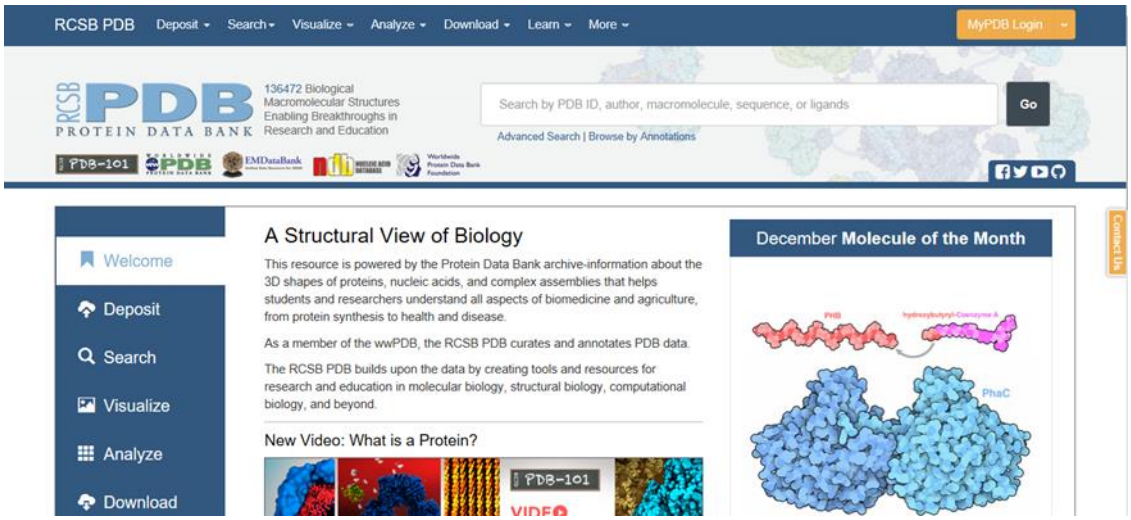


Figura 7: El Banco de datos de Proteínas (PDB) (Protein Data Bank) es un depósito mundial de información sobre las estructuras en 3D de grandes moléculas biológicas, incluyendo proteínas y ácidos nucleicos. Hay moléculas que son encontradas en todos los organismos incluyendo bacterias, levaduras, plantas, moscas, otros animales, y humanos.

Para las proteínas de las que no se dispone de estructura en RCSBPDB se realiza un reconocimiento de plegado con phyre2 (http://www.sbg.bio.ic.ac.uk/phyre2/html/page.cgi?id=index). Para realizar el reconocimiento de plegado es necesario introducir en la pàgina de phyre2 la secuencia de la proteína. La búsqueda de la secuencia de la proteína se realiza con el navegador genomico UCSC.

[4] Bibliografía 8,9,10,11,12,13,14,15

Figura 8. Navegador genómico UCSC

Figura 9: El modelado en modo "Normal" por Phyre2 produce un conjunto de modelos 3D potenciales de la proteína seleccionada basados en la alineación con estructuras de proteínas conocidas (reconocimiento de plegado, en inglés, threading)

2.3 Obtención de sitios de unión de las proteínas

Para poder obtener los sitios de unión de las proteínas se usa el webserber Raptor X (http://biosig.unimelb.edu.au/pkcsm/prediction)

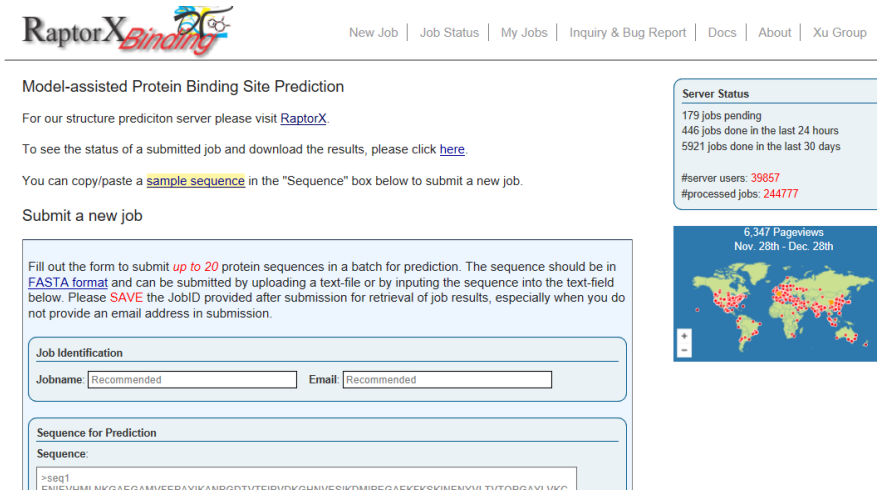


Figura 10: Página principal de binding-site de Raptor X

Para obtener los sitios de unión con este servidor introducimos la secuencia de las proteínas diana y por homología con otros sitios de unión de otras proteínas el servidor nos proporciona los resultados encontrados, en ellos se especifía los siguiente parámetros:

- Pvalue es el valor p de alineación, mide la probabilidad de predicción del modelo, cuanto más pequeño mejor. Menor de 0,001 se considera bueno

- El uGDT es la medición GDT (Global Distance Test) no normalizado definido como 1 * N (1) + 0.75 * N (2) + 0.5 * N (4) + 0.25 * N (8), donde N (x) es el número de residuos con el RMSD local menor que x. GDT se calcula como uGDT dividido por la longitud del dominio y multiplicado por 100. Si un modelo tiene uGDT mayor que 50 puede considerarse razonablemente bueno.

- uSeqID/SeqID es el número de idénticos residuos en la alineación que realiza el programa, si es mayor del 30% y la proteína tiene más de 200 residuos se considera bueno.

- Multiplicidad del bolsillo “pocket” mide la frecuencia con la que se ha encontrado el bolsillo en un conjunto de proteínas-ligando, >40 se considera bueno.

- Coordenadas del sitio de unión.

2.4 Virtual Screening usando MTiOpenScreen (http://mobyle.rpbs.univ-paris-diderot.fr/cgi-in/portal.py#forms::MTiOpenScreen)

Introducimos la estructura en formato pdb de las proteínas diana y las coordenadas del sitio de unión y el servidor nos proporciona una tabla de 1000 moléculas con sus propiedades. Esta tabla se explica más adelante.

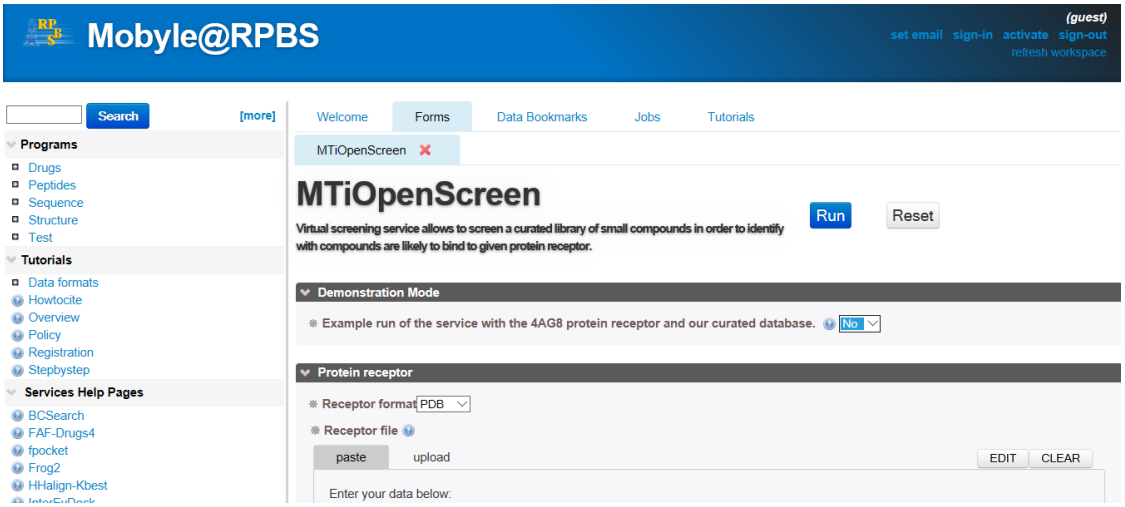


Figura 11: Página principal de MTiOpenScreen

2.4.1 AutoDockVina[5]

AutoDock Vina es el programa que utiliza MTiOpenscreen, el servidor que he escogido para realizar un screening "in silico" de las moléculas candidatas a unirse a las proteínas escogidas. El screening de posibles candidatos se realiza con la técnica de acoplamiento molecular (en inglés docking) que parte de una estructura de proteína en 3D conocida para, a través de métodos computacionales, predecir la orientación de los ligandos (moléculas candidatas) en los sitios de unión de las cavidades de las proteínas y su energía libre de unión..

El docking se basa en potenciales químicos, es decir, determina la conformación de enlace preferente y la energía libre de unión.

La función "score" de los distintos programas que existen tratan de aproximar las moléculas de tal forma que la energía libre de unión sea lo más pequeña posible.

.El funcionamiento de AutoDock Vina (la función Score) se basa en la energía libre de las contribuciones de los enlaces de los átomos tanto intramoleculares como intermoleculares, lo normal en otros programas es que sólo se use las intermoleculares.

[5] Bibliografía 16, 18

La función Score de Vina también tiene en cuenta la información empírica de las preferencias en la conformación receptor-ligando y las medidas de afinidad experimental. Utiliza también algoritmos de optimización (algoritomos genéticos, optimización de nubes de particulas, simulaciones “anneal” que simulan tensiones y fuerzas, y otros).

El resultado es un programa bastante robusto y rápido que ofrece buenos resultados.

2.4.2 Tabla de resultados MTiOpenScreen

El resultado de MTiOpenScreen es una tabla con un código de identificación del compuesto en donde aparecen una sería de propiedades fisicoquímicas del compuesto

Explicación de la tabla[6]:

Compound	**Es el número id del compuesto encontrado**
Model ID	**El número del modelo de acoplamiento presentado por este programa**
Energy	**Es la energía libre de unión del compuesto a la proteína**
nRot	**Número de átomos rotámero, con capacidad de rotacion**
Library	**La librería usada**
isLeadLike	**Si el compuesto es lead-like**
HBA	**Aceptores de enlaces de hidrógeno**
HBD	**Donadores de enlaces de hidrógeno**
LogP	**Es una medida de la lipofilidad de las moléculas que se mide con la fracción de molécula en octanol dividido entre la fracción de compuesto en agua. Cuanto más grande sea más lipofílico es el**

[6] Bibliografía 17,19,20,22

	compuesto.
MW	**Peso molecular**
TPSA	**Total/Topological Polar Surface Area–TPSA**

Las normas que explico a continuación son usadas para identificar moléculas que son posibles candidatos a fármacos (lead-like):

La norma de cinco de Lipinski

- No más de 5 donadores de hidrógeno, el número total de N-H y O-H.
- No más de 10 aceptores de hidrógeno (todos los átomos de nitrógeno y oxígeno.
- Masa molecular menor de 500 daltons.
- La partición de octanol-agua, log P , no mayor de 5

La norma de 3 (RO3)

- La partición de octanol-agua no mayor log P no mayor de 3
- Masa molecular menor de 300 daltons.
- No más de 3 donadores de hidrógeno.
- No mas de 3 aceptores de hidrógeno.
- No más de 3 enlaces con posibilidad de rotación

Lead like MTiOpenScreen

Las librerias Diverse-Lib y iPPI-lib contienen las propiedades de las moléculas, entre ellas, está la propiedad lead-like.

2.5 Identificación de moléculas

Para poder identificar las moléculas he utilizado la web pubchem, se han escogido el top5 de moléculas identificadas en pubchem que en su mayoría se encuentran entre los 20 primeros compuesto de la tabla de MTiOpenScreen. El ID del compuesto se introduce en la página pubchem.y nos proporciona, entre otras cosas, su nombre, estructura y código SMILES.

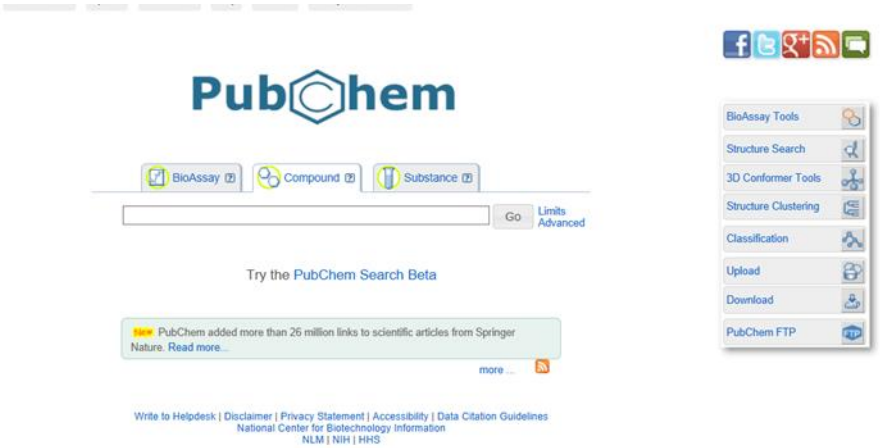


Figura 12 Web pubchem

2.6 Propiedades ADMET[7]

He escogido el servidor pKCSM (http://biosig.unimelb.edu.au/pkcsm/prediction) para obtener las propiedades ADMET: absorción, distribución, metabolismo, excreción y toxicidad de los moléculas elegidos.

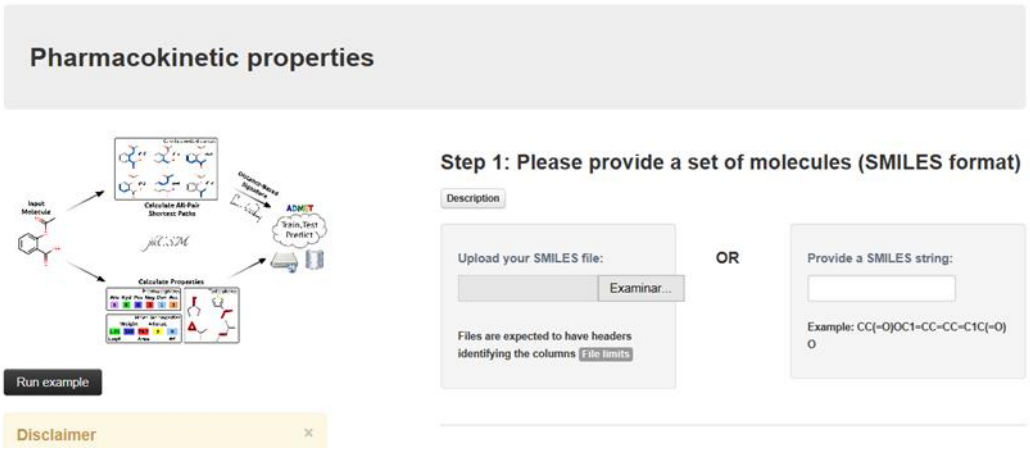


Figura 13 Servidor pkCSM

Los codigos SMILES de entrada los he obtenido de pubchem. A continuación se presenta una tabla con la explicación de las propiedades:

[7] Bibliografía 21

Características ADMET	**Valores recomendados y explicación**
Water solubility	Log mol/L (Valores pequeños de solubilidad en agua son peor absorbidos)
Caco2 permeability	>0,90 log cm/s Las células Caco2 provienen de un adenocarcinoma de células epiteliales colonrectales y se usan para medir la absorción de fármacos administrados oralmente.
Intestinal absorption (human)	≥30% Se usan para medir la absorción de fármacos en el intestino delgado en porcentaje
Skin Permeability	logKp>-2,5 cm/h, logKp es la constante de permeabilidad de la piel
P-glycoprotein substrate	Si el sustrato es transportado por esta proteína que protege de toxinas (es una proteína de unión-ATP de cajas ABC)
P-glycoprotein I inhibitor	Este dato puede ser útil para conocer ventajas terapeúticas o contraindicaciones.
P-glycoprotein II inhibitor	Este dato puede ser útil para conocer ventajas terapeúticas o contraindicaciones.
VDss (human)	Es el volumen teórico total que un fármaco necesitaría para distribuirse uniformemente para dar la misma concentración que en plasma. Cuanto más alto sea más fármaco hay en tejidos que en plasma. Se considera bajo log VDs<-0,15 L/kg y alto >0,45 L/kg
Fraction unbound (human)	Es la fracción de fármaco que no se une a proteínas de la sangre. Cuanto menor sea peor será su capacidad para el transporte transmembrana y su difusión.
BBB permeability	Mide la capacidad de pasar la barrera hematoencefálica. LogBB>0,3 se considera que puede pasar y logBB<-1 se considera que no pasa. Son valores teóricos. Log BB (relación logarítmica de las concentraciones del fármaco en cerebro y plasma)
CNS permeability	Mide también la capacidad de pasar la barrera hematoencefálica sin factores sistémicos de distribución. Log PS>-2 penetra en el Sistema nervioso central y log PS<-3 no penetra. (PS área del producto permeabilidad-superficie del fármaco en el cerebro)
CYP2D6 substrate	Si/No el fármaco es metabolizado por el citocromo p450, que es una enzima responsable de la detoxificación.
CYP3A4 substrate	Si/No el fármaco es metabolizado por el citocromo p450, que es una enzima responsable de la detoxificación.

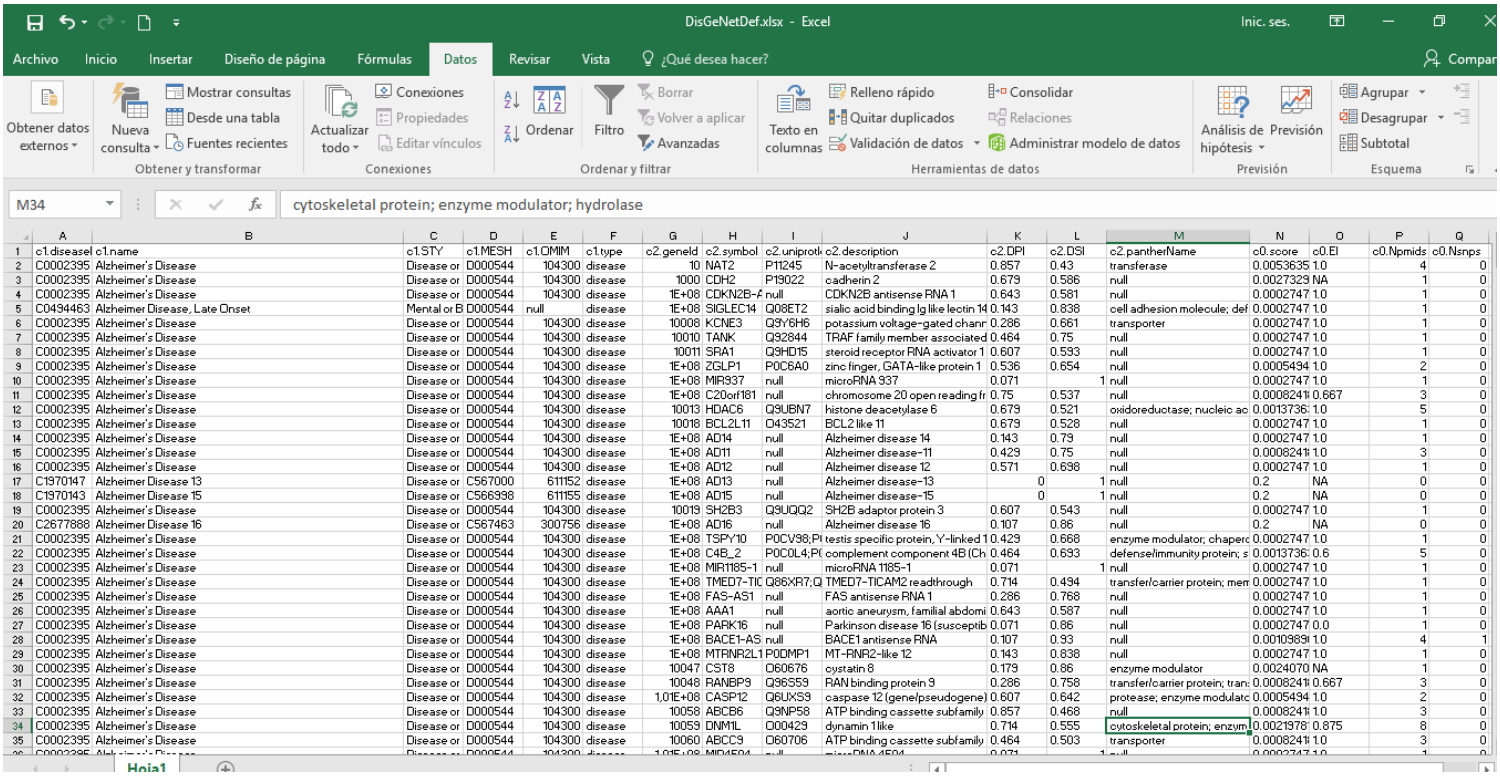
Características ADMET	**Valores recomendados y explicación**
CYP1A2 inhibitior	Si inhiben el citocromo p450, no se debe inhibir está contraindicado p450 debe ser <10mM
CYP2C19 inhibitior	Si inhiben el citocromo p450, no se debe inhibir está contraindicado p450 debe ser <10mM
CYP2C9 inhibitior	Si inhiben el citocromo p450, no se debe inhibir está contraindicado p450 debe ser <10mM
CYP2D6 inhibitior	Si inhiben el citocromo p450, no se debe inhibir está contraindicado p450 debe ser <10mM
CYP3A4 inhibitior	Si inhiben el citocromo p450, no se debe inhibir está contraindicado p450 debe ser <10mM
Total Clearance	Combina la eliminación renal y la hepática/biliar se mide en log ml/min/kg
Renal OCT2 substrate	Organic catión transporter 2 juega un papel importante en la función renal. Está contraindicado que los fármacos sean sustrato de esta enzima.
AMES toxicity	Si el compuesto es mutagéncico.
Max. tolerated dose (human)	Máxima dosis recomendada en humanos <0,477 baja, >0,477 alta.(log mg/kg/day)
hERG I inhibitor	Inhibidor de los canales de potasio hERG, síndrome QT y arritmia fatal.
hERG II inhibitor	Inhibidor de los canales de potasio hERG, síndrome QT y arritmia fatal
Oral Rat Acute Toxicity (LD50)	Lethal dosage value (mol/kg)
Oral Rat Chronic Toxicity (LOAEL)	Dosis mínima de un compuesto usado por un largo periodo de tiempo en donde se aprecian efectos adversos. (log mg/kg_bw/day)
Hepatotoxicity	Si provoca mal funcionamiento del hígado
Skin Sensitisation	Se utiliza sobre todo para productos dermatológicos, si son capaces de producir efectos adversos en la piel.
T.Pyriformis toxicity	Mide la inhibición del crecimiento del 50% de esta especie >-0.5 se considera toxico (log ug/L)
Minnow toxicity	LD50 para este tipo de pez (log mM)

3. Resultados

3.1 Base de datos de DisGeNet

Aplicando el código de R (Anexo 1) con el paquete RCurl se obtiene una tabla que tiene 17 columnas (característica y códigos de cada gen implicado en la enfermedad de Alzheimer) y 1764 filas que corresponden a cada gen.

Cabecera de la tabla:



	c1.diseaseI	c1.name	c1.STY	c1.MESH	c1.OMIM	c1.type	c2.geneId	c2.symbol	c2.uniprotk	c2.description	c2.DPI	c2.DSI	c2.pantherName	c0.score	c0.EI	c0.Npmids	c0.Nsnps
2	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	10	NAT2	P11245	N-acetyltransferase 2	0.857	0.43	transferase	0.0053635	1.0	4	0
3	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	1000	CDH2	P19022	cadherin 2	0.679	0.586	null	0.0027329	NA	1	0
4	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	1E+08	CDKN2B-A	null	CDKN2B antisense RNA 1	0.643	0.581	null	0.0002747	1.0	1	0
5	C0494463	Alzheimer Disease, Late Onset	Mental or B	D000544	null	disease	1E+08	SIGLEC14	Q08ET2	sialic acid binding Ig like lectin 14	0.143	0.838	cell adhesion molecule; def	0.0002747	1.0	1	0
6	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	10008	KCNE3	Q9Y6H6	potassium voltage-gated chann	0.286	0.661	transporter	0.0002747	1.0	1	0
7	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	10010	TANK	Q92844	TRAF family member associated	0.464	0.75	null	0.0002747	1.0	1	0
8	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	10011	SRA1	Q9HD15	steroid receptor RNA activator 1	0.607	0.593	null	0.0002747	1.0	1	0
9	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	1E+08	ZGLP1	P0C6A0	zinc finger, GATA-like protein 1	0.536	0.654	null	0.0005494	1.0	2	0
10	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	1E+08	MIR937	null	microRNA 937	0.071	1	null	0.0002747	1.0	1	0
11	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	1E+08	C20orf181	null	chromosome 20 open reading fr	0.75	0.537	null	0.0008241	0.667	3	0
12	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	10013	HDAC6	Q9UBN7	histone deacetylase 6	0.679	0.521	oxidoreductase; nucleic ac	0.0013736	1.0	5	0
13	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	10018	BCL2L11	O43521	BCL2 like 11	0.679	0.528	null	0.0002747	1.0	1	0
14	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	1E+08	AD14	null	Alzheimer disease 14	0.143	0.79	null	0.0002747	1.0	1	0
15	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	1E+08	AD11	null	Alzheimer disease-11	0.429	0.75	null	0.0008241	1.0	3	0
16	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	1E+08	AD12	null	Alzheimer disease 12	0.571	0.698	null	0.0002747	1.0	1	0
17	C1970147	Alzheimer Disease 13	Disease or	C567000	611152	disease	1E+08	AD13	null	Alzheimer disease-13	0	1	null	0.2	NA	0	0
18	C1970143	Alzheimer Disease 15	Disease or	C566398	611155	disease	1E+08	AD15	null	Alzheimer disease-15	0	1	null	0.2	NA	0	0
19	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	10019	SH2B3	Q9UQQ2	SH2B adaptor protein 3	0.607	0.543	null	0.0002747	1.0	1	0
20	C2677888	Alzheimer Disease 16	Disease or	C567463	300756	disease	1E+08	AD16	null	Alzheimer disease 16	0.107	0.86	null	0.2	NA	0	0
21	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	1E+08	TSPY10	P0CV98;P(	testis specific protein, Y-linked 1	0.429	0.668	enzyme modulator; chaperc	0.0002747	1.0	1	0
22	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	1E+08	C4B_2	P0C0L4;P(	complement component 4B (Ch	0.464	0.693	defense/immunity protein; s	0.0013736	0.6	5	0
23	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	1E+08	MIR1185-1	null	microRNA 1185-1	0.071	1	null	0.0002747	1.0	1	0
24	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	1E+08	TMED7-TIC	Q86XR7;Q	TMED7-TICAM2 readthrough	0.714	0.494	transfer/carrier protein; mer	0.0002747	1.0	1	0
25	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	1E+08	FAS-AS1	null	FAS antisense RNA 1	0.286	0.768	null	0.0002747	1.0	1	0
26	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	1E+08	AAA1	null	aortic aneurysm, familial abdomi	0.643	0.587	null	0.0002747	1.0	1	0
27	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	1E+08	PARK16	null	Parkinson disease 16 (susceptib	0.071	0.86	null	0.0002747	0.0	1	0
28	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	1E+08	BACE1-AS	null	BACE1 antisense RNA	0.107	0.93	null	0.0010989	1.0	4	1
29	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	1E+08	MTRNR2L1	P0DMP1	MT-RNR2-like 12	0.143	0.838	null	0.0002747	1.0	1	0
30	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	10047	CST8	O60676	cystatin 8	0.179	0.86	enzyme modulator	0.0024070	NA	1	0
31	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	10048	RANBP9	Q96S59	RAN binding protein 9	0.286	0.758	transfer/carrier protein; tran	0.0008241	0.667	3	0
32	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	1,01E+08	CASP12	Q6UXS9	caspase 12 (gene/pseudogene)	0.607	0.642	protease; enzyme modulato	0.0005494	1.0	2	0
33	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	10058	ABCB6	Q9NP58	ATP binding cassette subfamily	0.857	0.468	null	0.0008241	1.0	3	0
34	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	10059	DNM1L	O00429	dynamin 1 like	0.714	0.555	cytoskeletal protein; enzym	0.0021978	0.875	8	0
35	C0002395	Alzheimer's Disease	Disease or	D000544	104300	disease	10060	ABCC3	O60706	ATP binding cassette subfamily	0.464	0.503	transporter	0.0008241	1.0	3	0

3.2 Elección de dianas[8]

He escogido las siguientes proteínas diana porque juegan un papel importante en el desarrollo de la enfermedad según la bibliografía disponible.

3.2.1 Proteína precursora de la proteína amiloide β, APP

La APP (amiloyd precursor protein) se ha descrito en numerosos artículos como una de las proteínas implicadas en el desarrollo de la enfermedad de Alzheimer. No obstante la función de esta proteína no está del todo clara. A partir de ella se forma por proteolisis la proteína amiloide β por interacción con BACE-1 y la γ-secretasa. Sin embargo la APP parece estar implicada en la adhesión intercelular de células, se expresa en todos los tejidos y es transportada a sitios de presinapsis.

[8] Bibliografía 8, 9, 10, 11, 12, 13, 14, 15

Por estudios específicos de las proteínas APP, APLP-1 y APLP-2 se sabe que estas proteínas forman homodímeros y heterodímeros y el dominio proteico implicado en todas ellas es el E1, (N-terminal).
El papel de estas interacciones en la enfermedad de Alzheimer no es conocido, no obstante si está interacción de APP no se produce se ha comprobado en ratones Knockout que gracias a las interacciones de las otras proteínas el ratón sigue siendo viable.
El objetivo es buscar una molécula capaz de evitar la formación de dímeros de APP a través de la unión al dominio E1.

3.2.2 Proteína amiloide de suero A1

La proteína amiloide de suero está implicada en la formación de agregados de proteína amiloide. La región N-Terminal de las hélices 1 y 3 son las que están implicadas en la generación de péptidos amiloidogénicos.

Moléculas que puedan evitar la formación de agregados amiloides a través de la unión a estos sitios puede favorecer la reducción de la deposición de placas amiloides.

3.2.3 Proteína Kinasa-1 con afinidad por microtúbulos

Está proteína está implicada en la fosforilación de microtúbulos asociados a la proteína Tau, está fosforilación a su vez forma parte del proceso de formación de ovillos en la enfermedad de Alzheimer.
El dominio asociado a ubiquinona (UBE) se une al dominio catalítico en el extremo N-terminal.
Inhibiendo la acción de esta kinasa es posible que se redujera la formación de ovillos.

3.2.4 Preselinina-1

Está proteína forma parte del complejo γ-secretasa, responsable de la proteolisis de la APP y la secreción de proteína β-amiloide.

Se ha comprobado que su extremo carboxi-terminal está implicado en esta secreción, en experimentos donde se ha eliminado dicho extremo ha disminuido la producción de proteína β-amiloide.

En este caso se busca una molécula capaz de unirse en este extremo e inhibir la secreción de proteína β-amiloide.

3.2.5 Proteína RAMP3, forma parte del receptor de amilina 3 (AMY3)

Se ha descubierto que la enfermedad de Alzheimer y la diabetes tipo II tienen alguna característica similar, las dos depositan proteínas amiloidogénicas: la proteína amiloide β42 y la amilina.
Estas dos proteínas tienen en común el receptor AMY3 y se ha visto experimentalmente que pueden desencadenar sus efectos a través de éste. Los efectos son la transducción de señales a través de mediadores: proteína kinase A, MAPK, Akt y cFos.

AMY3 está formado por el receptor CTR like receptor y las proteína modificadora de actividad RAMP3.

Si se disminuye el efecto de la proteína amiloide-β sobre las células sería posible una disminución de los síntomas de la enfermedad de Alzheimer, en este caso mi propuesta va encaminada a inhibir la proteína RAMP3, parte del receptor, esta acción no perjudicaría a la otra parte del receptor con funciones positivas para la célula.

3.3 Obtención de los códigos PDB

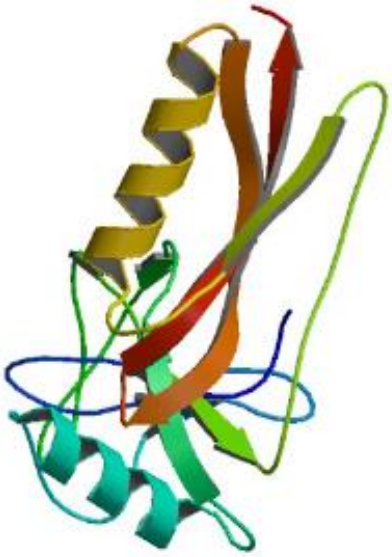
Para obtener los códigos PDB de las proteínas anteriormente elegidas he usado el paquete Uniprot.ws del proyecto Bioconductor de R (Anexo 2). Introduciendo los códigos de uniprot obtenidos en la tabla de genes de DisGeNet implicados en la enfermedad de Alzheimer se obtiene el correspondiente código PDB.

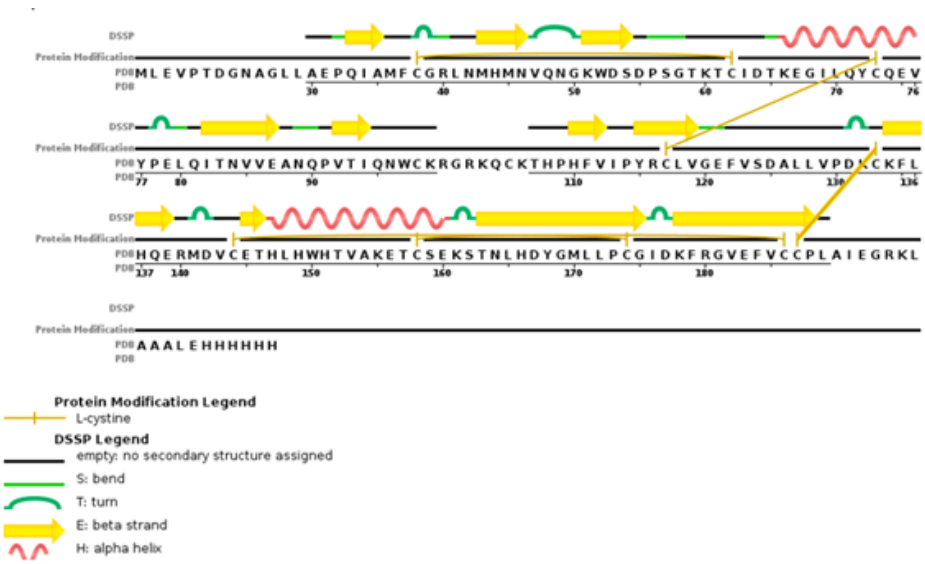
UniprotID	Descripción	PDB
P05067	amyloid beta precursor protein	4PWQ
P0DJI8	serum amyloid A1	4IP8
Q9P0L2	microtubule affinity regulating kinase 1	2HAK
P49768	presenilin 1	2KR6

La proteína RAMP3 no está descrita en PDB

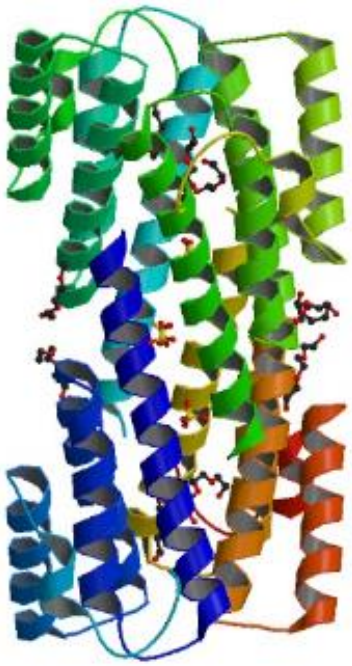
3.4 Estructuras de los dominios de la proteínas diana

APP dominio E1

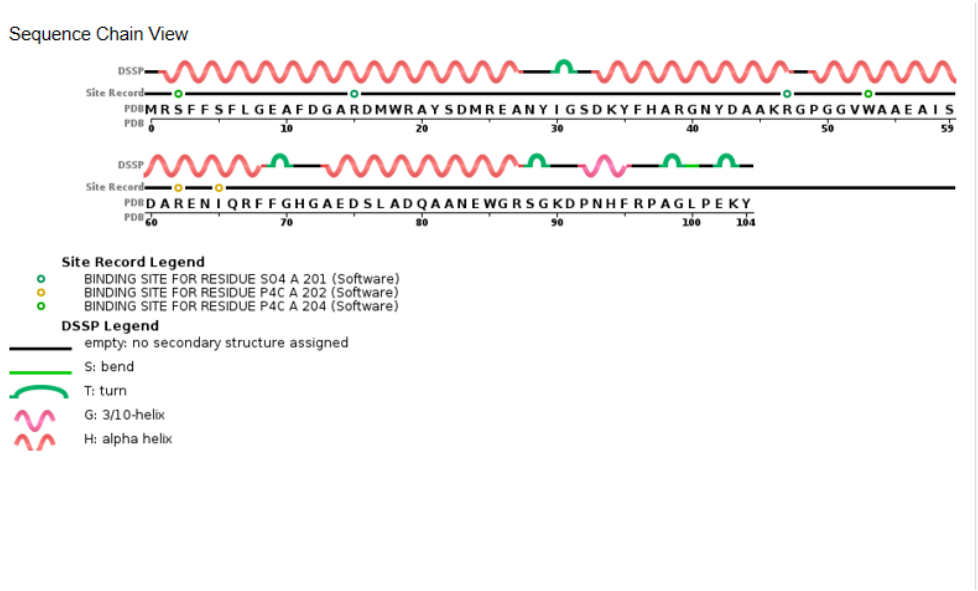




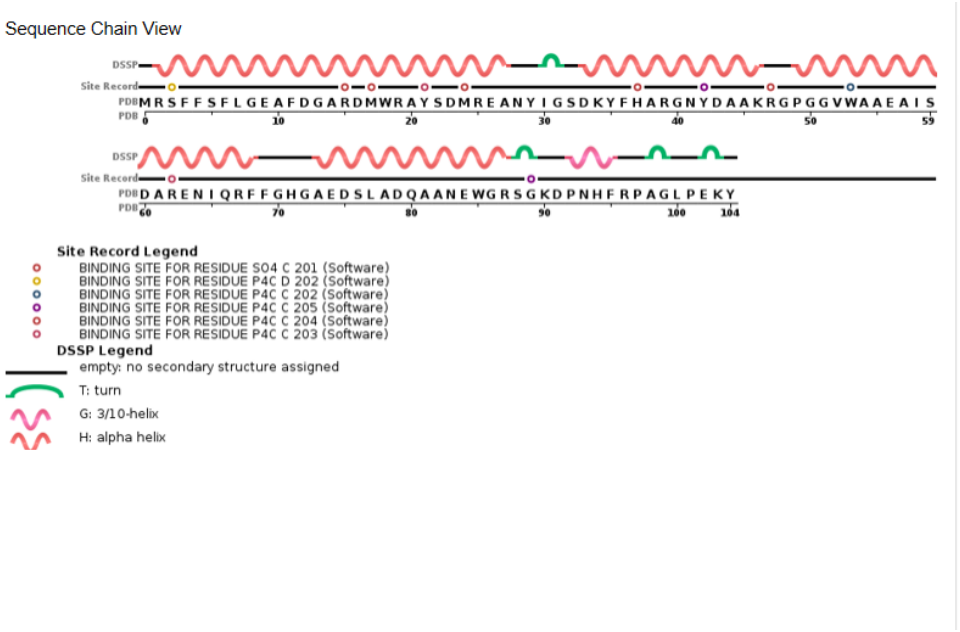
Proteína amiloide A1 de suero (Cuatro subunidades A,B y D son idénticas)



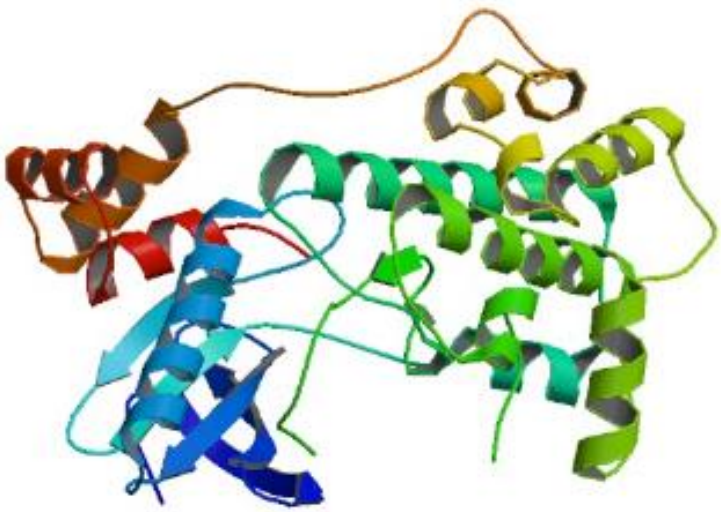
A,B y D


Sequence Chain View
DSSP
Site Record
PDB
M R S F F S F L G E A F D G A R D M W R A Y S D M R E A N Y I G S D K Y F H A R G N Y D A A K R G P G G V W A A E A I S
PDB
0
10
20
30
40
50
59
DSSP
Site Record
PDB
D A R E N I Q R F F G H G A E D S L A D Q A A N E W G R S G K D P N H F R P A G L P E K Y
PDB
60
70
80
90
100
104
Site Record Legend
BINDING SITE FOR RESIDUE SO4 A 201 (Software)
BINDING SITE FOR RESIDUE P4C A 202 (Software)
BINDING SITE FOR RESIDUE P4C A 204 (Software)
DSSP Legend
empty: no secondary structure assigned
S: bend
T: turn
G: 3/10-helix
H: alpha helix

C

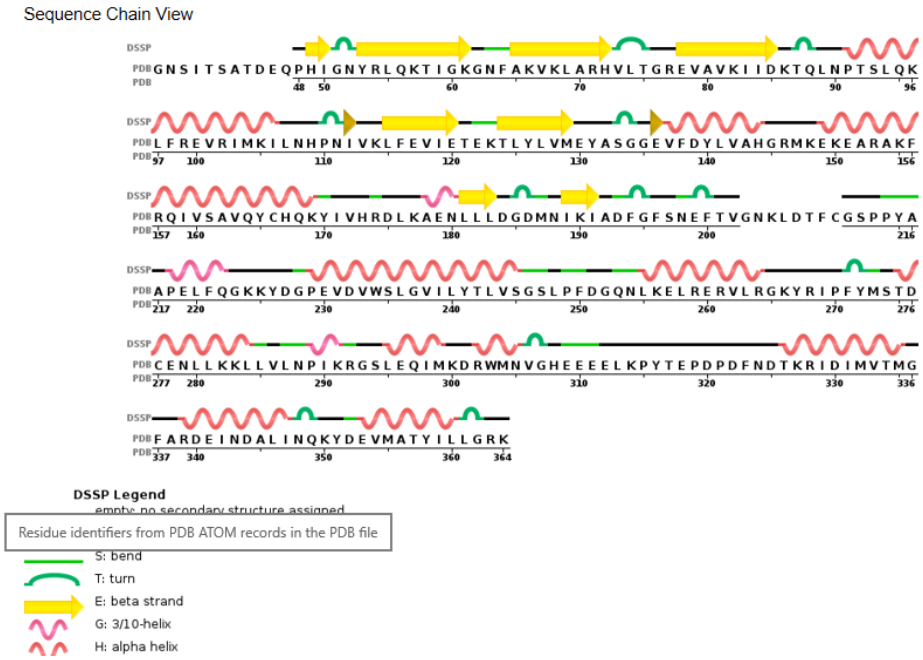


Proteína Kinasa-1 asociada a microtúbulos (MARK-1)

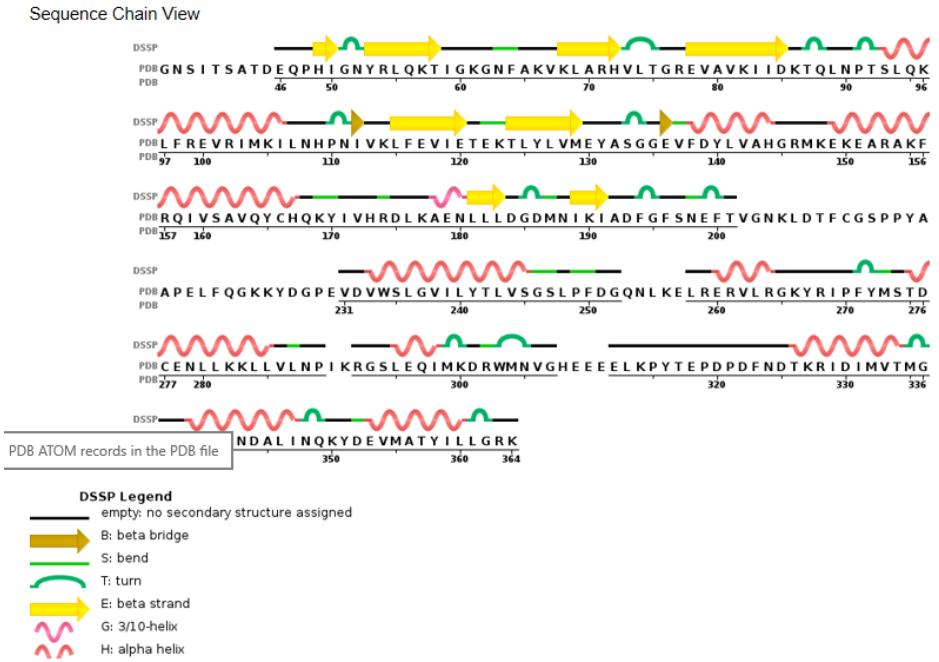


Tiene subunidad A,B,C,D,E,F,G, todas son idénticas excepto la B.

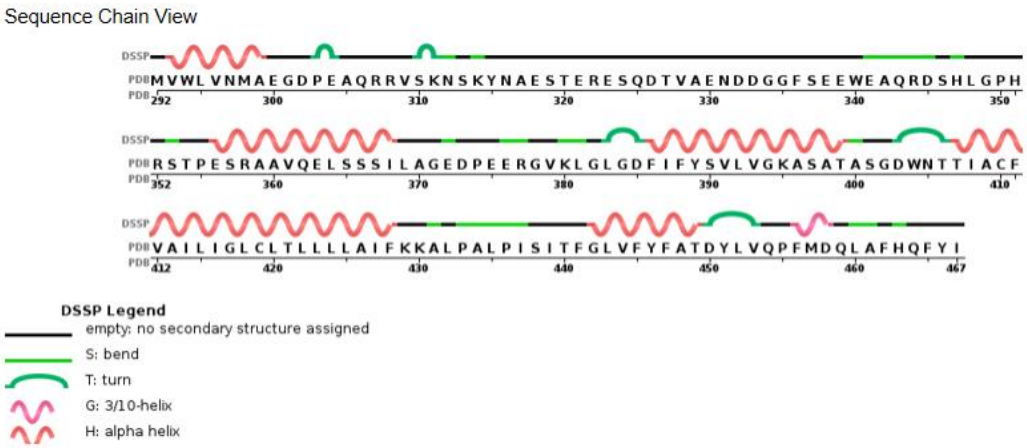
A


Sequence Chain View
DSSP
PDB GNSITSATDEQPHIGNYRLQKTIGKGNFAKVKLARHVLTGREVAVKIIDKTQLNPTSLQK
PDB
48 50 60 70 80 90 96
DSSP
PDB LFREVRIMKILNHPNIVKLFEVIETEKTLYLVMEYASGGEVFDYLVAHGRMKEKEARAKF
PDB
97 100 110 120 130 140 150 156
DSSP
PDB RQIVSAVQYCHQKYIVHRDLKAENLLLDGDMNIKIADFGFSNEFTVGNKLDTFCGSPPYA
PDB
157 160 170 180 190 200 216
DSSP
PDB APELFQGKKYDGPEVDVWSLGVILYTLVSGSLPFDGQNLKELRERVLRGKYRIPFYMSTD
PDB
217 220 230 240 250 260 270 276
DSSP
PDB CENLLKKLLVLNPIKRGSLEQIMKDRWMNVGHEEEELKPYTEPDPDFNDTKRIDIMVTMG
PDB
277 280 290 300 310 320 330 336
DSSP
PDB FARDEINDALINQKYDEVMATYILLGRK
PDB
337 340 350 360 364
DSSP Legend
empty: no secondary structure assigned
Residue identifiers from PDB ATOM records in the PDB file
S: bend
T: turn
E: beta strand
G: 3/10-helix
H: alpha helix

B


Sequence Chain View
DSSP
PDB GNSITSATDEQPHIGNYRLQKTIGKGNFAKVKLARHVLTGREVAVKIIDKTQLNPTSLQK
PDB
46 50 60 70 80 90 96
DSSP
PDB LFREVRIMKILNHPNIVKLFEVIETEKTLYLVMEYASGGEVFDYLVAHGRMKEKEARAKF
PDB
97 100 110 120 130 140 150 156
DSSP
PDB RQIVSAVQYCHQKYIVHRDLKAENLLLDGDMNIKIADFGFSNEFTVGNKLDTFCGSPPYA
PDB
157 160 170 180 190 200
DSSP
PDB APELFQGKKYDGPEVDVWSLGVILYTLVSGSLPFDGQNLKELRERVLRGKYRIPFYMSTD
PDB
231 240 250 260 270 276
DSSP
PDB CENLLKKLLVLNPIKRGSLEQIMKDRWMNVGHEEEELKPYTEPDPDFNDTKRIDIMVTMG
PDB
277 280 300 320 330 336
DSSP
PDB NDALINQKYDEVMATYILLGRK
350 360 364
PDB ATOM records in the PDB file
DSSP Legend
empty: no secondary structure assigned
B: beta bridge
S: bend
T: turn
E: beta strand
G: 3/10-helix
H: alpha helix

Preselinina-1 dominio CTF



RAMP 3

Para la obtención de la secuencia se ha utilizado el servidor genómico UCSC y para la obtención de la estructura el servidor de reconocimiento de plegado Phyre2.

Secuencia de proteína:

```
>NP_005847.1
METGALRRPQLLPLLLLLCGGCPRAGGCNETGMLERLPLCGKAFADMMGK
VDVWKWCNLSEFIVYYESFTNCTEMEANVVGCYWPNPLAQGFITGIHRQF
FSNCTVDRVHLEDPPDEVLIPLIVIPVVLTVAMAGLVVWRSKRTDTLL
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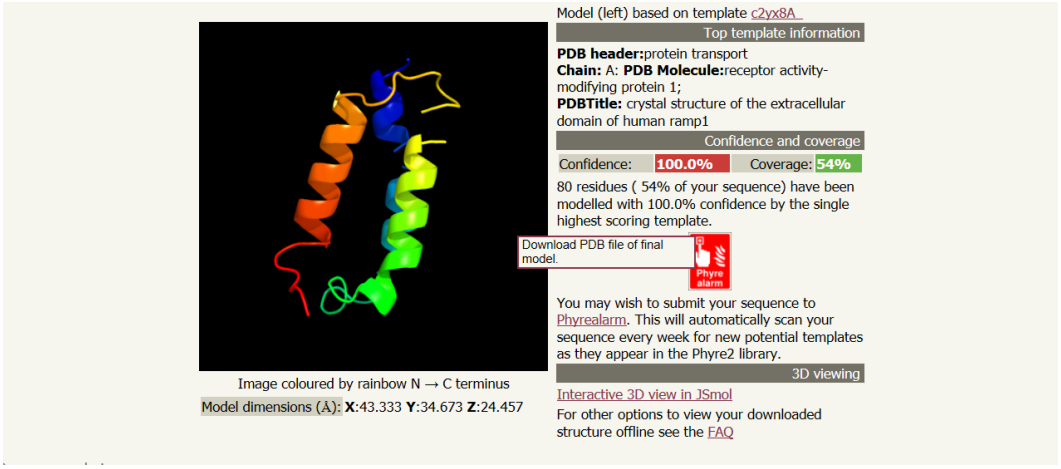


#	Template	Alignment Coverage	3D Model	Confidence	% i.d.	Template Information
1	c2yx8A	Alignment		100.0	29	**PDB header:**protein transport **Chain:** A: **PDB Molecule:**receptor activity-modifying protein 1; **PDBTitle:** crystal structure of the extracellular domain of human rar Run Investigator
2	c2xvtC	Alignment		100.0	25	**PDB header:**membrane protein **Chain:** C: **PDB Molecule:**receptor activity-modifying protein 2; **PDBTitle:** structure of the extracellular domain of human ramp2 Run Investigator
3	c4rwgC	Alignment		99.9	26	**PDB header:**membrane protein/hormone **Chain:** C: **PDB Molecule:**maltose-binding periplasmic protein, rece activity- **PDBTitle:** crystal structure of the clr:ramp1 extracellular domain heterodimer2 with bound high affinity cgrp analog Run Investigator

3.5 Sitios de unión

Se utiliza Raptor X para buscar los sitios de unión. A continuación se presentan los datos.

Dominio E1 de la proteína precursora amiloide (4PWQ)

Domain	P-value	uGDT/GDT	uSeqID/SeqID
1	3.6e-23	162/87	172/90

Pocket 1 (multiplicidad 4) coordenadas:

Cluster 0 -> 17.048 23.440 -33.372

Proteína amiloide de suero A1 dominio C (4IP8 C)

Domain	P-value	uGDT/GDT	uSeqID/SeqID
1	1.6e-07	101/91	102/97

Pocket 1 (multiplicidad 38) coordenadas:

Cluster 0 -> -25.779 5.646 39.531

Proteína Kinasa 1 con afinidad por microtúbulos dominio A (2HAK A)

Domain	P-value	uGDT/GDT	uSeqID/SeqID
1	1.0e-11	283/94	309/94

Pocket 1 (multiplicidad 85) coordenadas:

Cluster 0 -> 35.265 80.621 3.447

Proteína Kinasa 1 con afinidad por microtúbulos dominio B (2HAK B)

Domain	P-value	uGDT/GDT	uSeqID/SeqID
1	1.0e-11	283/94	309/94

Pocket 1 (mutiplicidad 85) coordenadas:

Cluster 0 -> 35.265 80.621 3.447

Preselinina-1 dominio CTF (2KR6)

Domain	P-value	uGDT/GDT	uSeqID/SeqID
1	2.8e-04	154/87	176/100

Pocket 1 (multiplicidad 2) coordenadas

Cluster 0 -> -9.081 74.214 4.295

RAMP3

Domain	P-value	uGDT/GDT	uSeqID/SeqID
1	9.0e-05	72/55	27/18

Pocket 1 (multiplicidad 9) coordenadas

Cluster 0 -> 52.234 38.122 29.599

3.6 Búsqueda de moléculas candidatas

Utilizamos el formato pdb de las proteínas para insertarlo en la aplicación de MTiOpenScreen con las coordenadas de los sitios de unión. El resultado para cada proteína es una tabla con las propiedades de las moléculas y el código de identificación del compuesto.

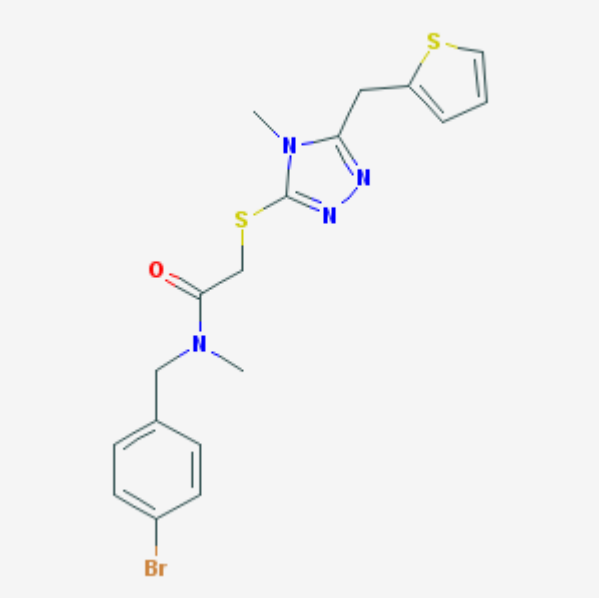
Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24339291_Intermediate	1	-9.3	1	diverse-lib	N	4	0	4.74	351.40058	47.26
17479619_Intermediate	1	-9.3	3	iPPI-lib	N	6	1	5.51	474.30614	76.61
57288056_Intermediate	1	-9.2	4	iPPI-lib	N	4	0	5.44	410.48762	81.29
22407743_Intermediate	1	-9.2	6	iPPI-lib	N	5	1	5.62	441.51828	68.54
14728891_Intermediate	1	-9.2	5	diverse-lib	N	5	1	5.74	431.50354	88.33
144187793_Intermediate	1	-9.0	5	iPPI-lib	Y	4	1	5.1	383.4855	44.7
24316306_Intermediate	1	-8.9	2	diverse-lib	N	4	1	4.66	366.41192	51.22
26538709_Intermediate	1	-8.9	5	iPPI-lib	N	6	2	5.95	455.89242	91.24
14745808_Intermediate	1	-8.8	6	diverse-lib	N	4	1	5.1	382.45438	49.41
24281040_Intermediate	1	-8.8	4	diverse-lib	N	3	1	5.72	395.47298	71.47
24314034_Intermediate	1	-8.8	3	diverse-lib	N	5	1	4.96	419.49284	84.76
24323848_Intermediate	1	-8.8	2	diverse-lib	Y	5	2	3.49	407.50858	126.7
26643902_Intermediate	1	-8.8	1	diverse-lib	N	5	3	4.69	393.43726	91.9
144116892_Accepted	1	-8.8	6	iPPI-lib	Y	4	1	5.12	406.4030896	50.7
22413596_Intermediate	1	-8.8	3	diverse-lib	N	4	1	5.81	429.94126	49.25
134216419_Accepted	1	-8.8	10	iPPI-lib	N	7	1	4.65	586.6417896	84.94
24413076_Intermediate	1	-8.8	6	diverse-lib	N	6	1	4.03	410.46778	76.88
26732350_Accepted	1	-8.8	5	diverse-lib	N	3	0	5.93	441.5.365232	29.54
124948818_Accepted	1	-8.7	5	diverse-lib	N	5	1	4.17	406.86156	68.29

Tabla 1: Ejemplo de resultado para la proteína amiloide de suero A1 dominio C

3.7 Identificación de compuestos en pubchem

La identificación de compuests en la página pubchen proporciona el nombre, la estructura del compuesto y su código SMILES. Ejemplo de resultado para proteína amiloide de suero A1:

24339291_Intermediate (ID proporcionado por MTiOpenScreen)



Nombre: N-[(4-bromophenyl)methyl]-N-methyl-2-[[4-methyl-5-(thiophen-2-ylmethyl)-1,2,4-triazol-3-yl]sulfanyl]acetamide

SMILES: CN1C(=NN=C1SCC(=O)N(C)CC2=CC=C(C=C2)Br)CC3=CC=CS3

3.7 Propiedades ADMET de las moléculas

Con los códigos SMILES obtenidos de la página Web pubchem de las moléculas se usa la aplicación pkCSM para conocer la propiedades ADMET de las moléculas. A continuación se muestra un ejemplo:

Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	**-5.565**	Numeric (log mol/L)
Absorption	Caco2 permeability	**1.271**	Numeric (log Papp in 10^{-6} cm/s)
Absorption	Intestinal absorption (human)	**90.657**	Numeric (% Absorbed)
Absorption	Skin Permeability	**-2.757**	Numeric (log Kp)
Absorption	P-glycoprotein substrate	**No**	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	**Yes**	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	**Yes**	Categorical (Yes/No)

Property	Model Name	Predicted Value	Unit
Distribution	VDss (human)	**-0.124**	Numeric (log L/kg)
Distribution	Fraction unbound (human)	**0**	Numeric (Fu)
Distribution	BBB permeability	**0.063**	Numeric (log BB)
Distribution	CNS permeability	**-2.296**	Numeric (log PS)
Metabolism	CYP2D6 substrate	**No**	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	**Yes**	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	**Yes**	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	**Yes**	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	**Yes**	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	**No**	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	**Yes**	Categorical (Yes/No)
Excretion	Total Clearance	**0.116**	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	**No**	Categorical (Yes/No)
Toxicity	AMES toxicity	**No**	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	**0.753**	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	**No**	Categorical (Yes/No)
Toxicity	hERG II inhibitor	**Yes**	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	**2.028**	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	**0.783**	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	**Yes**	Categorical (Yes/No)
Toxicity	Skin Sensitisation	**No**	Categorical (Yes/No)
Toxicity	*T.Pyriformis* toxicity	**0.559**	Numeric (log ug/L)
Toxicity	Minnow toxicity	**-2.079**	Numeric (log mM)

Tabla 2 Ejemplo de resultado para el compuesto contra la proteína de suero amiloide A1 dominio C

3.8 Resumen de resultados

En el anexo 3 se muestra las tablas resumen de los resultados obtenidos con el docking realizado con MTiOpenScreen , la identificacion de las moléculas en la pàgina Web pubchem y las propiedades ADMET obtenidas de la aplicación pkCSM. Se han escogido las cinco primeras moléculas que se presentan en la tabla de MTiOpenScreen y que se han podido identificar en pubchem.

3.9 Elección de moléculas

La elección de las moléculas se ha realizado en base a:

- Moléculas lead-like según las librerias de MTiOpenScreen
- Compuesto que cumplen la regla de cinco de Lipinski
- Moléculas que sean capaces de pasar la barrera hematoencefálica, propiedades de permeabilidad BBB y permeabilidad CNS.
- Moléculas que no sean mutagénicas y no causen daño hepático, AMES y hepatotoxicidad.

Los moléculas lead-like o que cumplen la regla de cinco de Lipinski tiene más posibilidades de ser candidatos a fármacos.

Las propiedades ADMET seleccionades han sido elegidas para priorizar que no causen daños irreparables y que sean capaces de pasar la barrera hematoencefálica.

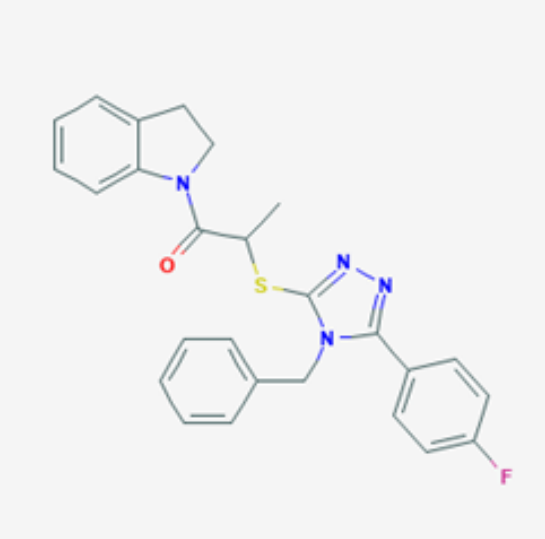
En algunos casos no se cumplen todas las propiedades antes indicadas, se ha intentado que se cumplan el máximo de ellas.

Los compuesto elegidos son los siguientes:

3.9.1 Dominio E1 de la proteína precursora amiloide

24377816_Intermediate

2-[[4-benzyl-5-(4-fluorophenyl)-1,2,4-triazol-3-yl]sulfanyl]-1-(2,3-dihydroindol-1-yl)propan-1-one



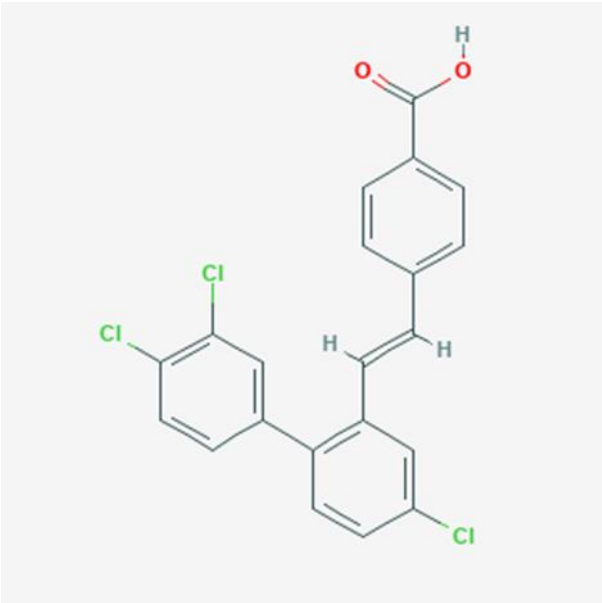
Propiedad	Valor
Lead-like	Sí
Regla de cinco	Sí
Librería	iPPI
Permeabilidad BBB	0.182
Permeabilidad CNS	-1.994
AMES	No
Toxicidad hepática	Yes

3.9.2 Proteina de suero amiloide A1

- Dominio A

22400820_Intermediate

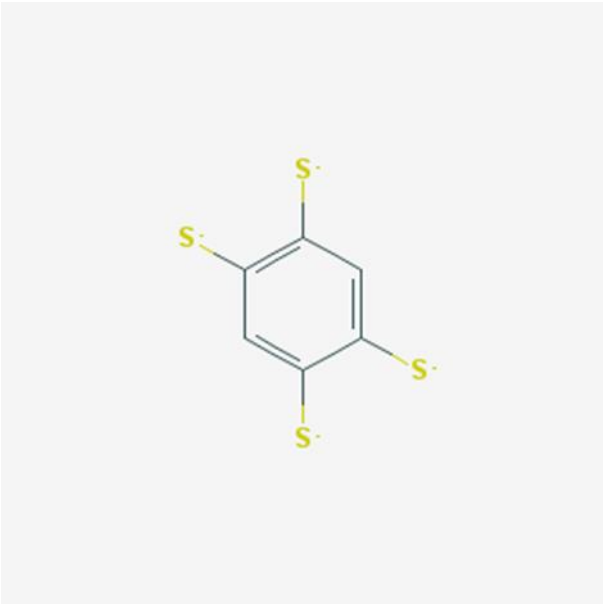
4-[(E)-2-[5-chloro-2-(3,4-dichlorophenyl)phenyl]ethenyl]benzoic acid



Propiedad	Valor
Lead-like	No
Regla de cinco	No (valor de log p es 5,37)
Librería	Diverse-lib
Permeabilidad BBB	0,214
Permeabilidad CNS	-1,234
AMES	No
Toxicidad hepática	No

- Dominio C

22407743_Intermediate
benzene-1,2,4,5-tetrathiolate

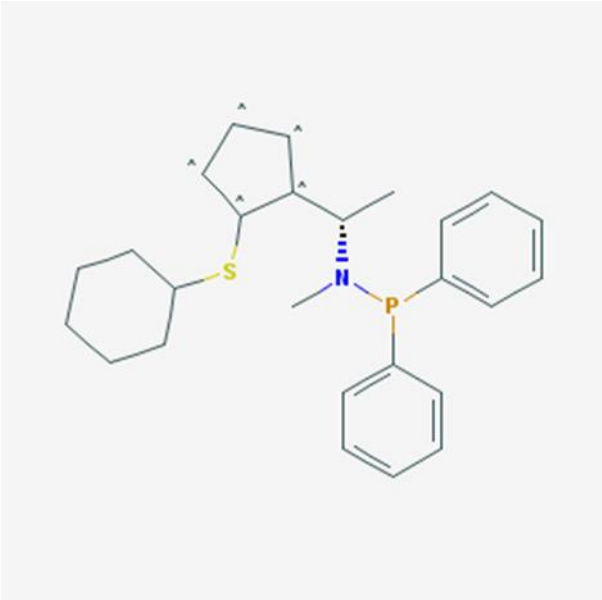


Propiedad	Valor
Lead-like	No
Regla de cinco	No (log P 5,62)
Librería	iPPI
Permeabilidad BBB	0,084
Permeabilidad CNS	-1,74
AMES	No
Toxicidad hepática	No

3.9.3 Proteína Kinasa 1 con afinidad por microtúbulos

- Dominio A

24805332_Intermediate
(1S)-1-(2-cyclohexylsulfanylcyclopentyl)-N-diphenylphosphanyl-N-methylethanamine



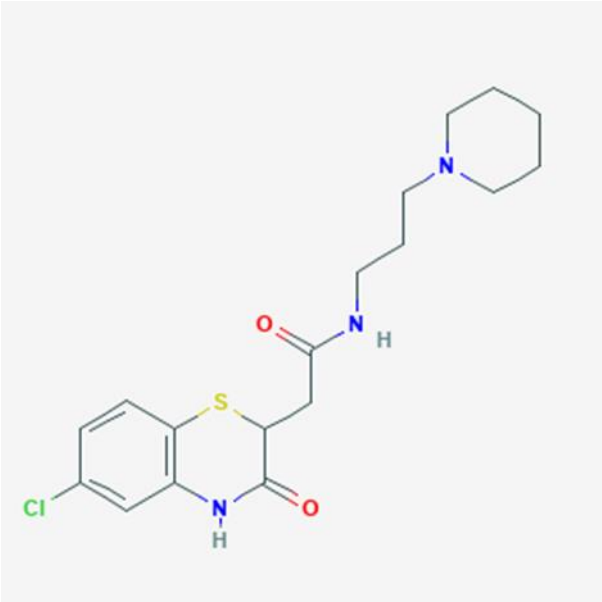
Propiedad	Valor
Lead-like	No
Regla de cinco	Si
Librería	iPPI
Permeabilidad BBB	1,293
Permeabilidad CNS	-1,218
AMES	No
Toxicidad hepática	No

- Dominio B

No he escogido ninguno porque presentaban demasiados valores que no cumplían con el criterio establecido.

3.9.4 Preselinina-1

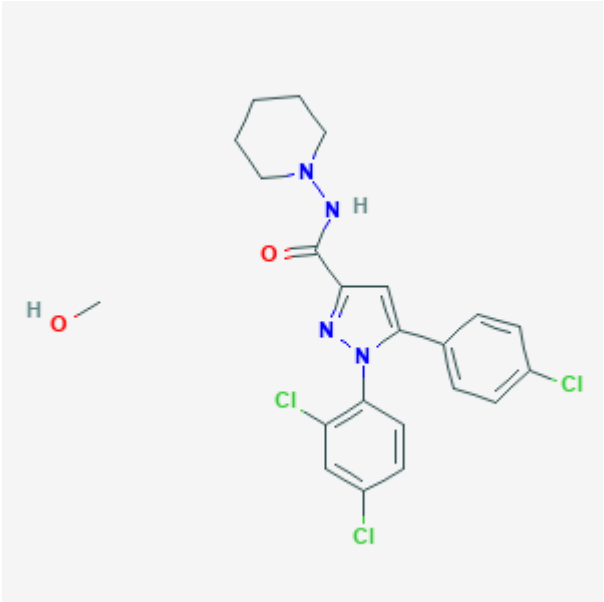
17480197_Accepted
2-(6-chloro-3-oxo-4H-1,4-benzothiazin-2-yl)-N-(3-piperidin-1-ylpropyl)acetamide



Propiedad	Valor
Lead-like	No
Regla de cinco	Si
Librería	Diverse-lib
Permeabilidad BBB	-0,078
Permeabilidad CNS	-2,478
AMES	No
Toxicidad hepática	No

3.9.5 Ramp 3

24799411_Intermediate
5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-piperidin-1-ylpyrazole-3-carboxamide;metanol



Propiedad	Valor
Lead-like	Si
Regla de cinco	Si
Librería	Diverse-lib
Permeabilidad BBB	-1,064
Permeabilidad CNS	-1,964
AMES	No
Toxicidad hepática	No

4. Conclusiones

En este trabajo se han obtenido siete dianas y seis moleculas que pueden ser candidatos a fármacos para la enfermedad de Alzheimer.

Las dianas elegidas han sido:

Dominio E1 de la proteína precursora amiloide, proteína amiloide de suero A1 dominio A y C , proteína Kinasa-1 con afinidad por microtúbulos dominio A y B, Preselinina-1 dominio CTF y RAMP3.

Las moléculas elegidas han sido:

1. 2-[[4-benzyl-5-(4-fluorophenyl)-1,2,4-triazol-3-yl]sulfanyl]-1-(2,3-dihydroindol-1-yl)propan-1-one.
2. 4-[(E)-2-[5-chloro-2-(3,4-dichlorophenyl)phenyl]ethenyl]benzoic acid.

3. benzene-1,2,4,5-tetrathiolate
4. (1S)-1-(2-cyclohexylsulfanylcyclopentyl)-N-diphenylphosphanyl-N-methylethanamine.
5. 2-(6-chloro-3-oxo-4H-1,4-benzothiazin-2-yl)-N-(3-piperidin-1-ylpropyl)acetamide.
6. 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-piperidin-1-ylpyrazole-3-carboxamide;metanol.

Los objetivos principales se han cumplido no obstante ha habido desviaciones con respecto a la planificación inicial.

El objetivo secundario de buscar en Gene Expression Omnibus (GEO) genes diferencialmete expresados en la enfermedad de Alzheimer no se ha realizado pues con la bibliografia al respecto había suficiente información para elegir las dianas.
DrugBank no se ha utilizado pues las librerías de moléculas utilizadas han sido las proporcionadas por MTiOpenScreen.

Otra de las desviaciones ha sido que solo se han elegido 5 moléculas por target, esto ha sido debido a que el servidor MTiOpenScreen dejo de fucionar durante la realización del trabajo durante al menos una semana. Debido a esto también se tuvo que descartar por falta de tiempo la tarea de comprobar si las moléculas elegidas podían funcionar para Parkinson y Ataxia.
La comprobación de la toxicidad en el servidor Vega no fue necesaria pues el servidor pkCSM proporciona también esta información.

En general la planificación del trabajo se ha seguido con un buen grado de cumplimiento.

Para la búsqueda de moléculas se pueden utilizar más parámetros. En este trabajo se han incluido los necesarios para poder elegir moléculas candidatas. Los resultados de MTiOpenScreen son muy amplios (1000 moléculas) y se pueden realizar estudiós de acoplamiento posteriores para afinar aún más la elección de los moléculas.

Con respecto a las propiedades ADMET también se pueden ampliar los conocimientos y realizar un estudio más exhaustivo usando otros servidores.

El futuro de la cura de la enfermedad de Alzheimer requiere el uso de toda la tecnología disponible, este estudio pretende ser un acercamiento al descubrimiento de fármacos a través de la bioinformàtica. Se puede ampliar usando más librerías de moléculas, mayor información sobre las dianas y uso de mayor número de aplicaciones para comparar resultados.

5. Glosario

Diana (target): compuesto sobre el que actúan una o varias moléculas (fármacos)

Cribado vidual (virtual screening): proceso informático automatizado para buscar moléculas que puedan unirse a dianas seleccionadas.

Acomplamiento molecular (Docking): proceso que parte de una estructura de proteína en 3D conocida para, a través de métodos computacionales, predecir la orientación de los ligandos (moléculas candidatas) en los sitios de unión de las cavidades de las proteínas y su energía libre de unión.

Propiedades ADMET: son las propiedades de las moléculas que determinan su absorción, distribución, metabolismo, excrecion y toxicidad en el organismo.

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16. MTiOpenScreen: a web server for structure-based virtual screening

C´eline M. Labb´e, Julien Rey, David Lagorce, Marek Vavruˇsa, J´erome Becot1,2, Olivier Sperandio1,2, Bruno O. Villoutreix, Pierre Tuff ´ery and Maria A. Miteva.

Universit ´e Paris Diderot, Sorbonne Paris Cit ´ e, Mol´ecules Th´ erapeutiques In Silico, INSERM UMR-S 973, Paris,
France, 2INSERM, U973, Paris, France and 3RPBS, 75205 Paris, France
Received February 11, 2015; Revised March 27, 2015; Accepted March 28, 2015

W448–W454 Nucleic Acids Research, 2015, Vol. 43, Web Server issue Published online 08 April 2015
doi: 10.1093/nar/gkv306

17. iPPI-DB: an online database of modulators of protein–protein interactions
C´eline M. Labb´e, M´elaine A. Kuenemann, Barbara Zarzycka3, Gert Vriend4, Gerry A.F. Nicolaes3, David Lagorce, Maria A.Miteva, Bruno O. Villoutreix and Olivier Sperandio.
Universit ´e Paris Diderot, Sorbonne Paris Cit ´ e, Mol´ecules Th´ erapeutiques, In Silico, INSERM UMR-S 973, Paris,
France, 2INSERM, U973, Paris, France, 3Department of Biochemistry, Cardiovascular Research Institute Maastricht
(CARIM), Maastricht University, Maastricht, The Netherlands and 4Centre for Molecular and Biomolecular Informatics
(CMBI), Radboudumc, PO Box 9101, 6500 HB Nijmegen, The Netherlands
Received August 02, 2015; Revised September 18, 2015; Accepted September 19, 2015

Nucleic Acids Research, 2015 1doi: 10.1093/nar/gkv982, pag 1-6

18. AutoDock Vina: Improving the Speed and Accuracy of Docking with a New Scoring Function, Efficient Optimization, and Multithreading
OLEG TROTT, ARTHUR J. OLSON
Department of Molecular Biology, The Scripps Research Institute, La Jolla, California
Received 3 March 2009; Accepted 21 April 2009
DOI 10.1002/jcc.21334
Published online 4 June 2009 in Wiley InterScience (www.interscience.wiley.com).
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19. Are there physicochemical differences between allosteric and competitive ligands?
Richard D. Smith1, Jing Lu2, Heather A. Carlson
Department of Medicinal Chemistry, University of Michigan, Ann Arbor, MI, United States of America,
Department of Computational Medicine and Bioinformatics, University of Michigan, Ann Arbor, MI, United
States of America
PLoS Comput

Biol 13(11): e1005813. https://doi.org/10.1371/journal.pcbi.1005813, pag 1-18

20. LOG P
    Supriyo Saha
    Department of Pharmaceutical Sciences, Sardar Bhagwan Singh Post Graduate Institute of
    Biomedical Sciences and Research, Dehradun, Uttarakhand, India
    Dilipkumar Pal
    Department of Pharmaceutical Sciences, Guru Ghasidash Vishwavidyalaya, (A Central University),
    Bilaspur, Chhattisgarh, India
    Encyclopedia of Physical Organic Chemistry, First Edition. Edited by Zerong Wang.
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21. pkCSM: predicting small-molecule pharmacokinetic properties using graph-based signatures
    Douglas E. V. Pires*, Tom L. Blundell and David B. Ascher*
    *Correspondence: douglas.pires@cpqrr.fiocruz.br , dascher@svi.edu.au. Poner la página.
    J. Med. Chem., 2015, 58 (9), pp 4066–4072
    DOI: 10.1021/acs.jmedchem.5b00104
    Publication Date (Web): April 10, 2015
    Copyright © 2015 American Chemical Society

22. Lipinski' s rule of five

https://en.m.wikipedia.org/wiki/Lipinski%27s_rule_of_five

Last edited 1 month ago

7. Anexos

Anexo 1 Código R (RCurl) base de datos DisGeNet

```
require(RCurl)
doQuery = function(inputFile, outFile, entity, identifier){
  #print(inputFile)
  #print(outFile)
  #print(entity)
  #print(identifier)


  # read in all data
  inFile = read.csv(file=paste(getwd(), inputFile, sep="/"), sep=",", header=TRUE)
  dataFin <- data.frame(matrix(nrow=0, ncol=14))

  STR = "";
  if (entity == "gene"){
    if (identifier == "entrez"){
      STR = "c2.geneId = '"
    }
    else  if (identifier == "hgnc"){
      STR = "c2.symbol = '"
    }
    else{
      stop ( "the type of identifier must be entrez gene identifiers or gene symbols \n")
    }
  }
  else if (entity == "disease"){
    if (identifier == "cui"){
      STR = "c1.diseaseId = '"
    }
    else  if (identifier == "mesh"){
      STR = "c1.MESH = '"
    }
    else  if (identifier == "omim"){
      STR = "c1.OMIM = '"
    }

    else{
      stop  ("the type of identifier must be cui or mesh or omim identifiers\n")
    }
  }
  else{
    stop ("the type of entity must be disease or gene \n");
  }

  for (ent in inFile$ent ){
    url <- "http://www.disgenet.org/oql"
    oql <- paste( "DEFINE
                  c0='/data/gene_disease_summary',
                  c1='/data/diseases',
                  c2='/data/genes',
                  c4='/data/sources'
                  ON
                  'http://www.disgenet.org/web/DisGeNET'
                  SELECT
                  c1 (diseaseId, name, STY, MESH, OMIM, type),
                  c2 (geneId, symbol,uniprotId, description, DPI, DSI, pantherName),
                  c0 (score, EI, Npmids, Nsnps)

                  FROM
```

```
            c0
            WHERE
            (
            c4 = 'ALL'
            AND ", STR, ent , "' )
            ORDER BY
            c0.score DESC" , sep = "")

   dataTsv <-  getURLContent(url, readfunction =charToRaw(oql), upload = TRUE, customrequest = "POST")
   #dataTsv <- rawToChar( getURLContent(url, readfunction =charToRaw(oql), upload = TRUE, customrequest = "POST"))
   myTextConnection <- textConnection( dataTsv )
   data <-  read.csv( myTextConnection, header = TRUE, sep = "\t" )
   close(myTextConnection)

   if (dim(data)[1] == 0 ){
     print ( paste (entity , ent, " is not in DisGeNET ", sep = " "))
   }
   else  {
     data$c0.EI <- ifelse(data$c0.EI == "null", NA, as.character(data$c0.EI) )
     dataFin <- rbind(dataFin, data)
   }

 }
 address <-  paste(getwd(), outFile, sep="/")
 print(address)

 write.table(dataFin,  address, sep="\t", row.names = FALSE,dec = ".", quote = FALSE)

}

myargs = commandArgs()
inputFile = "PrRCurl.csv"
outputFile = "resultados2"
entity = "disease"
identifier = "mesh"


print("Querying the database ")
doQuery(inputFile, outputFile, entity, identifier)
print("Finished")
```

Anexo 2 Codigo R (Uniprot.ws Bioconductor)

```
library(UniProt.ws)
availableUniprotSpecies(pattern="sapien")
Up<-UniProt.ws(9606)
Especie<- availableUniprotSpecies(pattern="sapien")
egs = keys(up, "UNIPROTKB")
egs = keys(Up, "UNIPROTKB")
keys <- c("P51693","P10997","P0DJI8", "Q9P0L2", "Q9NZ42", "P06727")
columns <- c("PDB","UNIGENE","SEQUENCE")
kt <- "UNIPROTKB"
res <- select(Up, keys, columns, kt)
```

Anexo 3 Resultados obtenidos

Proteína precursora amiloide dominio E1

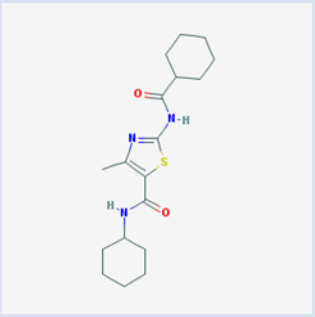
2-(cyclohexanecarbonylamino)-N-cyclohexyl-4-methyl-1,3-thiazole-5-carboxamide

CC1=C(SC(=N1)NC(=O)C2CCCCC2)C(=O)NC3CCCCC3

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
857180_Interm	1	-8.1	3	iPPI-lib	Y	5	2	4.25	412.407 6696	65.04

ADMET

Structure



Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	**-3.361**	Numeric (log mol/L)
Absorption	Caco2 permeability	**0.884**	Numeric (log Papp in
Absorption	Intestinal absorption	**90.458**	Numeric (%
Absorption	Skin Permeability	**-3.107**	Numeric (log Kp)
Absorption	P-glycoprotein	**Yes**	Categorical (Yes/No)
Absorption	P-glycoprotein I	**No**	Categorical (Yes/No)
Absorption	P-glycoprotein II	**No**	Categorical (Yes/No)
Distribution	VDss (human)	**0.424**	Numeric (log L/kg)
Distribution	Fraction unbound	**0.346**	Numeric (Fu)
Distribution	BBB permeability	**-0.108**	Numeric (log BB)
Distribution	CNS permeability	**-2.819**	Numeric (log PS)
Metabolism	CYP2D6 substrate	**No**	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	**No**	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	**No**	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	**No**	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	**No**	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	**No**	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	**No**	Categorical (Yes/No)
Excretion	Total Clearance	**-0.026**	Numeric (log
Excretion	Renal OCT2	**No**	Categorical (Yes/No)
Toxicity	AMES toxicity	**No**	Categorical (Yes/No)
Toxicity	Max. tolerated dose	**-0.516**	Numeric (log
Toxicity	hERG I inhibitor	**No**	Categorical (Yes/No)
Toxicity	hERG II inhibitor	**No**	Categorical (Yes/No)
Toxicity	Oral Rat Acute	**2.44**	Numeric (mol/kg)
Toxicity	Oral Rat Chronic	**0.419**	Numeric (log
Toxicity	Hepatotoxicity	**No**	Categorical (Yes/No)
Toxicity	Skin Sensitisation	**No**	Categorical (Yes/No)
Toxicity	*T.Pyriformis* toxicity	**0.629**	Numeric (log ug/L)
Toxicity	Minnow toxicity	**0.589**	Numeric (log mM)

3-(2,5-dioxopyrrolidin-1-yl)-N-prop-2-enyl-N-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl)benzamide

C=CCN(C1=NC2=C(S1)CCCC2)C(=O)C3=CC(=CC=C3)N4C(=O)CCC4=O

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24393329_Intermediate	1	-8.0	5	iPPI-lib	Y	6	1	5.93	426.396032	91.66

ADMET

Structure

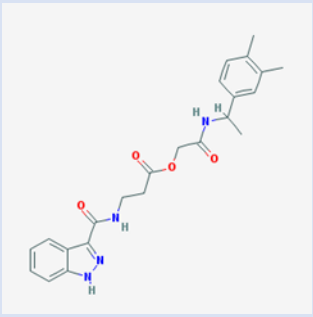
Property	Model Name	Predicted	Unit
Absorption	Water solubility	**-5.12**	Numeric (log mol/L)
Absorption	Caco2 permeability	**1.259**	Numeric (log Papp in 10^{-6}
Absorption	Intestinal	**96.5**	Numeric (% Absorbed)
Absorption	Skin Permeability	**-2.747**	Numeric (log Kp)
Absorption	P-glycoprotein	**No**	Categorical (Yes/No)
Absorption	P-glycoprotein I	**Yes**	Categorical (Yes/No)
Absorption	P-glycoprotein II	**Yes**	Categorical (Yes/No)
Distribution	VDss (human)	**0.008**	Numeric (log L/kg)
Distribution	Fraction unbound	**0.053**	Numeric (Fu)
Distribution	BBB permeability	**-0.729**	Numeric (log BB)
Distribution	CNS permeability	**-2.282**	Numeric (log PS)
Metabolism	CYP2D6 substrate	**No**	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	**Yes**	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	**Yes**	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	**Yes**	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	**Yes**	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	**No**	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	**Yes**	Categorical (Yes/No)
Excretion	Total Clearance	**-0.137**	Numeric (log ml/min/kg)
Excretion	Renal OCT2	**No**	Categorical (Yes/No)
Toxicity	AMES toxicity	**No**	Categorical (Yes/No)
Toxicity	Max. tolerated	**0.374**	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	**No**	Categorical (Yes/No)
Toxicity	hERG II inhibitor	**No**	Categorical (Yes/No)
Toxicity	Oral Rat Acute	**2.766**	Numeric (mol/kg)
Toxicity	Oral Rat Chronic	**2.188**	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	**Yes**	Categorical (Yes/No)
Toxicity	Skin Sensitisation	**No**	Categorical (Yes/No)
Toxicity	*T.Pyriformis*	**0.55**	Numeric (log ug/L)
Toxicity	Minnow toxicity	**0.424**	Numeric (log mM)

[2-[1-(3,4-dimethylphenyl)ethylamino]-2-oxoethyl] 3-(1H-indazole-3-carbonylamino)propanoate

CC1=C(C=C(C=C1)C(C)NC(=O)COC(=O)CCNC(=O)C2=NNC3=CC=CC=C32)C

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
56422362_Acc	1	-7.8	4	iPPI-lib	Y	9	1	1.4	462.90666	120.93

Structure



ADMET

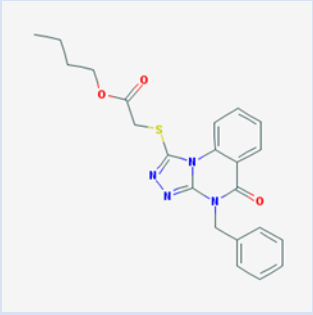
Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-4.198	Numeric (log mol/L)
Absorption	Caco2 permeability	0.901	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	70.134	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.744	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	No	Categorical (Yes/No)
Distribution	VDss (human)	0.037	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0	Numeric (Fu)
Distribution	BBB permeability	-1.125	Numeric (log BB)
Distribution	CNS permeability	-2.957	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	No	Categorical (Yes/No)
Excretion	Total Clearance	0.384	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.409	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.211	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	3.158	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.311	Numeric (log ug/L)
Toxicity	Minnow toxicity	-2.118	Numeric (log mM)

butyl 2-[(4-benzyl-5-oxo-[1,2,4]triazolo[4,3-a]quinazolin-1-yl)sulfanyl]acetate

CCCCOC(=O)CSC1=NN=C2N1C3=CC=CC=C3C(=O)N2CC4=CC=CC=C4

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24343126_Inte	1	-7.7	4	iPPI-lib	Y	5	1	4.05	413.51148	56.03

Structure



ADMET

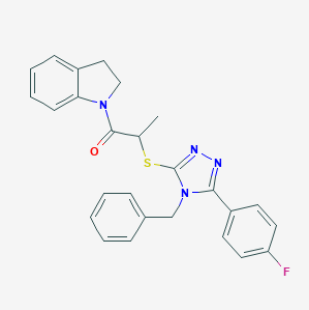
Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-4.293	Numeric (log mol/L)
Absorption	Caco2 permeability	1.169	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	98.655	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.735	Numeric (log Kp)
Absorption	P-glycoprotein substrate	No	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	-0.016	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.175	Numeric (Fu)
Distribution	BBB permeability	-1.152	Numeric (log BB)
Distribution	CNS permeability	-2.842	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	Yes	Categorical (Yes/No)
Excretion	Total Clearance	0.478	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.771	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.648	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	0.859	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.286	Numeric (log ug/L)
Toxicity	Minnow toxicity	-3.18	Numeric (log mM)

2-[[4-benzyl-5-(4-fluorophenyl)-1,2,4-triazol-3-yl]sulfanyl]-1-(2,3-dihydroindol-1-yl)propan-1-one

CC(C(=O)N1CCC2=CC=CC=C21)SC3=NN=C(N3CC4=CC=CC=C4)C5=CC=C(C=C5)F

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24377816_Inte	1	-7.7	4	iPPI-lib	Y	6	2	4.05	388.4159	92.17

Structure



ADMET

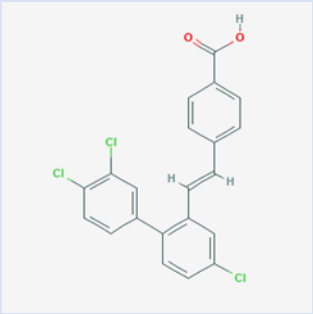
Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-5.033	Numeric (log mol/L)
Absorption	Caco2 permeability	1.064	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	94.117	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.735	Numeric (log Kp)
Absorption	P-glycoprotein substrate	No	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	-0.163	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.149	Numeric (Fu)
Distribution	BBB permeability	0.182	Numeric (log BB)
Distribution	CNS permeability	-1.994	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	Yes	Categorical (Yes/No)
Excretion	Total Clearance	-0.059	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.801	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.736	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	0.521	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.285	Numeric (log ug/L)
Toxicity	Minnow toxicity	-1.243	Numeric (log mM)

4-[(E)-2-[5-chloro-2-(3,4-dichlorophenyl)phenyl]ethenyl]benzoic acid

C1=CC(=CC=C1C=CC2=C(C=CC(=C2)Cl)C3=CC(=C(C=C3)Cl)Cl)C(=O)O

Compound	Model ID	Energy	nRot	Library	isLead Like	HBA	HBD	LogP	MW	TPSA
22400820_Int	1	-8.9	4	diverse-lib	N	5	2	5.37	424.49106	71.19

Structure



ADMET

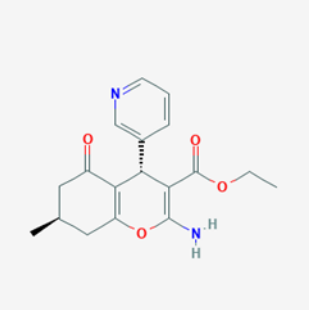
Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-3.272	Numeric (log mol/L)
Absorption	Caco2 permeability	1.162	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	95.441	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.735	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	No	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	No	Categorical (Yes/No)
Distribution	VDss (human)	-1.743	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0	Numeric (Fu)
Distribution	BBB permeability	0.214	Numeric (log BB)
Distribution	CNS permeability	-1.234	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	No	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	No	Categorical (Yes/No)
Excretion	Total Clearance	-0.035	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.661	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	No	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.381	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	0.608	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	No	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.288	Numeric (log ug/L)
Toxicity	Minnow toxicity	-1.97	Numeric (log mM)

ethyl (4S,7R)-2-amino-7-methyl-5-oxo-4-pyridin-3-yl-4,6,7,8-tetrahydrochromene-3-carboxylate

CCOC(=O)C1=C(OC2=C(C1C3=CN=CC=C3)C(=O)CC(C2)C)N

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
849702_Accepted	1	-8.9	1	iPPI-lib	Y	6	0	2.91	450.28474	73.43

Structure



ADMET

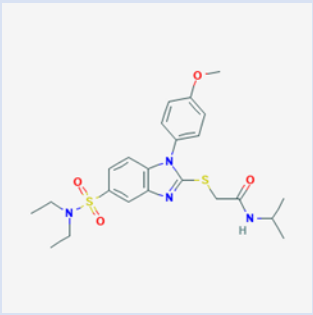
Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-3.38	Numeric (log mol/L)
Absorption	Caco2 permeability	1.309	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	79.876	Numeric (% Absorbed)
Absorption	Skin Permeability	-3.261	Numeric (log Kp)
Absorption	P-glycoprotein substrate	No	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	No	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	No	Categorical (Yes/No)
Distribution	VDss (human)	-0.145	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.316	Numeric (Fu)
Distribution	BBB permeability	-0.496	Numeric (log BB)
Distribution	CNS permeability	-2.972	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	No	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	No	Categorical (Yes/No)
Excretion	Total Clearance	0.55	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.322	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	No	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	3.162	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	1.412	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.338	Numeric (log ug/L)
Toxicity	Minnow toxicity	1.362	Numeric (log mM)

2-[5-(diethylsulfamoyl)-1-(4-methoxyphenyl)benzimidazol-2-yl]sulfanyl-N-propan-2-ylacetamide

CCN(CC)S(=O)(=O)C1=CC2=C(C=C1)N(C(=N2)SCC(=O)NC(C)C)C3=CC=C(C=C3)OC

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24384458_Int	1	-8.9	4	iPPI-lib	Y	6	1	5.79	494.4156	62.53

Structure



ADMET

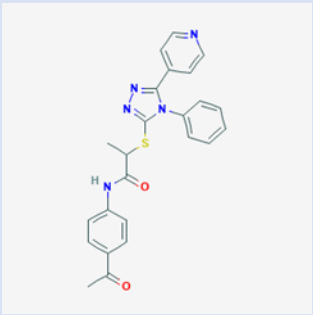
Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-2.941	Numeric (log mol/L)
Absorption	Caco2 permeability	1.013	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	91.424	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.735	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	-0.637	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.208	Numeric (Fu)
Distribution	BBB permeability	-0.833	Numeric (log BB)
Distribution	CNS permeability	-2.825	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	Yes	Categorical (Yes/No)
Excretion	Total Clearance	0.363	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	Yes	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.008	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.237	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	0.763	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.285	Numeric (log ug/L)
Toxicity	Minnow toxicity	-2.221	Numeric (log mM)

N-(4-acetylphenyl)-2-[(4-phenyl-5-pyridin-4-yl-1,2,4-triazol-3-yl)sulfanyl]propanamide

CC(C(=O)NC1=CC=C(C=C1)C(=O)C)SC2=NN=C(N2C3=CC=CC=C3)C4=CC=NC=C4

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24368587_Int	1	-8.9	4	iPPI-lib	N	5	2	4.46	443.5606	100.15

Structure



ADMET

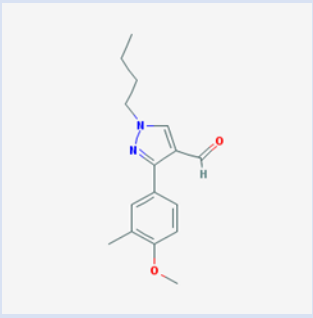
Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-3.917	Numeric (log mol/L)
Absorption	Caco2 permeability	1.13	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	94.632	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.735	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	0.213	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.14	Numeric (Fu)
Distribution	BBB permeability	-0.684	Numeric (log BB)
Distribution	CNS permeability	-2.477	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	Yes	Categorical (Yes/No)
Excretion	Total Clearance	-0.217	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.827	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.998	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	1.036	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.285	Numeric (log ug/L)
Toxicity	Minnow toxicity	0.737	Numeric (log mM)

1-butyl-3-(4-methoxy-3-methylphenyl)pyrazole-4-carbaldehyde

CCCCN1C=C(C(=N1)C2=CC(=C(C=C2)OC)C)C=O

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
104232068_A	1	-8.9	4	diverse-lib	N	5	0	4.25	558.38332	51.66

Structure



ADMET

Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-3.658	Numeric (log mol/L)
Absorption	Caco2 permeability	1.413	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	95.995	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.391	Numeric (log Kp)
Absorption	P-glycoprotein substrate	No	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	No	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	No	Categorical (Yes/No)
Distribution	VDss (human)	0.091	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.172	Numeric (Fu)
Distribution	BBB permeability	0.334	Numeric (log BB)
Distribution	CNS permeability	-1.701	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	No	Categorical (Yes/No)
Excretion	Total Clearance	0.449	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	Yes	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.703	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	No	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.152	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	1.972	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	1.096	Numeric (log ug/L)
Toxicity	Minnow toxicity	0.014	Numeric (log mM)

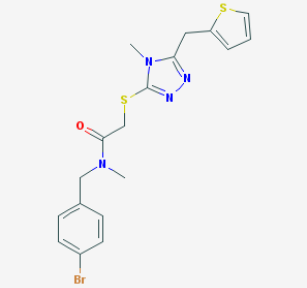
N-[(4-bromophenyl)methyl]-N-methyl-2-[[4-methyl-5-(thiophen-2-ylmethyl)-1,2,4-triazol-3-yl]sulfanyl]acetamide

CN1C(=NN=C1SCC(=O)N(C)CC2=CC=C(C=C2)Br)CC3=CC=CS3

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24339291_Int	1	-9.3	1	diverse-lib	N	4	0	4.74	351.40058	47.26

ADMET

Structure



Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-5.565	Numeric (log mol/L)
Absorption	Caco2 permeability	1.271	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	90.657	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.757	Numeric (log Kp)
Absorption	P-glycoprotein substrate	No	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	-0.124	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0	Numeric (Fu)
Distribution	BBB permeability	0.063	Numeric (log BB)
Distribution	CNS permeability	-2.296	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	Yes	Categorical (Yes/No)
Excretion	Total Clearance	0.116	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.753	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.028	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	0.783	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.559	Numeric (log ug/L)
Toxicity	Minnow toxicity	-2.079	Numeric (log mM)

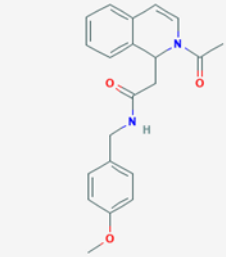
2-(2-acetyl-1H-isoquinolin-1-yl)-N-[(4-methoxyphenyl)methyl]acetamide

CC(=O)N1C=CC2=CC=CC=C2C1CC(=O)NCC3=CC=C(C=C3)OC

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
17479619_Int	1	-9.3	3	iPPI-lib	N	6	1	5.51	474.30614	76.61

ADMET

Structure



Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-4.385	Numeric (log mol/L)
Absorption	Caco2 permeability	1.67	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	92.386	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.893	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	0.009	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0	Numeric (Fu)
Distribution	BBB permeability	-0.123	Numeric (log BB)
Distribution	CNS permeability	-2.158	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	Yes	Categorical (Yes/No)
Excretion	Total Clearance	0.38	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	Yes	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	-0.172	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.086	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	1.372	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.821	Numeric (log ug/L)
Toxicity	Minnow toxicity	1.149	Numeric (log mM)

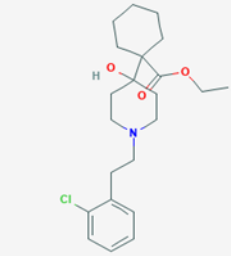
ethyl1-[1-[2-(2-chlorophenyl)ethyl]-4-hydroxypiperidin-4-yl]cyclohexane-1-carboxylate

CCOC(=O)C1(CCCCC1)C2(CCN(CC2)CCC3=CC=CC=C3Cl)O

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
57288056_Int	1	-9.2	4	iPPI-lib	N	4	0	5.44	410.48762	81.29

ADMET

Structure



Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-4.013	Numeric (log mol/L)
Absorption	Caco2 permeability	1.332	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	90.728	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.765	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	0.859	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.2	Numeric (Fu)
Distribution	BBB permeability	0.23	Numeric (log BB)
Distribution	CNS permeability	-2.023	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	No	Categorical (Yes/No)
Excretion	Total Clearance	1.021	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	Yes	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	-0.426	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	3.047	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	0.692	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.519	Numeric (log ug/L)
Toxicity	Minnow toxicity	-0.796	Numeric (log mM)

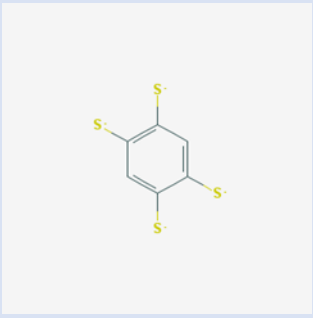
benzene-1,2,4,5-tetrathiolate

C1=C(C(=CC(=C1[S-])[S-])[S-])[S-]

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
22407743_Int	1	-9.2	6	iPPI-lib	N	5	1	5.62	441.51828	68.54

ADMET

Structure



Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-2.657	Numeric (log mol/L)
Absorption	Caco2 permeability	1.584	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	100	Numeric (% Absorbed)
Absorption	Skin Permeability	-1.467	Numeric (log Kp)
Absorption	P-glycoprotein substrate	No	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	No	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	No	Categorical (Yes/No)
Distribution	VDss (human)	0.036	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.409	Numeric (Fu)
Distribution	BBB permeability	0.084	Numeric (log BB)
Distribution	CNS permeability	-1.74	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	No	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	No	Categorical (Yes/No)
Excretion	Total Clearance	1.12	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.697	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	No	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.368	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	0.978	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	No	Categorical (Yes/No)
Toxicity	Skin Sensitisation	Yes	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	2.127	Numeric (log ug/L)
Toxicity	Minnow toxicity	1.069	Numeric (log mM)

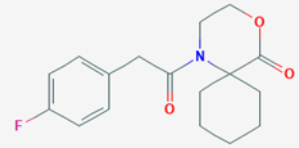
1-[2-(4-fluorophenyl)acetyl]-4-oxa-1-azaspiro[5.5]undecan-5-one

C1CCC2(CC1)C(=O)OCCN2C(=O)CC3=CC=C(C=C3)F

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24316306_Int	1	-8.9	2	diverse-lib	N	4	1	4.66	366.41192	51.22

ADMET

Structure



Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-3.339	Numeric (log mol/L)
Absorption	Caco2 permeability	1.364	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	94.74	Numeric (% Absorbed)
Absorption	Skin Permeability	-3.812	Numeric (log Kp)
Absorption	P-glycoprotein substrate	No	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	No	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	No	Categorical (Yes/No)
Distribution	VDss (human)	0.006	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.21	Numeric (Fu)
Distribution	BBB permeability	0.283	Numeric (log BB)
Distribution	CNS permeability	-2.353	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	No	Categorical (Yes/No)
Excretion	Total Clearance	1.331	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	Yes	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	-0.003	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	No	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.971	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	1.273	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	No	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.811	Numeric (log ug/L)
Toxicity	Minnow toxicity	0.958	Numeric (log mM)

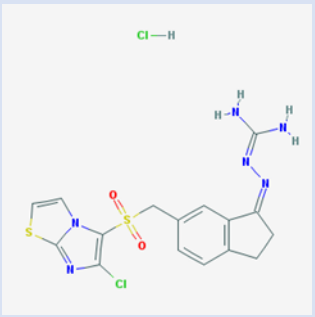
2-[(Z)-[6-[(6-chloroimidazo[2,1-b][1,3]thiazol-5-yl)sulfonylmethyl]-2,3-dihydroinden-1-ylidene]amino]guanidine;hydrochloride

C1CC(=NN=C(N)N)C2=C1C=CC(=C2)CS(=O)(=O)C3=C(N=C4N3C=CS4)Cl.Cl

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24794437_Ac	1	-10.1	4	diverse-lib	Y	6	0	3.77	447.4798264	63.39

ADMET

Structure



Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-2.913	Numeric (log mol/L)
Absorption	Caco2 permeability	0.611	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	78.227	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.735	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	No	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	No	Categorical (Yes/No)
Distribution	VDss (human)	0.349	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.371	Numeric (Fu)
Distribution	BBB permeability	-1.525	Numeric (log BB)
Distribution	CNS permeability	-2.815	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	No	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	No	Categorical (Yes/No)
Excretion	Total Clearance	0.461	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	Yes	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.697	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.482	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	0.581	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	No	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.285	Numeric (log ug/L)
Toxicity	Minnow toxicity	2.119	Numeric (log mM)

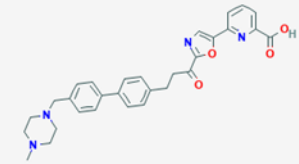
6-[2-[3-[4-[4-[(4-methylpiperazin-1-yl)methyl]phenyl]phenyl]propanoyl]-1,3-oxazol-5-yl]pyridine-2-carboxylic acid

CN1CCN(CC1)CC2=CC=C(C=C2)C3=CC=C(C=C3)CCC(=O)C4=NC=C(O4)C5=NC(=CC=C5)C(=O)O

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24801219_Ac	1	-9.7	4	iPPI-lib	Y	6	0	3.87	452.4284696	59.73

ADMET

Structure



Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-2.995	Numeric (log mol/L)
Absorption	Caco2 permeability	0.674	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	61.546	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.735	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	No	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	0.305	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.104	Numeric (Fu)
Distribution	BBB permeability	-1.324	Numeric (log BB)
Distribution	CNS permeability	-2.616	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	No	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	No	Categorical (Yes/No)
Excretion	Total Clearance	0.551	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.675	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	No	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.457	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	1.84	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.285	Numeric (log ug/L)
Toxicity	Minnow toxicity	4.281	Numeric (log mM)

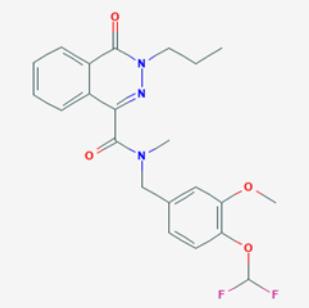
N-[[4-(difluoromethoxy)-3-methoxyphenyl]methyl]-N-methyl-4-oxo-3-propylphthalazine-1-carboxamide

CCCN1C(=O)C2=CC=CC=C2C(=N1)C(=O)N(C)CC3=CC(=C(C=C3)OC(F)F)OC

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
26614200_Ac	1	-9.7	4	diverse-lib	N	8	0	2.49	402.44908	84.22

ADMET

Structure



Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-5.409	Numeric (log mol/L)
Absorption	Caco2 permeability	1.305	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	93.151	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.782	Numeric (log Kp)
Absorption	P-glycoprotein substrate	No	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	-0.229	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.002	Numeric (Fu)
Distribution	BBB permeability	-0.936	Numeric (log BB)
Distribution	CNS permeability	-2.514	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	No	Categorical (Yes/No)
Excretion	Total Clearance	0.481	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.392	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.193	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	0.972	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.423	Numeric (log ug/L)
Toxicity	Minnow toxicity	-0.189	Numeric (log mM)

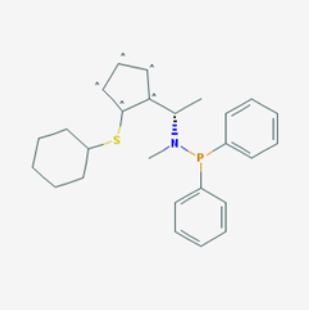
(1S)-1-(2-cyclohexylsulfanylcyclopentyl)-N-diphenylphosphanyl-N-methylethanamine

CC([C]1[CH][CH][CH][C]1SC2CCCCC2)N(C)P(C3=CC=CC=C3)C4=CC=CC=C4

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24805332_Int	1	-9.7	2	iPPI-lib	N	4	1	4.54	348.39994	49.97

ADMET

Structure



Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-6.493	Numeric (log mol/L)
Absorption	Caco2 permeability	1.101	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	97.106	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.714	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	1.042	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0	Numeric (Fu)
Distribution	BBB permeability	1.293	Numeric (log BB)
Distribution	CNS permeability	-1.218	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	No	Categorical (Yes/No)
Excretion	Total Clearance	-0.122	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.278	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.489	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	0.356	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	No	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.395	Numeric (log ug/L)
Toxicity	Minnow toxicity	-1.448	Numeric (log mM)

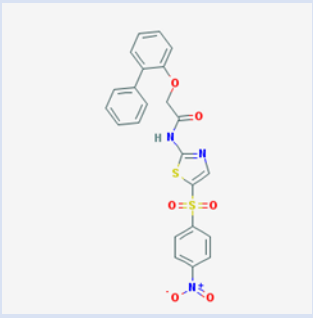
N-[5-(4-nitrophenyl)sulfonyl-1,3-thiazol-2-yl]-2-(2-phenylphenoxy)acetamide

C1=CC=C(C=C1)C2=CC=CC=C2OCC(=O)NC3=NC=C(S3)S(=O)(=O)C4=CC=C(C=C4)[N+](=O)[O-]

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24403989_Int	1	-9.6	3	diverse-lib	Y	6	0	3.63	357.2894096	69.63

ADMET

Structure



Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-4.887	Numeric (log mol/L)
Absorption	Caco2 permeability	0.78	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	96.168	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.735	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	-1.026	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.143	Numeric (Fu)
Distribution	BBB permeability	-1.486	Numeric (log BB)
Distribution	CNS permeability	-2.447	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	Yes	Categorical (Yes/No)
Excretion	Total Clearance	0.153	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.616	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.556	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	0.257	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.285	Numeric (log ug/L)
Toxicity	Minnow toxicity	-0.785	Numeric (log mM)

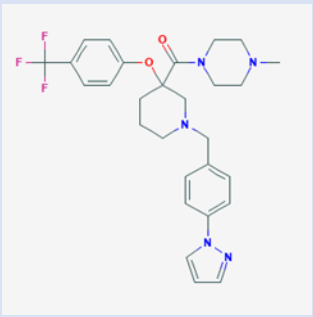
(4-methylpiperazin-1-yl)-[1-[(4-pyrazol-1-ylphenyl)methyl]-3-[4-(trifluoromethyl)phenoxy]piperidin-3-yl]methanone

CN1CCN(CC1)C(=O)C2(CCCN(C2)CC3=CC=C(C=C3)N4C=CC=N4)OC5=CC=C(C=C5)C(F)(F)F

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24823970_Int	1	-10.1	1	iPPI-lib	Y	5	1	4.73	404.45506	68.9

ADMET

Structure



Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-4.355	Numeric (log mol/L)
Absorption	Caco2 permeability	1.244	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	92.048	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.701	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	1.285	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.084	Numeric (Fu)
Distribution	BBB permeability	0.436	Numeric (log BB)
Distribution	CNS permeability	-2.139	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	Yes	Categorical (Yes/No)
Excretion	Total Clearance	0.291	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	Model Name	Predicted Value	Unit
Toxicity	Water solubility	-4.355	Numeric (log mol/L)
Toxicity	Caco2 permeability	1.244	Numeric (log Papp in 10-6 cm/s)
Toxicity	Intestinal absorption (human)	92.048	Numeric (% Absorbed)
Toxicity	Skin Permeability	-2.701	Numeric (log Kp)
Toxicity	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Toxicity	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Toxicity	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Toxicity	VDss (human)	1.285	Numeric (log L/kg)
Toxicity	Fraction unbound (human)	0.084	Numeric (Fu)

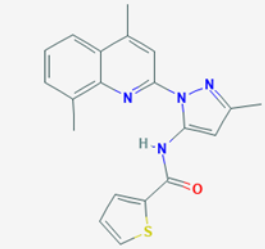
N-[2-(4,8-dimethylquinolin-2-yl)-5-methylpyrazol-3-yl]thiophene-2-carboxamide

CC1=CC=CC2=C1N=C(C=C2C)N3C(=CC(=N3)C)NC(=O)C4=CC=CS4

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24294355_Int armadi	1	-9.9	4	iPPI-lib	Y	4	1	5.52	393.43396	47.56

ADMET

Structure

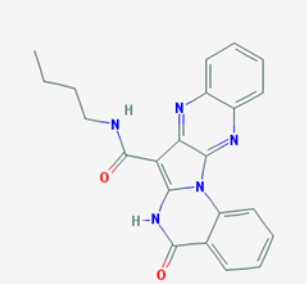


Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-4.373	Numeric (log mol/L)
Absorption	Caco2 permeability	1.291	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	94.837	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.71	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	0.374	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.164	Numeric (Fu)
Distribution	BBB permeability	0.011	Numeric (log BB)
Distribution	CNS permeability	-1.713	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	Yes	Categorical (Yes/No)
Excretion	Total Clearance	0.052	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	-0.228	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.572	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	1.199	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.349	Numeric (log ug/L)
Toxicity	Minnow toxicity	0.602	Numeric (log mM)

CCCCNC(=O)C1=C2NC(=O)C3=CC=CC=C3N2C4=NC5=CC=CC=C5N=C14

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24279494_Int	1	-9.8	3	iPPI-lib	Y	6	0	3.9	381.3835	78.11

Structure



ADMET

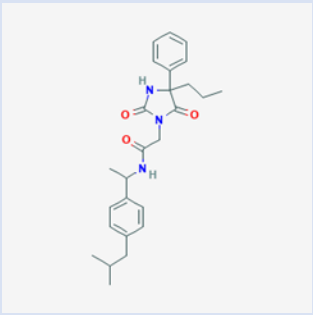
Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-3.378	Numeric (log mol/L)
Absorption	Caco2 permeability	1.385	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	87.958	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.735	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	0.117	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.111	Numeric (Fu)
Distribution	BBB permeability	-1.096	Numeric (log BB)
Distribution	CNS permeability	-2.383	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	Yes	Categorical (Yes/No)
Excretion	Total Clearance	0.687	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	Yes	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.436	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.502	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	0.965	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.285	Numeric (log ug/L)
Toxicity	Minnow toxicity	2.259	Numeric (log mM)

2-(2,5-dioxo-4-phenyl-4-propylimidazolidin-1-yl)-N-[1-[4-(2-methylpropyl)phenyl]ethyl]acetamide

CCCC1(C(=O)N(C(=O)N1)CC(=O)NC(C)C2=CC=C(C=C2)CC(C)C)C3=CC=CC=C3

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
143472101_A	1	-9.7	6	diverse-lib	N	5	1	4.92	415.48914	63.59

Structure



ADMET

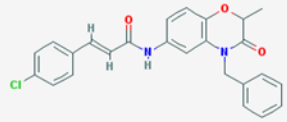
Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-5.886	Numeric (log mol/L)
Absorption	Caco2 permeability	0.856	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	91.535	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.743	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	0.04	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0	Numeric (Fu)
Distribution	BBB permeability	-0.361	Numeric (log BB)
Distribution	CNS permeability	-2.364	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	Yes	Categorical (Yes/No)
Excretion	Total Clearance	0.794	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-5.886	Numeric (log mol/L)
Absorption	Caco2 permeability	0.856	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	91.535	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.743	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	0.04	Numeric (log L/kg)

(E)-N-(4-benzyl-2-methyl-3-oxo-1,4-benzoxazin-6-yl)-3-(4-chlorophenyl)prop-2-enamide

CC1C(=O)N(C2=C(O1)C=CC(=C2)NC(=O)C=CC3=CC=C(C=C3)Cl)CC4=CC=CC=C4

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24308557_Intermodi	1	-9.7	3	iPPI-lib	Y	4	1	3.69	392.3980264	49.41

Structure



ADMET

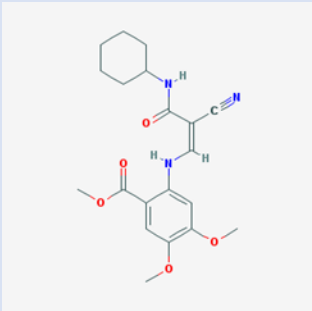
Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-5.179	Numeric (log mol/L)
Absorption	Caco2 permeability	1.543	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	94.346	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.736	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	-0.472	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0	Numeric (Fu)
Distribution	BBB permeability	-0.183	Numeric (log BB)
Distribution	CNS permeability	-1.719	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	Yes	Categorical (Yes/No)
Excretion	Total Clearance	-0.257	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	-0.067	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.361	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	1.173	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.315	Numeric (log ug/L)
Toxicity	Minnow toxicity	-2.933	Numeric (log mM)

methyl2-[[(Z)-2-cyano-3-(cyclohexylamino)-3-oxoprop-1-enyl]amino]-4,5-dimethoxybenzoate

COC1=C(C=C(C(=C1)C(=O)OC)NC=C(C#N)C(=O)NC2CCCCC2)OC

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24279458_Int	1	-10.1	5	iPPI-lib	Y	7	1	4.64	441.50496	101.2

Structure



ADMET

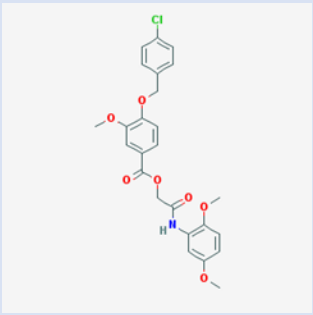
Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-3.981	Numeric (log mol/L)
Absorption	Caco2 permeability	0.932	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	85.002	Numeric (% Absorbed)
Absorption	Skin Permeability	-3.197	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	No	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	No	Categorical (Yes/No)
Distribution	VDss (human)	-0.282	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.231	Numeric (Fu)
Distribution	BBB permeability	-0.424	Numeric (log BB)
Distribution	CNS permeability	-2.789	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	No	Categorical (Yes/No)
Excretion	Total Clearance	0.578	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.013	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	No	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.635	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	1.741	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.613	Numeric (log ug/L)
Toxicity	Minnow toxicity	1.809	Numeric (log mM)

[2-(2,5-dimethoxyanilino)-2-oxoethyl] 4-[(4-chlorophenyl)methoxy]-3-methoxybenzoate

COC1=CC(=C(C=C1)OC)NC(=O)COC(=O)C2=CC(=C(C=C2)OCC3=CC=C(C=C3)Cl)OC

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24330502_Ac	1	-9.7	3	diverse-lib	Y	5	0	3.9	422.4024896	50.5

Structure



ADMET

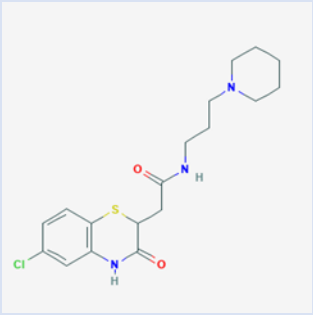
Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-6.617	Numeric (log mol/L)
Absorption	Caco2 permeability	0.961	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	93.003	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.736	Numeric (log Kp)
Absorption	P-glycoprotein substrate	No	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	-0.678	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0	Numeric (Fu)
Distribution	BBB permeability	-1.285	Numeric (log BB)
Distribution	CNS permeability	-3.11	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	Yes	Categorical (Yes/No)
Excretion	Total Clearance	0.276	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.763	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.334	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	0.972	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	No	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.297	Numeric (log ug/L)

2-(6-chloro-3-oxo-4H-1,4-benzothiazin-2-yl)-N-(3-piperidin-1-ylpropyl)acetamide

C1CCN(CC1)CCCNC(=O)CC2C(=O)NC3=C(S2)C=CC(=C3)Cl

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
17480197_Accepted	1	-9.6	3	diverse-lib	N	3	0	4.45	308.2304328	38.92

Structure



ADMET

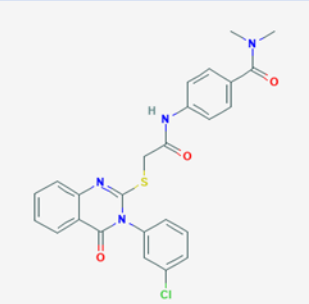
Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-3.492	Numeric (log mol/L)
Absorption	Caco2 permeability	1.402	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	91.58	Numeric (% Absorbed)
Absorption	Skin Permeability	-3.802	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	No	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	No	Categorical (Yes/No)
Distribution	VDss (human)	0.712	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.214	Numeric (Fu)
Distribution	BBB permeability	-0.078	Numeric (log BB)
Distribution	CNS permeability	-2.478	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	No	Categorical (Yes/No)
Excretion	Total Clearance	1.135	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	-0.401	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.927	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	1.076	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	No	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.814	Numeric (log ug/L)
Toxicity	Minnow toxicity	2.653	Numeric (log mM)

4-[[2-[3-(3-chlorophenyl)-4-oxoquinazolin-2-yl]sulfanylacetyl]amino]-N,N-dimethylbenzamide

CN(C)C(=O)C1=CC=C(C=C1)NC(=O)CSC2=NC3=CC=CC=C3C(=O)N2C4=CC(=CC=C4)Cl

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24329822_Intermedi	1	-9.5	3	diverse-lib	N	3	0	4.33	363.3535896	45.76

Structure



ADMET

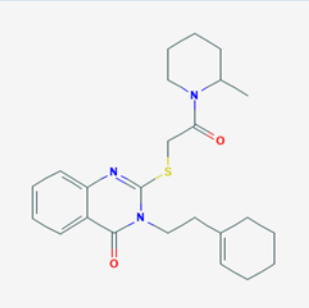
Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-4.253	Numeric (log mol/L)
Absorption	Caco2 permeability	1.149	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	93.57	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.735	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	-0.526	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.165	Numeric (Fu)
Distribution	BBB permeability	-0.659	Numeric (log BB)
Distribution	CNS permeability	-2.25	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	Yes	Categorical (Yes/No)
Excretion	Total Clearance	0.063	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.446	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.794	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	1.172	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.286	Numeric (log ug/L)
Toxicity	Minnow toxicity	0.718	Numeric (log mM)

3-[2-(cyclohexen-1-yl)ethyl]-2-[2-(2-methylpiperidin-1-yl)-2-oxoethyl]sulfanylquinazolin-4-one

CC1CCCCN1C(=O)CSC2=NC3=CC=CC=C3C(=O)N2CCC4=CCCCC4

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24386664_Intermadi	1	-9.5	6	iPPI-lib	Y	4	1	4.93	418.55114	66.87

Structure



ADMET

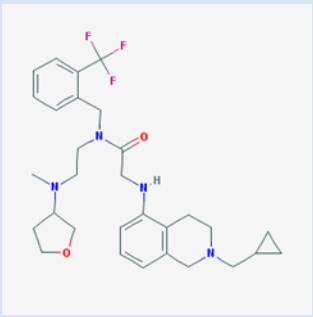
Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-5.018	Numeric (log mol/L)
Absorption	Caco2 permeability	1.332	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	93.259	Numeric (% Absorbed)
Absorption	Skin Permeability	-3.071	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	0.667	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.058	Numeric (Fu)
Distribution	BBB permeability	0.216	Numeric (log BB)
Distribution	CNS permeability	-2.086	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	Yes	Categorical (Yes/No)
Excretion	Total Clearance	0.049	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	-0.106	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.968	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	0.883	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.659	Numeric (log ug/L)
Toxicity	Minnow toxicity	0.363	Numeric (log mM)

2-[[2-(cyclopropylmethyl)-3,4-dihydro-1H-isoquinolin-5-yl]amino]-N-[2-[methyl(oxolan-3-yl)amino]ethyl]-N-[[2-(trifluoromethyl)phenyl]methyl]acetamide

CN(CCN(CC1=CC=CC=C1C(F)(F)F)C(=O)CNC2=CC=CC3=C2CCN(C3)CC4CC4)C5CCOC5

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
121283528_A	1	-7.9	2	iPPI-lib	Y	7	2	0.85	320.25582	109.41

Structure



ADMET

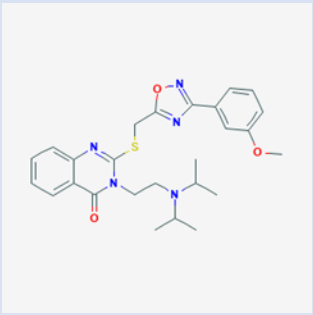
Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-3.79	Numeric (log mol/L)
Absorption	Caco2 permeability	0.901	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	88.358	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.736	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	1.661	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.251	Numeric (Fu)
Distribution	BBB permeability	-0.052	Numeric (log BB)
Distribution	CNS permeability	-1.111	Numeric (log PS)
Metabolism	CYP2D6 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	No	Categorical (Yes/No)
Excretion	Total Clearance	1.2	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	-0.178	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.736	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	1.154	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.3	Numeric (log ug/L)
Toxicity	Minnow toxicity	2.594	Numeric (log mM)

3-[2-[di(propan-2-yl)amino]ethyl]-2-[[3-(3-methoxyphenyl)-1,2,4-oxadiazol-5-yl]methylsulfanyl]quinazolin-4-one

CC(C)N(CCN1C(=O)C2=CC=CC=C2N=C1SCC3=NC(=NO3)C4=CC(=CC=C4)OC)C(C)C

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24366176_Intermedi	1	-7.8	4	iPPI-lib	N	7	1	5.03	438.49618	109.6

Structure



ADMET

Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-4.431	Numeric (log mol/L)
Absorption	Caco2 permeability	1.33	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	94.017	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.735	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	0.584	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.234	Numeric (Fu)
Distribution	BBB permeability	-1.218	Numeric (log BB)
Distribution	CNS permeability	-2.496	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	Yes	Categorical (Yes/No)
Excretion	Total Clearance	0.442	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	Yes	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.899	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.663	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	0.524	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.286	Numeric (log ug/L)
Toxicity	Minnow toxicity	-2.5	Numeric (log mM)

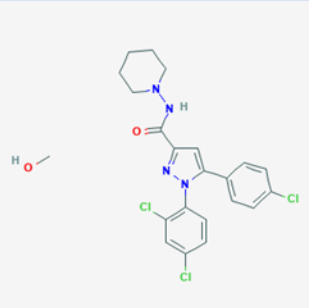
5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-piperidin-1-ylpyrazole-3-carboxamide;methanol

CO.C1CCN(CC1)NC(=O)C2=NN(C(=C2)C3=CC=C(C=C3)Cl)C4=C(C=C(C=C4)Cl)Cl

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24799411_Intermedi	1	-7.8	3	diverse-lib	Y	6	1	2.21	389.44702	

ADMET

Structure



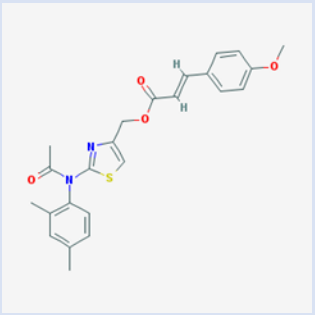
Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-4.463	Numeric (log mol/L)
Absorption	Caco2 permeability	1.258	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	87.739	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.731	Numeric (log Kp)
Absorption	P-glycoprotein substrate	No	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	0.42	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.112	Numeric (Fu)
Distribution	BBB permeability	-1.064	Numeric (log BB)
Distribution	CNS permeability	-1.964	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	No	Categorical (Yes/No)
Excretion	Total Clearance	0.025	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.702	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.561	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	0.367	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	No	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.303	Numeric (log ug/L)
Toxicity	Minnow toxicity	1.398	Numeric (log mM)

[2-(N-acetyl-2,4-dimethylanilino)-1,3-thiazol-4-yl]methyl (E)-3-(4-methoxyphenyl)prop-2-enoate

CC1=CC(=C(C=C1)N(C2=NC(=CS2)COC(=O)C=CC3=CC=C(C=C3)OC)C(=O)C)C

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24363501_Intermedi	1	-7.7	2	iPPI-lib	N	4	0	4.43	385.3656264	47.26

Structure



ADMET

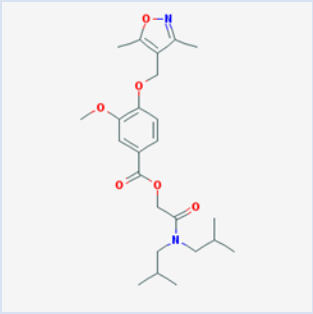
Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-6.406	Numeric (log mol/L)
Absorption	Caco2 permeability	0.665	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	95.026	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.673	Numeric (log Kp)
Absorption	P-glycoprotein substrate	No	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	-0.162	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0	Numeric (Fu)
Distribution	BBB permeability	-0.877	Numeric (log BB)
Distribution	CNS permeability	-1.93	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	Yes	Categorical (Yes/No)
Excretion	Total Clearance	-0.012	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.287	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.593	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	1.303	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.487	Numeric (log ug/L)
Toxicity	Minnow toxicity	-1.607	Numeric (log mM)

[2-[bis(2-methylpropyl)amino]-2-oxoethyl] 4-[(3,5-dimethyl-1,2-oxazol-4-yl)methoxy]-3-methoxybenzoate

CC1=C(C(=NO1)C)COC2=C(C=C(C=C2)C(=O)OCC(=O)N(CC(C)C)CC(C)C)OC

Compound	Model ID	Energy	nRot	Library	isLeadLike	HBA	HBD	LogP	MW	TPSA
24384915_Intermediate	1	-7.7	4	diverse-lib	N	6	1	4.58	451.4668232	101.83

Structure



ADMET

Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-5.86	Numeric (log mol/L)
Absorption	Caco2 permeability	0.729	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	93.669	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.949	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	-0.236	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0	Numeric (Fu)
Distribution	BBB permeability	-0.961	Numeric (log BB)
Distribution	CNS permeability	-2.759	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	Yes	Categorical (Yes/No)
Excretion	Total Clearance	0.977	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.183	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.463	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	1.292	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	T.Pyriformis toxicity	0.498	Numeric (log ug/L)
Toxicity	Minnow toxicity	-0.862	Numeric (log mM)