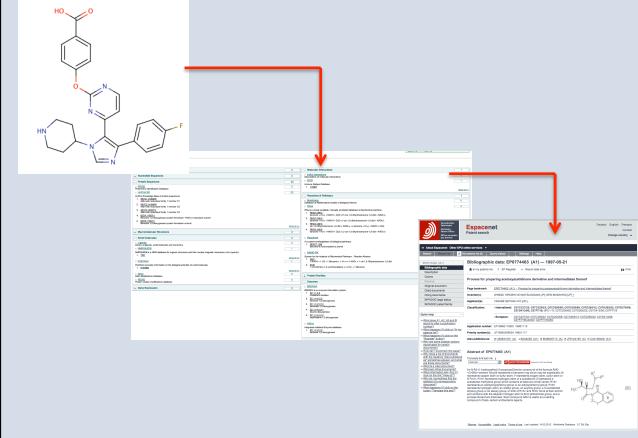


**Chemical Entities Databases at the EBI
Patent Searching**

bioinformatics.ca

Dr. Louisa Bellis
Patent Informatics: Sequence and Chemical Databases for
Prior Art Searching
April 19, 2012



The screenshot shows a chemical structure of a complex molecule on the left, which is then used to search the ChEMBL database. The search results page displays various pharmacological data and properties for the molecule.

EMBL-EBI

ChEMBL

ChEBI

ChEBI and ChEMBL



ChEBI

Chemical Entities of Biological Interest (ChEBI) is a freely available dictionary of molecular entities focused on 'small' chemical compounds.

ChEMBL

ChEMBL is a database of bioactive, drug-like small molecules.

- Dictionary of molecular entities, focused on 'small molecules'
- Incorporates an ontological classification
- Uses nomenclature, symbolism and terminology endorsed by international scientific bodies, such as IUPAC
- Database of bioactive, drug-like small molecules
- Contains 2D structures, calculated properties and abstracted bioactivities
- Curates structures from published primary literature

Chemical Entities Databases at the EBI

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ChEBI and ChEMBL

- All of the ChEMBL compounds have been submitted into ChEBI's database
- So, searching on either database will give you the same results
- ChEBI and ChEMBL link out to each other via hyperlinks on their compound pages
- Both databases encourage user suggestions and comments on quality, errors and new features
- ChEBI is focused on the ontology of the compounds, whilst ChEMBL is focused on the associated bioactivity data.

Chemical Entities Databases at the EBI

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ChEBI Background...

<http://www.ebi.ac.uk/chebi/>

Chemical Entities Databases at the EBI

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What is ChEBI?

- Freely available, reference dictionary of small molecules

Focused on:

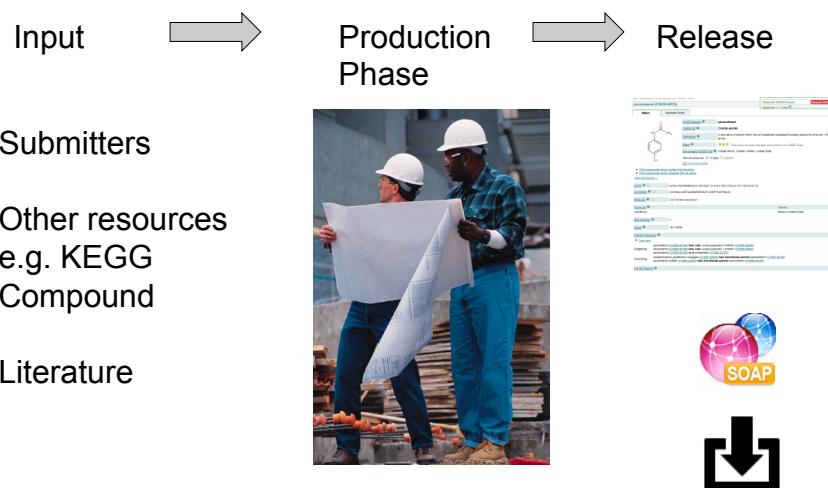
- Manual annotation of chemical compound information from the literature and other web resources
- Structural and biological classification of its compounds
- A complete set of synonyms and cross-references for each compound

<http://www.ebi.ac.uk/chebi/>

Chemical Entities Databases at the EBI

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How is ChEBI maintained?



Chemical Entities Databases at the EBI

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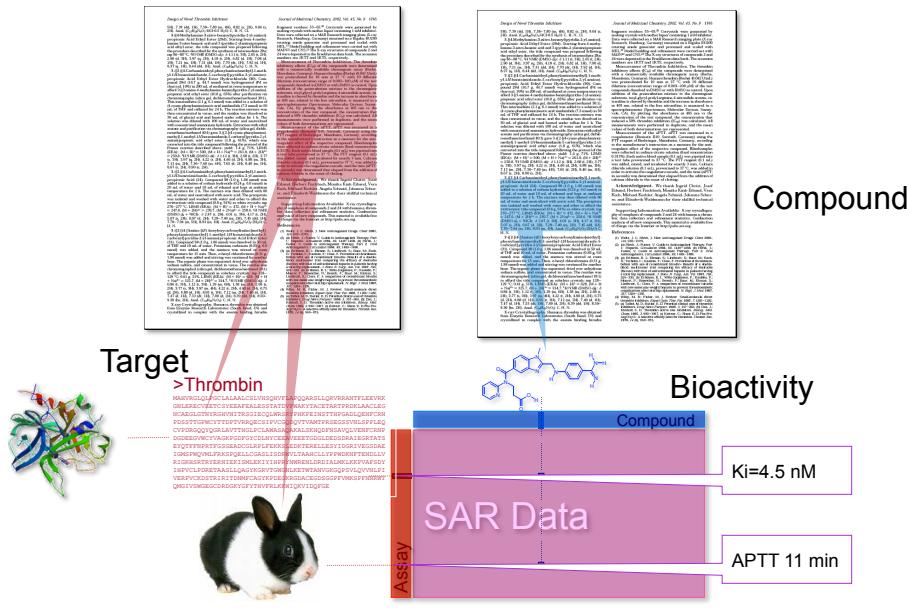
ChEMBL Background...

<http://www.ebi.ac.uk/chembldb/>

Chemical Entities Databases at the EBI

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What is ChEMBL data?



Chemical Entities Databases at the EBI

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Data Statistics

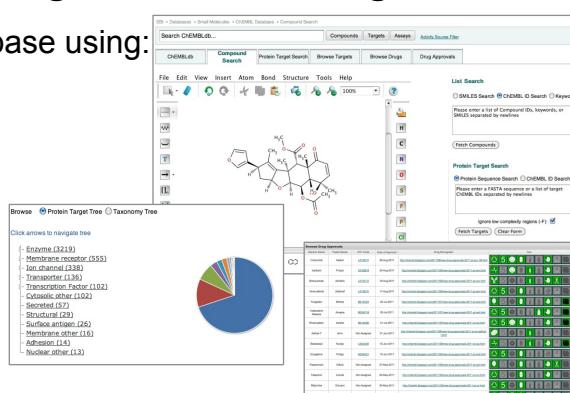
- Focused towards compounds with drug-like properties by extraction from medicinal chemistry journals
- Includes small molecules (~92%) and peptides (~7%)
- Compounds can be clustered into chemical series from same publications, allowing compound structures to be related to activity (SAR).
- Abstracted from 44,682 papers across 34 journals
- 1,296,266 compound records
 - 1,143,682 distinct compound structures
- 6,933,088 activities
 - binding measurements, functional assays and ADMET
- 8,845 targets, inc 5,668 protein targets and 2,570 human targets
- Deposition of PubChem Substances and Bioassay assays

Chemical Entities Databases at the EBI

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Searching and Downloading

- Search the database using:
 - Protein targets
 - BLAST
 - Compounds
 - Substructure
 - Exact match
 - SMILES
 - Keywords
- Webservices, using Java, Perl and Python
- Download the data files and the Oracle/MySQL data dumps from the FTP website for incorporation into external databases



Chemical Entities Databases at the EBI

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ChEMBL External Links

- ChEMBL includes links to external databases within its interface.
- Links included are:
 - ChEBI
 - DrugBank
 - ChemSpider
 - PDBe
 - PubChem
 - Wikipedia

Molecule Forms

CHEMBL192 CHEMBL1737

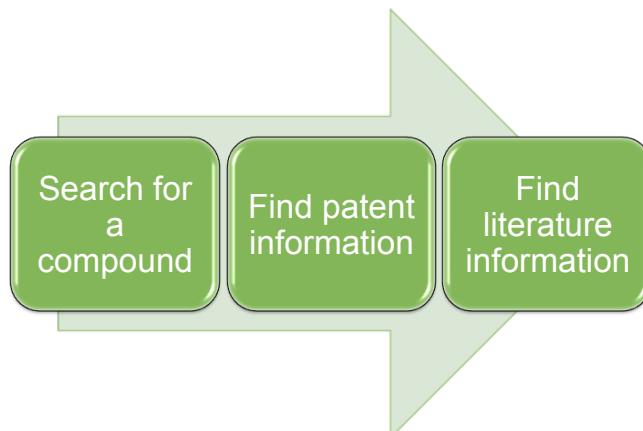
Database Links

ChEBI	ChEBI:9139
ChemSpider	ChemSpider:BNRNXUUZRGQAQC-UHFFFAOYSA-N
DrugBank	DB00203
PDBe	VIA - VIA (PDBe Entries)
PubChem	SID: 26748898 SID: 50085897
Wikipedia	Sildenafil

Chemical Entities Databases at the EBI

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Workflow 1



Chemical Entities Databases at the EBI

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ChEBI homepage

Type your search term

Search for ★★★ only

Entity of the month
5th September 2011, Tetraethyllead



The recently deceased Emeritus Professor Derek Bryson had a long and distinguished career at the University of Reading, spanning a wide variety of interests including organometallic chemistry, radical chemistry and photochemistry.
[Read more ...](#)

<http://www.ebi.ac.uk/chebi/>

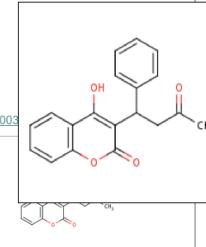
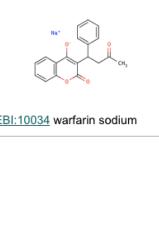
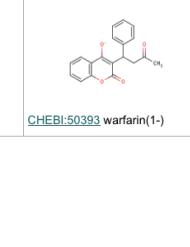
Chemical Entities Databases at the EBI bioinformatics.ca

Search results

You searched for **warfarin in All, 3 in Stars**

Download your search results: [Tab-delimited](#), [XML](#), [SDF](#)

4 entries found, displaying 1 to 4.

 CHEBI:1003 warfarin potassium	 CHEBI:10034 warfarin sodium	 CHEBI:50393 warfarin(1-)
--	--	--

Chemical Entities Databases at the EBI bioinformatics.ca

ChEBI entry for Warfarin

[View biological role classification](#)

ChEBI Ontology	
Tree view warfarin (CHEBI:10033) has role NAD(P)H:quinone oxidoreductase inhibitor (CHEBI:50390) warfarin (CHEBI:10033) is a chromenone (CHEBI:38445) warfarin (CHEBI:10033) has role rodenticide (CHEBI:33288) warfarin (CHEBI:10033) has role anticoagulant (CHEBI:50249) warfarin (CHEBI:10033) is conjugate acid of warfarin(1-) (CHEBI:50393) warfarin(1-) (CHEBI:50393) is conjugate base of warfarin (CHEBI:10033)	
Outgoing	
Incoming	
IUPAC Name	
4-hydroxy-3-(3-oxo-1-phenylbutyl)-2H-1-benzopyran-2-one	
INNs	
warfarin	Sources
warfarina	ChemIDplus
warfarine	ChemIDplus
warfarinum	ChemIDplus
Synonyms	
(Phenyl-1-acetyl-2 ethyl) 3-hydroxy-4 coumarine	ChemIDplus
1-(4'-Hydroxy-3'-coumarinyl)-1-phenyl-3-butanol	ChemIDplus
2H-1-Benzopyran-2-one, 4-hydroxy-3-(3-oxo-1-phenylbutyl)-	ChemIDplus
3-(1'Phenyl-2'-acetylethyl)-4-hydroxycoumarin	ChemIDplus
3-(alpha-Phenyl-beta-acetylethyl)-4-hydroxycoumarin	ChemIDplus
3-(alpha-Phenyl-beta-acetylethyl)-4-hydroxycoumarin	ChemIDplus
4-Hydroxy-3-(3-oxo-1-phenyl-butyl)-cumarin	ChemIDplus

Chemical Entities Databases at the EBI bioinformatics.ca

ChEBI entry for Warfarin

[Manually annotated patent identifiers](#)

[Click to see more auto-generated patent identifiers](#)

[View more database links](#)

4-Hydroxy-3-(3-oxo-1-phenyl-butyl)-cumarin	ChemIDplus	
4-Hydroxy-3-(3-oxo-1-phenylbutyl)coumarin	ChEBI	
Coumafene	ChemIDplus	
Zoocoumarin	ChemIDplus	
Brand Name	Source	
Warf 10	DrugBank	
Database Links	Databases	
DB00682	DrugBank	
US2427578	Patent	
US2765321	Patent	
US2777659	Patent	
US3239529	Patent	
494165	ChEMBL	
View more database links		
Registry Number	Type	Source
1293536	Beilstein Registry Number	Beilstein
Last Modified		
29 June 2010		

Chemical Entities Databases at the EBI bioinformatics.ca

Automatically generated cross-references

EBI > Databases > Small Molecules > ChEBI > Automatically Generated warfarin (CHEBI:10033)

Search ChEBI here! Search for ★★ only

Main Automatic Xrefs

+ Expand relevant - Collapse all

Genomes 0	Molecular Interactions 0
Nucleotide Sequences 0	Reactions & Pathways 3
Protein Sequences 7	BioModels 3
PRIDE 0 Proteomics Identification Database	Database of Mathematical models of biological interest.
UniProt KB 7 UniProt Knowledge Base of protein sequences.	1. BIOMD0000000338 Wajima2009_BloodCoagulation_aPTTtest
1. ARSE_HUMAN Arylsulfatase E	2. BIOMD0000000339 Wajima2009_BloodCoagulation_PTtest
2. ARSF_HUMAN Arylsulfatase F	3. BIOMD0000000340 Wajima2009_BloodCoagulation_warfarin_heparin
3. CP2C9_HUMAN Cytochrome P450 2C9	show all >>
4. VKOR1_BOVIN Vitamin K epoxide reductase complex subunit 1	Rhea 0 Rhea is a freely available, manually annotated database of biochemical reactions.
5. VKOR1_HUMAN Vitamin K epoxide reductase complex subunit 1	Reactome 0 A curated knowledgebase of biological pathways.
show all >>	SABIO-RK 0 System for the Analysis of Biochemical Pathways
	- Reaction Kinetics

Chemical Entities Databases at the EBI bioinformatics.ca

Automatically generated cross-references

Small molecules

- Ligands 0
- NMRShiftDB 0
- PubChem 1
PubChem provides information on the biological activities of small molecules.
1. 53801150 [show all >>](#)
- RESID 0
- Protein residue modifications database

Gene Expression 0

Auto-generated patents

Enzymes

- BRENDA 12
BRENDA is an enzyme information system.
 - EC 1.1.1.184 carbonyl reductase (NADPH)
 - EC 1.1.1.188 prostaglandin-F synthase
 - EC 1.1.4.1 vitamin-K-epoxide reductase (warfarin-sensitive)
 - EC 1.6.5.2 NAD(P)H dehydrogenase (quinone)
 - EC 1.6.5.5 NADPH:quinone reductase [show all >>](#)
- IntEnz 0
Integrated relational Enzyme database.

Literature

- Medline 0
Citations and abstracts from many life-science journals
- Patents 61
Biology-related abstracts of patent applications.
 - EP1438982 DRUGS COMPRISING COMBINATION OF TRIAZASPIRO 5,5 UDECANE DERIVATIVE WITH CYTOCHROME P450 ISOZYME 3A4 INHIBITOR AND/OR P−GLYCOPROTEIN INHIBITOR
 - EP1625870 Needle for intradermal delivery of substances having penetration limiting means
 - EP1719526 Pharmaceutical combinations comprising a P2T receptor antagonist and another anti-thrombotic agent
 - EP1743639 Use of substituted pyrazoline compounds for the treatment of coagulation related diseases
 - EP1894567 CONCOMITANT PHARMACEUTICAL AGENTS AND USE THEREOF [show all >>](#)

Ontologies 0

Chemical Entities Databases at the EBI bioinformatics.ca

Go to ChEMBL for more literature

4-Hydroxy-3-(3-oxo-1-phenyl-butyl)-cumarin	ChemIDplus	
4-Hydroxy-3-(3-oxo-1-phenylbutyl)coumarin	ChEBI	
Coumafene	ChemIDplus	
Zoocoumarin	ChemIDplus	
Brand Name	Source	
Warf 10	DrugBank	
Database Links	Databases	
DB00682	DrugBank	
US2427578	Patent	
US2765321	Patent	
US2777859	Patent	
US3239529	Patent	
494165	ChEMBL	
View more database links		
Registry Number	Type	Source
1293536	Beilstein Registry Number	Beilstein
Last Modified		
29 June 2010		

ChEMBL link

Chemical Entities Databases at the EBI

bioinformatics.ca

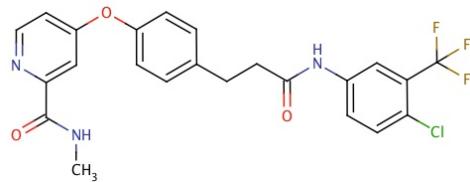
Compound Report Card

Summary					
Compound ID	CHEMBL1464				
Compound Name	Warfarin				
Synonyms	Warfarin, Warfarin sodium, Warfarin Potassium				
Approved Drug	Yes				
Trade Names	Coumadin, Jantoven				
 CHEMBL1464					
Approved Drug Features					
Clinical Trials					
Number of clinical trials registered at clinicaltrials.gov 260					
Parent Properties					
Mol. Weight	ALogP	Num Ro5 Violations	Num Rotatable Bonds	Passes Rule-Of-Three	Med Chem Friendly
308.3	2.83	0	4	No	Yes
Parent ACD Properties					
Acidic pKa	Basic pKa	LogP	LogD	Species	
4.5	-	3.129	.326	ACID	

Chemical Entities Databases at the EBI

bioinformatics.ca

Workflow 2

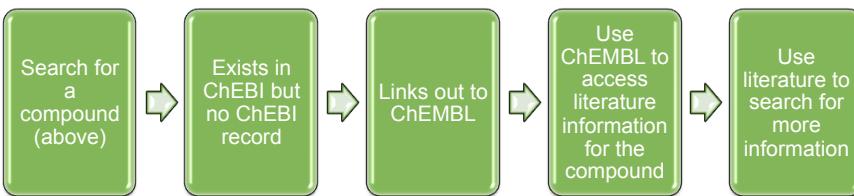
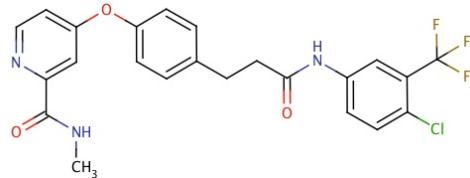


- Searching for this compound in ChEBI doesn't give any data but does give a direct link to ChEMBL
- In ChEMBL, you can download literature information for further investigation

Chemical Entities Databases at the EBI

bioinformatics.ca

Workflow 2



Chemical Entities Databases at the EBI

bioinformatics.ca

Searching in ChEBI:

The screenshot shows the ChEBI search interface. On the left, a chemical structure editor displays a complex molecule with various functional groups. Below it is a periodic table of elements. On the right, the search results are shown under the heading "ChEBI Results". It says "You searched for structures similar to" and shows a preview of the query structure. Below this, it says "8 entries found, displaying 1 to 8." A list of compounds is shown, with the first one being "CHEBI:117680" (CHEMBL1688862). A red box highlights this entry, and an arrow points from the text "Clicking on this compound will take you straight to ChEMBL" to the compound's name.

Chemical Entities Databases at the EBI bioinformatics.ca

The screenshot shows the ChEMBL Compound Report Card for Compound CHEMBL1688862. It includes sections for Summary, Clinical Trials, Parent Properties, Parent ACD Properties, and Representations. A large "Bioactivity Summary" section is highlighted with a red box. Inside this box, a pie chart titled "ChEMBL Activity Types for Compound CHEMBL1688862" shows three categories. One category, "IC50 (3)", is circled with a red oval, and an arrow points from the text "Hyperlink to bioactivity results" to this circle.

Chemical Entities Databases at the EBI bioinformatics.ca

Access to Literature

Literature links

ChEMBL Bioactivity Search Results: 3

Parent	Ingredient	Bioactivity	Activity Comment	Operator	Value	Units	Assay CHEMBL ID	Assay Source	Assay Type	Description	ChEMBL Target ID	Target Name	Organism	Target Mapping	BP Reference	Reference	Name in Reference
		IC50		>	25000	nM	CHEMBL1693570	Scientific Literature	B	Inhibition of Raf kinase in human A375 cells assessed by growth inhibition of MEK-mediated ERK phosphorylation after 3 hrs using 3,3'-5,5'-tetrazine/benzodiazepine liquid substrate.	CHEMBL1905	Serine/threonine-protein kinase RAF	Homo sapiens	Homologous protein Autocuration	J. Med. Chem. (2011) 54:6;1838	2	
		IC50		>	25000	nM	CHEMBL1693570	Scientific Literature	B	Inhibition of Raf kinase in human A375 cells assessed by growth inhibition of MEK-mediated ERK phosphorylation after 3 hrs using 3,3'-5,5'-tetrazine/benzodiazepine liquid substrate.	CHEMBL1905	Serine/threonine-protein kinase RAF	Homo sapiens	Homologous protein Autocuration	J. Med. Chem. (2011) 54:6;1838	2	
		IC50		>	25000	nM	CHEMBL1693570	Scientific Literature	B	Inhibition of Raf kinase in human A375 cells assessed by growth inhibition of MEK-mediated ERK phosphorylation after 3 hrs using 3,3'-5,5'-tetrazine/benzodiazepine liquid substrate.	CHEMBL1905	Serine/threonine-protein kinase RAF	Homo sapiens	Homologous protein Autocuration	J. Med. Chem. (2011) 54:6;1838	2	

Document Report Card

Doc ID: CHEMBL1687927

Journal: J. Med. Chem. (2011) 54:1836-1846

Title: Design and optimization of potent and orally bioavailable tetrahydronaphthalene Raf inhibitors.

Authors: Gould AE, Adams R, Adhikari S, Aertgeerts K, Afroze R, Blackburn C, Calderwood EF, Chau R, Choultar J, Duffey MO, England DB, Farmer C, Forsyth N, Garcia K, Gaulin J, Greenspan PD, Guo R, Harrison SJ, Huang SC, Iartchouk N, Janowick D, Kim MS, Kulkarni B, Langston SP, Liu JX, Ma LT, Menon S, Mizutani H, Paske E, Renou CC, Rezaei M, Rowland RS, Sintchak MD, Smith MD, Stroud SG, Tregay M, Tian Y, Velby OP, Vos JT, Vyskocil S, Williams J, Xu T, Yang JH, Yan Q, Zeng H, Zhang DM, Zhang Q, Galvin KM

Abstract: Inhibition of mutant B-Raf signaling, through either direct inhibition of the enzyme or inhibition of MEK, the direct substrate of Raf, has been demonstrated preclinically to inhibit tumor growth. Very recently, treatment of B-Raf mutant melanoma patients with a selective B-Raf inhibitor has resulted in promising preliminary evidence of antitumor activity. This article describes the design and optimization of tetrahydronaphthalene-derived compounds as potent inhibitors of the Raf pathway *in vitro* and *in vivo*. These compounds can inhibit B-Raf mutants.

CiteXplore: [21341678](#)

DOI: [https://doi.org/10.1021/jm200700z](#)

Hyperlinks from ChEMBL to CiteXplore

Access to Literature

The image shows three overlapping web pages:

- ChEMBL - PubChem Compound Details:** Shows compound 21341678, a homologous inhibitor of B-Raf mutant. It includes tabs for 'Abstract', 'Chemical', 'Similar Compounds', and 'PubChem Compound'.
- CiteXplore - citation details:** Shows the publication record for 'Design and Optimization of Potent and Orally Bioavailable Tetrahydrophthalimide Raf Inhibitors'. It includes sections for 'Abstract', 'Keywords (MeSH)', and 'Chemicals'.
- Journal of Medicinal Chemistry website:** Shows the full article 'Design and Optimization of Potent and Orally Bioavailable Tetrahydrophthalimide Raf Inhibitors' by Jia, Yano, Li, Zeng, et al. The page includes navigation links like 'Home', 'About & Authors', 'Search', and 'Submit Manuscript'.

A red arrow points from the ChEMBL page to the CiteXplore page. Another red arrow points from the CiteXplore page to the journal website. A third red circle highlights the 'CiteXplore' link on the ChEMBL page.

Hyperlinks from ChEMBL to CiteXplore

Any Questions?