

NIAID's Anti-HIV/OI/TB Therapeutics Database: ChemDB

A publicly available, web searchable
chemical/biological database

<http://chemdb.niaid.nih.gov>

Mohamed Nasr



History of ChemDB

- 1988 - Started by Dr. Mohamed Nasr to track HIV drug development
- 1993 - Expanded to cover compounds tested against AIDS-related opportunistic pathogens
- 2002 - Expanded to cover additional viral pathogens
- 2002 - ChemDB available over the web
- 2010 - ChemDB 2.0 website released
- 2015 - Re-focused on HIV and *Mycobacterium tuberculosis*
 - Legacy pathogens are still available for searching



Development of the Database

- Data sources include journals, meeting abstracts, and patents.
- References describing compounds tested against pathogens of interest are identified using database searches.
- Articles are abstracted if they contain original quantitative biological data on well-defined chemicals or plant abstracts.



Bibliographic Statistics

- Over 29,000 references have been chosen for abstraction.
 - References from over 2,000 different journals
 - Includes over 2,000 patents
- The top five journals cited in ChemDB are:
 - Antimicrobial Agents and Chemotherapy (2,177 references)
 - Journal of Medicinal Chemistry (1,913 references)
 - Bioorganic and Medical Chemistry Letters (1,608 references)
 - Antiviral Research (947 references)
 - European Journal of Medicinal Chemistry (825 references)



Chemical Compound Statistics

- Currently over 377,000 compounds in the database:
 - Nearly 262,000 public compounds
 - Over 115,000 proprietary compounds

Public Compounds in ChemDB

Compound Type	Number
Compounds containing anti-HIV data	>130,000*
Tested in a cellular assay	>41,000
Tested in a cell-free assay	>109,000
Tested for latent HIV reactivation	>90
Compounds containing anti- <i>Mycobacterium tuberculosis</i> data	>38,000*
Tested in a cellular assay	>36,000
Tested in a cell-free assay	>3,000
Compounds tested against other pathogens	>107,000

*Some compounds are tested in multiple pathogens or multiple assay types.



Biological Data Statistics

- Biological data is linked to both structural and bibliographic data
- A “line” of data is a database entry containing biological testing data
 - One compound may have many lines of data

Public Biological Data in ChemDB	
Biological Data Type	Lines
Anti-HIV data	
Tested in a cellular assay	>236,000
Tested in a cell-free assay	>78,000
Tested for latent HIV reactivation	>230
Anti- <i>Mycobacterium tuberculosis</i> data	
Tested in a cellular assay	>75,000
Tested in a cell-free assay	>4,600
Compounds tested against other pathogens	>345,000




Other Pathogens

Top 20 Other Pathogens in ChemDB

Pathogens	Compounds	Lines
Hepatitis C virus	29,872	49,277
<i>Candida albicans</i>	24,662	50,407
Herpes simplex virus 1	9,505	21,999
<i>Plasmodium falciparum</i>	9,122	18,713
Human cytomegalovirus	6,237	12,378
<i>Cryptococcus neoformans</i>	5,713	9,961
<i>Aspergillus fumigatus</i>	4,801	8,350
Herpes simplex virus 2	4,560	9,583
<i>Aspergillus niger</i>	4,539	6,430
<i>Mycobacterium avium</i>	3,972	8,618
<i>Toxoplasma gondii</i>	3,766	7,372
<i>Mycobacterium smegmatis</i>	3,062	4,449
Hepatitis B virus	3,047	6,454
Varicella zoster virus	2,569	7,131
Influenza A virus	2,420	6,684
<i>Aspergillus flavus</i>	2,330	3,627
Vaccinia virus	2,321	3,610
Rhinovirus	2,297	9,195
Poliovirus	2,064	2,652
<i>Candida parapsilosis</i>	1,992	3,984

Home Page

U.S. Department of Health and Human Services • National Institutes of Health



National Institute of Allergy and Infectious Diseases
Leading research to understand, treat, and prevent infectious, immunologic, and allergic diseases.

Division of AIDS Anti-HIV/OI/TB Therapeutics Database

HOME

About ChemDB

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- User Guide
- Announcements

Advanced Search

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- Literature

Drugs in Development

- HIV
- HCV
- TB
- Herpes
- Protozoal
- Fungal

Surveillance Memos

Other Links

- NIAID/Division of AIDS Home Page
- NLM/ChemID Plus Chemical Database
- NCI/DTP Open Chemical Repository
- NIST HIV Structural Database
- NIH Home Page

Welcome to the new ChemDB HIV, Opportunistic Infection and Tuberculosis Therapeutics Database. This database contains information extracted from scientific literature on the structure and activity of compounds that have been tested against HIV, HIV enzymes or opportunistic pathogens.

There are three main search portals for the database: the chemical portal allows searches by compound structure or chemical characteristics, the biological portal performs searches based on compound activity against a specific pathogen or enzyme, and the literature portal supports searches based on publication information, such as author name or journal.

Simple Search:



Compounds Literature

Advanced Search:


Structures and data for informational purposes only.

Last Updated: August 2015



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National Institute of Allergy and Infectious Diseases



U.S. Department of Health and Human Services
National Institutes of Health




Searchable fields

- The search fields are divided into three sections:
 - Compound search
 - Chemical details search
 - Chemical structure search
 - Biological data search
 - Literature reference search



Chemical Details Search

Division of AIDS Anti-HIV/OI/TB Therapeutics Database

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• NCI/DTP Open Chemical Repository
• NIST HIV Structural Database
• NIH Home Page

Chemical Search **Biological Search** **Literature Search**

Go to [Boolean Search](#)

Compound Data

Chemical Name: Search By: Include:

Company:

Chemical Class:
Beta-Lactams
Acetanilides
Adamantanes
Alcohols
Aliphatic Amines
Alkaloids
Alkenes
Alynes

Target Class:
Bacteria
DNA Intercalators
DNA Replication
Folate Biosynthesis
Fungi
HIV, Assembly
HIV, Entry
HIV, Interaction

AIDS #: NSC #:

Molecular Formula: CAS #:

Molecular Weight: Value:

Symyx LogP?: Value:

Lipinski "Score"?:

Chemical Structure Search

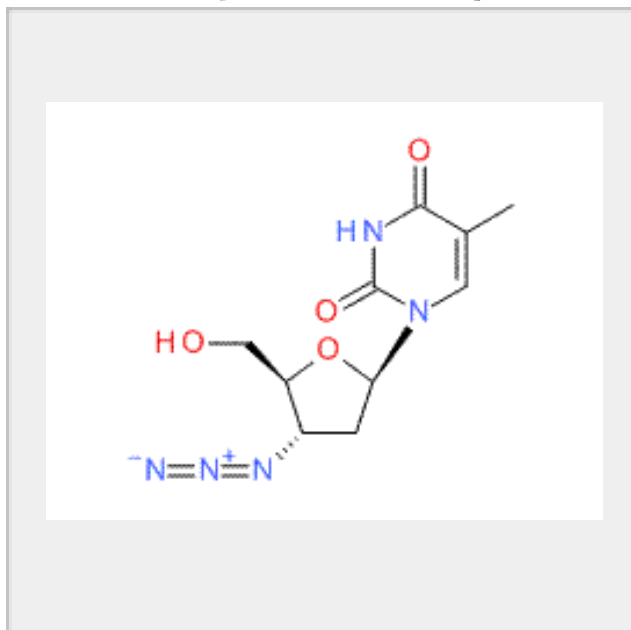
Structure Search

Search

Clear Section

MarvinSketch courtesy of [ChemAxon](#) requires [Java](#)

Click structure input box below to show/hide the MarvinSketch
Select File->Open to load .mol files from your PC



Select Type:

Similarity ▼

Flexmatch ▼

Substructure Search

Exact Match

SMILES string:

Load SMILES



Biological Data Search

Chemical Search | **Biological Search** | **Literature Search**

Go to [Boolean Search](#)

Compound Data
 Structure Search
 Cell Based Anti-HIV Assay Data

HIV Target:

Select a Target

- 26S Proteasome
- Alpha-glucosidase
- Binding, target not specified
- CCR3
- CCR5
- CD4
- CX3CR1
- CXCR4

Cell Type:

Select Cell Type

- ATH8
- C8166
- CBMC
- CEM
- Ghost
- H9
- HEK 293
- HEp-2

EC50: Value:

IC50: Value:

TI: Value:

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Anti-HIV Enzyme Inhibition Data

Target:

Select EI Target



Literature Search

Chemical Search

Biological Search

Literature Search

Literature

LitRef #:

Year:

Author:

Title:

Journal:

Volume:

Search

Clear



Results

- The data for each compound is displayed in several sections:
 - Compound details
 - Biological testing data
 - HIV cellular data
 - HIV enzyme (cell-free) data
 - Opportunistic infection and other pathogen data
 - Literature Citations

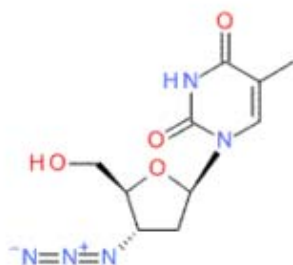


Compound Details

Division of AIDS Anti-HIV/OI/TB Therapeutics Database

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Chemical Structure



Zoom

Transfer to Search

Compound

Molecular Formula: C₁₀ H₁₃ N₅ O₄ AIDS#: 000001
Molecular Weight: 267.24 NSC#: 602670
CAS#: 30516-87-1

Chemical Name

1-[(2R,4S,5S)-4-azido-5-(hydroxymethyl)tetrahydrofuran-2-yl]-5-methyl-pyrimidine-2,4-dione

Stereochemical, Salt and/or Other Information

BETA-D; RIBOFURANOSYL

Compound Details

HIV Cellular Data

HIV Enzyme Data

Opportunistic Infection Data

Literature

Details

Chemical Class: Pyrimidine Nucleosides
Target Class: HIV, Reverse Transcription
Company: GLAXO WELLCOME
Synonyms: AZT
Azidothymidine
BW A509U
Retrovir(TM)
Thymidine, 3'-azido-3'-deoxy-
ZDV
Zidovudine

Calculated Parameters

H-Bond Donors: 2
H-Bond Acceptors: 6
Symyx LogP estimate?: -0.64
Lipinski (Score, out of 4)? : 4

Links

PubChem via AIDS#: [000001](#)
ChemID Plus by CAS#: [30516-87-1](#)
PubMed by CAS#: [30516-87-1](#)
DTP by NSC#: [602670](#)



Biological Data

Division of AIDS Anti-HIV/OI/TB Therapeutics Database

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Chemical Structure



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Compound

Molecular Formula: C10 H13 N5 O4 **AIDS#:** 000001
Molecular Weight: 267.24 **NSC#:** 602670
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[Compound Details](#) | [HIV Cellular Data](#) | [HIV Enzyme Data](#) | [Opportunistic Infection Data](#) | [Literature](#)

Reference (LitRef#)	HIV Strain	Cell Type	EC ₅₀	IC ₅₀	TI	Target	Mutation	Other
Journal of Medicinal Chemistry 1987 (1)	HIV-1(IIIB)	MT-4	.008 uM	4 uM	666.66	Reverse transcriptase	N	Anti-Viral Assay: CPE(TR) Comments: SHOWED SE HIV-1. (REF. 1394)
Journal of Medicinal Chemistry 1987 (2)	HIV-1(IIIB)	ATH8	2.4 uM	45 uM	19	Reverse transcriptase	N	Anti-Viral Assay: CPE
Biochemical and Biophysical Research Communications 1987 (3)	HIV-1(IIIB)	MT-4	.008 uM	3.5 uM	583	Reverse transcriptase	N	Anti-Viral Assay: CPE(TR)
Journal of Medicinal Chemistry 1988 (8)	HIV-1(LAV)	PBMC(MITOGEN STIM.)	.002 uM	> 100 uM	> 50000	Reverse transcriptase	N	Anti-Viral Assay: RT/CPE
FEBS Letters 1988 (13)	HIV-1(IIIB)	MT-4	.007 uM	12 uM	1714	Reverse transcriptase	N	Anti-Viral Assay: CPE
Journal of Medicinal Chemistry 1987 (14)	HIV-1(LAV)	HuT-78	.23 uM			Reverse transcriptase	N	Anti-Viral Assay: RT-ACT Comments: MULV: EC50
Lancet 1987 (35)	HIV-1(IIIB)	C3				Reverse transcriptase	N	Anti-Viral Activity: 99 % In Anti-Viral Assay: IFA(HIV-1) Anti-Viral Activity: 80 % In

There are three biological data tabs:

- HIV Cellular Data
- HIV Enzyme Data
- Opportunistic Infection Data

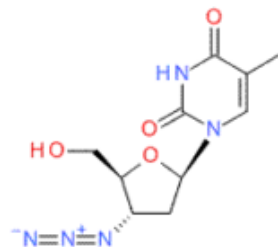


Literature Citations

Division of AIDS Anti-HIV/OI/TB Therapeutics Database

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Chemical Structure



[Zoom](#)

[Transfer to Search](#)

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[Compound Details](#)

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[Literature](#)

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Author	Title	Journal	Volume	Pages	Year	Link
HERDEWIJN, P; PAUWELS, R; BABA, M; BALZARINI, J; DE CLERCQ, E	SYNTHESIS AND ANTI-HIV ACTIVITY OF VARIOUS 2' AND 3'-SUBSTITUTED 2',3'-DIDEOXYADENOSINES: A STRUCTURE-ACTIVITY ANALYSIS	Journal of Medicinal Chemistry	30(11)	2131-2137	1987	Medline Abstract
HERDEWIJN, P; BALZARINI, J; DE CLERCQ, E; PAUWELS, R; BABA, M; BRODER, S; VANDERHAEGHE, H	3'-SUBSTITUTED 2',3'-DIDEOXYNUCLEOSIDE ANALOGUES AS POTENTIAL ANTI-HIV(HTLV-III/LAV) AGENTS	Journal of Medicinal Chemistry	30(8)	1270-1278	1987	Medline Abstract
BABA, M; PAUWELS, R; HERDEWIJN, P; DE CLERCQ, E; DESMYTER, J; VANDEPUTTE, M	BOTH 2',3'-DIDEOXYTHYMIDINE AND ITS 2',3'-UNSATURATED DERIVATIVE (2',3'-DIDEOXYTHYMINENE) ARE POTENT AND SELECTIVE INHIBITORS OF HIV REPLICATION IN VITRO	Biochemical and Biophysical Research Communications	142(1)	128-134	1987	Medline Abstract
LIN, T-S; GUO, J-Y; SCHINAZI, RF; CHU, CK; XIANG, J-N; PRUSOFF, WH	SYNTHESIS AND ANTIVIRAL ACTIVITY OF VARIOUS 3'-AZIDO ANALOGUES OF PYRIMIDINE DEOXYRIBONUCLEOSIDES AGAINST HUMAN IMMUNODEFICIENCY VIRUS (HIV-1,HTLV-III/LAV)	Journal of Medicinal Chemistry	31(2)	338-340	1988	Medline Abstract
TORRENCE, PF; KENJO, J-E; LESIAK, K; BALZARINI, J; DE CLERCQ, E	AIDS DEMENTIA: SYNTHESIS AND PROPERTIES OF A DERIVATIVE OF 3'-AZIDO-3'-DEOXYTHYMIDINE(AZT) THAT MAY BECOME LOCKED IN THE CENTRAL NERVOUS SYSTEM	FEBS Letters	234(1)	135-140	1988	Medline Abstract
LIN, T-S; CHEN, MS; MCLAREN, C; GAO, Y-S; GHAZZOULI, I; PRUSOFF, WH	SYNTHESIS AND ANTIVIRAL ACTIVITY OF VARIOUS 3'-AZIDO, 3'-AMINO, 2',3'-UNSATURATED, AND 2',3'-DIDEOXY ANALOGUES OF PYRIMIDINE DEOXYRIBONUCLEOSIDES AGAINST	Journal of Medicinal Chemistry	30(2)	440-444	1987	Medline Abstract



Benefits and Uses of ChemDB

- ChemDB is useful for scientists within NIAID and around the world:
 - Structure activity relationship studies
 - Identifying novel mechanisms of action
 - Verification of structural and chemical information
 - Identifying emerging therapeutic classes
 - Literature surveillance

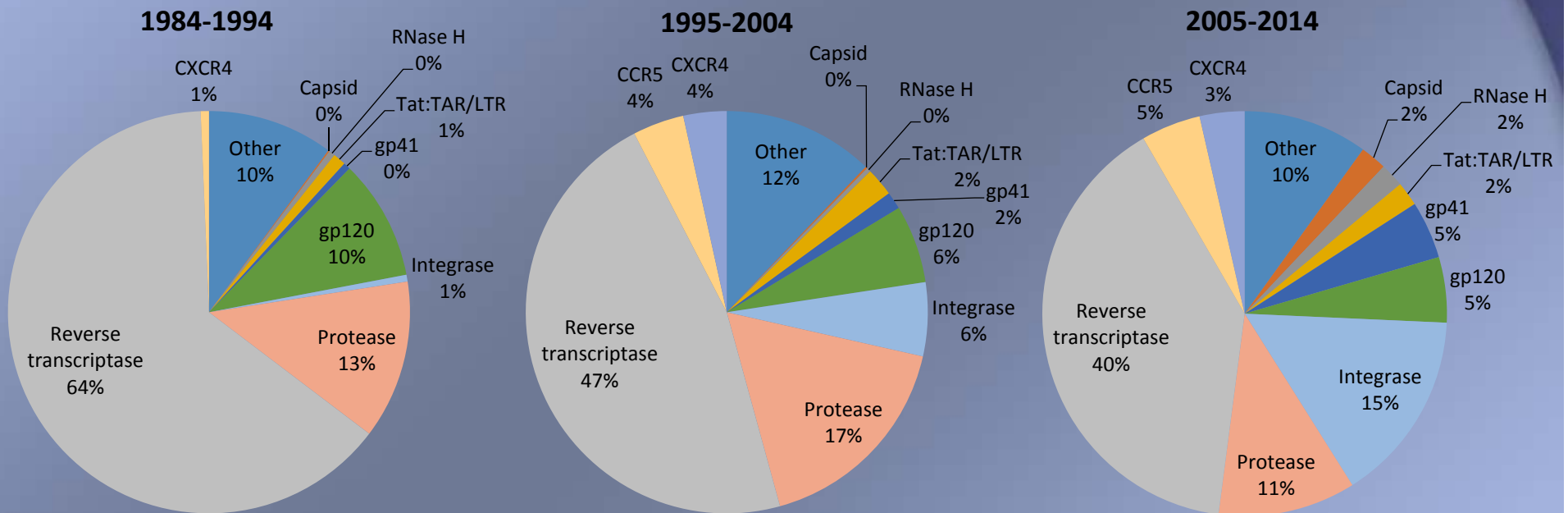


Benefits and Uses of ChemDB

- The data in ChemDB also can be used to analyze research trends over time.
- Example:
 - Data describing the targets of anti-HIV studies (e.g. RT, protease, integrase) were collected from ChemDB sources between 1983 and 2014.
 - These data were compared with the timing of FDA drug approvals.



Proportions of Targets Referenced by Decade, 1984-2014



Publications and Data Transfers

- ChemDB is an important tool within NIAID and in the scientific community
- In the past seven years, ChemDB has:
 - Provided 16 data transfers to government and non-government research entities
 - Been cited in peer-reviewed publications 17 times
 - Seen a steady increase in website usage, and is now typically >200 users per day



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