The anti-intellectual effects of intellectual property

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Intellectual property dynamics

- Academic sector
  - becoming more business like
  - getting into drug discovery
- Chemistry databases
  - private / public synergy
- Precompetitive initiatives
  - can compounds be shared?
- Conclusion

Where did this title come from?

ELSEVIER

The anti-intellectual effects of intellectual property

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Intellectual property considerations decrease research productivity in subtle and unanticipated ways. Chemical probe exchange between Pharma and academia is hindered by academic IP interests. These are perceived as a subtle nuisance by the academic researcher. Novel ligands for oral targets are historically few and numbers of economically attractive oral drug targets are limited. Economically speculative targets lie in the academic domain but the medicinal chemistry to explore these in a drug discovery sense lies in Pharma and cooperation between the two is hindered by very different academic and Pharma views on chemical quality. Tools and probes for academic target validation can accommodate looser chemical quality criteria as opposed to the very strict chemical quality criteria required in Pharma drug discovery.

Libraries Screening Center Network and associated Molecular Library Repository of screening compounds exemplify important efforts to address this deficit [2]. The anti-intellectual effects of intellectual property (IP) considerations are the topics broadly covered by this commentary. Too often, this type of topic is treated as if it were only a technical, legal or factual issue and the very important effects of people's attitudes are ignored. This commentary deals with some of the softer, people issues. Hence, it is unapologetically subjective and very much an opinion piece by this author.

Profitability limits the number of oral drug targets

IP considerations have always been a core value of

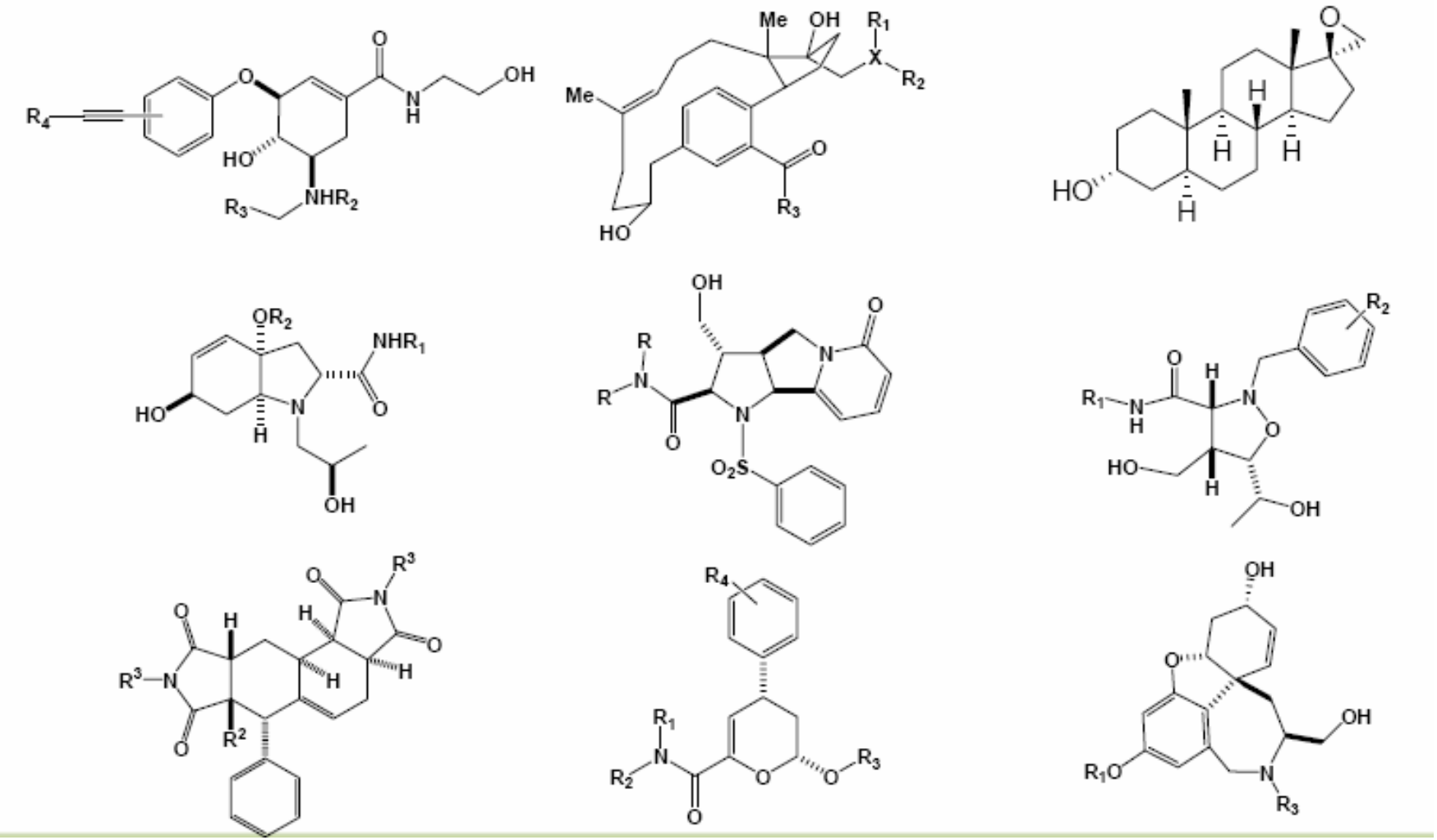
IP and subtle productivity effects

- Intellectual property considerations decrease research productivity in subtle and unanticipated ways.
- Chemical probe exchange between Pharma and academia is hindered by academic IP interests.
- These are perceived as a subtle nuisance by the academic researcher.

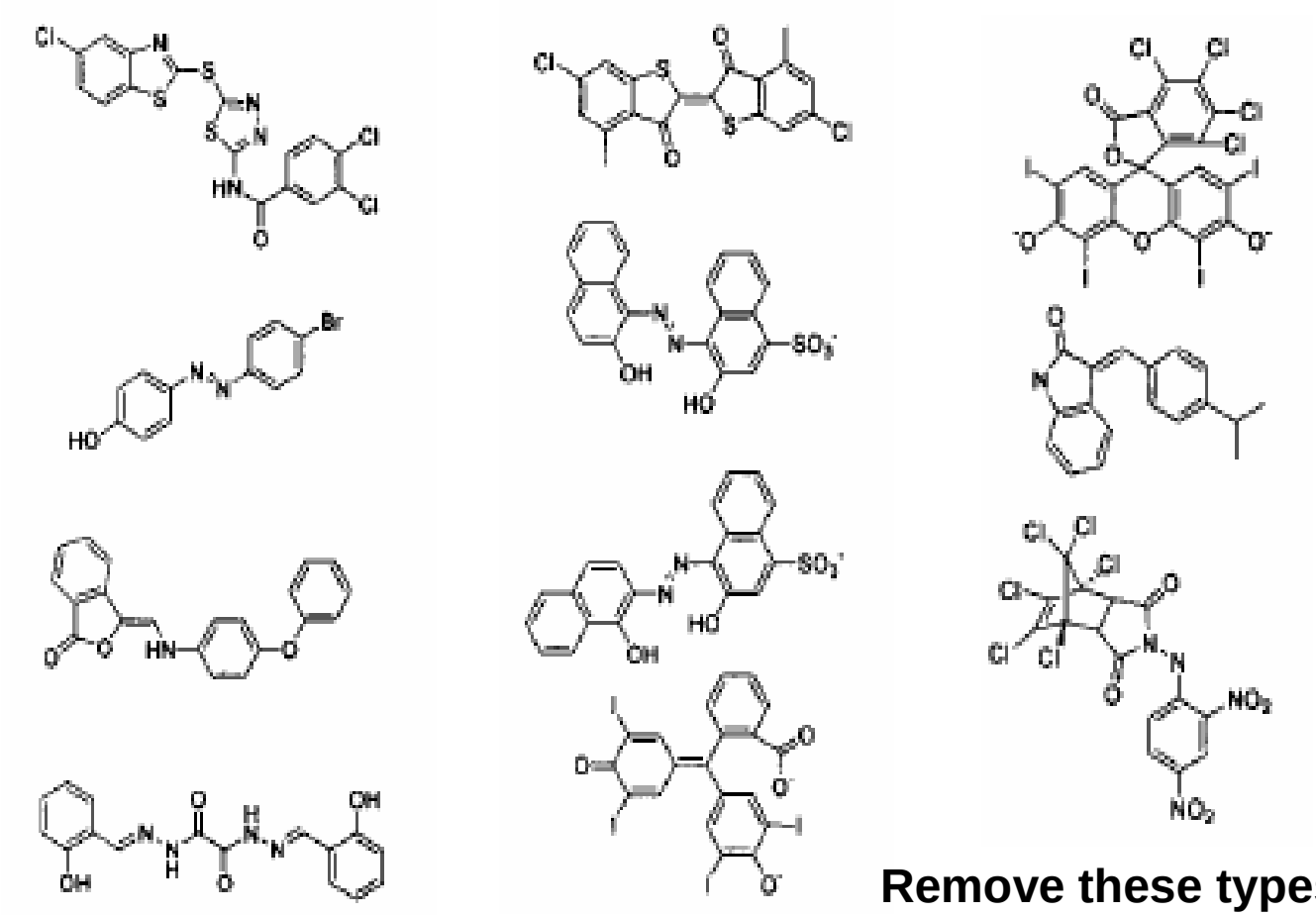
Academic biology - chemistry disconnect

- Economically speculative targets lie in the academic domain
- The medicinal chemistry to explore these in a drug discovery sense lies in Pharma
- Cooperation between the two is hindered by very different academic and Pharma views on chemical quality.

Beautiful chemistry



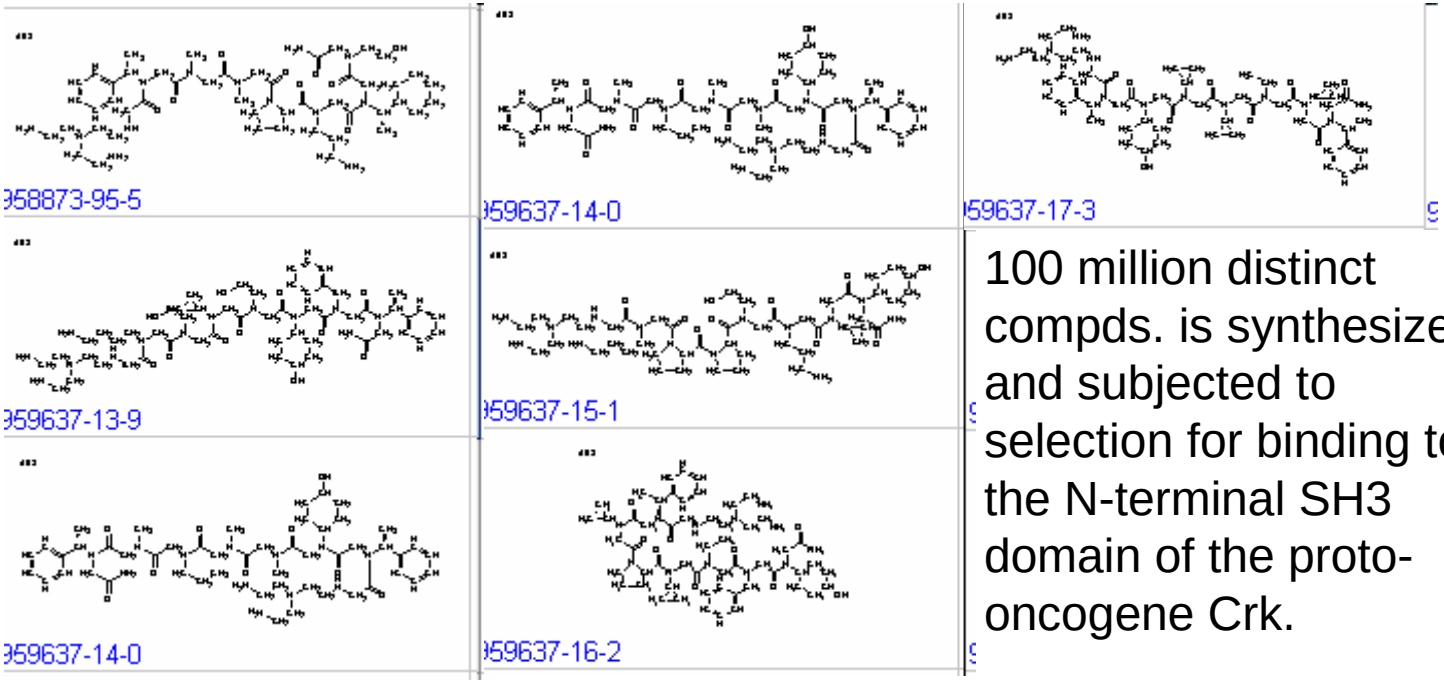
Horrible chemistry



Remove these types of compounds from any assays

These look good to biologists

Academic biology enthusiasism versus drug discovery reality



100 million distinct compds. is synthesized and subjected to selection for binding to the N-terminal SH3 domain of the proto-oncogene Crk.

Synthetic Ligands Discovered by in Vitro Selection. Wrenn, S. Jarrett; Weisinger, Rebecca M.; Halpin, David R.; Harbury, Pehr B. Journal of the American Chemical Society (2007), 129(43), 13137-13143.

"The evolutionary approach has the potential to drastically simplify and accelerate small-mol. discovery."

Evolving public private cooperation

Wikipedia talk:WikiProject Chemistry/CAS validation

From Wikipedia, the free encyclopedia
< Wikipedia talk:WikiProject Chemistry

Contents [hide]

CAS Discourages Using SciFinder for curating 3rd party databases (e.g. Wikipedia)

New announcement from CAS

CAS, a division of the American Chemical Society, is pleased to announce that it will contribute to the Wikipedia project. CAS will work with Wikipedia to help provide accurate CAS Registry Numbers® for current substances listed in Wikiprojects-Chemicals section of the Wikipedia Chemistry Portal that are of widespread general public interest.

Academic drug discovery efforts

- University of Dundee, Scotland
  - treatment of African sleeping sickness
- Medical Research Council Technology UK
  - health of the UK population
- Catholic University of Leuven, Belgium
  - CD3 (center for drug discovery and development)

Needed for academic drug discovery

wellcome trust

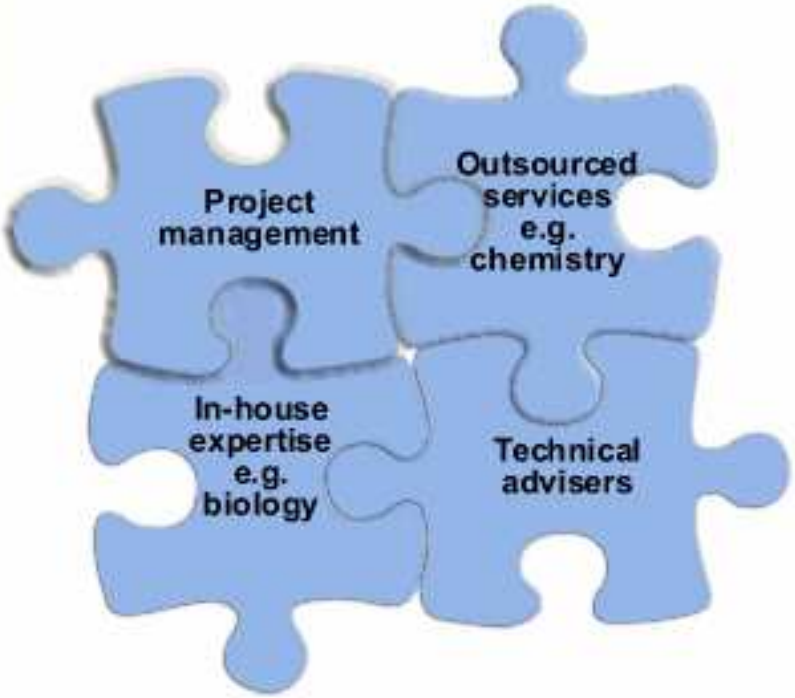
Funding | Strategy | Funded activities | Knowledge centre | What's on | About us

Home > Funding > Technology transfer > Seeding Drug Discovery scheme

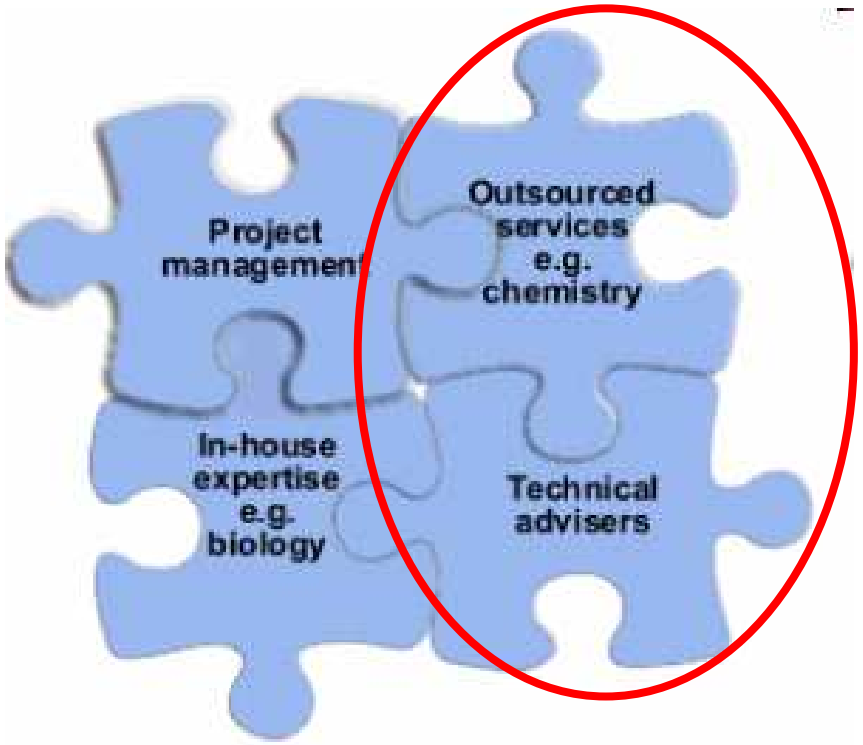
- Biomedical science
- **Technology transfer**
  - Translation awards
  - Strategic translation awards
  - **Seeding Drug Discovery scheme**
- Medical humanities
- Public engagement

ABOUT SEEDING DRUG DISCOVERY

For further information about the application process plea
the Wellcome Trust: techtransfer@wellcome.ac.uk.



Analytical opportunities



In 2004 at the Society for Biomolecular Sciences meeting 10% of attendees were academics. In 2008 at the SBS meeting 35% were academics.

Precompetitive initiatives

- Cooperation among pharma for activities viewed as clearly precompetitive
  - safety biomarkers
  - imaging technologies
- Cooperation among pharma for activities viewed as proprietary / IP sensitive?
  - **"Pathways Across the Valley of Death: Novel Intellectual Property Strategies for Accelerated Drug Discovery"**

    Arti K. Rai, Duke University Law School

Share chemistry without IP effect?

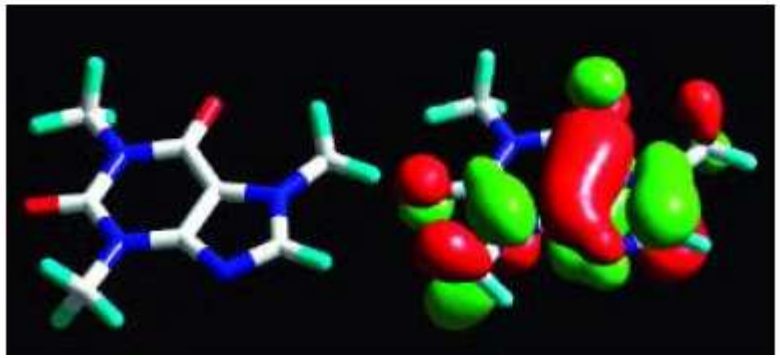
Science & Technology

April 25, 2005
Volume 83, Number 17
pp. 24-29

ACS MEETING NEWS

IS SAFE EXCHANGE OF DATA POSSIBLE?

Modelers in need of proprietary compounds seek ways to share information, but not structure



Share?
Maybe!

It depends on context

InChIKey for Ivermectin

SPBDXSGPUHCETR-VHJJIYNUBB

Richness in chemistry databases

- Cooperation between proprietary and publically accessible data sources
- New batch mode chemistry search options
- New linking of structures to calculated and experimental data
- Late breaking press release July 23, 2008

Open Access ChEMBL Databases

- Free access to large scale drug discovery chemogenomics data
  - Five year grant from Wellcome Trust to the European Bioinformatics Institute
  - www.ebi.ac.uk
- StARlite – Medicinal chemistry
  - ~430,000 unique compounds
- CandiStore – Clinical development candidates
- DrugStore – Launched drugs

- SARfari – integration platform for gene family chemogenomics and 3-D structural data
  - Kinases
  - Rhodopsin-like GPCRs

New chemistry batch abilities

SubScape™... Available to SciFinder Subscribers

SubScape is a new substance visualization tool available to subscribers who are using SciFinder 2007. SubScape allows you to easily visualize substances and manage substance answer sets retrieved in SciFinder to speed the discovery process.

With SubScape, you can:

- Identify novel substances which are structurally similar for the purposes of lead discovery
- Explore secondary uses for existing substances
- Research potential adverse effects for a drug
- Investigate competitive intelligence related to all of the substances listed in a patent

CAS Subscape™ allows one to process a SciFinder answer set of 20,000 compounds and map these against any CAS field.

New options for name search

Registry Number:	70288-86-7
	No Structure Diagram Available
Formula:	Unspecified
CA Index Name:	Ivermectin
Other Names:	22,23-Dihydroavermectin B1; Cardomec; Cardotek 30; Cevamec; Equimec; Equimec Paste; Eqvalan; Heartgard; Heartgard 30; Hyvermectin; Ivectin; Ivertin; Ivomec; Ivosint; Jetamec; L 640471; MK 933; Mectizan; Noramectin; Oramec; Pandex; Phoenectin; Stromectol; Uvemec; Vermic; Zimecterin

CAS SciFinder did not give a structure for Ivermectin

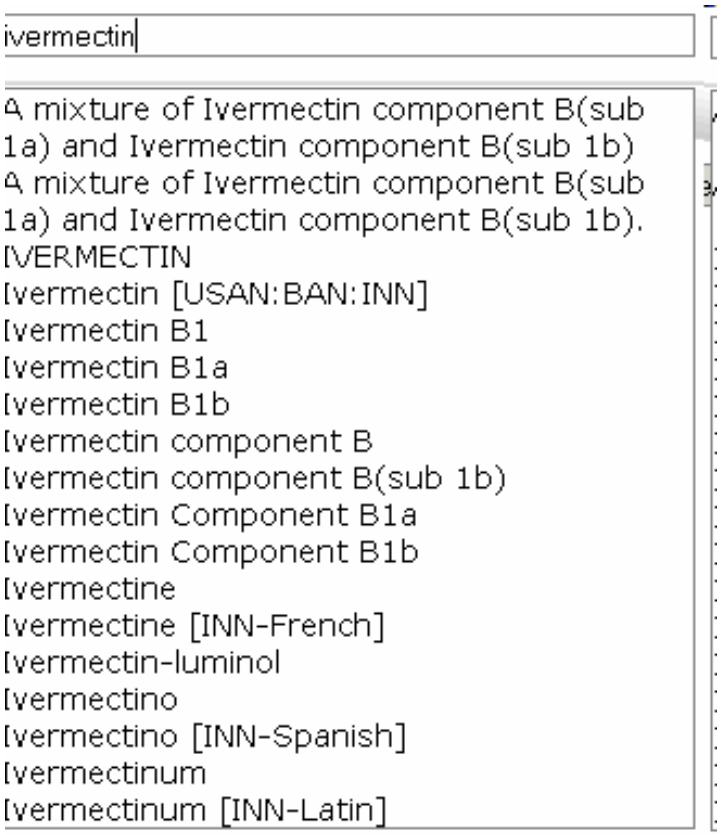
ChemSpider™

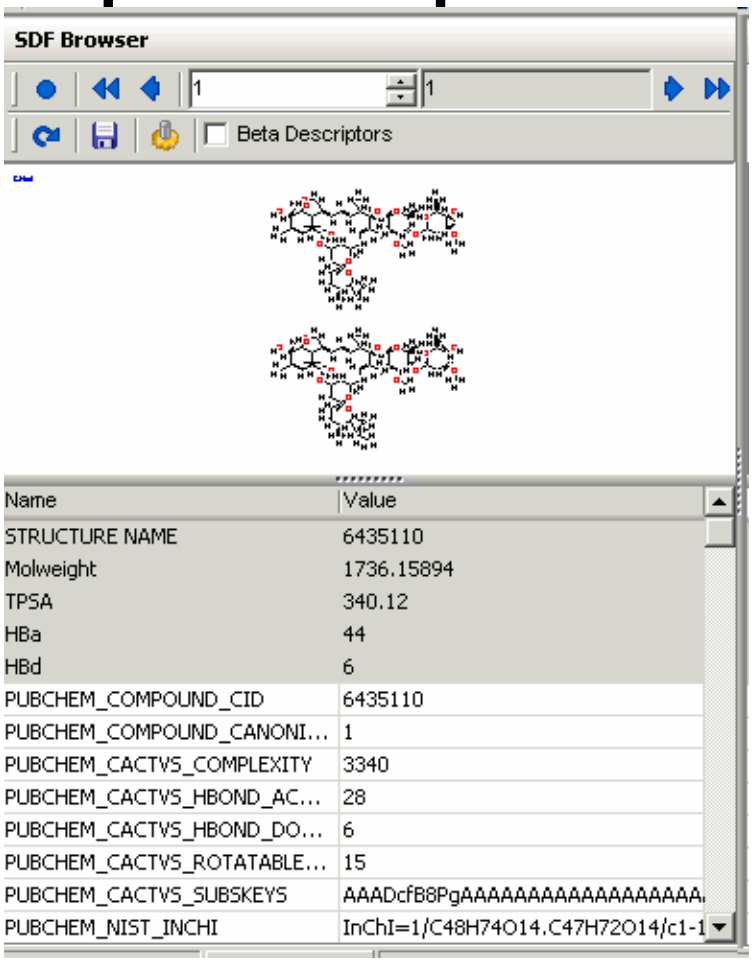
Building a Structure Centric Community for Chemists

Home Search Services Resources About

ChemSpider is a free access service providing a structure centric community for chemists. Providing access to millions of chemical structures and integration to a multitude of other online services ChemSpider is the richest single source of structure-based chemistry information.

New structure capture options





Ivermectin name search in Chemspider, then link directly to PubChem

Structure, data from PubChem and can then link to Medline

Analytically useful properties

Names and Synonyms

Validated by Experts, Validated by Users, Non-Validated, ~~Removed by Users~~, Redirected by Users, **Redirect Approved by Experts**

IVERMECTIN *[Wiki]*
Ivermectin B1a

Predicted Properties

LogP:	ACD/LogP: 6.61 XLogP: 2.80	**# of Rule of 5 Violations:**	3
ACD/LogD (pH 5.5):	6.61	**ACD/LogD (pH 7.4):**	6.61
ACD/BCF (pH 5.5):	62318.94	**ACD/BCF (pH 7.4):**	62318.05
ACD/KOC (pH 5.5):	94095.72	**ACD/KOC (pH 7.4):**	94094.38
#H bond acceptors:	14	**#H bond donors:**	3
#Freely Rotating Bonds:	11	**Polar Surface Area:**	137.06 $Å^2$
Index of Refraction:	1.564	**Molar Refractivity:**	230.72 cm^3
Molar Volume:	708.3 cm^3	**Polarizability:**	91.46 $10^{-24} cm^3$
Surface Tension:	51.9 dyne/cm	**Density:**	1.23 g/cm^3
Flash Point:	267.3 °C	**Enthalpy of Vaporization:**	155.25 kJ/mol
Boiling Point:	940.4 °C at 760 mmHg	**Vapour Pressure:**	0 mmHg at 25°C

41 Natural Products 1990-2000

CAS	Name	Indication/Use	MWT
[illegible]	Miglitol	Diabetes	[illegible]
[illegible]	Mizoribine	Arthritis	[illegible]
[illegible]	Voglibose	Diabetes, obesity	[illegible]
[illegible]	Pentostatin	Leukemia	[illegible]
[illegible]	Artemisinin	Malaria	[illegible]
[illegible]	Galantamine	Alzheimer's disease, arthritis	[illegible]
[illegible]	Masoprocol	Cancer	[illegible]
[illegible]	Donepezil	Alzheimer's disease	[illegible]
[illegible]	Carbenin	Antibiotic	[illegible]
[illegible]	Gospenimus	Arthritis	[illegible]
[illegible]	Podophyllotoxin	Human papillomavirus	[illegible]
[illegible]	Topotecan	Diabetes	[illegible]
[illegible]	Mycophenolate mofetil	Arthritis	[illegible]
[illegible]	Orlistat	Obesity	[illegible]
[illegible]	Cromolyn sodium	Asthma	[illegible]
[illegible]	Cefetamet pivoxil	Antibiotic	[illegible]
[illegible]	Cefozopran	Antibiotic	[illegible]
[illegible]	Cefsulodin	Antibiotic	[illegible]
[illegible]	Irinotecan	Cancer	[illegible]
[illegible]	Tirilazad	Subarachnoid haemorrhage	[illegible]
[illegible]	Acarbose	Diabetes	[illegible]
[illegible]	Cefpirimzole	Antibiotic	[illegible]
[illegible]	Clarithromycin	Antibiotic	[illegible]
[illegible]	Azithromycin	Antibiotic	[illegible]
[illegible]	Vinorelbine	Cancer	[illegible]
[illegible]	Tacrolimus	Immunomodulation	[illegible]
[illegible]	Docetaxel	Cancer	[illegible]
[illegible]	Paclitaxel	Cancer	[illegible]
[illegible]	Sirolimus	Immunomodulation	[illegible]
[illegible]	Everolimus	Immunomodulation	[illegible]
[illegible]	Cyfetrolu	Antibiotic	1022.24
[illegible]	Mepartricin	Benign prostatic hyperplasia	1141.34
[illegible]	Oxiam	Cancer, HIV/AIDS	[illegible]
[illegible]	Ivermectin	Parasitiche	[illegible]
[illegible]	Teicoplanin	Antibiotic	[illegible]
[illegible]	Policosanol	Hyperlipidaemia	
[illegible]	Lentinan	Cancer	
[illegible]	Sizofiran	Cancer, hepatitis-B virus	
[illegible]	Z-100	Immunomodulation	
[illegible]	Sobrerol	Arthritis	
[illegible]	LW-30020	Immunomodulation	

MWT < 350

MWT 350-500

MWT > 500

Polymers

Conclusions

- Academia, public sector, pharma
  - rapidly changing and dynamic scenario
- Academic drug discovery
  - growth and new opportunities for analytical
- Greater chemistry database synergies
- Better database batch mode capability
- Intellectual property
  - a nuisance sometimes, but also a positive change facilitator in unexpected ways