Metodologie di Sintesi e Sviluppo Farmaceutico

Synthesis and Development Pharmaceutical Methodologies

Laurea Magistrale in Chimica a.a. 2019/2019

How to acquire and product scientific knowledge

"SCIENTIFIC KNOWLEDGE IS IN PERPETUAL EVOLUTION; IT FINDS ITSELF CHANGED FROM ONE DAY TO THE NEXT."

JEAN PIAGET

Marco L. Lolli *University of Torino* (UniTO)

The scientific knowledge

- Someone that pay the bill
- A knowledge transfer/discussion
- Some technology involved

The Alchemist (N. C. Wyeth – 1937)

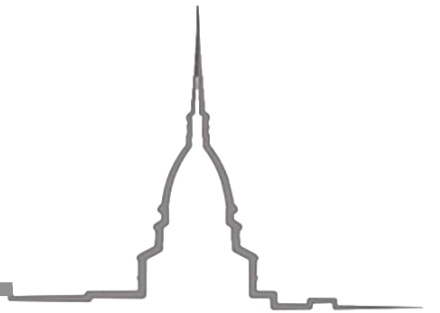
Modern times

The scientific knowledge

Primary Sources

A primary source provides direct or firsthand evidence about an event, object, person, or work of art.
Primary sources include results of experiments, statistical data and empirical studies—research where an experiment was performed or a direct observation was made. The results of empirical studies are typically found in scholarly articles or papers delivered at conferences.

- Articles

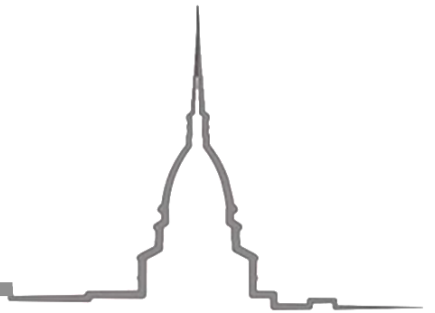


The scientific knowledge

Secondary Sources

Secondary sources describe, discuss, interpret, comment upon, analyze, evaluate, summarize, and process primary sources.

- Patents
- Internal reports/publicatoions
- Technical or research reports;
- Research projects;
- Meeting abstracts;
- PhD / Master Thesis
- Books and educational material
- Lab guedelines
- pre-print manuscript



Scientific paper

A scientific paper is a written and published report describing **original research results.** That short definition must be qualified, however, by noting that a scientific paper **must be written in a certain way** and it **must be published in a certain way**, as defined by three centuries of developing tradition, editorial practice, scientific ethics, and the interplay of printing and publishing procedures.

A **Journal** is a periodical publication that contain articles on a specific topic.

Year, *volume*, page

J. Med. Chem. **2015**, *58*, 4590−4609

http://pubs.acs.org/journal/jmcmar

Protect (or NOT) yourself!!!

You make money your research???

The fact that the **privately owed** journals are **highly expansive** create a limitation of knowledge diffusions.

This fact create a big controversial inside th4 scientific community that if supporting the rising on the **open access Journals**

DOAJ DIRECTORY OF OPEN ACCESS JOURNALS

DOAJ is an online directory that indexes and provides access to high quality, open access, peer-reviewed journals.

https://doaj.org/

Reading a scientific paper

"**First name**": this author is supposed to have a primary role in the all study.

"**Affiliations**": the single groups involved. More are, better is…

IF 5,248

Journal of
Medicinal
Chemistry

Article

pubs.acs.org/jmc

Studies on the ATP Binding Site of Fyn Kinase for the Identification of New Inhibitors and Their Evaluation as Potential Agents against Tauopathies and Tumors

Cristina Tintori,[†] Giuseppina La Sala,[†] Giulia Vignaroli,[†] Lorenzo Botta,[†] Anna Lucia Fallacara,[†,‡] Federico Falchi,[†,‡] Marco Radi,[†,∥] Claudio Zamperini,[†] Elena Dreassi,[†] Lucia Dello Iacono,[†] Donata Orioli,[§] Giuseppe Biamonti,[§] Mirko Garbelli,[§] Andrea Lossani,[§] Francesca Gasparrini,[‡,∥] Tiziano Tuccinardi,[⊥] Ilaria Laurenzana,[#] Adriano Angelucci,[▽] Giovanni Maga,[§] Silvia Schenone,[*,○] Chiara Brullo,[○] Francesca Musumeci,[○] Andrea Desogus,[○] Emmanuele Crespan,[*,§] and Maurizio Botta[†,◆]

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[‡]Dipartimento di Chimica e Tecnologie del Farmaco, Università La Sapienza, Piazzale Aldo Moro 5, I-00185 Roma, Italy
[§]Istituto di Genetica Molecolare, IGM-CNR, Via Abbiategrasso 207, I-27100 Pavia, Italy
[∥]Dipartimento di Medicina Molecolare, Sapienza Università di Roma, Piazzale Aldo Moro 5, 00185 Roma, Italy
[⊥]Dipartimento di Farmacia, Università di Pisa, Via Bonanno 6, 56126 Pisa, Italy
[#]Laboratory of Preclinical and Translational Research, IRCCS-Centro di Riferimento Oncologico Basilicata (CROB), Via Padre Pio 1, Rionero in Vulture 85028 Potenza Italy
[▽]Dipartimento di Scienze Cliniche Applicate e Biotecnologiche, Università dell'Aquila, Via Vetoio, 67100 Coppito, L'Aquila, Italy
[○]Dipartimento di Farmacia, Università di Genova, Viale Benedetto XV 3, I-16132 Genova, Italy
[◆]Biotechnology College of Science and Technology, Temple University, Biolife Science Building, Suite 333, 1900 N 12th Street, Philadelphia, Pennsylvania 19122, United States

Supporting Information

"**Asterisc**": this is named "Reference author", the one that is coordinating the all project and whose must direct any further question. In a complex study, as this, could be more then one.

"**Supporting information**": some material (NMR, recipes, figures, …), that just support the study but that can be heavy in the manuscript is placed in a separate, free of charge, editor web site.

Reading a scientific paper

"**Title**": The title of a paper is important because it is one of the first things that an editor/ reviewer/reader sees when they look at your manuscript. Therefore, it is important to grab their attention right away and give them an idea of why your paper is a scientific breakthrough! Be specific, not too technical, and concise. Must be included inside the keywords for web search.

IF 5,248

Journal of
Medicinal
Chemistry

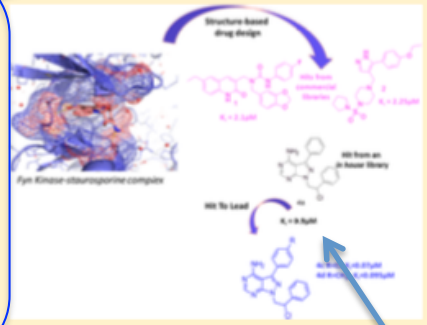
Article

pubs.acs.org/jmc

Studies on the ATP Binding Site of Fyn Kinase for the Identification of New Inhibitors and Their Evaluation as Potential Agents against Tauopathies and Tumors

Cristina Tintori,[†] Giuseppina La Sala,[†] Giulia Vignaroli,[†] Lorenzo Botta,[†] Anna Lucia Fallacara,[†,‡] Federico Falchi,[†,+] Marco Radi,[†,¶] Claudio Zamperini,[†] Elena Dreassi,[†] Lucia Dello Iacono,[†] Donata Orioli,[§] Giuseppe Biamonti,[§] Mirko Garbelli,[§] Andrea Lossani,[§] Francesca Gasparrini,[‡,∥] Tiziano Tuccinardi,[⊥] Ilaria Laurenzana,[#] Adriano Angelucci,[▽] Giovanni Maga,[§] Silvia Schenone,*[,○] Chiara Brullo,[○] Francesca Musumeci,[○] Andrea Desogus,[○] Emmanuele Crespan,*[,§] and Maurizio Botta[†,◆]

ABSTRACT: Fyn is a member of the Src-family of nonreceptor protein–tyrosine kinases. Its abnormal activity has been shown to be related to various human cancers as well as to severe pathologies, such as Alzheimer's and Parkinson's diseases. Herein, a structure-based drug design protocol was employed aimed at identifying novel Fyn inhibitors. Two hits from commercial sources (**1**, **2**) were found active against Fyn with K_i of about 2 μM, while derivative **4a**, derived from our internal library, showed a K_i of 0.9 μM. A hit-to-lead optimization effort was then initiated on derivative **4a** to improve its potency. Slightly modifications rapidly determine an increase in the binding affinity, with the best inhibitors **4c** and **4d** having K_is of 70 and 95 nM, respectively. Both compounds were found able to inhibit the phosphorylation of the protein Tau in an Alzheimer's model cell line and showed antiproliferative activities against different cancer cell lines.



"**Abstract**": Imagine you have twenty seconds to explain the project you have been working on for months or years to another scientist who is not familiar with your area of research. You would probably try and tell them the one or two main outcomes without going into excessive technical detail.

Just grab the reader's attention with the first statement and then leave them with the overall message of the manuscript in the last sentence.

"**Graphical abstract**": Explain everything in just a nice attractive image!

Reading a scientific paper

Journal of Medicinal Chemistry — Article — pubs.acs.org/jmc

Studies on the ATP Binding Site of Fyn Kinase for the Identification of New Inhibitors and Their Evaluation as Potential Agents against Tauopathies and Tumors

- **INTRODUCTION**

What was before and what this study is proposing to do. Must not be a review on the topic

What the authors have done for support the claim. A nice readable story must be written here where any question had found a good explanation

IF 5,248

- **RESULTS AND DISCUSSION**

What we have done and what we will do in future inside this research topic

- **CONCLUSIONS**

- **EXPERIMENTAL SECTION**

All the experimental data supporting the authors claims and the protocols used to obtain them

Some protocols or data are placed here because heavy inside the manuscript (for example the synthetic strategies inside a pharmacological journal). Because free of charge, is also a way to disseminate the group research

- **ASSOCIATED CONTENT**

- **ACKNOWLEDGMENTS**

Who paid the bill?
One your friend was helpful?

- **REFERENCES**

Inside a manuscript there are no personal opinions but just correlations between already published fact!

Each journal has a specific scope

IF 5,248

Journal Scope

The *Journal of Medicinal Chemistry* publishes studies that contribute to an understanding of the relationship between molecular structure and biological activity or mode of action.

Some specific areas that are appropriate include the following:

- Design, synthesis, and biological evaluation of novel biologically active compounds, diagnostic agents, or labeled ligands employed as pharmacological tools.
- Molecular modifications of reported series that lead to a significantly improved understanding of their structure-activity relationships (SAR). Routine extensions of existing series that do not utilize novel chemical or biological approaches or do not add significantly to a basic understanding of the SAR of the series will normally not be accepted for publication.
- Structural biological studies (X-ray, NMR, etc.) of relevant ligands and targets with the aim of investigating molecular recognition processes in the action of biologically active compounds.
- Molecular biological studies (e.g., site-directed mutagenesis) of macromolecular targets that lead to an improved understanding of molecular recognition.
- Computational studies that provide fresh insight into the SAR of compound series that are of current general interest or analysis of other available data that subsequently advance medicinal chemistry knowledge.
- Substantially novel computational chemistry methods with demonstrated value for the identification, optimization, or target interaction analysis of bioactive molecules.
- Effect of molecular structure on the distribution, pharmacokinetics, and metabolic transformation of biologically active compounds. This may include design, synthesis, and evaluation of novel types of prodrugs.
- Novel methodology with *broad* application to medicinal chemistry, but only if the methods have been tested on relevant molecules.

If you want to publish on JMC, your study MUST contain novelty in design and synthesis of new bioactive candidates. The compound must be fully characterized for the pharmacological/ Biochemistry profile. X-ray crystallography and cell based study are well accepted…

Each journal has a specific scope

IF 4.721

Journal Scope

The Journal of Organic Chemistry (*JOC*) welcomes original contributions of fundamental research in all branches of the theory and practice of organic chemistry.

Since mid-2011, *JOC* has been publishing Brief Communications—preliminary results of unusual novelty and urgency that justify immediate disclosure, and *JOC*Synopses—focused short reviews of current topics, in addition to Articles, Notes, and Perspectives.

The *Journal of Organic Chemistry* now publishes *JOC* Featured Articles—full papers selected by Editor-in-Chief C. Dale Poulter and the *JOC* Associate Editors for special consideration as exceptional contributions to the journal as identified during the review process. Upon acceptance, the galley proofs of these selected manuscripts are prepared and sent to the author on an expedited schedule to facilitate more rapid online and print publication. In addition to being identified as Featured Articles on the index page of each issue, they are posted on a special *JOC* Featured Articles Web page.

Authors may choose to have the accepted version of the manuscript file appear on the Web as a *Just Accepted* manuscript until the copyedited, proof-corrected version is published as an ASAP Article or in an issue. If this option is selected, the official publication date is the date the manuscript is posted on the ACS Publications Web site as *Just Accepted*.

If you want to publish on JOC, your study MUST contain novelty in chemistry related topic. In this case the bio part is less important.

Other journals are more general and ready to accept everything of high profile inside the scientific research..

Impact Factor is 42.351
(2014)

Impact Factor is 33.611
(2014)

Full article, *short article* or *communication* (Letter)?

An **article**, both full or short (less pages) is a complete study where all the literature and the experimental material supporting are included.
Difficult to do, high value.

Editor-in-Chief:
Gunda I. Georg
and
Shaomeng Wang

Editors & Editorial Board
Recommend this Journal
Author Index

Current Issue View Articles ASAP

Total Citations	Impact Factor	Articles Published
63,060	5.447	773

2014 Journal Citation Reports® by Thomson Reuters, 2015

A Letter or Communication is a form of fast and short article used to block a specific topic. It doesn't contain any experimental part., be careful in that sense. Usually is followed by a full article.

Editor-in-Chief:
Dennis C. Liotta

Editors & Editorial Board
Recommend this Journal
Author Index

Current Issue View Articles ASAP

Total Citations	Impact Factor	Articles Published
2,385	3.120	226

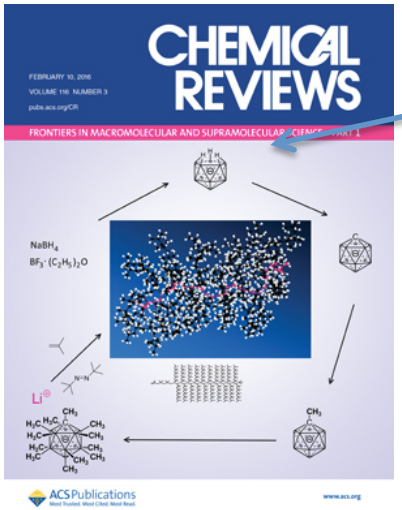
2014 Journal Citation Reports® by Thomson Reuters, 2015

What about writing a Review?

Review articles are an attempt to summarize the current state of understanding on a topic. As example of grey literature, a review article re-presents previously published material, rather that reporting new facts or analysis. Academic publications that specialize in review articles are known as review journals.

Recent Update on Human Lactate Dehydrogenase Enzyme 5 (hLDH5) Inhibitors: A Promising Approach for Cancer Chemotherapy
Reshma Rani and Vinit Kumar
pp 487-496
Publication Date (Web): September 4, 2015 (Perspective)
DOI: 10.1021/acs.jmedchem.5b00168

JMC "perspective" series



ACS Chemical Review
IF 48.6

Will the journal accept my manuscript? (unlucky, probably not ☺☺ !!!)

The Impact Factor

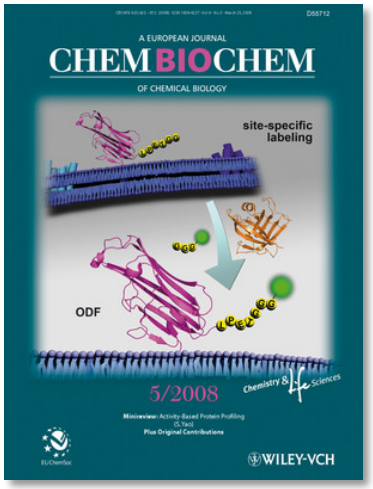
Impact factor (IF). Introduced from ISI (Institute for Scientific Information), and published each year inside Journal Citation Reports. The IF is correlated from the citation inside the bibliography parts of the specific journal. More the research inside the journal has a high impact, more the article is cited and by reflex the IF go higher.

High IF journals are selective ...

Will the journal accept my manuscript? (unlucky, probably not ☺☺ !!!)

The Impact Factor

IF 5.447



IF 3,944

IF 3,346

IF 3,151

IF 2,921

Will the journal <u>accept</u> my manuscript (probably not ☺)?

The Impact Factor

Impact Factor is 5.447
(2014)

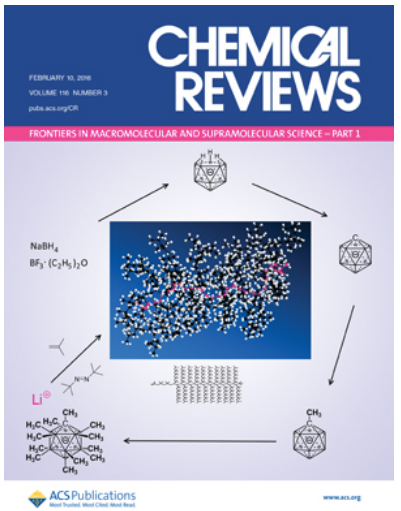
Impact Factor is 42.351
(2014)

The IF are <u>not perfectly comparable</u> and **must** be considered inside a specific field. If a good research inside is inside a field with low impact inside the research community, it will be receive the a low IF

Will the journal accept my manuscript (probably not ☺)?

The Impact Factor

Impact Factor is 5.447
(2014)

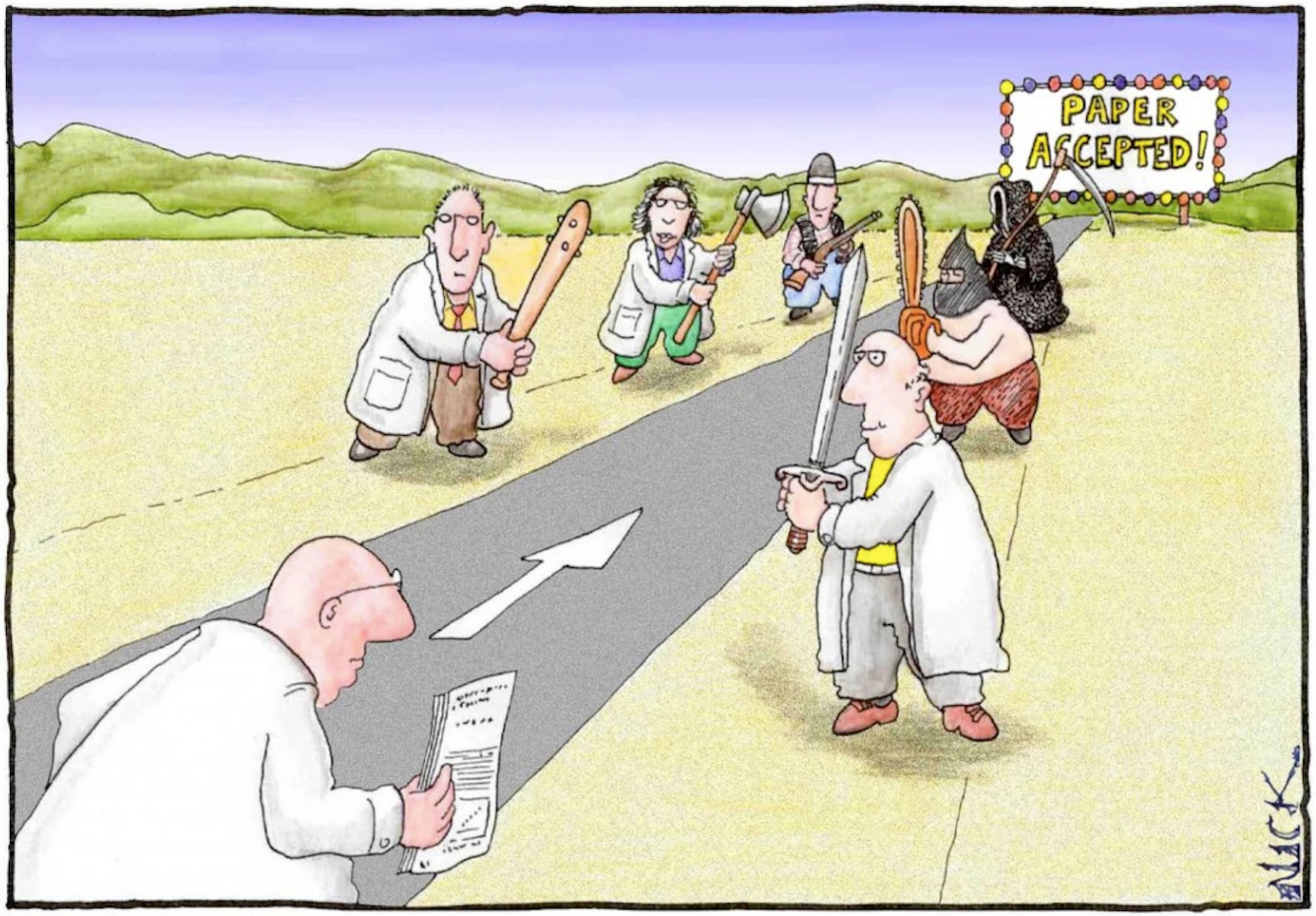


Impact Factor is 48.6
(2016)

Beside the fact that is not containing novelty, a good review has always an high impact on the field.

How be sure that real is real?

The **peer review** vs **IF** mechanism



Most scientists regarded the new streamlined peer-review process as "quite an improvement."

The **peer review** system

A blind judgment of three field expert (reviews) will judge:

- if the article fit the journal requisite
- if the article fit the journal value (IF)
- if the study is coherent and well done
- the novelty of the proposal research
- if the study is complete or some important parts are missing
- if the experimental protocols are complete and well written
- if the general manuscript editing is acceptable for publication (figures, mistakes, …)

- Then propose to the editor to "**accept for publication** " of "**reject**" it.

Manuscript Submission

Editor Judgement STEP 1

OUT

Rejection

IN

Referee (3x) Judgement

Editor Judgement STEP 2

Accepted for publication!!!

Marco L. Lolli

University of Torino (UniTO)

The **peer review** system: example

The editor answer

Dear Dr. Lolli:

Below are the editor's comments and reviews for your manuscript. The reviewers have suggested major revisions before your manuscript can be accepted. Please submit a revised version of your manuscript along with a cover letter that explains point-by-point how you have responded to the comments.

Please also note that the editors are encouraging authors to submit molecular formula strings and the associated biochemical and biological data as supporting information. Providing these data is of great value to readers and can increase an article's discoverability and citability. See complete submission instructions here: http://pubs.acs.org/page/jmcmar/submission/jmcmar_mfstrings.html

We would like to receive your revision as soon as possible, 17-May-2016 at the latest.

The **peer review** system: example

The referee# 1 answer

This manuscript is describing the design, synthesis and evaluation of 7 inhibitors of DHODH. The results presented here are worth a publication in J. Med. Chem. although along with decent science, a lot of "noise" has been slipped in the paper. For instance all the comments on the Scaffold similarity and in silico ADME/ Toxicity evaluation are absolutely useless and are only lending to computer science was it does not do: proper prediction of these properties. The same goes for the content of the figure 6. This is only a fancy method to state that the series of compounds are original. Still about the computer use, several docking poses are described in the manuscript and are thus providing nice pictures. This is the only thing they do, docking calculations are still not accurate enough, despite the many useless academic papers pretending the contrary. Moreover, it would be remarkably ludicrous to try to pretend that the chemists did not designed and start to prepare the analogues (fairly obvious in view of the inhibitors reported in ref 17) in this manuscript before the docking calculations. In other words, this manuscript would be much better as a note or with much more X-ray structure which would confirm (or not) the calculations provided. This referee would also suggest to test compound 17 for its possible effect on DHODH.

The **peer review** system… limits

Feature: Physics fraud physicsworld.com

The rise and fall of a physics fraudster

Seven years after rumours of massive fraud began to surface, the repercussions of Jan Hendrik Schön's lies still reverberate. In her new book *Plastic Fantastic*, abridged and edited here, **Eugenie Samuel Reich** chronicles how his fraud shook the scientific world

Referee (3x) Judgement

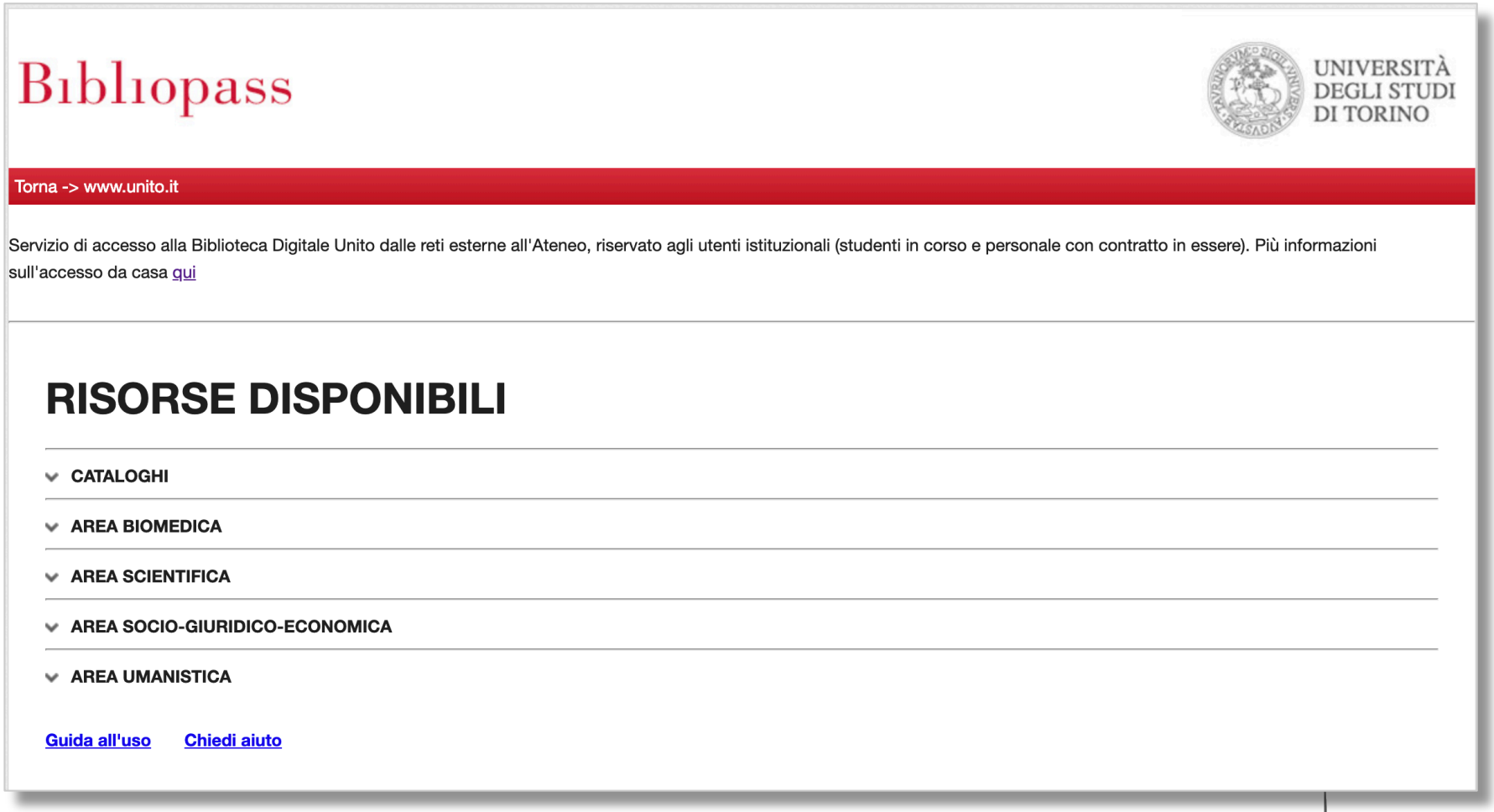
The Schön scandal concerns German physicist Jan **Hendrik Schön** who briefly rose to prominence after a series of apparent breakthroughs with semiconductors that were later discovered to be fraudulent. The scandal provoked discussion in the scientific community about the degree of responsibility of coauthors and reviewers of scientific papers. The debate centered on whether **peer review**, traditionally designed to find errors and Determine relevance and originality of papers, should also be required to detect deliberate fraud.

How judge the value of a single article (not only Journal Impact Factor)

Science Citation Index

The **Science Citation Index** (SCI) is a sub-set of the Science Citation Index Expanded (SCIE), containing journals that rank competitively among the most highly-cited core journals in their category or categories. The Science Citation Index Expanded is essentially the web version of what used to be a database available only on CDRom/ Diskette.

Searching the literature



https://login.bibliopass.unito.it/menu

Searching the literature

https://login.bibliopass.unito.it/menu

Sezione area biomedica

- Dizionari Zanichelli online - Vocabolari, dizionari monolingue e bilingue, dizionari tecnici di Italiano, Inglese, Francese, Russo, Tedesco.
- Elsevier - Ebook - Accesso agli ebook dell'editore Elsevier
- Elsevier Science Direct - Accesso a periodici elettronici e ebook di uno dei fornitori di contenuti più importanti per le discipline scientifiche, tecniche e mediche. Anche le scienze umane e sociali sono rappresentate con alcuni titoli.
- Embase - Embase è una banca dati biomedica e farmacologica che indicizza letteratura biomedica internazionale dal 1947 ad oggi.
- Harrison's Principles of Internal Medicine - Principale manuale di riferimento per la medicina interna per medici, specializzandi e studenti.
- In Pratica - Pensiero Scientifico Editore - Collezione di e-books per medici e bibliotecari.
- JAMA Network - Pacchetto di riviste elettroniche pubblicate dall'American Medical Association.
- JOVE - Journal of Visual Experiments - JOVE pubblica video scientifici sottoposti a peer-review in campo biomedico, chimico e fisico. L'Ateneo sottoscrive la sezione Neuroscience e la banca dati Science Education.
- Micromedex - Informazioni evidence-based su farmaci e loro interazioni, tossicologia, analisi di laboratorio e medicina alternativa.
- Nature - Accesso ai periodici dell'editore Nature, di riferimento per le scienze biologiche, mediche e naturali.
- New England Journal of Medicine - Il NEJM è la più antica e una delle più importanti pubblicazioni di Medicina generale al mondo.
- Oxford English Dictionary (OED) - Dizionario della lingua inglese: fornisce definizione, storia e pronuncia di oltre 600.000 parole.
- Oxford Scholarship Online - Accesso a una selezione di ebook dell'Oxford University Press per le Neuroscienze.
- PLOS Public Library of Science - Periodici ad accesso aperto di area scientifica e biomedica.
- ProQuest - PILOTS - Fornisce indici, abstracts e full-text di periodici inerenti le discipline psicologiche.
- Proceedings of the National Academy of Sciences (PNAS) - Rivista ufficiale della National Academy of Sciences degli Stati Uniti.
- PsycInfo - Contiene abstracts di riviste accademiche, libri e tesi nell'ambito delle scienze comportamentali e della salute mentale.
- PubMed - Banca dati che comprende più di 25 milioni di citazioni di letteratura biomedica, tra cui Medline, curata dalla National Library of Medicine (USA). Le citazioni possono essere corredate da link al full-text in PubMed Central o sul sito dell'editore.
- SciVal - SciVal offre strumenti per l'analisi dei risultati della ricerca a partire dai dati della produzione scientifica.
- Scopus - Database di citazioni ed abstracts dell'editore Elsevier. Indicizza riviste e conference papers.
- SpringerLink - Piattaforma di accesso ai contenuti digitali (ejournals e ebook) dell'editore Springer.
- Taylor and Francis Online - Piattaforma di periodici elettronici gestita da Taylor & Francis, gruppo editoriale internazionale.
- UpToDate - Banca dati di informazioni evidence-based per il supporto alle decisioni cliniche sul point of care.
- Web of Science - Banca dati interdisciplinare a carattere citazionale. Comprende i tre indici disciplinari Science Citation Index Expanded (SCIE), Social Science Citation Index (SSCI), Arts and Humanities Citation Index (AHCI) e il Journal Citation Reports (JCR) per la ricerca dell'Impact Factor delle riviste.
- Wiley - Ebooks - Piattaforma di ebooks dell'editore Wiley.
- Wiley Online - Piattaforma che rende disponibili online i contenuti dell'editore Wiley.

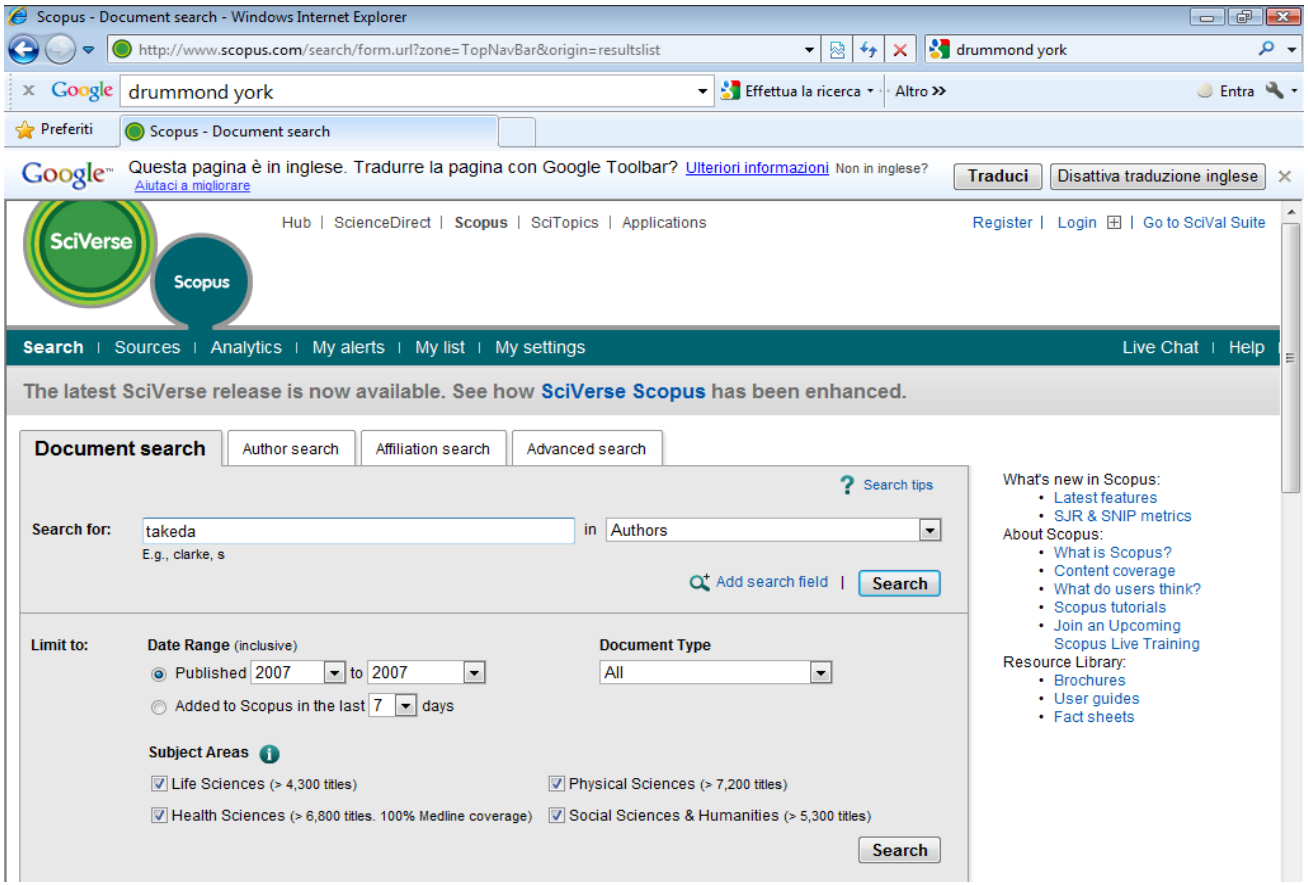
Screenshot

Search engines

Scopus

www.scopus.com

Elsevier ha introdotto nel 2004 in rete Scopus che combina le caratteristiche di PubMed e Web of Science.



Example of a SCOPUS related research

Scopus
www.scopus.com

Answering:
"*what happen in drug design inside the malaria topic in the last five years?*"

Here is the topic where we start:
"**Malaria**"

Keyword TITLE-ABS-KEY (malaria)

Only article and review, no Patent

DOCTYPE (ar OR re)

In which field are we looking?

SUBJAREA
(mult OR agri OR bioc OR immu OR neur OR phar OR mult OR medi OR nurs OR vete OR dent OR heal)

PUBYEAR > 2009

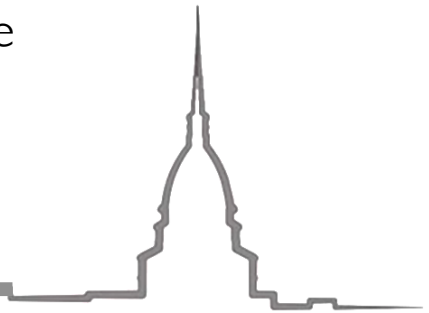
Since the 2009

Keyword ((drug target))

We are interested in new "drug targets", in order to include some innovation

Keyword (j med CHEM)

We are restrict the field….



Example of a SCOPUS related research

Scopus
www.scopus.com

Answering:
"*what happen in drug design inside the malaria topic in the last five years?*"

Hit number# 1

The citation number reflex the impact of this paper on the field. Already 40 citation in only two years

Click here and get the PDF

IF 2.42, medium level

Example of a SCOPUS related research

Scopus
www.scopus.com

Answering:
"*what happen in drug design inside the malaria topic in the last five years?*"

Only 1 citation in the same two years ☹

Hit number#53

53	Synthesis of gallinamide A analogues as potent falcipain inhibitors and antimalarials	Conroy, T., Guo, J.T., Elias, N., (...), Hunt, N.H., Payne, R.J.	2014	Journal of Medicinal Chemistry	1

TROVA

Click here and get the PDF

IF 5.44, high level

Protect yourself!!!

Submit a PATENT!

A **patent** is an exclusive right given by law to inventors to make use of, and exploit, their inventions for a limited period of time. By granting the inventor a temporary monopoly in exchange for a full description of how to perform the invention, patents play a key role in developing industry around the world.

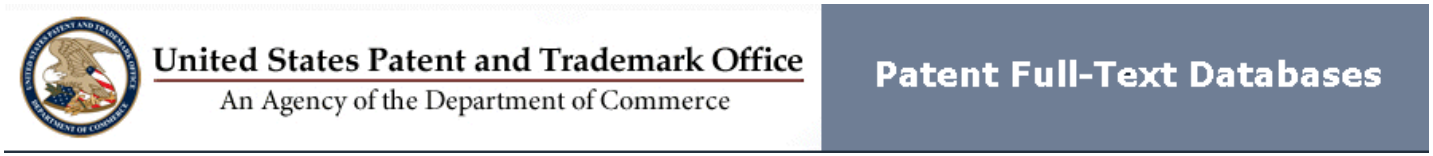
- A patent is done to **protect** knowledge and not to **share**
- A patent coverage is quite expansive
- Patented literature is also **source of information,** not always reliable

Protect yourself!!!

Submit a PATENT!

Few engines allow to search the patent world:

- Esp@cenet: European Patent Office (EPO) database (http://www.epo.org/searching/free/espacenet.html)
- US Patent and Trademark Office (USPTO) (http://www.uspto.gov/patft/)
- The World Intellectual Property Organization (WIPO) (http://www.wipo.int/about-wipo/en/what_is_wipo.html).



Searching the literature

https://login.bibliopass.unito.it/menu

Sezione area Scientifica

AREA SCIENTIFICA

- APS Journals - Accesso ai periodici dell'American Physical Society.
- AdisInsight - Database che raccoglie dati su farmaci in via di sperimentazione a livello globale (studi clinici, casi di reazioni avverse a farmaci...).
- American Chemical Society - Accesso al full text delle riviste pubblicate dall'American Chemical Society, una fra le più importanti società scientifiche nel campo della chimica.

- Cambridge Structural Database (CSD) - Contiene dati cristallografici di composti organici, organometallici e di complessi metallici.
- DigiZeitschriften - Archivio retrospettivo di periodici accademici in lingua tedesca, in ambito umanistico, scientifico e nelle scienze sociali.
- Dizionari Zanichelli online - Vocabolari, dizionari monolingue e bilingue, dizionari tecnici di Italiano, Inglese, Francese, Russo, Tedesco.
- Elsevier Science Direct - Accesso a periodici elettronici e ebook di uno dei fornitori di contenuti più importanti per le discipline scientifiche, tecniche e mediche. Anche le scienze umane e sociali sono rappresentate con alcuni titoli.

- PubMed - Banca dati che comprende più di 25 milioni di citazioni di letteratura biomedica, tra cui Medline, curata dalla National Library of Medicine (USA). Le citazioni possono essere corredate da link al full-text in PubMed Central o sul sito dell'editore.
- Reaxys - Database bibliografico e fattuale per le scienze chimiche.
- Royal Society of Chemistry - Piattaforma di riviste online dell'editore Royal Society of Chemistry.
- SciFinder - Banca dati prodotta dal Chemical Abstract Service, contiene il repertorio della letteratura chimica a partire dalla fine dell'Ottocento applicata alle diverse scienze. Per la consultazione, è necessaria la creazione di un account individuale previa registrazione a questo link.
- SciVal - SciVal offre strumenti per l'analisi dei risultati della ricerca a partire dai dati della produzione scientifica.
- Science Online - Accesso alle riviste della American Association for the Advancement of Science, dedicate alle discipline scientifiche, con particolare riguardo per le scienze biologiche e mediche.
- Scopus - Database di citazioni ed abstracts dell'editore Elsevier. Indicizza riviste e conference papers.
- SpringerLink - Piattaforma di accesso ai contenuti digitali (ejournals e ebook) dell'editore Springer.
- Taylor and Francis Online - Piattaforma di periodici elettronici gestita da Taylor & Francis, gruppo editoriale internazionale.
- UlrichsWeb - Repertorio di informazioni relative a periodici pubblicati a livello internazionale.
- Walter De Gruyter Journals - Pacchetto multidisciplinare di riviste pubblicate dall'editore tedesco De Gruyter.
- Web of Science - Banca dati interdisciplinare a carattere citazionale. Comprende i tre indici disciplinari Science Citation Index Expanded (SCIE), Social Science Citation Index (SSCI), Arts and Humanities Citation Index (AHCI) e il Journal Citation Reports (JCR) per la ricerca dell'Impact Factor delle riviste.
- Wiley Online - Piattaforma che rende disponibili online i contenuti dell'editore Wiley.

How it work?

CAS
A DIVISION OF THE AMERICAN CHEMICAL SOCIETY

Chemical Abstracts

- Since 1907 the Chemical Abstract Service (CAS) is published by the American Chemical Society. It fully cover the chemistry related scientific production, patent and more then 14 000 specific publication are covered.

https://www.cas.org/

How it work?

CAS
A DIVISION OF THE AMERICAN CHEMICAL SOCIETY

- Topic
- Author
- Structures
- **Abstract**: important to understand what happened also if the access to the article is impossible.
- Keywords

ACS Infectious Diseases

Letter

pubs.acs.org/journal/aidcbc

Onchocerca volvulus Molting Inhibitors Identified through Scaffold Hopping

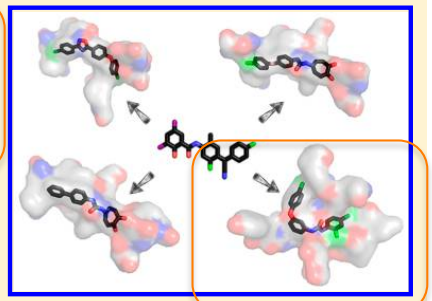
Major Gooyit,[†] Tyler L. Harris,[†] Nancy Tricoche,[‡] Sacha Javor,[†] Sara Lustigman,[‡] and Kim D. Janda*[,†]

[†]Departments of Chemistry and Immunology and Microbial Science, The Skaggs Institute for Chemical Biology, and The Worm Institute of Research and Medicine, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, California 92037, United States

[‡]Lindsley F. Kimball Research Institute, New York Blood Center, New York, New York 10065, United States

Supporting Information

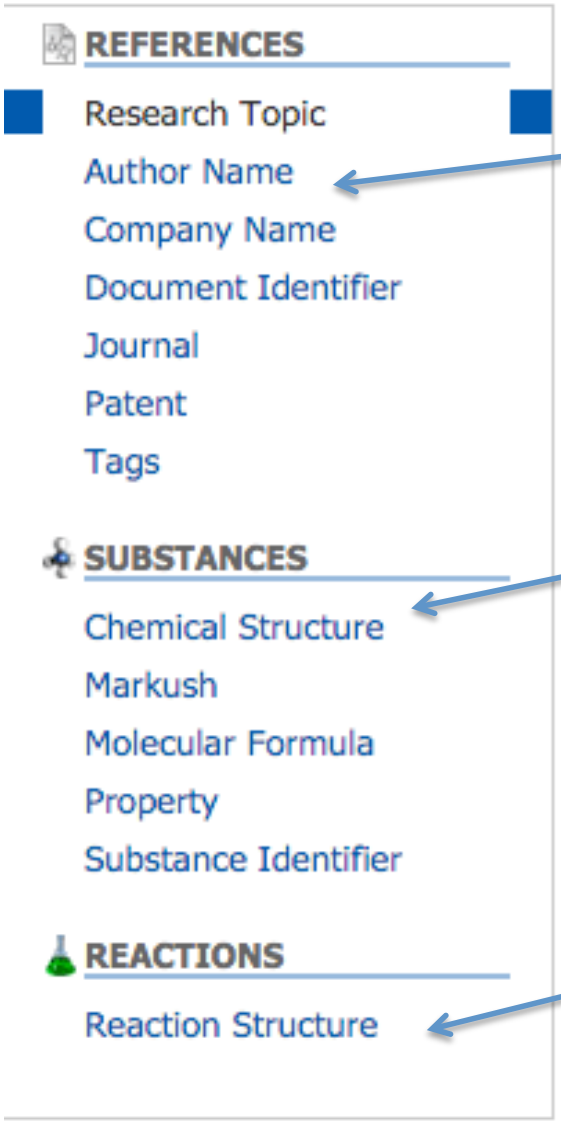
ABSTRACT: The anthelmintic closantel has shown promise in abrogating the L3 molting of *Onchocerca volvulus*, the causative agent of the infectious disease onchocerciasis. In our search for alternative scaffolds, we utilized a fragment replacement/modification approach to generate novel chemotypes with improved chitinase inhibitory properties. Further evaluation of the compounds unveiled the potential of urea-tropolones as potent inhibitors of *O. volvulus* L3 molting.



KEYWORDS: *onchocerciasis, tropolones, molting*

Search engines

SciFinder®



Topic research…. What we want to know??
A topic, a person, a field, a molecule name….

A specific structure is needed?

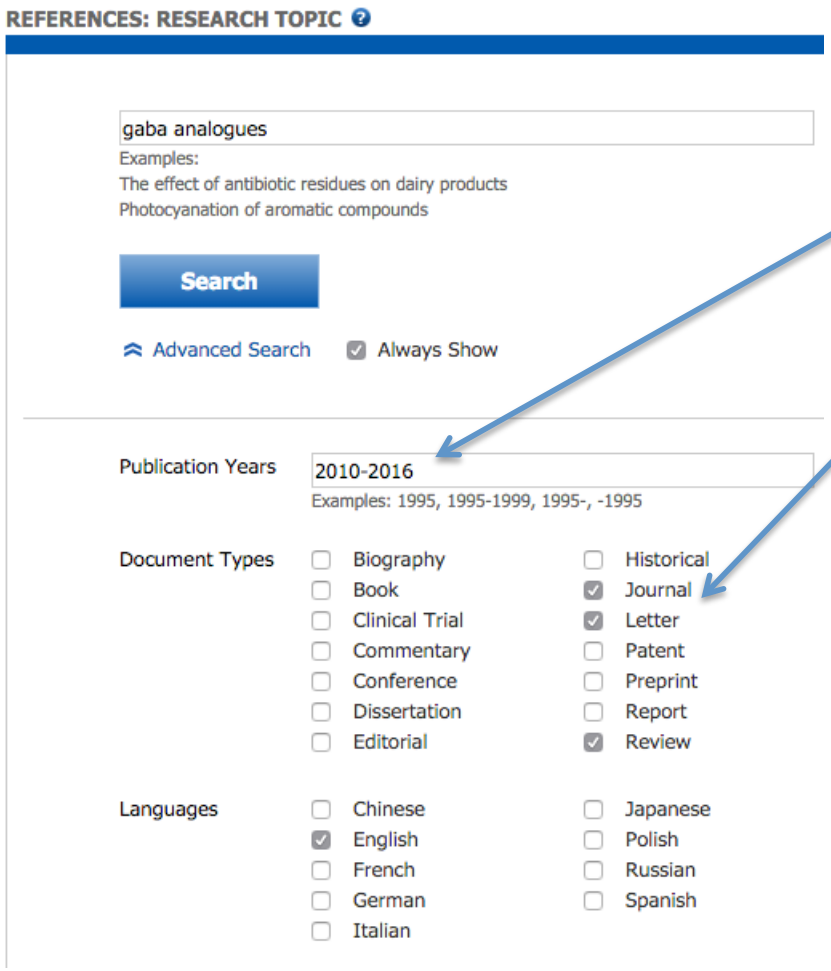
A specific reaction???

Example of a SciFinder related research

Answering:
"*Searching for GABA analogues in neurotrasmission*"

SciFinder®

www.scifinder.com



Let's limit to the last 6 years and only to papers

Example of a SciFinder related research

Answering:
"*Searching for GABA analogues in neurotrasmission*"

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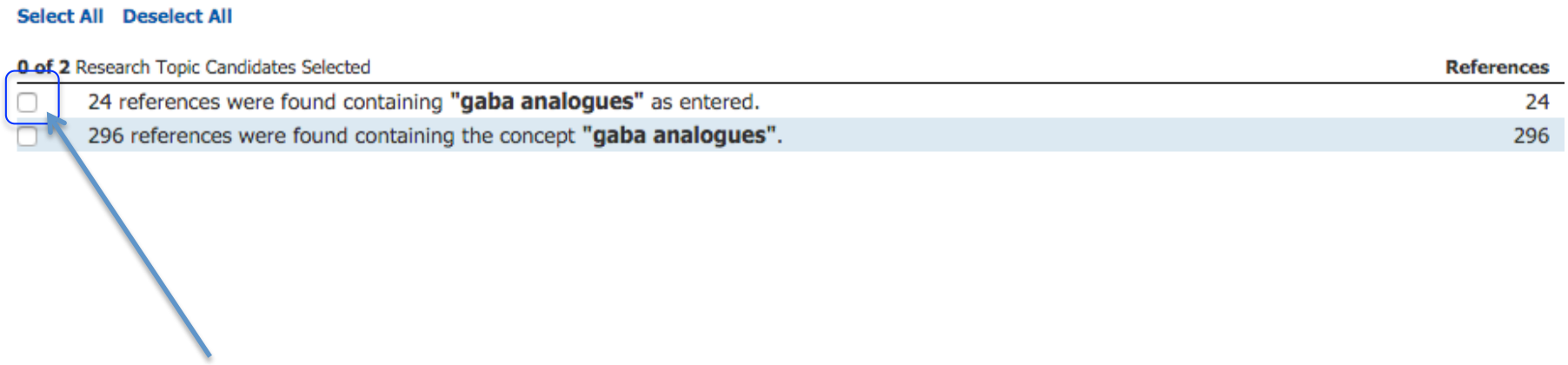

First here, then expand to the other 296

Example of a SciFinder related research

Answering:
"*Searching for GABA analogues in neurotrasmission*"

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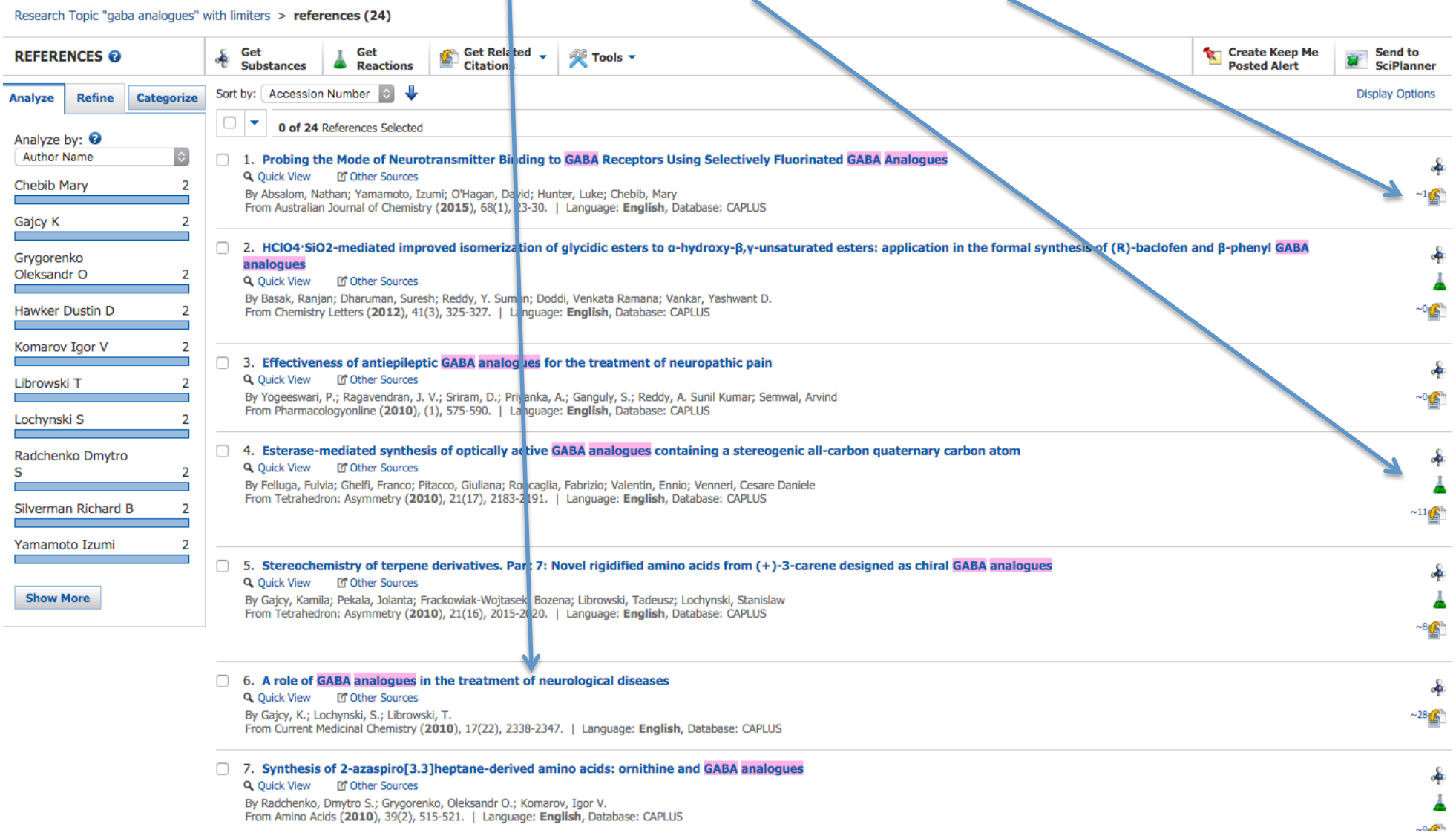
Here we are….

Reactions

Citated references



Example of a SciFinder related research

Answering:
"*Searching for GABA analogues in neurotrasmission*"

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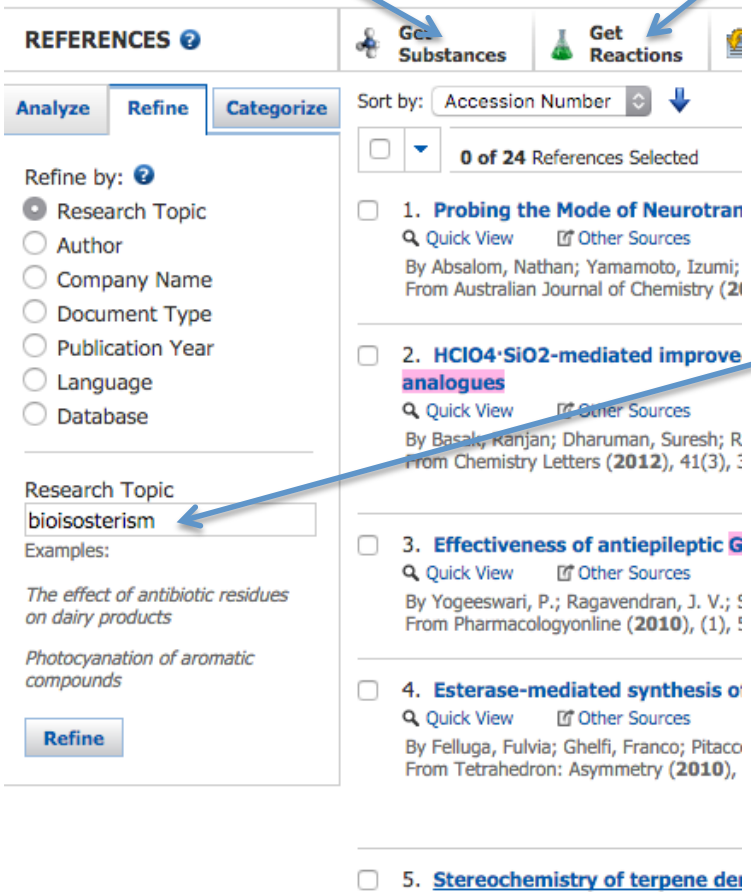
Substance involved

Reactions



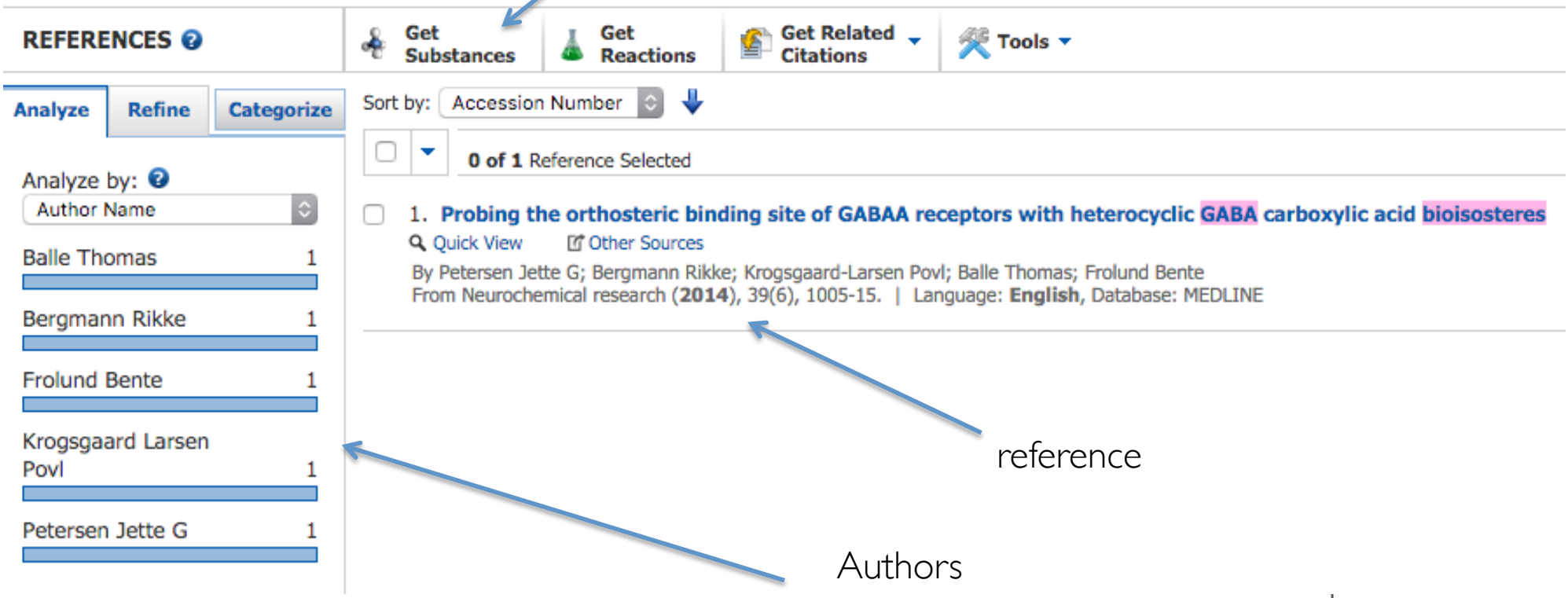
Refinement with the keyword "bioisosterism"

Example of a SciFinder related research

Answering:
"*Searching for GABA analogues in neurotrasmission*"

SciFinder®

www.scifinder.com



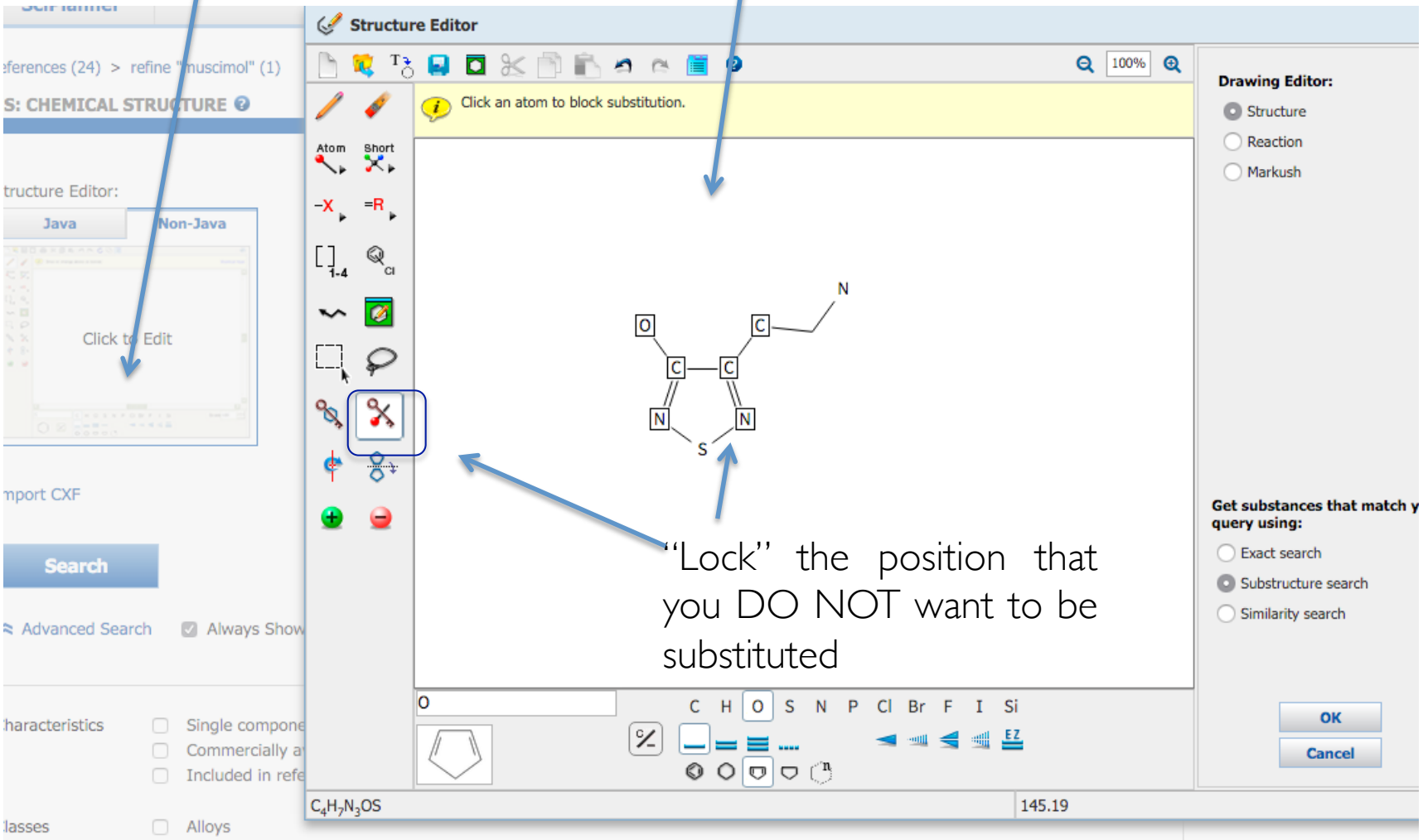
Example of a SciFinder related research

Answering:
Structure research

www.scifinder.com

Go on structure research

Write here your molecule



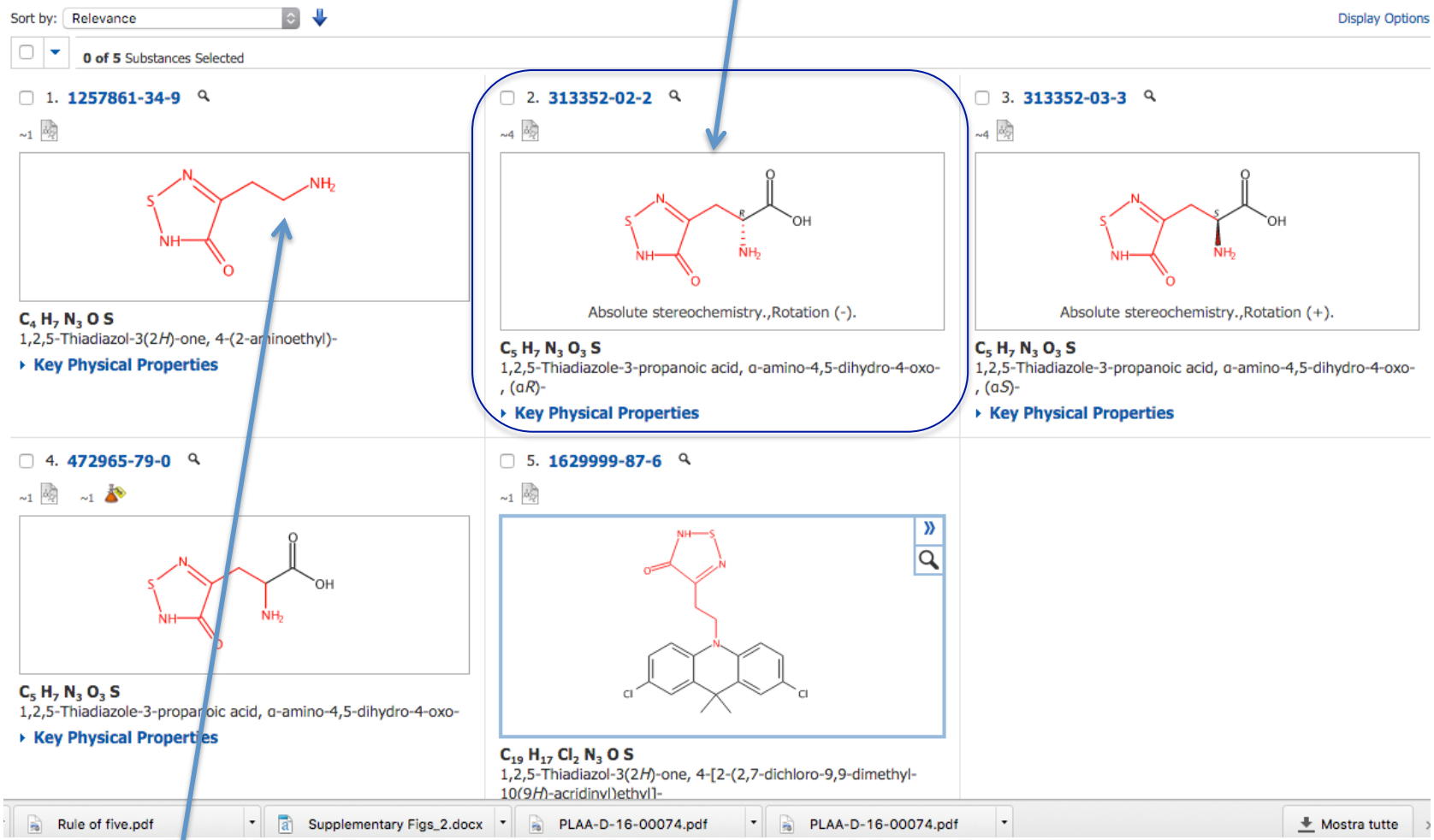
"Lock" the position that you DO NOT want to be substituted

Example of a SciFinder related research

Answering:
Structure research

www.scifinder.com

Go for the Glu analogue



We did not "Lock" this position

Example of a SciFinder related research

Answering:
Structure research

SciFinder®

www.scifinder.com

Be AWARE… predicted properties

CAS Registry Number 313352-02-2

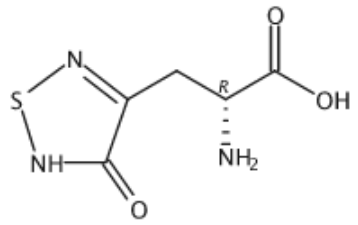
$C_5 H_7 N_3 O_3 S$

1,2,5-Thiadiazole-3-propanoic acid, α-amino-4,5-dihydro-4-oxo-, (α*R*)-

Molecular Weight
189.19

Density (Predicted)
Value: 1.94±0.1 g/cm3 | Condition: Temp: 20 °C Press: 760 Torr

pKa (Predicted)
Value: 1.97±0.10 | Condition: Most Acidic Temp: 25 °C

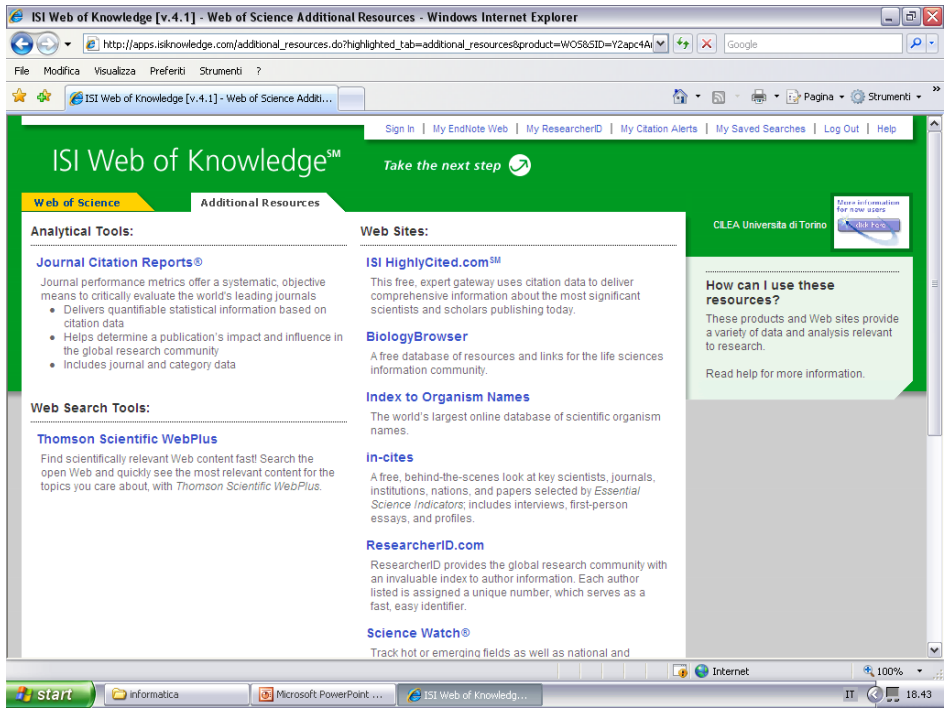


Rotation (-).,Absolute stereochemistry.

- PREDICTED PROPERTIES
- PREDICTED SPECTRA
- TARGET INDICATORS
- CAS REFERENCE ROLES
- ADDITIONAL DETAILS

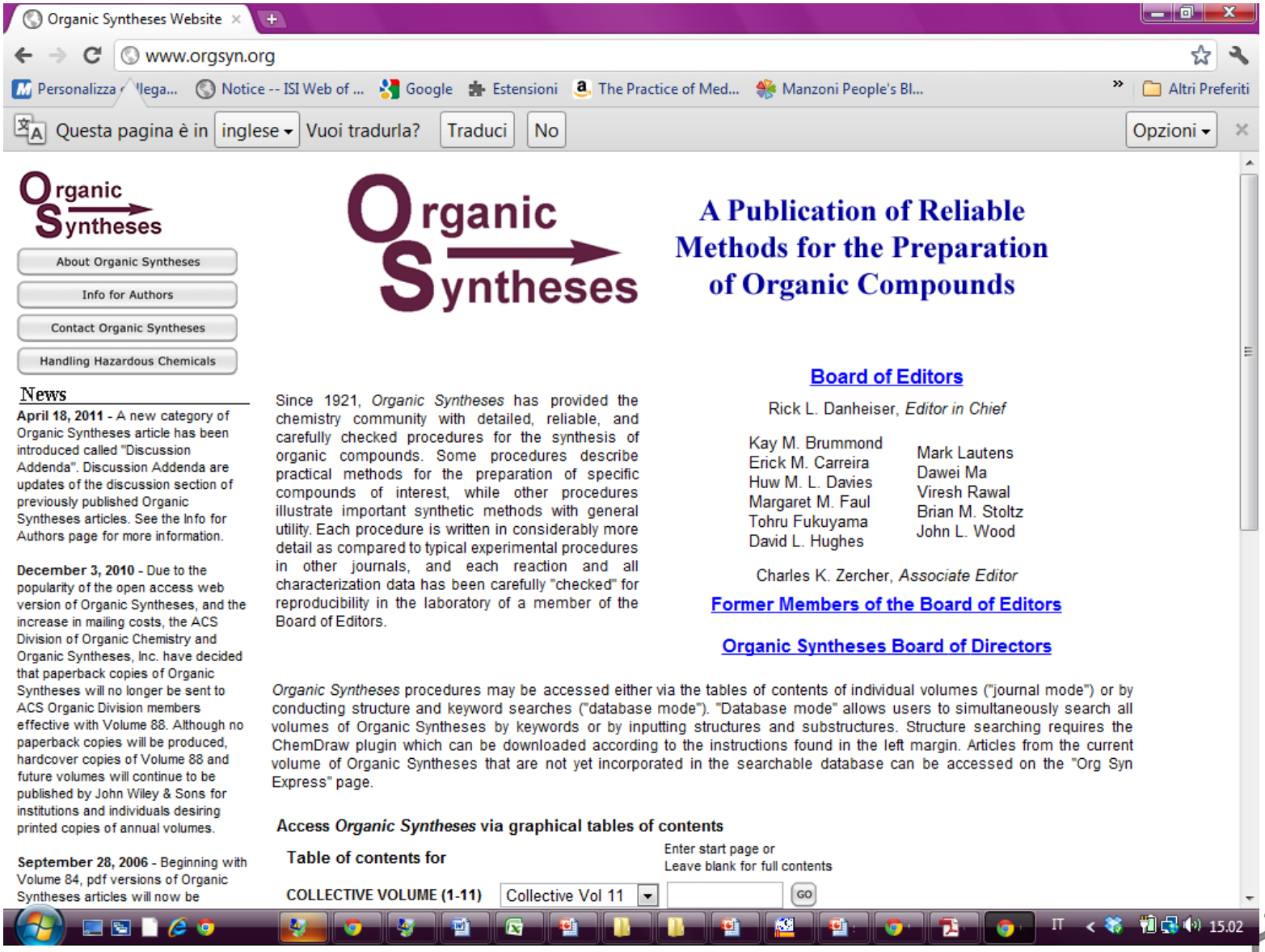
ISI Web of Science

L'Institute for Scientific Information (ISI) ha introdotto nel 2001 in rete il web ok knowledge, che è un sistema di segnalazione rapida dei documenti pubblicati in tutto il mondo dalle fonti primarie più importanti. Tale sistema è costituito da altri sottosistemi di alta utilità, tra cui: il Web of Science e il Journal Citation Reports.



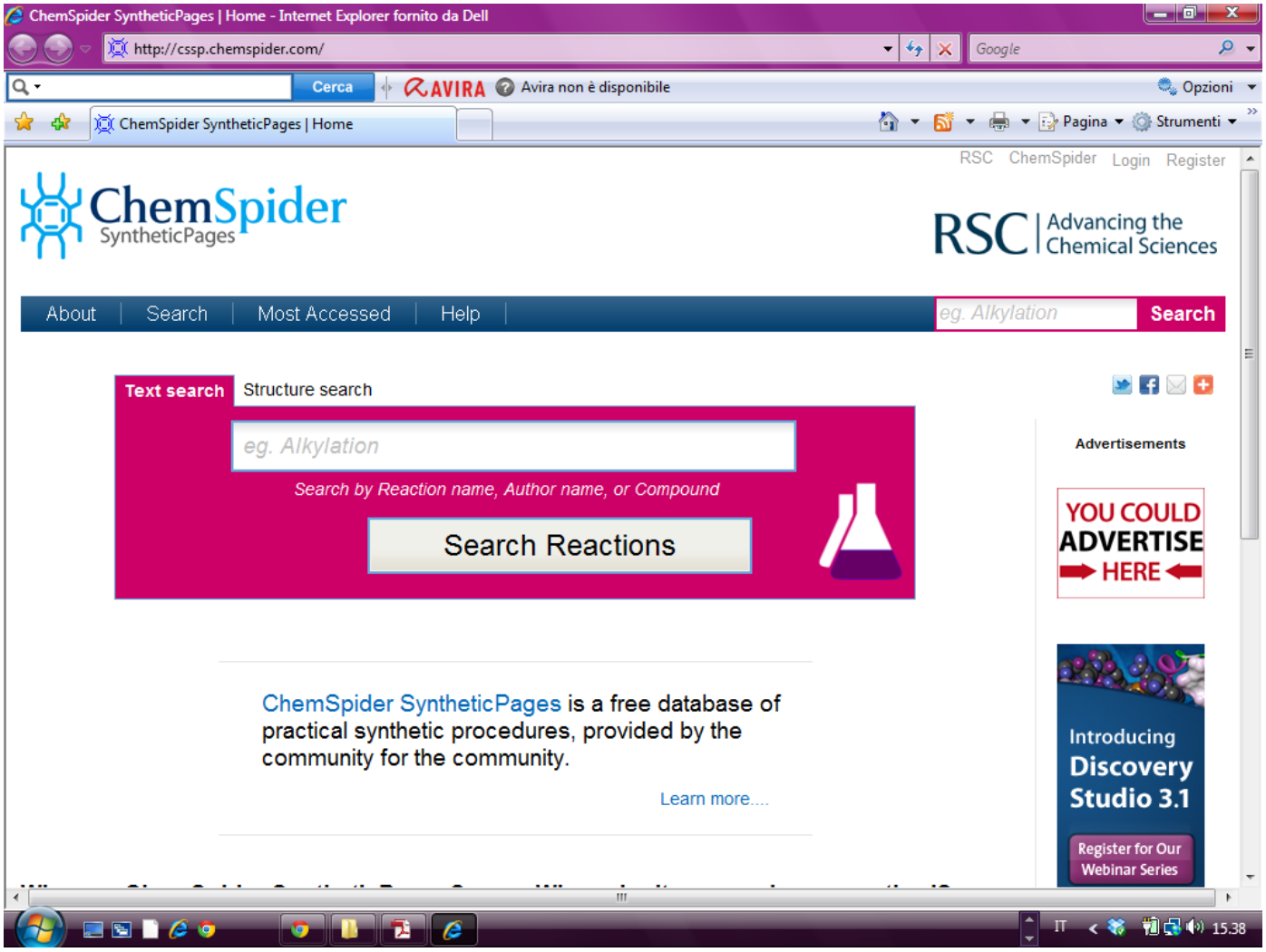
Property/Reactions search engines

http://www.orgsyn.org/



http://cssp.chemspider.com/

Property/Reactions search engines



Fund rising campaign

Someone that pay your research bill

- **University** based sources
  ex60%
- **Foundations** based sources
  San Paolo, CRT, Bill&Melinda Gates, …
- **European** based sources
  H2020, ITN, Marie Curie, …
- **Company** based sources
  Bayer, …
- ***Business Angels*** – seed accelerators
  BiovelocITA, AutoraTT, ..

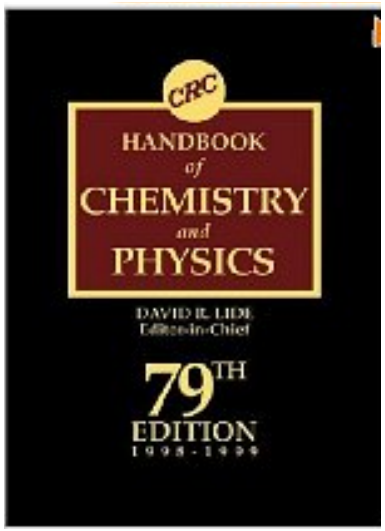
The Alchemist (N. C. Wyeth – 1937)

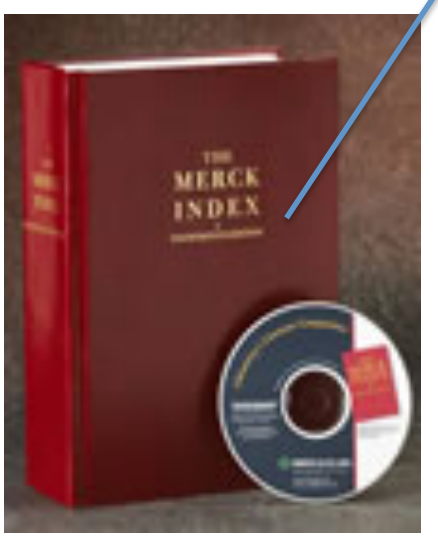
Other grey sources:

Manuals and Encyclopaedias

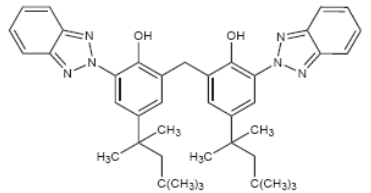
Manuals contain a significant amount of data scattered in diverse primary sources. Encyclopedias allow quick access to concise information. They are not updated to the latest data (eg .The Merck Index).

Good for properties….





1294. Bisoctrizole. [103597-45-1] 2,2′-Methylenebis[6-(2*H*-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol]; MBBT; Tinosorb M; Tinuvin 360. $C_{41}H_{50}N_6O_2$; mol wt 658.87. C 74.74%, H 7.65%, N 12.76%, O 4.86%. UV-A filter with dual mechanism of action. Photostable organic molecule with broad UV absorption; microfine structure causes light scattering and reflection. Prepn and use in light stabilizer formulations: N. Kubota, A. Nishimura, **EP 180992**; *eidem*, **US 4681905** (1986, 1987 both to Adeka Argus). Light stabilization of polymers: G. Rytz *et al.*, *Angew. Makromol. Chem.* **247**, 213 (1997). Skin photoprotection study: C. Gélis *et al.*, *Photodermatol. Photoimmunol. Photomed.* **19**, 242 (2003). HPLC determn in suncare formulations: C. G. Smyrniotakis, H. A. Archontaki, *J. Chromatogr. A* **1031**, 319 (2004). UV attenuating properties of microparticles: B. Herzog *et al.*, *J. Colloid Interface Sci.* **276**, 354 (2004).



Slightly yellow powder, mp 195°. Flash pt: >200°C. d^{20} 1.2. Vapor pressure (25°): 6×10^{-13} Pa. Soly at 20° (%w/w): water < 0.001; acetone 0.05; chloroform 100; *n*-hexane 0.03; methylene chloride 75; toluene 34. Absorption max (chloroform): 308, 349 nm (ε 31895). Absorption max (*n*-heptane): 348 nm (ε 31600).

USE: Light stabilizer in polymers and resins.

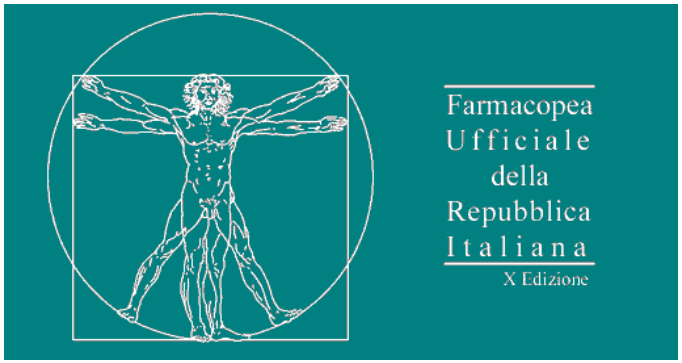
THERAP CAT: Ultraviolet screen.

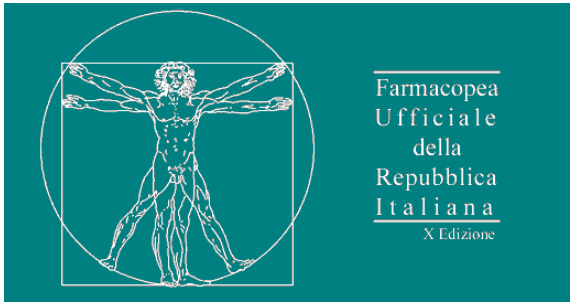
Other grey sources:

Manuals and Encyclopaedias

"La Farmacopea Ufficiale rappresenta la norma farmaceutica obbligatoria destinata ad assicurare, in una data entità politica, l'uniformità di contenuto, di composizione, di qualità e concentrazione dei principi attivi, nonché ad indicare i mezzi necessari al controllo tecnico ed analitico delle varie forme farmaceutiche"

La Farmacopea Ufficiale





CONTENUTO

CAPITOLI GENERALI

Apparecchiature, metodi generali fisici e chimicofisici

Identificazione

Reattivi

MONOGRAFIE

In certe monografie o altri testi, i termini "adeguato" o "appropriato" sono usati per qualificare un reattivo, microrganismo, un metodo, ecc.; se i criteri di adeguatezza non sono descritti nella monografia, l'adeguatezza stessa deve essere riconosciuta dall'Autorità competente.

1.2. ALTRE DISPOSIZIONI RELATIVE AI CAPITOLI GENERALI E MONOGRAFIE

Quantità. Nei saggi con limiti numerici e nei dosaggi, le quantità indicate, per l'esecuzione analitica, sono approssimate. La quantità realmente usata, che può differire per non più del 10 per cento da quella indicata, deve essere esattamente pesata o misurata; il risultato è calcolato in base a questa quantità esatta. Nei saggi dove il limite non è numerico, ma dipende usualmente dal confronto con il comportamento di una sostanza di riferimento nelle stesse condizioni, viene utilizzata la quantità indicata. I reattivi vengono utilizzati nelle quantità prescritte.

Le quantità sono pesate o misurate con una accuratezza corrispondente al grado di precisione indicato. Nel caso delle pesate, la precisione corrisponde a più o meno 5 unità dopo l'ultima cifra indicata (ad esempio 0,25 g deve essere interpretata come una quantità compresa tra 0,245 g e 0,255 g). Per la misura dei volumi, se la cifra dopo il punto decimale è zero o finisce con uno zero (per esempio 10,0 ml o 0,50 ml), si utilizza a seconda del caso una pipetta, un pallone tarato o una buretta; negli altri casi può essere impiegato un cilindro o una pipetta graduata. I volumi indicati in microlitri vengono misurati mediante una micropipetta o microsiringa.

E' tuttavia ammesso che, in certi casi, la precisione con la quale le quantità vengono indicate non corrisponda al numero di cifre significative indicato in uno specifico limite numerico. Le pesate e le misure vengono in questo caso effettuate con un sufficiente grado di accuratezza.

Apparecchi e procedure. La vetreria volumetrica soddisfa ai requisiti di Classe A delle appropriate Norme Internazionali stabilite dalla Organizzazione Internazionale di Normalizzazione.

Se non diversamente prescritto, le procedure analitiche vengono effettuate ad una temperatura compresa tra 15 °C e 25 °C.

Se non diversamente prescritto, i saggi comparativi vengono effettuati in tubi identici di vetro incolore, trasparente, neutro aventi un fondo piatto ed un diametro interno di 10 mm. Volumi uguali dei liquidi da comparare vengono esaminati secondo l'asse verticale dei tubi contro un fondo bianco o, se necessario, contro un fondo nero. L'esame viene effettuato con luce diffusa. Tutti i solventi impiegati in un saggio o dosaggio che prevede l'uso di un indicatore vengono preventivamente neutralizzati in presenza di quell'indicatore, a meno che non sia prescritto un saggio in bianco.

Bagno maria. Il termine "bagno-maria" significa un bagno di acqua bollente a meno che non venga indicata acqua ad un'altra temperatura. Possono essere usati altri metodi di riscaldamento a condizione che la temperatura sia vicina, ma non superiore ai 100 °C o alla temperatura prescritta.

Seccare e calcinare a massa costante. I termini "seccare a massa costante" e "calcinare a massa costante" significano che due pesate consecutive non differiscono per più di 0,5 mg; la seconda pesata viene effettuata dopo un ulteriore periodo di essiccamento o calcinazione appropriato alla natura e quantità del residuo.

Dove è prescritto l'essiccamento utilizzando una delle espressioni "in essiccatore" o "nel vuoto" esso viene effettuato usando le condizioni descritte in *2.2.32 Perdita all'essiccamento.*

REATTIVI

La realizzazione corretta delle procedure analitiche descritte nella Farmacopea e la attendibilità dei risultati dipende, in parte, dalla qualità dei reattivi usati. I reattivi sono descritti nel capitolo generale 4. Si assume che i reattivi utilizzati siano di qualità analitica; per alcuni reattivi sono inclusi nelle specifiche i saggi per determinare la loro adeguatezza.

SOLVENTI

Solventi. Il termine "soluzione", senza indicazione del solvente, indica una soluzione acquosa. Quando l'uso dell'acqua è prescritto o implicito per le procedure analitiche descritte nella Farmacopea o per la preparazione dei reattivi, l'acqua usata deve essere conforme alle specifiche della monografia *Acqua depurata (8)*. Il termine "acqua distillata" indica acqua depurata preparata mediante distillazione. Il termine "etanolo" senza altra qualificazione significa alcool contenente circa il 96 per cento *V/V* di etanolo (C_2H_6O). Altre diluizioni di etanolo sono indicate con il termine "alcool" seguito dall'indicazione della percentuale in volume di etanolo (C_2H_6O) richiesta.

Farmacopea Ufficiale della Repubblica Italiana
X Edizione

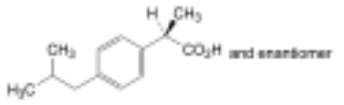
Prescrizioni generali

arco L. Lolli University of Torino (UniTO)

07/2002:0721

IBUPROFEN

Ibuprofenum



$C_{13}H_{18}O_2$ M_r 206.3

DEFINITION

(2*RS*)-2-[4-(2-Methylpropyl)phenyl]propanoic acid.

Content: 98.5 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white, crystalline powder or colourless crystals.

Solubility: practically insoluble in water, freely soluble in acetone, in methanol and in methylene chloride. It dissolves in dilute solutions of alkali hydroxides and carbonates.

IDENTIFICATION

First identification: *A*, *C*.

Second identification: *A*, *B*, *D*.

A. Melting point (*2.2.14*): 75 °C to 78 °C.

B. Dissolve 50.0 mg in a 4 g/l solution of *sodium hydroxide R* and dilute to 100.0 ml with the same alkaline solution. Examined between 240 nm and 300 nm (*2.2.25*), using a spectrophotometer with a band width of 1.0 nm and a scan speed of not more than 50 nm/min, the solution shows a shoulder at 258 nm and 2 absorption maxima, at 264 nm and 272 nm. The ratio of the absorbance measured at the maximum at 264 nm to that measured at the shoulder at 258 nm is 1.20 to 1.30. The ratio of the absorbance measured at the maximum at 272 nm to that measured at the shoulder at 258 nm is 1.00 to 1.10.

C. Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs.

Comparison: *ibuprofen CRS*.

D. Thin-layer chromatography (*2.2.27*).

Test solution. Dissolve 50 mg of the substance to be examined in *methylene chloride R* and dilute to 10 ml with the same solvent.

Reference solution. Dissolve 50 mg of *ibuprofen CRS* in *methylene chloride R* and dilute to 10 ml with the same solvent.

Plate: *TLC silica gel plate R*.

Mobile phase: *anhydrous acetic acid R*, *ethyl acetate R*, *hexane R* (5:24:71 *V/V/V*).

Application: 5 µl.

Development: over a path of 10 cm.

Drying: at 120 °C for 30 min.

Detection: lightly spray with a 10 g/l solution of *potassium permanganate R* in *dilute sulphuric acid R* and heat at 120 °C for 20 min. Examine in ultraviolet light at 365 nm.

Results: the principal spot in the chromatogram obtained with the test solution is similar in position, colour and size to the principal spot in the chromatogram obtained with the reference solution.

TESTS

Solution S. Dissolve 2.0 g in *methanol R* and dilute to 20 ml with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and colourless (*2.2.2*, *Method II*).

Angle of optical rotation (*2.2.7*): − 0.05° to + 0.05°. Dissolve 0.50 g in *methanol R* and dilute to 20.0 ml with the same solvent.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 20 mg of the substance to be examined in 2 ml of *acetonitrile R* and dilute to 10.0 ml with *mobile phase A*.

Reference solution (a). Dilute 1.0 ml of the test solution to 100.0 ml with *mobile phase A*.

Reference solution (b). Dissolve 20 mg of *ibuprofen CRS* in 2 ml of *acetonitrile R*, add 1.0 ml of a 0.06 g/l solution of *ibuprofen impurity B CRS* in *acetonitrile R* and dilute to 10.0 ml with *mobile phase A*.

Column:

- *size*: *l* = 0.15 m, Ø = 4.6 mm,
- *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase:

- *mobile phase A*: mix 0.5 volumes of *phosphoric acid R*, 340 volumes of *acetonitrile R* and 600 volumes of *water R*; allow to equilibrate and dilute to 1000 volumes with *water R*,
- *mobile phase B*: *acetonitrile R*,

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 25	100	0
25 - 55	100 → 15	0 → 85
55 - 70	15	85
70 - 75	15 → 100	85 → 0

Flow rate: 2 ml/min.

Detection: spectrophotometer at 214 nm.

Equilibration: for about 45 min with *mobile phase A*.

Injection: 20 µl.

System suitability: reference solution (b):

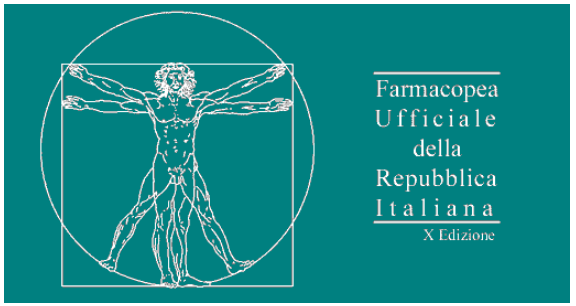
- *peak-to-valley ratio*: minimum of 1.5, where H_p = height above the baseline of the peak due to impurity B, and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to ibuprofen. If necessary, adjust the concentration of acetonitrile in *mobile phase A*.

Limits:

- *impurity B*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (b) (0.3 per cent),
- *any other impurity*: not more than 0.3 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.3 per cent),
- *total of all impurities apart from impurity B*: not more than 0.7 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.7 per cent),
- *disregard limit*: 0.05 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Impurity F. Gas chromatography (*2.2.28*): use the normalisation procedure.

Monographs D - R



Monografia

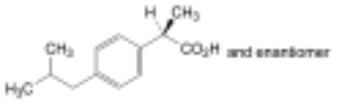
Ibuprofen

Marco L. Lolli *University of Torino* (UniTO)

07/2002:0721

IBUPROFEN

Ibuprofenum



$C_{13}H_{18}O_2$ M_r 206.3

DEFINITION

(2*RS*)-2-[4-(2-Methylpropyl)phenyl]propanoic acid.

Content: 98.5 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white, crystalline powder or colourless crystals.

Solubility: practically insoluble in water, freely soluble in acetone, in methanol and in methylene chloride. It dissolves in dilute solutions of alkali hydroxides and carbonates.

IDENTIFICATION

First identification: A.

Second identification: A, B, D.

A. Melting point (*2.2.14*): 75 °C to 78 °C.

B. Dissolve 50.0 mg in a 4 g/l solution of *sodium hydroxide R* and dilute to 100.0 ml with the same alkaline solution. Examined between 240 nm and 300 nm (*2.2.25*), using a spectrophotometer with a ba... width of 1.0 nm and a scan speed of not more than 50 nm/min, the solution shows a shoulder at 258 nm ... 2 absorption maxima, at 264 nm and 272 nm. The rati... the absorbance measured at the maximum at 264 nm ... that measured at the shoulder at 258 nm is 1.20 to 1.5... The ratio of the absorbance measured at the maximum at 272 nm to that measured at the shoulder at 258 nm is 1.00 to 1.10.

C. Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs.

Comparison: *ibuprofen CRS*.

D. Thin-layer chromatography (*2.2.27*).

Test solution. Dissolve 50 mg of the substance to be examined in *methylene chloride R* and dilute to 10 ml with the same solvent.

Reference solution. Dissolve 50 mg of *ibuprofen CRS* in *methylene chloride R* and dilute to 10 ml with the same solvent.

Plate: *TLC silica gel plate R*.

Mobile phase: *anhydrous acetic acid R, ethyl acetate R, hexane R* (5:24:71 *V/V/V*).

Application: 5 µl.

Development: over a path of 10 cm.

Drying: at 120 °C for 30 min.

Detection: lightly spray with a 10 g/l solution of *potassium permanganate R* in *dilute sulphuric acid R* and heat at 120 °C for 20 min. Examine in ultraviolet light at 365 nm.

Results: the principal spot in the chromatogram obtained with the test solution is similar in position, colour and size to the principal spot in the chromatogram obtained with the reference solution.

TESTS

Solution S. Dissolve 2.0 g in *methanol R* and dilute to 20 ml with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and colourless (*2.2.2, Method II*).

Angle of optical rotation (*2.2.7*): – 0.05° to + 0.05°. Dissolve 0.50 g in *methanol R* and dilute to 20.0 ml with the same solvent.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 20 mg of the substance to be examined in 2 ml of *acetonitrile R* and dilute to 10.0 ml with *mobile phase A*.

Reference solution (a). Dilute 1.0 ml of the test solution to ... *CRS* in ... dilute to ...

...

– *size*: *l* = 0.15 m, Ø = 4.6 mm,

– *stationary phase*: *octadecylsilyl silica gel for ...*

... *phosphoric acid R*, ... mixture of ... 1000 volumes ...

– *mobile phase B*: *acetonitrile R*,

Time	Mobile phase A	Mobile phase B
...	...	... (*V/V*)

Flow rate: 2 ml/min.

Detection: spectrophotometer at 214 nm.

Equilibration: for about 45 min with *mobile phase A*.

Injection: 20 µl.

System suitability: reference solution (b):

– *peak-to-valley ratio*: minimum of 1.5, where H_p = height above the baseline of the peak due to impurity B, and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to ibuprofen. If necessary, adjust the concentration of acetonitrile in *mobile phase A*.

Limits:

– *impurity B*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (b) (0.3 per cent),

– *any other impurity*: not more than 0.3 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.3 per cent),

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Impurity F. Gas chromatography (*2.2.28*): use the normalisation procedure.

Definizione

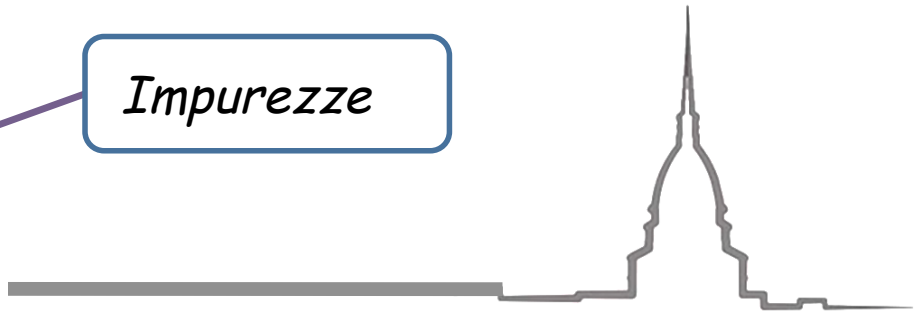
Caratteri

Identificazione

Monografia
Ibuprofen

Tests

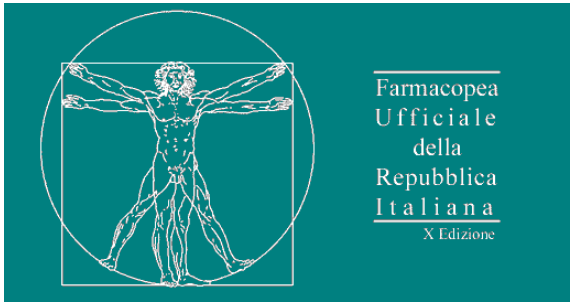
Impurezze



Marco L. Lolli *University of Torino* (UniTO)

Formula bruta

Formula di Struttura



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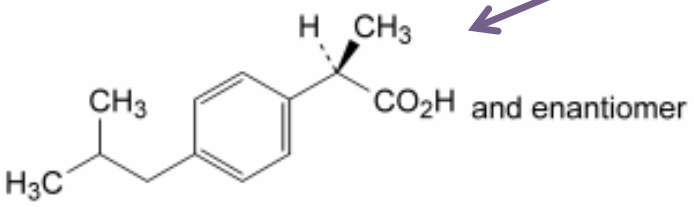

and enantiomer

$C_{13}H_{18}O_2$ M_r 206.3

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Solubility: practically insoluble in water, freely soluble in acetone, in methanol and in methylene chloride. It dissolves in dilute solutions of alkali hydroxides and carbonates.

IDENTIFICATION

First identification: A, C

TESTS

Solution S.

Angle of opt

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– *mobile p*

Monografia

Ibuprofen

PM

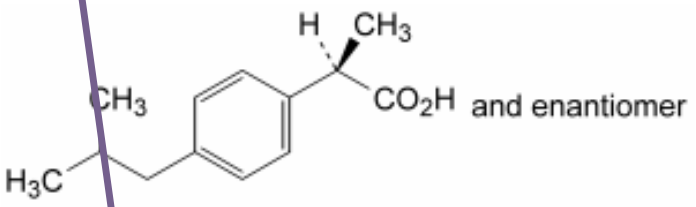
Nome IUPAC

Forma fisica

07/2002:0721

IBUPROFEN

Ibuprofenum



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First identification: A, C

TESTS

Solution S. I
with the sam

Appearance
colourless (2

Angle of opt
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Mobile phas
– *mobile ph*

Farmacopea Ufficiale della Repubblica Italiana
X Edizione

Monografia

Ibuprofen

Profilo di Solubilità

in dilute solutions of alkali hydroxide

IDENTIFICATION

First identification: A, C.

Second identification: A, B, D.

A. Melting point (*2.2.14*): 75 °C to 78 °C.

B. Dissolve 50.0 mg in a 4 g/l solution of *sodium hydroxide R* and dilute to 100.0 ml with the same alkaline solution. Examined between 240 nm and 300 nm (*2.2.25*), using a spectrophotometer with a band width of 1.0 nm and a scan speed of not more than 50 nm/min, the solution shows a shoulder at 258 nm and 2 absorption maxima, at 264 nm and 272 nm. The ratio of the absorbance measured at the maximum at 264 nm to that measured at the shoulder at 258 nm is 1.20 to 1.30. The ratio of the absorbance measured at the maximum at 272 nm to that measured at the shoulder at 258 nm is 1.00 to 1.10.

C. Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs.

Comparison: *ibuprofen CRS*.

D. Thin-layer chromatography (*2.2.27*).

Test solution. Dissolve 50 mg of the substance to be examined in *methylene chloride R* and dilute to 10 ml with the same solvent.

Reference solution. Dissolve 50 mg of *ibuprofen CRS* in *methylene chloride R* and dilute to solvent.

Plate: *TLC silica gel plate R*.

chromat

Mobile phas

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Injection: 2

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separatin
necessary
mobile ph

Identificazione (Prima e seconda)

Farmacopea Ufficiale della Repubblica Italiana X Edizione

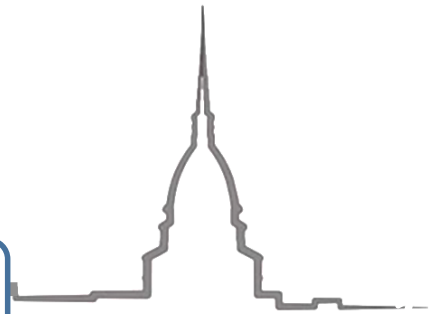
Monografia

Ibuprofen

Punto di fusione

Spettroscopie UV, IR

Cromatografia su strato sottile



University of Torino (UniTO)

Hydrochloric acid. *1043500.* [7647-01-0].
See *Concentrated hydrochloric acid (0002).*

Hydrochloric acid R1. *1043501.*
Contains 250 g/l of HCl.
Dilute 70 g of *hydrochloric acid R* to 100 m

Hydrochloric acid, brominated. *1043507.*
To 1 ml of *bromine solution R* add 100 ml of *hydrochloric acid R.*

Hydrochloric acid, dilute. *1043503.*
Contains 73 g/l of HCl.
Dilute 20 g of *hydrochloric acid R* to 100 ml with *water R.*

Hydrochloric acid, dilute, heavy metal-free. *1043509.*
Complies with the requirements prescribed for *dilute hydrochloric acid R* and with the following maximum contents of heavy metals:

CAS number

Reattivi

CAS number

Alcohol. *1002500.* [64-17-5].
See *Ethanol (96 per cent) R.*