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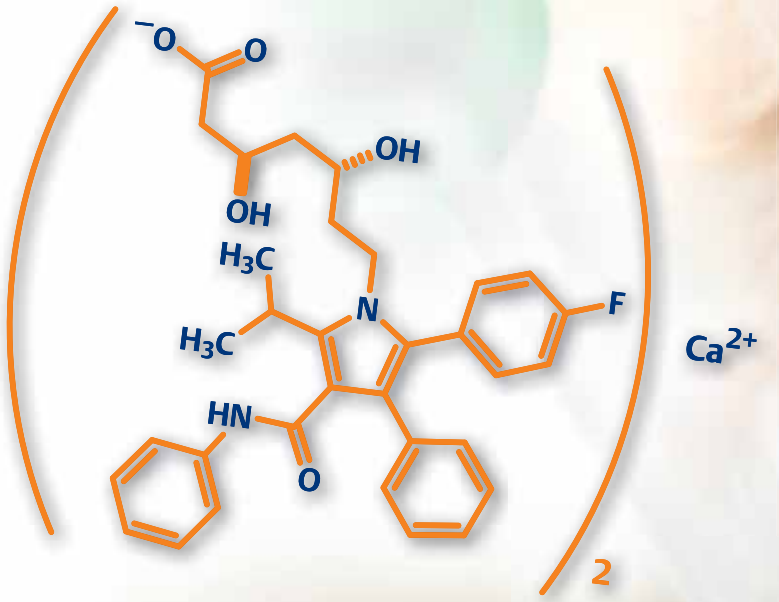
Pharmaceutical Substances

Syntheses• Patents• Applications

Approved APIs in focus



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Pharmaceutical Substances -

Pharmaceutical Substances is the first point of reference for any person wishing to screen information about drugs. Its online version provides ready access to syntheses, patents, and applications for more than 2400 active pharmaceutical ingredients (APIs), while the newly published print version focuses on newly approved APIs.

Since the work was first published in print in the 1970s the focus of the product has remained unchanged: Professors Axel Kleemann, Jürgen Engel, Bernhard Kutscher, and Dr. Dietmar Reichert present in a clear and concise manner highly evaluated information collected from all the relevant literature and commercial patent data. This includes synthetic routes and all intermediates for approved drugs from the six most important markets.

For more than 30 years, **Pharmaceutical Substances** has been the most authoritative resource for everyone involved in design, discovery, development, evaluation, and marketing of drugs. The structure searchable online version is updated biannually and is a standard reference in the chemical and pharmaceutical industry worldwide.

The 5th printed edition features the same highly evaluated content for the 1300 most relevant APIs. It is a handy add-on to the electronic version as well as an excellent stand-alone resource for the occasional user.

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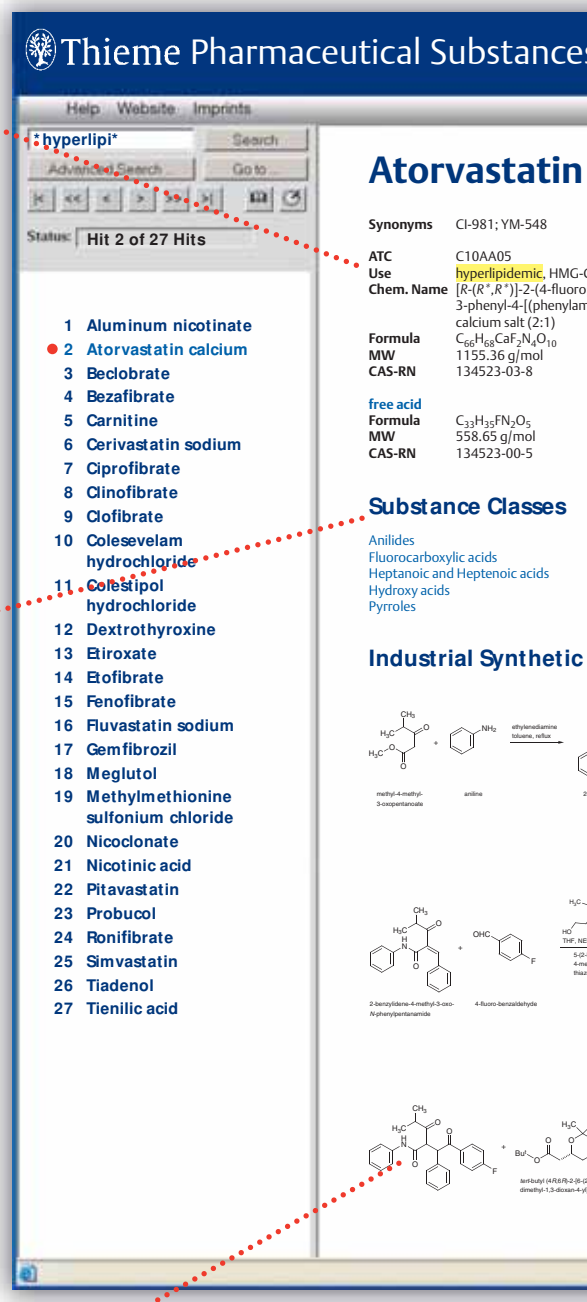
The International Nonproprietary Names (INN) of pharmaceutical substances form the title of each monograph. All the synonyms in use for the compounds are shown in the second line. Factual data, listed underneath the INN, include chemical name (written according to the IUPAC chemical substance naming convention), Anatomical Therapeutic Chemical (ATC) Codes, major uses, CAS and EINECS numbers, molecular formula (written in Hill System Order) and weight, and acute toxicity.

Clicking on one of the names in the Substance Class section provides access to all other drugs belonging to the same class. If enzymes, microorganisms, or plant or animal tissues are involved in a synthesis, they are also listed here and are linked to other syntheses in which they are involved.



Great care is taken by the authors to ascertain the synthetic route(s) used for industrial large-scale production of the drugs listed in **Pharmaceutical Substances**. A detailed description of the preparation of each substance is provided, including the synthesis of intermediates. In many cases, different synthetic routes are described, especially for the most economically important drugs.

* The content shown has been shortened for demonstration purposes.

– Evaluated for relevance

All substances referenced in the synthetic pathways are listed by their CAS number, molecular formula, and chemical and CAS index names to allow efficient searching for sources of supply. As all entries are text and structure searchable, this unique listing is also an essential tool for suppliers to find uses for their products and contract manufacturing organizations to find cooperation partners. Key Intermediates are highlighted with a blue background color.

s

calcium

CoA-reductase inhibitor
phenyl)-β,δ-dihydroxy-5-(1-methylethyl)-
hino)carbonyl]-1*H*-pyrrole-1-heptanoic acid

Intermediates (Excerpt*)

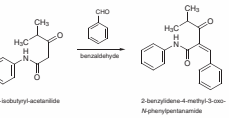
CAS-RN	Formula	Chem. Name	CAS Index Name
77-76-9	$C_5H_{12}O_2$	acetone dimethyl acetal	Propane, 2,2-dimethoxy-
95061-51-1	$C_{22}H_{20}O_3$	(*S*)-(+)-2-acetoxy-1,1,2-triphenylethanol	1,2-Ethanediol, 1,1,2-triphenyl-, 2-acetate, (S)-
41365-75-7	$C_7H_{17}NO_2$	3-aminopropionaldehyde diethyl acetal	1-Propanamine, 3,3-diethoxy-
62-53-3	C_6H_7N	aniline	Benzenamine
100-52-7	C_7H_6O	benzaldehyde	Benzaldehyde
4568-71-2	$C_{13}H_{16}ClNOS$	3-benzyl-5-(2-hydroxyethyl)-4-methylthiazolium chloride	—
125971-57-5	$C_{19}H_{19}NO_2$	2-benzylidene-4-methyl-3-oxo-*N*-phenylpentanamide	Pentanamide, 4-methyl-3-oxo-N-phenyl-2-(phenylmethylene)-
434935-49-6	$C_4H_7BrO_3$	(*S*)-4-bromo-3-hydroxybutanoic acid	—
540-88-5	$C_6H_{12}O_2$	*tert*-butyl acetate	Acetic acid, 1,1-dimethylethyl ester
125995-13-3	$C_{14}H_{27}NO_4$	*tert*-butyl (4*R*,6*R*)-2-[6-(2-aminoethyl)-2,2-dimethyl-1,3-dioxan-4-yl]acetate	1,3-Dioxane-4-acetic acid, 6-(2-aminoethyl)-2,2-dimethyl-, 1,1-dimethylethyl ester, (4R-cis)-
125971-94-0	$C_{14}H_{23}NO_4$	*tert*-butyl (4*R*,6*R*)-2-(6-cyanomethyl-2,2-dimethyl-1,3-dioxan-4-yl)acetate	1,3-Dioxane-4-acetic acid, 6-(cyanomethyl)-2,2-dimethyl-, 1,1-dimethylethyl ester, (4R-cis)-
125988-01-4	$C_{11}H_{17}NO_4$	*tert*-butyl 5(*R*)-hydroxy-6-cyano-3-oxohexanoate	Hexanoic acid, 6-cyano-5-hydroxy-3-oxo-, 1,1-dimethylethyl ester, (R)-

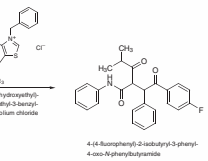
For the six most important markets trade names and the names of companies that produce and market the product are given. Years of introduction are added in those cases where they differ from the date the original patent was granted. A trade name displayed with wfm (withdrawn from market) beside it indicates that the pharmaceutical substance is no longer available on the market through this company under this trade name.

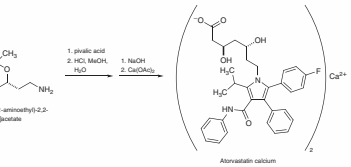
Trade Names & Vendors

Country	Trade Name	Vendor
D	Sortis	Parke Davis; Gödecke; Pfizer; Mack, Illert.
F	Tahor	Pfizer
GB	Lipitor	Pfizer
I	Lipitor	Warner-Lambert
	Torvast	Pfizer
	Totalip	Guidotti
J	Lipitor	Yamanouchi
USA	Lipitor	Parke Davis; Pfizer

Path (Excerpt*)







Formulations

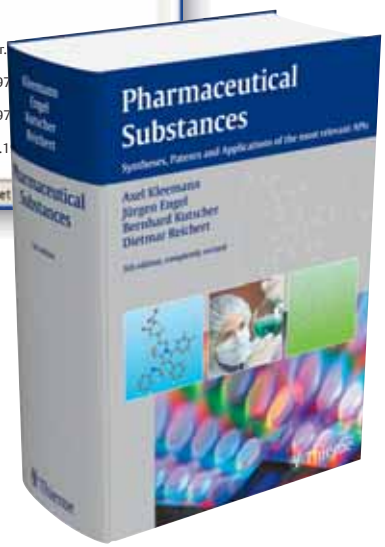
tabl. 5 mg, 10 mg, 20 mg, 40 mg, 80 mg

The most important pharmaceutical dosage forms are provided to enable the user to assess the order of magnitude a compound is needed in and thus helping to estimate its commercial value.

References (Excerpt*)

US 4 681 893 (Warner-Lambert; 21.7.1987; appl. 30.5.1986).
US 5 273 995 (Warner-Lambert; 28.12.1993; appl. 26.2.1991; USA-prior. 21.7.1989).
EP 409 281 (Warner-Lambert; appl. 23.1.1991; USA-prior. 21.7.1989, 26.2.1991).
DE 1 061 073 (Warner-Lambert; appl. 20.7.1990; USA-prior. 21.7.1989).

improved process:
WO 2 005 087 723 (Apotex Pharmachem; appl. 11.3.2005; CA-prior. 15.3.2004).
CA 2 460 935 (Apotex Pharmachem; appl. 15.3.2004).
a4 US 4 681 893 (Warner-Lambert; appl. 21.7.1987; USA-prior. 30.5.1986).
bc1 US 5 155 251 (Warner-Lambert; 13.10.1992; appl. 11.10.1991).
c1 US 5 103 024 (Warner-Lambert; 7.4.1992; appl. 17.10.1990).
US 6 433 213 (Warner-Lambert; 13.8.2002; appl. 2.12.1998, 16.6.2000; USA-prior. 19.12.1997).
US 6 596 879 (Warner-Lambert; 22.7.2003; appl. 11.6.2002; USA-prior. 19.12.1997, 2.12.1998).
US 6 962 994 (Warner-Lambert; 8.11.2005; appl. 11.4.2003; USA-prior. 19.12.1997, 11.6.2002).
c2 US 5 248 793 (Warner-Lambert; 28.9.1993; appl. 21.12.1992; USA-prior. 17.10.1, 27.12.1991).



The references in **Pharmaceutical Substances** give an overview of the patents that apply to the synthetic route, the dates of issue of the US patents, as well as application and priority dates. When applicable, patent references for alternative syntheses are listed as well as references to non-patent literature.

Online Version:

– All approved APIs
– Constantly updated
– Structure searchable

Print Version:

– The most relevant APIs
– Convenient one-volume format
– Fully updated in August 2008

"As a process research and development chemist, I appreciate the detailed reaction schemes which inform me on how every drug on the market can be made and the detailed references to not only the published literature but to patents."

Dr. Trevor Laird, Scientific Update LLP and Editor of Organic Process Research and Development.

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Print version

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Online version

System Requirements:

PC: Win NT 4.0 / 95 / 98 / 2000 / XP,
Microsoft Internet Explorer 5.0 and above,
Mozilla 5.0 (e.g. Firefox) and above

Mac: OS X 10.3.9 and above, Safari 2.0 and above

Optional Drawing Software: ISIS Draw 2.5, ChemDraw 9.0 and 10.0

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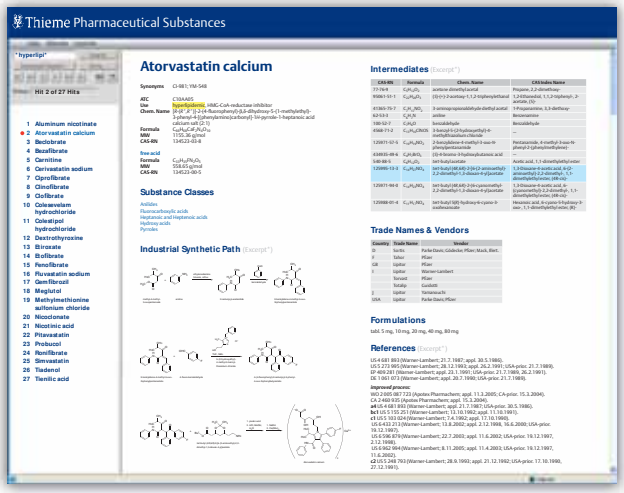
Designed for fast information retrieval

Online Version

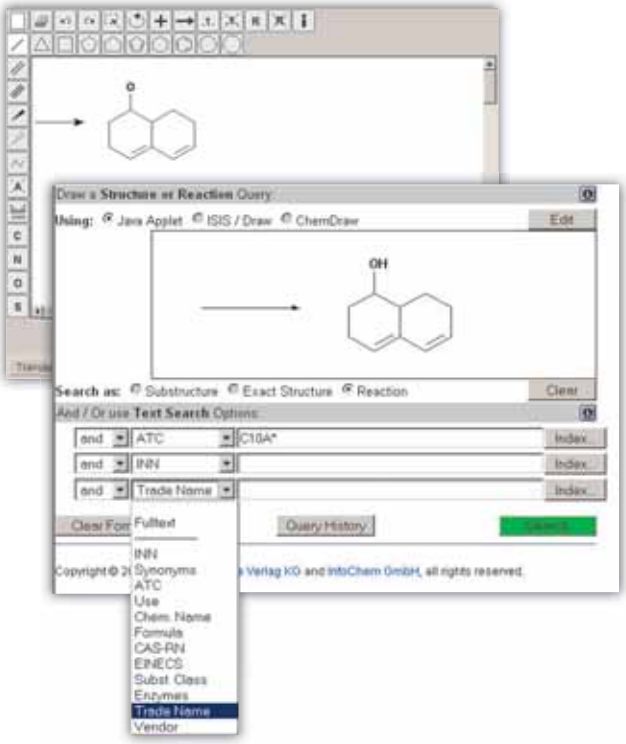
Pharmaceutical Substances makes use of the latest developments in information technology. Not only is this product easy to access using a standard browser interface, it also provides the user with search facilities that allow them to rapidly screen the data for relevant entries. Amongst the many innovations in the newly created electronic product is the ability to search for structures contained in the synthetic schemes.



The intuitive Quick Search permits the user to enter a query and search the entire text content of the database for relevant information. When entering a query, wild cards (*, ?, !) may also be used to achieve as broad a search as possible. The video buttons underneath allow efficient navigation in the list of hits and the history function gives access to queries performed earlier in the session.

Advanced Search Interface

The sophisticated Advanced Search interface allows refined and specific searches to be carried out. Both text and structure searches can be carried out together or individually. A built-in Java Applet allows structure queries to be carried out when ISIS/Draw and ChemDraw structure editors are not available. These detailed searches ensure that only the most relevant information is retrieved, saving time and providing an effective route to the database entries of interest.



InfoChem

The Pharmaceutical Substances reaction database is being constructed in collaboration with InfoChem.

Print Version

All compounds are organized alphabetically according to their International Nonproprietary Name (INN). For added ease of use the book features 4 additional indexes:

- Intermediates
- Trade Names
- Substance Classes
- Enzymes, Microorganisms, Plant and Animal Tissues

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