



Derwent

Drug File

An introduction to the Derwent Drug File

Edition 3

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Derwent User Guide

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An introduction to Derwent Information

Derwent, the leading specialist in scientific and patent information, has for over 50 years provided vital information to companies and research institutes across the world.

Derwent World Patents Index (DWPI) is unrivalled in its comprehensive, enhanced patent information covering more than 8 million separate inventions from 40 patent-issuing authorities including the USPTO, WIPO, EPO, Japanese and German patent offices.

Derwent's products are designed to meet the needs of not only the major multinationals, but equally importantly, to fulfil the information demands of smaller, more specialised organisations.

Used by a global audience, Derwent's information products give a comprehensive picture of technological innovations worldwide – providing critical advantage by highlighting new opportunities, identifying competitors and assisting R&D.

As part of The Thomson Corporation, Derwent works closely with global leaders in the information industry to guarantee customers access to unequalled business and technological intelligence.

An introduction to the Derwent Drug File

The Derwent Drug File (DDF) is a literature based information service which was conceived in 1964 to meet the demands of research based pharmaceutical companies.

The Derwent Drug File was developed together with the world's leading pharmaceutical companies to be the definitive source of drug literature and conference information.

DDF provides over a million references from the worldwide pharmaceutical literature covering all aspects of drug development, synthesis, evaluation, manufacture and use.

The highly focused coverage of the database ensures that all information retrieved from it is strongly drug oriented. In addition, the unique combination of biological and chemical information enables searchers to find data on all types of structure activity relationships.

Approximately 1,200 of the world's leading scientific and technical journals are scanned for relevant papers, together with conference proceedings and meeting reports.

Derwent's pharmaceutical drug specialists assess every journal article and conference report to ensure that the Derwent Drug File covers all the latest research in the drug field.

All articles giving significant information on novel or established drugs or vaccines are selected, in relation to treatment or prevention of disease, metabolism, toxicology, chemical synthesis, pharmaceuticals and analysis.

Every Derwent Drug File record is prepared by Derwent's team of experts to bring you:-

- original titles of all articles, or an English language translation
- full bibliographic data, including reprint address
- highly informative abstracts (~300 words) for every record outlining research methods and detailing results; frequently it is unnecessary to refer to the original article
- guaranteed Derwent-written English-language abstracts of articles originally in one of twenty-two different languages (approximately 19% of the database records are translations from foreign language journals) both chemical and biological information, together in one database
- chemical formulae (printed products only) which give an extra dimension to your information source

Who should use the Derwent Drug File?

The Derwent Drug File will be of particular interest to:

- Pharmaceutical companies
 - Drug development departments;
 - Clinical research departments;
 - Toxicology departments; Regulatory affairs departments; Marketing departments; Licensing departments
- Government agencies
- Hospitals
- Academic libraries
- Independent information consultants

The Derwent Drug File will be of particular interest to information managers, information scientists, research scientists, including chemists, medicinal chemists, pharmacologists, biologists etc. who work in the field of pharmaceuticals.

Availability of the Derwent Drug File

The Derwent Drug File is available in a variety of media – printed booklets, online, CD-ROM, Internet and diskette.

■ Printed Form

The DDF abstracts are classified in broad subject headings called Thematic Groups, or into 54 specific drug-related sections called Profiles.

Every week Derwent publishes Profile booklets for each of the 54 profile numbers; Thematic booklets for 4 of the 6 thematic groups; and Abstracts and Alerting Journals containing all the summary abstracts.

■ Online

The DDF database is available online through Datastar, Dialog, STN, Ovid PayGo and DIMDI. The database is made up of three separate files:-

Current File – This is the major DDF file and contains data from 1983 to date.

Backfile – This covers the period from the start of the service in 1964 up until 1982.

Registry File – This is a companion file to the DDF current file and is designed to be used in combination

with it. A record is created for every compound on its first occurrence in the main ongoing file.

■ CD-ROM

The DDF CD-ROM contains data from 1983 to date. The CD-ROM runs under SilverPlatter software, is fully text searchable and also contains images of formulae and tables of results.

■ Ovid

The DDF database is available via Ovid Online, containing data from 1964 to date. It is fully text searchable and also contains images of formulae and tables of results

■ Discovery

The DDF database is available via Discovery, containing data from 1964 to date. It is fully text and structure searchable.

The table below summarises the online availability of the Derwent Drug File.

HOST	CURRENT FILE 1983-PRESENT	BACKFILE 1964-1982	REGISTRY FILE
DATASTAR	DDFU (Subscribers)	DDBF (Subscribers) DDNS (Non-subscribers)	DDRR
DIALOG	912 (Subscribers) 377 (Non-subscribers)	913 (Subscribers) 376 (Non-subscribers)	911 (Subscribers) 375 (Non-subscribers)
STN	DRUGU (Subscribers; Literature and Registry segments combined) DDFU (Non-subscribers)	DRUGB (Subscribers) DDFB (Non-subscribers)	DRUGU (Subscribers; Literature and Registry segments combined)
DIMDI	DW83 (Subscribers; 1983-present) DW90 (Subscribers; 1990-present) DD83 (Non-subscribers; 1983-present) DD90 (Non-subscribers; 1990-present)	DH64 (Non-subscribers)	

Why use the Derwent Drug File?

- Guaranteed abstract in English for every record:

No cluttering of database with routine references repeating information already published elsewhere.
- Designed by and especially for the pharmaceutical industry:

DDF Abstracts are sufficiently detailed to be used as substitutes for the original article and are acceptable for regulatory bodies. Thus you can save money on journal subscription costs, document ordering, translation costs etc.
- Save time by searching a focused database:

The only database which focuses specifically on all aspects of pharmaceutical drugs.

The only drug file which contains comprehensive searchable chemical information.
- Worldwide literature coverage which is wider than most libraries:

Information for the database is compiled from 1,200 international journals and international conferences.
- The quality of Derwent's information is unbeatable:

Every record contains an abstract (other similar services have abstracts for approximately only 60% of their records).

Each abstract has been written by a Derwent subject specialist and provides information on methods used, results obtained and conclusions drawn.
- Abstracts available within a few weeks of publication of the original article
- Derwent Drug File printed products, DDF on STN and DDF on Discovery also includes chemical structures
- Precise indexing, thus precise retrieval without false drops – cost and time efficient
- Comprehensive classification and indexing – choice of very specific or very broad searching
- Drug and disease roles make specific searching easier and more efficient

Derwent Drug File – Profile Definitions

Each record in the Derwent Drug File is classified by drug related subject areas using one or more *Profile Numbers*. The Profile Numbers are used to define the printed Profile Booklets and for classification purposes in the online database and on the CD-ROM.

The Profile Numbers and their definitions follow.

Definition	Number	Description
Adverse Reactions	35	Papers reporting adverse reactions to drugs in humans.
Analgesics, Antipyretics and NSAID's	43	Pharmacology and therapeutic use of analgesics, antipyretics and NSAID's.
Anesthetics	45	Pharmacological and clinical evaluations of local and general anesthetics and premedication (routine anesthesia is not included).
Animal Toxicology	34	Toxicity of drugs in animals including LD50's.
Antiallergics	3	Pharmacology and therapeutic uses of H1 antagonists and antianaphylactics; therapy of allergy and hypersensitivity.
Antiarrhythmics	57	Pharmacology and therapeutic use of antiarrhythmic agents.
Antibiotics	6	All aspects of antibiotics, other than antitumor activity.
Antimicrobials in-vitro	23	In-vitro studies of production, evaluation, etc. of antimicrobial agents involving microorganisms other than viruses.
Antiseptics	54	Pharmacology and therapeutic use of antibacterials other than antibiotics (see Profile 6). Includes animal models.
Biological Response Modifiers	50	Pharmacological and clinical studies of immunomodulators, lymphokines and cell products in cancer biology and immunotherapy.
Cancer Chemotherapy – Clinical	51	Studies of antitumor agents in humans.
Cancer Chemotherapy – Non Clinical	52	Studies of antitumor agents in animals and animal or human tissue in-vitro.

Definition	Number	Description
Cardiants	56	Pharmacology and therapeutic use of drugs (e.g. coronary vasodilators) stimulating the heart.
Clinical Trials	64	Papers describing clinical trials of any drug.
Corticosteroids	46	Pharmacology, metabolism and therapeutic use of glucocorticoids, mineralocorticoids, ACTH and their antagonists.
Dermatological Agents	36	Pharmacological and therapeutic aspects of drugs acting on the skin.
Drug Analysis and Methodology	70	Chemical, physicochemical, serological and biological methods for assay and evaluation of drugs. Methodology of drug screening.
Drug Delivery Systems	65	Studies of osmotic pumps, controlled release systems, prodrugs, drug targeting, etc.
Drug Interactions	66	Reports of interactions (beneficial or deleterious) between drugs in-vitro or in-vivo.
Drug Receptors	63	All aspects of drug receptors.
Drugs acting on Bone and Joints	24	Pharmacology and therapeutic use of drugs affecting diseases of bones, joints and muscles, e.g. antirheumatics.
Drugs acting on Endogenous Compounds	22	Effects of drugs on mammalian intermediary metabolism. Includes metabolism of catecholamines but not drugs, hormones, vitamins or nucleic acids.
Drugs acting on Enzymes	14	Effects of drugs, including inhibitors, on enzymes in-vitro and in-vivo.
Drugs acting on the Kidney	39	Pharmacology and therapeutic use of diuretics and other drugs acting on the kidney and urinary system.
Drugs acting on the Respiratory System	33	Pharmacology and therapeutic uses of drugs acting on the respiratory system.

Definition	Number	Description
Drugs affecting the Autonomic Nervous System and Neurotransmitters	60	Parasympathetic and sympathetic drugs, neurotransmitters and their antagonists.
Drugs affecting the CNS and Motor System	59	Anticonvulsants, sedatives, analeptics, antiparkinsonians, relaxants, neuromuscular blockers and their antagonists.
Drugs in Children and the Elderly	67	All aspects of drug use in children or in the elderly.
Drugs in Fertility	15	Contraceptives and other drugs acting on the mammalian reproductive system. Drugs used in obstetrics and gynecology.
Drugs in Molecular Biology	27	Effects of drugs on nucleic acid metabolism, cell replication, cytogenetics, etc.
Fungicides, Protozoacides and Anthelmintics	55	Pharmacology and therapeutic use of antiinfective agents other than antibacterials and virucides. Includes animal models and ectoparasites.
Gastrointestinal Drugs	16	Pharmacology and therapeutic use of drugs acting on the gastrointestinal system (H ₂ antagonists and other antiulcer agents, antidiarrheics, antiemetics, etc.).
Hematological Agents	18	Pharmacology and therapeutic use of drugs affecting hemostasis (e.g. anticoagulants, antiaggregants, thrombolytics, hemostatics).
Immunopharmacology	20	Pharmacology and therapeutic effects of drugs on humoral and Immunotherapy and cellular immunity including transplantation, and vaccines.
Insulin, Glucagon and Diabetics	12	Pharmacology, metabolism and therapeutic uses of insulin, glucagon and antidiabetic agents. Therapy of diabetes mellitus.

Definition	Number	Description
Medicinal Chemistry	71	Chemistry, especially synthesis, of pharmacologically active compounds.
Mutagenic, Carcinogenic and Teratogenic Drugs	68	Studies of mutagenic, carcinogenic and teratogenic effects of drugs in man or animals.
Narcotics and Opioids	44	Pharmacology and therapeutic uses of narcotics, opioids and their antagonists.
New Drugs	72	Papers reporting for the first time any named drug or compound given a code number (trial preparation).
ORL Drugs	61	Pharmacology and therapeutic use of drugs acting on the ENT system.
Ophthalmological Drugs	62	Pharmacology and therapeutic use of drugs acting on the eye.
Peptide and Thyroid Hormones	49	Pharmacology, metabolism and therapeutic use of peptide hormones (except insulin and glucagon) and thyroid hormones.
Pharmaceutics	29	Preparation, formulation and examination of pharmaceutical products. Influence of dosage form on bioavailability, etc.
Pharmacokinetics	8	Biopharmaceutics/pharmacokinetics and metabolism of drugs.
Prostaglandins and Leukotrienes	48	Pharmacology, metabolism and therapeutic use of prostaglandins, thromboxanes, leukotrienes and their antagonists, unless used as antiinflammatories (see Profile 43).
Psychotropic Agents	32	Pharmacological and therapeutic aspects of psychotropic drugs.
Review of Drugs	69	Papers reviewing chemistry, pharmaceutics, pharmacokinetics, pharmacology, therapeutic use, etc. of drugs.

Definition	Number	Description
Sex Hormones and Analogs	47	Pharmacology, metabolism and therapeutic use of androgens, estrogens, progestogens and their antagonists. Includes anabolic steroids.
Structure-Activity	38	Correlation between chemical structure and biological activity of drugs.
Therapy of Infection	53	Clinical application of drugs in the treatment of infectious diseases.
Trial Preparations	73	Any paper describing the evaluation of a drug identified by a code number, including the first and all subsequent mentions of such drugs, until they are named.
Vasoactive Drugs	58	Pharmacology and therapeutic use of drugs affecting the vascular system (e.g. hypotensives, antiarteriosclerotics, peripheral vasodilators).
Virucides	41	Pharmacology and therapeutic use of antiviral drugs.
Vitamins	42	Pharmacology, metabolism and therapeutic use of vitamins and their antagonists.

Derwent Drug File – Thematic Groups and their Definitions

Each Derwent Drug File abstract is also classified using one or more broad subject headings called Thematic Groups. The Thematic Groups are searchable online or on the CD-ROM using either the Group letter or the Definition.

Groups B, C, M, and P and T are the most important and a weekly printed journal is published for these; groups T, A, E, G, S, N and V are used for classification purposes only.

Group	Definition	Description
B	BIOCHEMISTRY	and ENZYMOLOGY, including BIOPHYSICS, MOLECULAR BIOLOGY, METABOLISM (except for drug, vitamin, electrolyte, catecholamine and hormone metabolism), and metabolic disorders (except for vitamin and hormone disorders).
C	CHEMISTRY	organic and inorganic compounds, their synthesis, isolation, determination of structure.
M	MICROBIOLOGY	viruses, bacteria, fungi, algae, protozoa; infectious diseases including experimental infection; pharmacology and clinical application of chemotherapeutic agents (antibiotics antiseptics, disinfectants, sulfa drugs, etc.); technical fermentation.
N	NUTRITION	and feeding, food and feedstuffs, additives flavors, antioxidants, colors, preservation (not vitamins).
P	PHARMACOLOGY	and PHYSIOLOGY, experiments on animals and isolated organs, not covered by Thematic Groups B, E, M, N, V. Also used for the pharmacology of hormones and steroids but not antimicrobials.
T	THERAPEUTICS	pharmacotherapy (with Thematic Groups B, E, M, N, V assigned as required).
A	ANALYSIS	qualitative and quantitative; chemical, physical, physicochemical, biological and microbiological analysis.

Group	Definition	Description
E	ENDOCRINOLOGY	pharmacology of and therapy with natural and synthetic hormones, hormone-like compounds and their antagonists.
G	GALENICS	preparation and examination of pharmaceutical forms of drugs and packaging.
S	ADVERSE EFFECTS	and TOXICOLOGY, side effects; agranulocytosis; chronic, subacute and acute toxicity; radiolesion; embryopathy.
V	VITAMINS	pharmacology of and therapy with natural and synthetic vitamins, vitamin-like compounds and their antagonists.

Analysis of coverage

DDF covers the entire drug development process from synthesis to clinical trial. This makes it an essential source for information on all aspects of drugs:-

analysis	metabolism
mechanism of action	pharmacokinetics
adverse effects	drug comparisons
animal studies	biochemistry
interactions	pharmacology
toxicology	trial preparations
treatment of diseases	clinical studies

DDF coverage is truly international, with journals sourced from publishers in over 40 countries. The journals are selected through liaison with worldwide representatives of the pharmaceutical industry. The current coverage of nearly 1200 titles represents those journals in which virtually all relevant drug development is disclosed.

A major feature of DDF is the extensive conference coverage which together with the literature coverage provides a comprehensive picture of the state-of-the-art in pharmaceutical research and development.

The current database (1983-present) comprises over 840,000 records in total. The backfile (1964-1983) contains over 896,000 records. The companion registry file contains over 76,500 compounds of pharmaceutical use.

Every year approximately 50,000 new entries are added to the database.

Summary of the fields in the Derwent Drug File

Field	Definition
Accession Number	a unique number for every record in the database
Accession Year	when the record was added to the database
Title of research paper	original authors' title or English language translation
Author(s)	surname and initials of up to 10 authors
Language	original language of the article
Location	city, state, country location where the work took place
Reprint address	as given on the original paper and email
Corporate Affiliates	company, university, research institute etc.
Journal Name	standard abbreviations used
CODEN	international standard
ISSN number of journal	international standard
Publication year	year when the original article was published
Abstract	approximately 300 words, written by Derwent experts
Abstract summary	contains summary of the paper, plus qualitative data
Abstract extension	contains details of methods and results
Section Headings	broad subject groups (the Thematic Groups)
Classification Codes	classification into drug related topics (by Profile Number)
Common terms	indexing terms which apply to the entire document
Link terms	drug-specific indexing terms
CAS Registry Number	included where available

The companion file containing chemical and pharmacological information, the Derwent Drug Registry File, features the following fields:-

Field	Definition
Accession number	unique number for every record in the database
Derwent Drug Registry Name	unique identifier for a drug
Derwent Drug Name	preferred name for the drug e.g. INN
CAS Registry Number	included where available
Classification terms	activities of the drug
Sub-structure terms	chemical substructure keywords which define the drug - structure searchable on STN

Field labels may vary slightly according to the online host.

Sample Records

Example of typical records from the Derwent Drug File online database on STN and Dialog and from a DDF profile booklet are shown.

Dialog record

(c) 1999 DERWENT INFO LTD. All rts. reserv.
00860566 DERWENT ACCESSION NUMBER: 1999-45567
Postinoculation PMPA treatment, but not preinoculation immunomodulatory therapy, protects against development of acute disease induced by the unique simian immunodeficiency virus SIVsmmPBj.
Hodge S; de Rosayro J; Glenn A; Ojukwu I C; Dewhurst S; McClure H M; Bischofberger N; Anderson D C; Klumpp S A; Novembre F J
Univ.Rochester Yerkes-Region.Primate-Res.Cent. Univ.Atlanta Gilead (Rochester, N.Y., Atlanta, Ga.; Foster City, Cal., USA)
J.Virol. 73, No. 10, 8630-39, 1999
CODEN: JOVIAM ISSN: 0022-538X LANGUAGE: English RECORD TYPE: Abstract
REPRINT ADDRESS: Yerkes Regional Primate Research Center, 954 N. Gatewood Rd., Atlanta, GA 30322, U.S.A. (F.J.N.). (e-mail: fnovembr@rmy.emory.edu).
ABSTRACT:
A study was carried out to investigate the effect of immunosuppression and antiretroviral treatment in macaques with acute disease induced by the simian immunodeficiency virus (SIVsmmPBj). Suppression of the immune system with s.c. FK-506 (Prograf, tacrolimus; Fujisawa) prior to viral inoculation did not protect animals from acute SIVsmmPBj infection. However, s.c. treatment with the antiretroviral agent (R)-9-(2 - phosphonomethoxypropyl)adenine (PMPA; Gilead) protected against acutely lethal disease when given a few days after viral infection. The study demonstrates that the SIVsmmPBj model is useful for testing vaccines and other treatments.
EXTENDED ABSTRACT:
Methods
Juvenile pig-tailed macaques were inoculated i.v. with a high dose of SIV derived from the PBj6.6 molecular clone. Some animals were treated with FK-506 (0.75 mg/kg) (given on days -2 and -1 before viral inoculation and continued every other day thereafter). Other animals were treated with PMPA (30 mg/kg/day) (beginning on day 3 or 5 after infection and continued until day 14 after infection).
Results
FK-506 did not prevent acute infection and all animals died 10 days after viral inoculation. However, FK-506 may have had a partial effect on SIVsmmPBj induced immune activation as animals treated with FK-506 had lower levels of virus, CD25+ cells and FasL expressing cells in the ileum and colon. In animals treated with PMPA, there were no

signs of acute disease. Virus could not be isolated from PBMC of macaques that received PMPA beginning 3 days post-infection. When PMPA was started 5 days after infection, a less dramatic antiviral effect was observed. (E83)

SPECIAL FEATURES: 4 Fig. 5 Tab. 41 Ref.

COMMON TERMS:

IN-VIVO -FT; MACAQUE -FT; I.P. -FT; SIV-VIRUS -FT; LAB.ANIMAL -FT; MONKEY -FT; INJECTION -FT; VIRUS -FT; LEUKOVIRUS -FT

LINK TERMS:

01; TACROLIMUS -PH; PROGRAF -PH; FUJISAWA -FT; FK-506 -RN; IMMUNOSUPPRESSIVE -FT; IMMUNOSUPPRESSIVES -FT; PH -FT;*01*; 104987-11-3 *02*; PMPA -PH; GILEAD -FT; PMPA -RN; VIRUCIDE -FT; VIRUCIDES -FT; REVERSE-TRANSCRIPTASE-INHIBITORS -FT; PH -FT

CAS(R) REGISTRY NUMBERS: *01* 104987-11-3

SECTION HEADINGS: Immunological (20); Virucides (41); Biol. Response Modifiers (50)

THEMATIC GROUPS: M (Microbiology); P (Pharmacology)

STN record

L1 ANSWER 11 OF 630 DRUGU COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-34705 DRUGU P
TI Preclinical evaluation of PEG-L-asparaginase for pancreatic cancer.
AU Denis L J; Izbicka E; Davidson K; Lawrence R; Marty J; Barrera H; Medina L; Moore R; Weitman S; Von Hoff D D
CS Cancer-Therapy-Res.Cent.San-Antonio
LO San Antonio, Tex., USA
SO Proc.Am.Assoc.Cancer Res. (40, 90 Meet., 343-44, 1999)
ISSN: 0197-016X
AV Institute for Drug Development, Cancer Therapy and Research Center, San Antonio, TX 78245, U.S.A.
LA English
DT Journal
AB The aim of this study was to evaluate a polyethylene glycol modified L-asparaginase (PEG-L-ASNase, Oncaspar) in combination with gemcitabine in vitro and in vivo using mice. PEG-L-ASNase demonstrated significant inhibition of 3 human pancreatic cell lines in vitro and an additive effect was observed with gemcitabine. PEG-L-ASNase and gemcitabine exhibited additive tumor growth inhibition in the murine xenograft model. In conclusion, these data indicate that PEG-L-ASNase is a promising ***new*** ***drug*** formulation for the treatment of pancreatic cancer and warrants further study particularly in combination with gemcitabine. (conference abstract: 90th Annual Meeting of the American Association for Cancer Research, Philadelphia, Pennsylvania, USA, 1999).
ABEX Methods MiaPaCa human pancreatic cancer cells were implanted into nude mice and PEG-L-ASNase (12.5 IU/g or 25 IU/g on day 1 i.p.) and gemcitabine (80 mg/kg on days 1, 4, 7 and 10 i.p.) were administered alone or in combination. Results Tumor growth inhibition as compared to untreated controls was 59%, 63.5% and 85.9% for PEG-L-ASNase alone, gemcitabine alone and PEG-L-ASNase plus gemcitabine. Higher doses of PEG-L-ASNase did not induce greater inhibition. In vitro studies revealed 61% and 100% inhibition of PANC-1 and MiaPaC human pancreatic cell lines by 1.0 IU/ml PEG-L-ASNase and 51% inhibition of the BxPC-3 cell line when exposed to 10 IU/ml. IC50 values determined by MTT assay were 0.13 and 0.25 IU/ml for PEG-L-ASNase against MiaPaCa and PANC-1 cells respectively.
(JL)
SH P Pharmacology
CC 52 Chemotherapy - non-clinical
65 Drug Delivery
CT PANCREAS *OC; ANIMAL-NEOPLASM *OC; PANCREOPATHY *OC; IN-VIVO *FT; IN-VITRO *FT; CYTOSTATIC *FT; TUMOR-CELL *FT; MOUSE *FT; I.P. *FT; ADDITIVE *FT; SYNERGIST *FT; CYTOSTATIC-COMB. *FT; XENOGRAFT *FT; TISSUE-CULTURE *FT; LAB.ANIMAL *FT; INJECTION *FT; COMB. *FT

[01] ASPARAGINASE *PH; POLYETHYLENE-GLYCOL *PH; ASPARASE *RN;
DRUG-DELIVERY *FT; ONCASPAR *FT; CYTOSTATICS *FT; ENZYMES
*FT; EC-3.5.1.1 *FT; PH *FT

RN: 9015-68-3

[02] GEMCITABINE *PH; LY-188011 *RN; CYTOSTATICS *FT; PH *FT

RN: 95058-81-4

FA AB; LA; CT

FS Literature

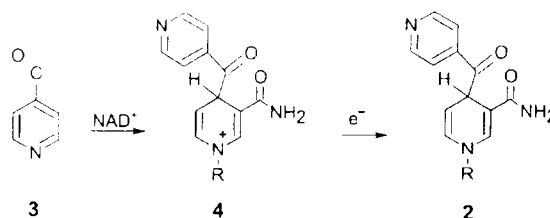
Profile Booklet

C M 54 71 1999-37541
Spontaneous formation of the bioactive form of the tuberculosis drug isoniazid.
Angew.Chem.Int.Ed.Engl. (38, No. 17, 2588-90, 1999)
/Univ.Bochum/ Wilming M; Johnsson K/ Bochum, Ger.

A study on the spontaneous formation of the bioactive form of isoniazid and the mechanism of the inhibition of the enoyl-acyl carrier protein (ACP) reductase, InhA with subsequent inhibition of the synthesis of mycolic acids, which form an integral part of the mycobacterial cell wall, is reported. The incubation of InhA with isoniazid, Mn^{2+} and either NADH or NAD^+ was performed and the reaction mixture analyzed by matrix assisted laser desorption/ ionization mass spectrometry (MALDI-MS). The efficient formation of the inhibitor (2) in the absence of InhA was used to interpret the mechanism of action of isoniazid as well as obtaining a better understanding of the molecular events leading to isoniazid resistance.

Reaction of InhA with isoniazid in the presence of Mn ions and either NADH or NAD^+ gave rise to a product corresponding in molecular mass to that of (2). HPLC showed that in addition to the oxidation of isoniazid to isonicotinic acid, NADH was rapidly oxidized to NAD^+ . The structure (2) was assigned to a product formed in an incubation performed in the absence of InhA on the basis of NMR spectroscopy and published crystal data for the InhA inhibitor complex. These results supported a mechanism whereby the isonicotinoyl radical (3) is formed spontaneously from isoniazid and then reacts with NAD^+ to form a radical cation (4), which is then reduced to (2). 2 Fig. 16 Ref. (BM)

Institut de Chimie Organique, Universite de Lausanne, CH-1015 Lausanne, Switzerland. (K.J.). (Email: kai.johnsson@ico.unil.ch).



How to get the best search results

The Derwent Drug File provides the most precise and relevant search results of all the databases available in this field. The unique arrangement of the keywords within the indexing fields, together with the use of 'linking' and 'roles' provides an exceedingly high degree of relevance.

In many databases, all keywords are simply grouped together in a single field. This is similar to finding two words in the same paragraph i.e. they may or may not be related. The Derwent Drug File separates keywords into a series of 'sentences' in each of which all data is contextually linked; each sentence contains a single drug together with all other terms relating to this drug.

In addition to this highly drug-specific indexing, the Derwent Drug File makes extensive use of 'roles'. These roles provide an indication of the context in which a keyword is used; for example, one role indicates that a drug is used in treatment or that a disease is being treated, while another signifies that a disease is an adverse effect of a drug.

Generic searching (e.g. groups of drug, types of disease etc.) is also provided for by the use of "Higher Terms". These are generic terms describing drugs, groups of diseases, types of organism etc., and every time a specific concept is indexed, the

appropriate higher terms are automatically assigned.

All keywords used in the indexing are controlled by means of the Derwent Drug File Thesaurus which lists all searchable keywords and non-searchable synonyms.

Due to the use of natural language and the comprehensive nature of the abstracts, very good results are also obtained when searching free text.

User Aids

The following additional user aids are available:-

- Derwent Literature Services - Journal List and Selection Guidelines
- Derwent Drug File Thesaurus (in 3 parts)
- DDF on Discovery user guide
- DDF on Ovid user guide

Detailed datasheets for assistance with online searching are available from STN, Orbit, Dialog and Datastar.

Training classes are provided upon request.

Appendix I

Derwent Drug File Core Journals

American Heart Journal
American Journal of Cardiology
American Journal of Clinical Oncology
American Journal of Gastroenterology
American Journal of Medicine
American Journal of Psychiatry
Annals of Internal Medicine
Anticancer Drug Design
Antimicrobial Agents and Chemotherapy
Arthritis and Rheumatism
Arzneimittel-Forschung
Biochemical Pharmacology
Bioorganic and Medicinal Chemistry Letters
Blood
British Journal of Cancer
British Journal of Clinical Pharmacology
British Journal of Pharmacology
British Medical Journal
Cancer
Cancer Research
Cardiovascular Drugs and Therapy
Chemical and Pharmaceutical Bulletin
Circulation
Clinical Cancer Research
Clinical Infectious Diseases
Clinical Pharmacology and Therapeutics
Current Therapeutic Research
Drug Metabolism and Disposition
European Heart Journal
European Journal of Medicinal Chemistry
European Journal of Cancer
European Journal of Pharmacology
FEBS Letters
Gastroenterology
Heart
Hypertension
Infection and Immunity
International Journal of Pharmaceutics
Journal of American College of Cardiology
Journal of American Medical Association
Journal of Antibiotics
Journal of Antimicrobial Chemotherapy
Journal of Cancer Research and Clinical
Oncology
Journal of Clinical Oncology
Journal of Clinical Pharmacology
Journal of Hypertension
Journal of Internal Medicine
Journal of Investigative Dermatology
Journal of Medicinal Chemistry
Journal of Pharmacy and Pharmacology
Journal of Pharmaceutical Sciences
Journal of Rheumatology

Journal of Urology
Japanese Journal of Antibiotics
Japanese Journal of Pharmacology
Japanese Journal of Chemotherapy
Lancet
Life Sciences
New England Journal of Medicine
Nature
Neynyn-Shmied.
Pharmacology Biochemistry and Behavior
Pharmacological Research
Proceedings of the National Academy of
Science
Science
Southern Medical Journal
Tetrahedron
Tetrahedron Letters
Thrombosis and Hemostasis

Appendix II

Derwent Drug File selection guidelines

The aim of Derwent Drug File is to provide a database meeting the scientific documentation needs of the pharmaceutical industry, which includes all important articles relating to drug development, evaluation and use. This principle governs the selection of articles concerned with analysis, biochemistry, chemistry, endocrinology, immunology, medicine, microbiology, pharmaceuticals, pharmacology, physiology, and toxicology. To this end, the articles are selected in such a way as to ensure that the database contains the important papers from as wide a range of journals as possible.

All articles giving significant information on one or more drugs (including vaccines) are selected whether the subject of the paper is chemistry, biochemistry, pharmaceuticals, pharmacology, medicine, etc.

This means that all papers describing isolation, synthesis, formulation, pharmacology, toxicology, metabolism, clinical trials, etc. of novel or established drugs are included. Routine references to established drugs (e.g. case reports, discussions, editorials, commentaries) are

not included unless the paper reports some significant result (e.g. an adverse effect). Review papers are treated on their merits, but generally only those discussing drugs in some detail and giving a significant number of references are selected.

The following are not selected:

- a Papers which do not mention drugs, unless they are concerned with topics of related importance such as potential screening methods, aspects of formulation, etc.
- b Papers containing relatively trivial references to drugs, e.g. use as reagents or pharmacological tools.
- c Purely incidental drug therapy unrelated to the subject of study.
- d Routine use of anaesthetics and diagnostic agents.
- e Generic drug groups (e.g. steroids, cardioglycosides) unless these are the main subject of the paper.
- f Drug legislation, regulatory affairs, documentation, sales.
- g Letters containing no original data.
- h Drug abuse, alcoholism, tobacco smoking.

- i Environmental pollutants, poisons, non-drug carcinogens.
- j Items of interest only to Derwent Veterinary Drug File (veterinary) or Derwent Crop Protection File (pesticides, plant protection and related subjects), or Derwent Biotechnology Abstracts.

Customer Support

Derwent Help Desk Assistance

Expert advice and support is available via our Derwent Help Desk staff, to provide a fast and efficient response to all your enquiries. The experienced Help Desk staff have an in-depth knowledge of all Derwent's products and services and are familiar with the command languages of the various online hosts

In addition to your online and other product queries, the staff will assist with delivery and invoice enquiries, take details of amendments to contact address details, and action correction of any reported errors. In fact, from general customer queries through to technical questions on chemical or polymer indexing or how to set up your internet browser, the Help Desk is there to help you.

Contact your local Help Desk by phone, fax or e-mail or visit the Customer Services area on the Derwent World Wide Web Site.

Universal Freephone

The European Help Desk has recently launched a Universal Freephone Number

+800 33 44 2999

At Present this is available in the following countries:

Belgium	- 00800 33 44 2999
Denmark	- 00800 33 44 2999
France	- 00800 33 44 2999
Germany	- 00800 33 44 2999
Norway	- 001800 33 44 2999
Sweden	- 009800 33 44 2999
Switzerland	- 00800 33 44 2999
The Netherlands	- 00800 33 44 2999
UK*	- 00800 33 44 2999

Additional countries will be made available as they join the Universal Freephone system

(* UK users should note that it is necessary to dial the international prefix '00')

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Derwent Word Wide Web Site

<http://www.derwent.com/>

<http://www.derwent.co.jp/>

Customer Training

Specialist staff run regular training programmes to help you search our online databases effectively and comprehensively. Training classes are held in major towns and cities in Europe, North America and Japan. Training sessions can be found at <http://www.derwent.com/training.html>

A wide range of classes are available introducing Derwent files to both beginners and experienced searchers. Subject specialist classes are also available providing specialist training on Derwent's indexing. We can also develop training classes or presentations tailored to your company's specific needs.