

(19)



Europäisches Patentamt

European Patent Office

Office européen des brevets



(11)

EP 1 344 830 A1

(12)

EUROPEAN PATENT APPLICATION

(43) Date of publication:

17.09.2003 Bulletin 2003/38

(51) Int Cl.7: **C12P 35/02**, C12P 35/06,

C12P 39/00, C12N 9/08,

C12N 9/80, C12N 9/06,

C12N 11/02, C12N 11/18,

C07D 501/20, C07D 501/04

(21) Application number: **02075989.0**

(22) Date of filing: **12.03.2002**

(84) Designated Contracting States:

**AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU
MC NL PT SE TR**

Designated Extension States:

AL LT LV MK RO SI

(71) Applicant: **Bioferma Murcia, S.A.**

30840 Alhama de Murcia, Murcia (ES)

• **Fernandez-Lorente, Gloria**

28030 Madrid (ES)

• **Betancort, Lorena Dutrenit**

28028 Madrid (ES)

• **Hidalgo, Aurelio Huertas**

48013 Bilbao (ES)

• **Mateo, Cesar Gonzalez**

28005 Madrid (ES)

(72) Inventors:

• **Guisan Seijas, Jose M.**

28002 Madrid (ES)

• **Fernandez-Lafuente, Roberto**

28914 Madrid (ES)

(74) Representative: **Davila Baz, Angel et al**

c/o Clarke, Modet & Co.,

Goya, 11

28001 Madrid (ES)

(54) **A process for the preparation of cephalosporan acid derivatives from cephalosporin C**

(57) A process for the preparation of cephalosporin acid derivatives comprises the step of enzymatically converting cephalosporin C into 7 cephalosporin acid derivatives in the presence of two biocatalysts, wherein

one biocatalyst comprises co-immobilised D-amino acid oxidase and a catalase enzyme, and the other biocatalyst comprises immobilised glutaryl acylase.

EP 1 344 830 A1



European Patent
Office

EUROPEAN SEARCH REPORT

Application Number
EP 02 07 5989

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
X	WO 90 12110 A (BIOPURE CORPORATION) 18 October 1990 (1990-10-18) see especially p. 1-7, Example 7 and the claims) * the whole document *	1-14	C12P35/02 C12P35/06 C12P39/00 C12N9/08 C12N9/80 C12N9/06 C12N11/02 C12N11/18 C07D501/20 C07D501/04
X,D	GOLINI P. ET AL.: "Immobilization of D-amino acid oxidase from different yeasts: Characterization and application in the deamination of cephalosporin C." ENZYME AND MICROBIAL TECHNOLOGY, vol. 17, 1995, pages 324-329, XP002209698 see especially p. 324 and 325. * the whole document *	13,14	
Y		1-12	
Y,D	FERNANDEZ-LAFUENTE R. ET AL.: "The coimmobilization of D-amino acid oxidase and catalase enables the quantitative transformation of D-amino acids (D-phenylalanine) into alpha-keto-acids (phenylpyruvic acid)." ENZYME AND MICROBIAL TECHNOLOGY, vol. 23, 1998, pages 28-33, XP002209699 * the whole document *	1-12	
X	EP 0 322 032 A (MERCK & CO. INC.) 28 June 1989 (1989-06-28) * page 6 - page 9; claim 1 *	13	
A		1-12,14	
Y,D	MATEO C. ET AL.: "Increase in conformational stability of enzymes immobilized on epoxy-activated supports by favoring additional multipoint covalent attachment." ENZYME AND MICROBIAL TECHNOLOGY, vol. 26, 2000, pages 509-515, XP002209700 * the whole document *	5-9	
The present search report has been drawn up for all claims			
Place of search MUNICH		Date of completion of the search 13 August 2002	Examiner Douschan, K
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

EPO FORM 1503 03.82 (P04C01)



European Patent
Office

EUROPEAN SEARCH REPORT

Application Number
EP 02 07 5989

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Y	FERNANDEZ-LAFUENTE R. ET AL.: "Stabilization of enzymes (DAAO) against hydrogen peroxide via immobilization and post-immobilization techniques." JOURNAL OF MOLECULAR CATALYSIS B: ENZYMATIC, vol. 7, 1999, pages 173-179, XP002209701 * the whole document *	5-9	
X	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; May 1998 (1998-05) BIANCHI DANIELE ET AL: "Enzymatic transformation of cephalosporin C to 7-ACA by simultaneous action of immobilized D-amino acid oxidase and glutaryl-7-ACA acylase." Database accession no. PREV199800478069 XP002209702	13	
Y	* abstract * & APPLIED BIOCHEMISTRY AND BIOTECHNOLOGY, vol. 73, no. 2-3, May 1998 (1998-05), pages 257-268, ISSN: 0273-2289 --- -/--	1-12	
The present search report has been drawn up for all claims.			TECHNICAL FIELDS SEARCHED (Int.Cl.7)
Place of search MUNICH		Date of completion of the search 13 August 2002	Examiner Douschan, K
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons ----- & : member of the same patent family, corresponding document			

EPO FORM 1503 03 82 (P/M/C01)



European Patent
Office

EUROPEAN SEARCH REPORT

Application Number
EP 02 07 5989

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
X	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1994 NIKOLOV ALEXANDER ET AL: "Enzymatic transformation of cephalosporin C to 7-amino-cephalosporanic acid: Part II: Single-step procedure using a coimmobilized enzyme system." Database accession no. PREV199598033966 XP002209703	13	
Y	* abstract * & ENZYME AND MICROBIAL TECHNOLOGY, vol. 16, no. 12, 1994, pages 1037-1041, ISSN: 0141-0229 -----	1-12	
			TECHNICAL FIELDS SEARCHED (Int.Cl.7)
The present search report has been drawn up for all claims			
Place of search MUNICH		Date of completion of the search 13 August 2002	Examiner Douschan, K
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

EPO FORM 1503 03/82 (P04/C01)