(12) UK Patent Application (19) GB (11) 2 073 191 A

(21) Application No **8109980**
(22) Date of filing **31 Mar 1981**
(30) Priority data
(31) **21096**
(32) **1 Apr 1980**
(33) **Italy (IT)**
(43) Application published
14 Oct 1981
(51) **INT CL³**
C07D 501/22 A61K
31/545
(52) Domestic classification
C2C 1314 214 220 22Y
256 25Y 292 29Y 30Y 33Y
340 342 34Y 351 352 365
366 367 36Y 628 662 801
80Y AA KE
(56) Documents cited
None
(58) Field of search
C2C
(71) Applicant
Dobfar SpA.,
via Marzabotto,
Vimercate 20059 (Milan),
Italy
(72) Inventors
Marco Falciani,
Renato Broggi
(74) Agent
Gill, Jennings & Every,
53/64 Chancery Lane,
London WC2A 1HN

(54) **Cephadroxyl Derivative**

(57) The novel disodium salt of N-carboxycephadroxyl can be administered, e.g. parenterally, as an antiobiotic.

GB 2 073 191 A

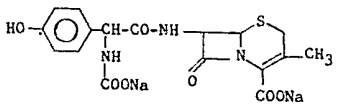
SPECIFICATION

Cephadroxyl Derivatives

The antibiotic cephadroxyl, i.e. *p*-hydroxycephalexin, is described in US Patent Specification No. 3,489,752. It is a broad-spectrum antibiotic which is administered orally. It would be desirable to provide a cephadroxyl derivative which could be administered parenterally.

Disodium salts of N-carboxycephalexin and N-carboxycephradine are disclosed in Dutch Patent Application No. 72.10416.

The novel compound of this invention is the disodium salt of N-carboxycephadroxyl. This compound has the formula



I

The novel salt may be prepared by reacting a suitable derivative of cephadroxyl with sodium carbonate. The reaction may be conducted in an aqueous system from which the product can be isolated by precipitation.

For administration to a subject, e.g. parenterally, the salt of this invention may be provided, in association with a physiologically acceptable excipient, in the form of a pharmaceutical composition.

The following Examples illustrate how the novel compound may be prepared.

Example 1

To a suspension of cefadroxil monohydrate (38.1 g, 0.1 mole) in water (110 ml) at 15°C, sodium carbonate (10.6 g, 0.1 mole) was added portion-wise. After stirring for 0.5 hours at 15—20°C, acetone (280 ml) was added over 15 minutes. After stirring for 2 hours, a white crystalline material was obtained. On cooling to 0°C and further dilution with acetone (250 ml), the solution was allowed to crystallise for 24 hours. The precipitate was separated by filtration, washed with acetone (50 ml) and submitted to vacuum-drying at 40°C. 26 g of N-carboxycefadroxil disodium salt were obtained.

Water content: 7.5%
Sodium content: 13.6%
N-carboxycefadroxil: 78.9%
$[\alpha]_D$ (C=1, H_2O)=+147° (on a dry basis)
$E^{1\%}_{1\,cm}$ at 262 nm=196
Microbiological titre=789 mcg/mg as cefadroxil

Example 2

To a suspension of cefadroxil dimethylformamide solvate (43.6 g, 0.1 mole) in water (110 ml), sodium carbonate (10.6 g, 0.1 mole) was added drop-wise. After stirring for 0.5 hours at 10—15°C, acetone (300 ml) was added over 20 minutes. After stirring for 1.5 hours, a white crystalline material crystallised out. After cooling at 0°C and further dilution with acetone (250 ml), the solution was allowed to crystallise for 2 hours. The precipitate was separated by filtration, washed with acetone (50 ml) and submitted to vacuum-drying at 40°C. 27.5 g of N-carboxycefadroxil disodium salt were obtained.

Water content: 7.8%
Sodium carbonate: 13.4%
N-carboxycefadroxil: 78.8%
$[\alpha]_D$ (C=1, H_2O)=+145° (on a dry basis)
$E^{1\%}_{1cm}$ at 262 nm=193
Microbiological titre=787 mcg/mg as cefadroxil.

Claims

1. The disodium salt of N-carboxycephadroxyl.
2. The compound of formula I as herein defined.
3. A pharmaceutical composition comprising the compound of claim 1 or claim 2 in association with a physiologically acceptable excipient.

Printed for Her Majesty's Stationery Office by the Courier Press, Leamington Spa, 1981. Published by the Patent Office, 25 Southampton Buildings, London, WC2A 1AY, from which copies may be obtained.