66584/86

(CONVENTION. By one or more persons and/or a Compa:

APPLICATION ACCEPTED AND AMENDMENTS

ALLOWED 19-4-90

598499

COMMONWEALTH OF AU:

Patents Act 1952-1969

PATENT OFFICE PATENT OFFICE
ONE HUNDRED DOLLARS ONE HUNDRED DOLLARS
16 DEC Melbourne

CONVENTION APPLICATION FOR A PATENT

FEE STAMP TO VALUE OF $100.00 ATTACHED
MAIL OFFICER

LODGED AT SUB-OFFICE
16 DEC 1986
Melbourne

(1) Here insert (in full) Name or Names of Applicant or Applicants, followed by Address (es).

We (1) LABORATOIRES HOECHST S.A. and BEHRINGWERKE AKTIENGESELLSCHAFT, of Tour Roussel Nobel, 3, Avenue du General de Gaulle, F-92800 Puteaux, France and D-3550 Marburg Federal Republic of Germany, respectively

(2) Here insert Title of Invention.

hereby apply for the grant of a Patent for an invention entitled: (2) NEW ANTHRACYCLINES AND DRUGS CONTAINING THEM

(3) Here insert number(s) of basic application(s)

which is described in the accompanying complete specification. This application is a Convention application and is based on the application numbered (3) 8518661

(4) Here insert Name of basic Country or Countries, and basic date or dates

for a patent or similar protection made in (4) France on 17th December 1985

My/Our address for service is Messrs. Edwd. Waters & Sons, Patent Attorneys, 50 Queen Street, Melbourne, Victoria, Australia.

DATED this 15th day of December 1986

(5) Signature (s) of Applicant (s) or Seal of Company and Signatures of its Officers as prescribed by its Articles of Association

(5) LABORATOIRES HOECHST S.A. and BEHRINGWERKE AKTIENGESELLSCHAFT

by James Murray

James Murray

Registered Patent Attorney

Form 7

COMMONWEALTH OF AUSTRALIA

Patents Act 1952

DECLARATION IN SUPPORT OF A CONVENTION APPLICATION UNDER PART XVI. FOR A PATENT

In support of the Convention application made under Part XVI. of the Patents Act 1952 by 1) LABORATOIRES HOECHST S.A. of Tour Roussel Nobel, 3, Avenue du Général de Gaulle, F-92800 Puteaux, France and 2) BEHRINGWERKE AKTIENGESELLSCHAFT of D-3550 Marburg, Federal Republic of Germany for a patent for an invention entitled:

NEW ANTHRACYCLINES AND DRUGS CONTAINING THEM

We, 1) Bernard WINICKI of 34 rue Saint-James - 92200 NEUILLY S/SEINE- FRANCE

2) Heribert Bug of 7 Amselweg, D-3551 Niederweimar)
3) Philipp Stein of 28 Höhenweg, D-3550 Marburg) Federal Republic of Germany

do solemnly and sincerely declare as follows:

1. We are authorized 1) by LABORATOIRES HOECHST S.A. and 2) and 3) by BEHRINGWERKE AKTIENGESELLSCHAFT the applicants for the patent to make this declaration on their behalf.

2. The basic application as defined by Section 141 of the Act was made in France
under No. 85-18 661 on December 17, 1985
by LABORATOIRES HOECHST S.A.

3. a) Jean-Pierre Gesson, La Germonière, Montamisé, F-86360 Chasseneuil du Poitou
b) Martine Mondon, 9, Rue de Pontreau - App. 529, F-86000 Poitiers
c) Jean-Claude Jacquesy, 46, Rue du Planty, F-86180 Bruxerolles
d) Hans Peter Kraemer, 16 Birkenweg, D-3550 Marburg
a) - c) France, d) Federal Republic of Germany

are the actual inventors of the invention and the facts upon which LABORATOIRES HOECHST S.A. and BEHRINGWERKE AKTIENGESELLSCHAFT are entitled to make the application are as follows:

The said LABORATOIRES HOECHST S.A. and BEHRINGWERKE AKTIENGESELLSCHAFT are the assignees of the said Jean-Pierre Gesson, Martine Mondon, Jean-Claude Jacquesy, Hans Peter Kraemer

4. The basic application referred to in paragraph 2 of this Declaration was the first application made in a Convention country in respect of the invention the subject of the application.

Declared at Puteaux, France, this 3rd day of December 1986
and at Marburg, Federal Republic of Germany, this 26th day of November 1986.

LABORATOIRES HOECHST S.A.

Winicki - President

BEHRINGWERKE AKTIENGESELLSCHAFT

ppa. Stein
Prokurist

ppa. Bug
Prokurist

To the Commissioner of Patents

(12) PATENT ABRIDGMENT (11) Document No. AU-B-66584/86
(19) AUSTRALIAN PATENT OFFICE (10) Acceptance No. 598499

(54) Title
DAUNORUBICIN DERIVATIVES AND PHARMACEUTICAL COMPOSITIONS THEREOF

International Patent Classification(s)
(51)[4] C07H 015/252 A61K 031/71 C07D 309/14

(21) Application No. : 66584/86 (22) Application Date : 16.12.86

(30) Priority Data

(31) Number (32) Date (33) Country
85 18661 17.12.85 FR FRANCE

(43) Publication Date : 18.06.87

(44) Publication Date of Accepted Application : 28.06.90

(71) Applicant(s)
LABORATOIRES HOECHST S.A.; BEHRINGWERKE AKTIENGESELLSCHAFT

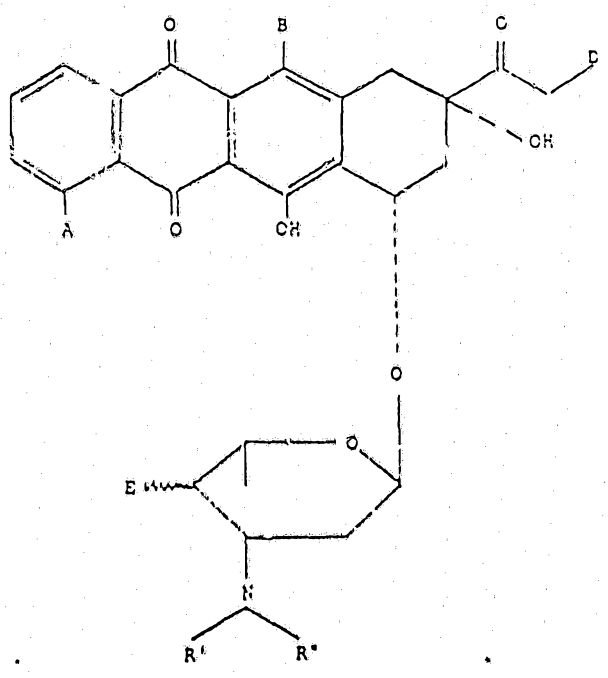
(72) Inventor(s)
JEAN-PIERRE GESSON; MARTINE MONDON; JEAN-CLAUDE JACQUESY; HANS PETER KRAEMER

(74) Attorney or Agent
WATERMARK MELBOURNE

(56) Prior Art Documents
AU 65100/86 C07H 31/70 C07C 79/36
AU 22164/83 C07H 15/252 C07D 309/10
EP 254484

(57) Claim

1. A new anthracycline represented by the formula I below:



(I)

.../2

in which:

A denotes OCH_3 or OH or H groups,

B denotes an OH group or a hydrogen atom,

D denotes a hydrogen atom or an OH group,

E denotes an OH group or a hydrogen atom,

and R' and R", which may be identical or different, denote a hydrogen atom (and in this case R' is different from R") or the group $-(CH_2)_n-R_1-(CH_2)_m-R_2$

where

n is between 1 and 6,

m is between 0 and 4 (with the proviso, of course, that if m = 0, R_2 is nonexistent)

R_1 denotes one of the following groups:

$-\overset{\overset{O}{\|}}{C}-O-$

$-\overset{\overset{O}{\|}}{C}-OH$ (in this case, m = 0)

$-\overset{\overset{O}{\|}}{C}-N\begin{matrix}R_3\\R_4\end{matrix}$ (in this case m = 0 where R_3 and R_4, which may be identical or different, denote a hydrogen atom or a substituted or unsubstituted alkyl group)

$-C\equiv N$ (in this case m = 0)

$-S-$

$-O-$ (with the proviso that m is other than 0)

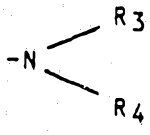
$-N\begin{matrix}R_3\\R_4\end{matrix}$ (m = 0 and R_3 and R_4 have the same meaning as above)

$-N\begin{matrix}COR_3\\R_4\end{matrix}$ (m = 0 and R_3 and R_4 have the same meaning as above)

and

R_2 denotes (in the case where m is other than 0)

a hydrogen atom or alkyl or alkoxy groups or



(R_3 and R_4 having the same meaning as above).

598499

Form 10

COMMONWEALTH OF AUSTRALIA

PATENTS ACT 1952-69

COMPLETE SPECIFICATION

(ORIGINAL)

Class Int. Class

Application Number: 66584/86.
Lodged:

Complete Specification Lodged:
Accepted:
Published:

Priority :

Related Art :

This document contains the amendments made under Section 49 and is correct for printing.

Name of Applicant : LABORATOIRES HOECHST S.A. and BEHRINGWERKE AKTIENGESELLSCHAFT

Address of Applicant : Tour Roussel Nobel, 3, Avenue du General de Gaulle, F-92800 Puteaux, France and D-3550 Marburg, Federal Republic of Germany, respectively

Actual Inventor:

Address for Service : EDWD. WATERS & SONS,
50 QUEEN STREET, MELBOURNE, AUSTRALIA, 3000.

Complete Specification for the invention entitled:

NEW ANTHRACYCLINES AND DRUGS CONTAINING THEM

The following statement is a full description of this invention, including the best method of performing it known to :- us

HOE 85/B 750

LABORATOIRES HOECHST S.A. and BEHRINGWERKE AKTIENGESELLSCHAFT

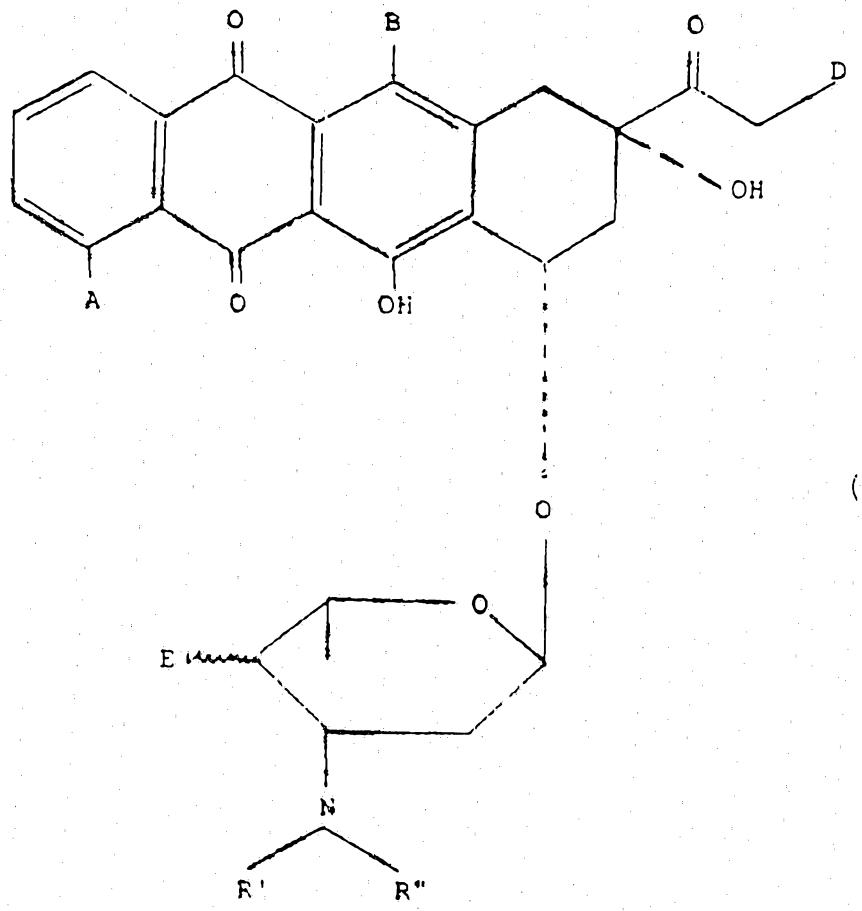
NEW ANTHRACYCLINES AND DRUGS CONTAINING THEM

The present invention relates to new anthracyclines and to drugs containing them.

A great deal of effort, continuously expended during recent years by different research teams, has enabled the anthracycline family to be enlarged, these compounds nowadays constituting one of the most promising classes of drugs in respect of its anticancer activity.

Continuing the study which has already been proceeding for several years (see, in particular, French Patents 83/05,217, 83/13,877, 84/03,634, 84/09,405 and 85/10,063), the Applicant has developed new anthracycline derivatives in which the pharmacological properties of this family are advantageously modified.

The subject of the present invention is new anthracyclines represented by the formula I below:



(I)

in which:

A denotes OCH_3 or OH or H groups,

B denotes an OH group or a hydrogen atom,

D denotes a hydrogen atom or an OH group,

E denotes an OH group or a hydrogen atom,

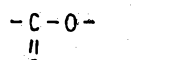
and R' and R", which may be identical or different, denote a hydrogen atom (and in this case R' is different from R") or the group $-(CH_2)_n-R_1-(CH_2)_m-R_2$

where

n is between 1 and 6,

m is between 0 and 4 (with the proviso, of course, that if m = 0, R_2 is nonexistent)

R_1 denotes one of the following groups:



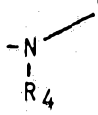
(in this case, m = 0)

(in this case m = 0 where R_3 and R_4, which may be identical or a different, denote a hydrogen atom or substituted or unsubstituted alkyl group)

(in this case m = 0)

(with the proviso that m is other than 0)

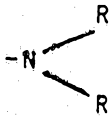
(m = 0 and R_3 and R_4 have the same meaning as above)



(m = 0 and R_3 and R_4 have the same meaning as above)

and

R_2 denotes (in the case where m is other than 0) a hydrogen atom or alkyl or alkoxy groups or



(R_3 and R_4 having the same meaning as above)

Some of these new derivatives have exceptional cytotoxic properties, as described later in the cell proliferation test. The Applicant has been able to achieve these results by means of the "functionalization" of the alkyl radicals R' and R".

Among the different derivatives according to the present invention which are endowed with very advantageous pharmacological effects, it is appropriate to mention the following in particular:

3'-N-(cyanomethyl)daunorubicin

3'-N,N-bis(cyanomethyl)daunorubicin

3'-N-(2-methoxyethyl)daunorubicin
3'-N-cyanomethyl-3'-N-(2-methoxyethyl)daunorubicin
3'-N-[(N,N-diethylcarbamoyl)methyl]daunorubicin
3'-N,N-bis[(N,N-diethylcarbamoyl)methyl]daunorubicin
3'-N-(carbomethoxymethyl)daunorubicin
3'-N-[2-(2-methoxyethoxy)ethyl]daunorubicin
3'-N,N-bis[2-(2-methoxyethoxy)ethyl]daunorubicin

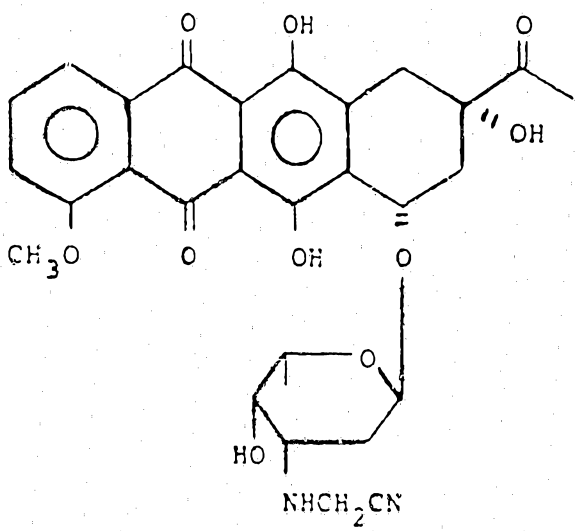
The invention will be better understood with the aid of the additional description which follows, which relates to examples of implementing the processes or of preparations of the derivatives according to the present invention, and also to an account of pharmacological experiments.

It must nevertheless be clearly understood that these examples of implementation and this account of pharmacological experiments are given exclusively by way of illustration of the subject of the invention, and in no way constitute a limitation thereof.

EXAMPLES

PREPARATION OF 3'-N-(CYANOMETHYL)- AND 3'-N,N-BIS(CYANOMETHYL)DAUNORUBICIN

Iodoacetonitrile (10 eq.) is added to a mixture of daunorubicin hydrochloride (100 mg; 0.18 mmol) and Et_3N (0.54 mmol) in 15 ml of DMF. After 48 h at room temperature, 3'-N,N-bis(cyanomethyl)daunorubicin (7 mg, 6.3%), 3'-N-(cyanomethyl)daunorubicin (58 mg, 57%) and unreacted daunorubicin (16 mg, 16.6%) are separated in order of increasing polarity.



3'-N-(CYANOMETHYL)DAUNORUBICIN

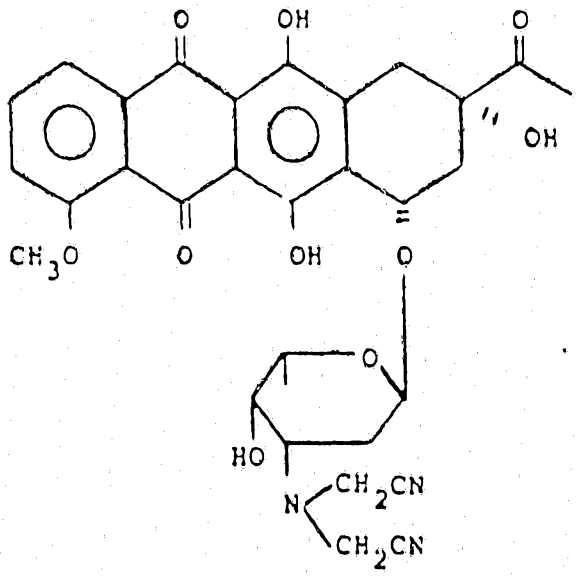
Yld. = 57%

Melting point: 134-140°C (dec.)

MS: (FAB -): 566

NMR ($CDCl_3$) 200 MHz: 1.35 (doublet, J = 5 Hz, 3H); 2.42 (singlet, 3H); 3.00 (ABq, 2H); 3.59 (singlet, 1H); 3.69 (singlet, 1H); 4.07 (singlet, 3H); 5.25 (sharp signal, 1H); 5.50 (sharp signal, 1H); 7.38 (doublet, J = 7.5 Hz, 1H); 7.77 (triplet, J = 7.5 Hz, 1H); 8.00 (doublet, J = 7.5 Hz, 1H); 13.23 (singlet, 1H); 13.95 (singlet, 1H).

IR (CH_2Cl_2): 3600, 3500, 1710, 1610, 1550, 1440 cm^{-1}.



3'-N,N-BIS(CYANOMETHYL)DAUNORUBICIN

Yld. = 6.3%

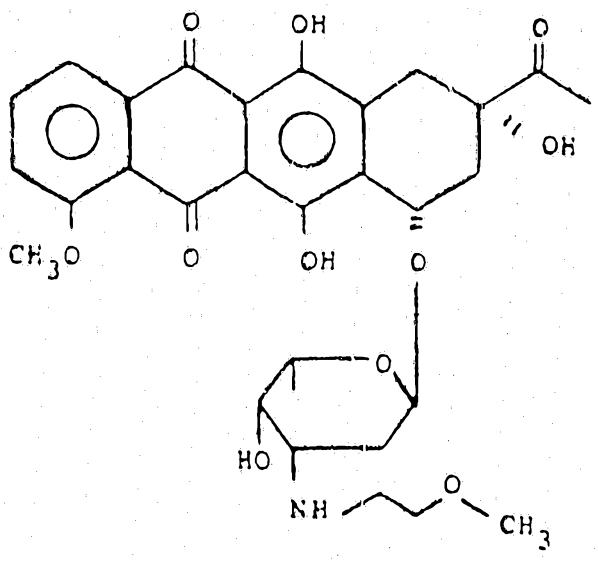
Melting point: 155-165°C

NMR ($CDCl_3$) 200 MHz: 1.34 (doublet, J = 5.5 Hz, 3H); 2.40 (singlet, 3H); 3.10 (ABq, 2H); 3.80 (singlet); 4.08 (singlet, 3H); 4.29 (broad singlet, 1H); 5.26 (sharp signal, 1H); 5.57 (sharp signal, 1H); 7.38 (doublet, J = 7.5 Hz, 1H); 7.79 (triplet, J = 7.5 Hz, 1H); 8.03 (doublet, J = 7.5 Hz, 1H); 13.28 (singlet, 1H); 14.02 (singlet, 1H).

IR (CH_2Cl_2): 3700, 3500 (broad), 2980, 2920, 2840, 1710, 1610, 1580, 1420, 1380, 1350 cm^{-1}.

PREPARATION OF 3'-N-(2-METHOXYETHYL)DAUNORUBICIN

2-Iodoethyl methyl ether (15 eq.) is added to a mixture of daunorubicin hydrochloride (30 mg; 0.054 mmol) and Et_3N (0.16 mmol) in 1.5 ml of DMF. After 48 h at room temperature, 3'-N-(2-methoxyethyl)daunorubicin (60%) is separated from the residual daunorubicin (22%).



3'-N-(2-METHOXYETHYL)DAUNORUBICIN

Yld.: 60%

Melting point: (Kofler stage): 113°C (dec.)

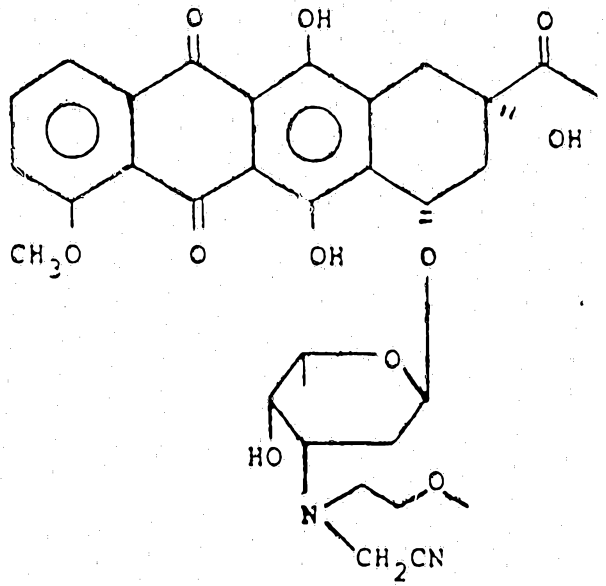
MS: (FAB -): 585 (12%); 515 (13%), 409 (9%), 380 (11%), 321 (12%), 301 (100%)

$[\alpha]_D$ = 253° (C = 0.15; $CHCl_3$)

NMR ($CDCl_3$) 200 MHz: 1.38 (doublet, J = 5.5 Hz, 3H); 2.41 (singlet, 3H); 2.74 (triplet, J = 5 Hz, 2H); 3.32 (singlet, 3H); 3.46 (triplet, J = 5 Hz, 2H); 4.09 (singlet, 3H); 4.73 (broad singlet, 1H); 5.31 (sharp signal, 1H); 5.53 (sharp signal, 1H); 7.40 (doublet, J = 7.5 Hz, 1H); 7.80 (triplet, J = 7.5 Hz, 1H); 8.06 (doublet, J = 7.5 Hz, 1H).

PREPARATION OF 3'-N-CYANOMETHYL-3'-N-(2-METHOXYETHYL)-DAUNORUBICIN

Iodoacetonitrile (15 eq.) is added to a mixture of 3'-N-(2-methoxyethyl)daunorubicin (10 mg; 0.017 mmol), obtained above, and Et_3N (0.05 mmol) in DMF (0.5 ml). After 48 h at room temperature, 3'-N-cyanomethyl-3'-N-(2-methoxyethyl)daunorubicin (10.2 mg; 98%) is obtained.



3'-N-CYANOMETHYL-3'-N-(2-METHOXYETHYL)DAUNORUBICIN

Yld. = 98%

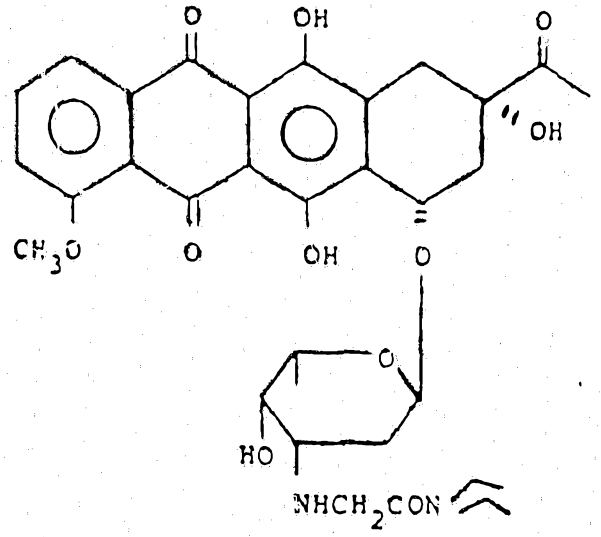
$[\alpha]_D$ = 378° (C = 0.07; $CHCl_3$)

NMR ($CDCl_3$) 200 MHz: 1.38 (doublet, J = 5.5 Hz, 3H); 2.43 (singlet, 3H); 3.10 (ABq, 2H); 3.35 (singlet, 3H); 3.66 (singlet); 4.10 (singlet, 3H); 4.57 (singlet, 1H); 5.31 (sharp signal, 1H); 5.59 (sharp signal, 1H); 7.40 (doublet, J = 7.5 Hz, 1H); 7.79 (triplet, J = 7.5 Hz, 1H); 8.05 (doublet, J = 7.5 Hz, 1H); 13.32 (singlet, 1H); 14.02 (singlet, 1H).

Melting point (Kofler stage): 120° (dec.)

The following were obtained in the same manner:

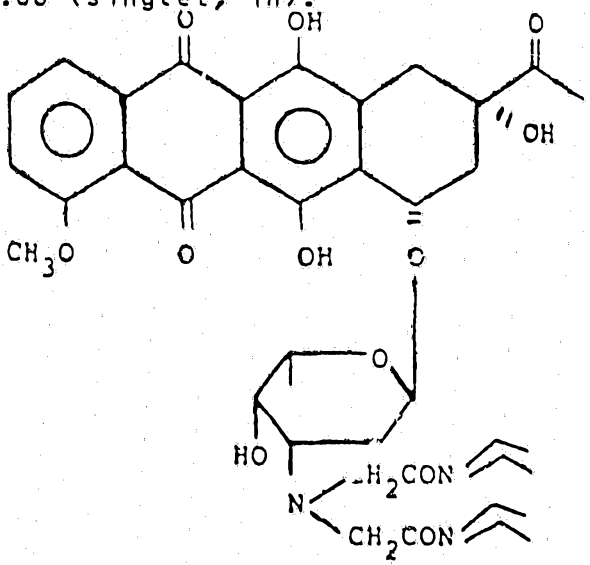
a)



3'-N-[(N,N-DIETHYLCARBAMOYL)METHYL]DAUNORUBICIN

NMR: 1.37 (doublet, J = 5.5 Hz, 3H); 2.41 (singlet, 3H); 4.08 (singlet, 3H); 4.77 (broad singlet, 1H); 5.31 (sharp signal, 1H); 5.53 (sharp signal, 1H); 7.39 (doublet, J = 7.5 Hz, 1H); 7.78 (triplet, J = 7.5 Hz, 1H); 8.03 (doublet, J = 7.5 Hz, 1H); 13.30 (singlet, 1H); 13.66 (singlet, 1H).

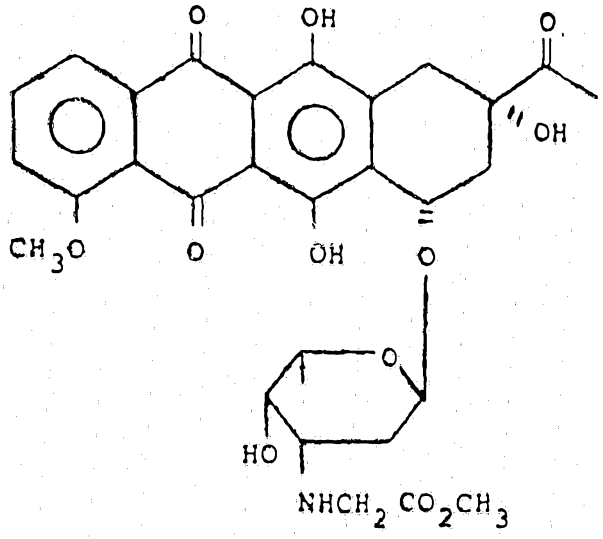
b)



3'-N,N-BIS[(N,N-DIETHYLCARBAMOYL)METHYL]DAUNORUBICIN

NMR: 2.40 (singlet, 3H); 4.09 (singlet, 3H); 5.30 (sharp signal, 1H); 5.57 (sharp signal, 1H); 7.38 (doublet, J = 7.5 Hz, 1H); 7.77 (triplet, J = 7.5 Hz, 1H); 8.05 (doublet, J = 7.5 Hz, 1H); 13.31 (singlet, 1H); 13.65 (singlet, 1H).

c)

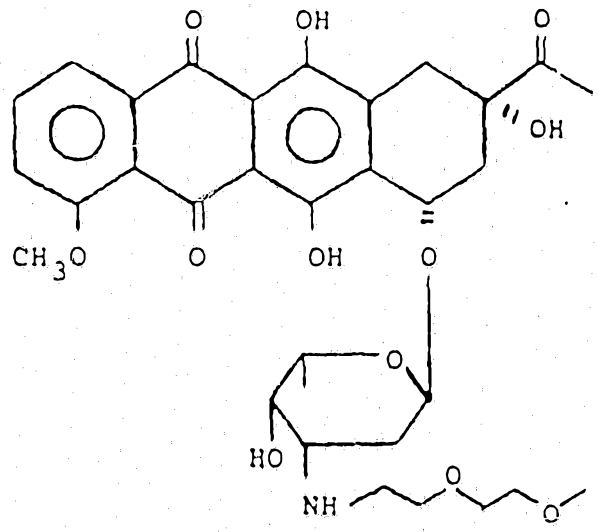


3'-N-(CARBOMETHOXYMETHYL)DAUNORUBICIN

Melting point: 142-148°C

NMR ($CDCl_3$) 200 MHz: 1.36 (doublet, J = 5.5 Hz, 3H); 2.41 (singlet, 3H); 3.10 (ABq, 2H); 3.41 (singlet, 2H); 3.52 (singlet, 1H); 3.70 (singlet, 3H); 4.09 (singlet, 3H); 5.29 (sharp signal, 1H); 5.52 (sharp signal, 1H); 7.40 (doublet, J = 7.5 Hz, 1H); 7.79 (triplet, J = 7.5 Hz, 1H); 8.06 (doublet, J = 7.5 Hz, 1H).

d)



3'-N-[2-(2-METHOXYETHOXY)ETHYL]DAUNORUBICIN

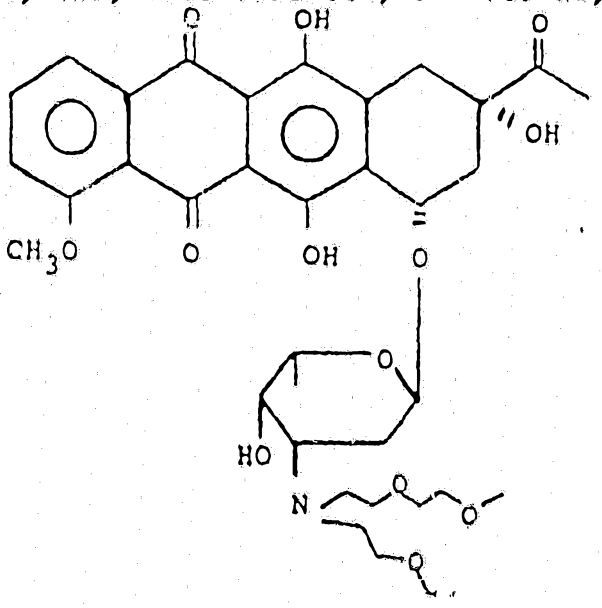
Yld. = 44%

Melting point: 70 - 75°C

$[\alpha]_D$ = 270° (C = 0.1; $CHCl_3$)

NMR ($CDCl_3$) 200 MHz: 1.36 (doublet, J = 5.5 Hz, 3H); 2.41 (singlet, 3H); 3.02 (ABq, 2H); 3.33 (singlet, 3H); 4.07 (singlet, 3H); 4.69 (broad singlet, 1H); 5.25 (sharp signal, 1H); 5.50 (sharp signal, 1H); 7.38 (doublet, J = 5 Hz, 1H); 7.76 (triplet, J = 7.5 Hz, 1H); 8.00 (doublet, J = 7.5 Hz, 1H).

e)



3'-N,N-BIS[2-(2-METHOXYETHOXY)ETH

Yld. = 9%

$[\alpha]_D$ = 294° (C = 0.07; $CHCl_3$)

NMR ($CDCl_3$) 200 MHz: 1.34 (doublet, J = 5 Hz, 3H); 2.42 (singlet, 3H); 3.12 (ABq, 2H); 3.31 (singlet, 6H); 4.09 (singlet, 3H); 4.74 (broad singlet, 1H); 5.30 (sharp signal, 1H); 5.58 (sharp signal, 1H); 7.40 (doublet, J = 7.5 Hz, 1H); 7.79 (triplet, J = 7.5 Hz, 1H); 8.02 (doublet, J = 7.5 Hz, 1H); 13.31 (singlet, 1H); 14.0 (singlet, 1H).

The cytotoxic properties of some derivatives claimed according to the invention are demonstrated in the cell proliferation tests which are summarized in Table I below.

The experimental protocol was performed according to the procedure of HAMBURGER and SALMON on leukemia L 1210 strain cells. Some modifications were introduced in the procedure of HAMBURGER and SALMON, and in particular:

the conditioned medium was replaced by McCoy5A. The number of cells in a dish was reduced to 5×10^2 cells per dish on account of the high covering efficiency of leukemia L 1210.

Cells were incubated with various concentrations of the test substance for 1 hour at 37°C. The cells were then washed twice with McCoy5A, and finally applied in an agar upper layer according to the method of HAMBURGER and SALMON.

In addition, parallel experiments were carried out with continuous incubation and with various concentrations of the test substance by mixing the latter with the upper layer before application.

The dishes were kept in an incubator with 5% CO_2, 20% O_2, at 95% relative humidity for 5 to 7 days at 37°C. After this period, the colonies having a diameter greater than 60 µm were counted with an inverted microscope.

The results were expressed as a percentage of the number of colonies formed from treated L 1210 relative to an untreated control. The coefficient of variation of repeated experiments was less than 15%.

The results are presented in Table I.

TABLE I

PRODUCT	IC_{50} in µg/ml (continuous exposure)
3'-N-(cyanomethyl)-daunorubicin	0.0028
3'-N,N-bis(cyanomethyl)-daunorubicin	0.08
3'-N-(2-methoxyethyl)-daunorubicin	0.01
3'-N-cyanomethyl-3'-N-(2-methoxy-ethyl)daunorubicin	0.09
3'-N-[(N,N-diethylcarbamoyl)-methyl]daunorubicin	0.28
3'-N,N-bis[(N,N-diethylcarbamoyl)-methyl]daunorubicin	0.65
3'-N-(carbomethoxymethyl)dauno-rubicin	0.24
3'-N-[2-(2-methoxyethoxy)ethyl]-daunorubicin	0.07
3'-N,N-bis[2-(2-methoxyethoxy)-ethyl]daunorubicin	0.22
DOXORUBICIN (reference)	0.02
DAUNORUBICIN (reference)	0.02

The drugs containing the derivatives according to the present invention are generally administered at doses of between 0.001 and 25 mg/kg/day.

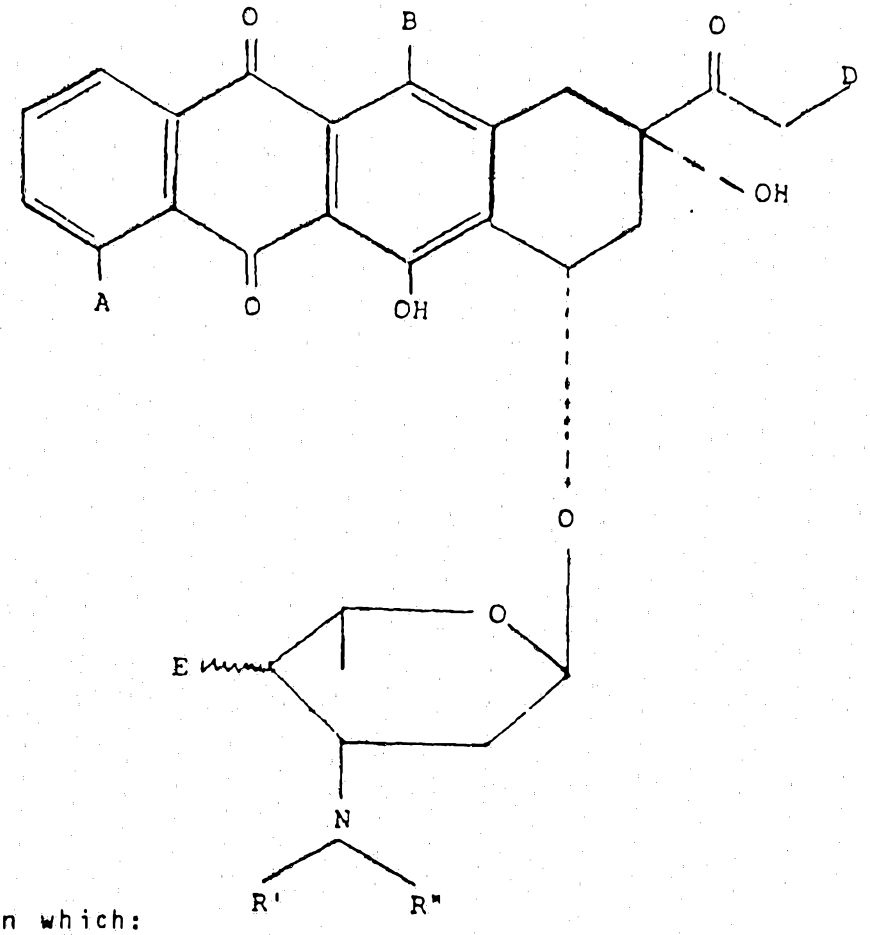
The derivatives according to the general formula I are preferably administered orally but, according to requirements, they can be administered by the other routes: parenterally, subcutaneously, intravenously, intramuscularly, intraperitoneally or transcutaneously.

This administration can also be carried out in combination with excipients or diluents which are pharmaceutically acceptable.

~~CLAIMS~~

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A new anthracycline represented by the formula I below:



(I)

in which:

A denotes OCH_3 or OH or H groups,

B denotes an OH group or a hydrogen atom,

D denotes a hydrogen atom or an OH group,

E denotes an OH group or a hydrogen atom,

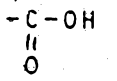
and R' and R", which may be identical or different, denote a hydrogen atom (and in this case R' is different from R") or the group $-(CH_2)_n-R_1-(CH_2)_m-R_2$ where

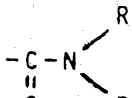
n is between 1 and 6,

m is between 0 and 4 (with the proviso, of course, that if m = 0, R_2 is nonexistent)

R_1 denotes one of the following groups:

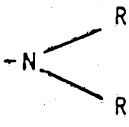
$$-\overset{\overset{O}{\|}}{C}-O-$$

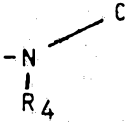

(in this case, m = 0)


(in this case m = 0 where R_3 and R_4, which may be identical or different, denote a hydrogen atom or a substituted or unsubstituted alkyl group)


(in this case m = 0)

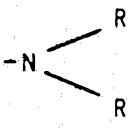

(with the proviso that m is other than 0)


(m = 0 and R_3 and R_4 have the same meaning as above)


(m = 0 and R_3 and R_4 have the same meaning as above)

and

R_2 denotes (in the case where m is other than 0) a hydrogen atom or alkyl or alkoxy groups or


(R_3 and R_4 having the same meaning as above).

2. An anthracycline as claimed in claim 1, which is a derivative of the doxorubicin family.

3. An anthracycline as claimed in claim 1, which is a derivative of the daunorubicin family.

4. An anthracycline as claimed in claim 1, which is a derivative of the carminomycin family.

5. An anthracycline as claimed in claim 1, which is a 4'-epi derivative.

6. An anthracycline as claimed in claim 1, which is a 4'-deoxy derivative.

7. An anthracycline as claimed in claim 1, which comprises 3'-N-(cyanomethyl)daunorubicin.

8. An anthracycline as claimed in claim 1, which comprises 3'-N,N-bis(cyanomethyl)daunorubicin.

9. An anthracycline as claimed in claim 1, which comprises 3'-N-(2-methoxyethyl)daunorubicin.

10. An anthracycline as claimed in claim 1, which comprises 3'-N-cyanomethyl-3'-N-(2-methoxyethyl)daunorubicin.

11. An anthracycline as claimed in claim 1, which comprises 3'-N-[(N,N-diethylcarbamoyl)methyl]daunorubicin.

12. An anthracycline as claimed in claim 1, which comprises 3'-N,N-bis[(N,N-diethylcarbamoyl)methyl]daunorubicin.

13. An anthracycline as claimed in claim 1, which comprises 3'-N-(carbomethoxymethyl)daunorubicin.

14. An anthracycline as claimed in claim 1, which comprises 3'-N-[2-(2-methoxyethoxy)ethyl]daunorubicin.

15. An anthracycline as claimed in claim 1, which comprises 3'-N,N-bis[2-(2-methoxyethoxy)ethyl]daunorubicin.

~~16. A drug comprising or containing an anthracycline as~~ claimed in any one of claims 1 to 15.

DATED this 15th day of December 1986.

LABORATOIRES HOECHST S.A. and
BEHRINGWERKE AKTIENGESELLSCHAFT

EDWD. WATERS & SONS
PATENT ATTORNEYS
50 QUEEN STREET
MELBOURNE, VIC. 3000.

16. A pharmaceutical composition comprising an effective amount of a compound of formula (1) as claimed in claim 1 in adjunct with a pharmaceutically acceptable carrier or excipient.

DATED this 4th day of April 1990.

LABORATOIRES HOECHST S.A. and
BEHRINGWERKE AKTIENGESELLSCHAFT

WATERMARK PATENT & TRADEMARK ATTORNEYS
THE ATRIUM
290 BURWOOD ROAD
HAWTHORN, VICTORIA 3122
AUSTRALIA

DBM/KJS/CH (1.13)