

[54] **MEDICINE COMPRISING LYSINE
DERIVATIVES**

[76] **Inventor:** Georges Tixier, 37, avenue d'Iena,
Paris, France

[22] **Filed:** Oct. 11, 1972

[21] **Appl. No.:** 296,583

[30] **Foreign Application Priority Data**
Oct. 13, 1971 France 71.36804

[52] **U.S. Cl.** 424/319

[51] **Int. Cl.²** A61K 15/12; A61K 27/00

[58] **Field of Search**..... 424/319, 56, 84

[56] **References Cited**
FOREIGN PATENTS OR APPLICATIONS
87M 1/1961 France 424/319

86M 1/1961 France 424/319
4,048M 4/1966 France 424/319
4,465M 9/1966 France

OTHER PUBLICATIONS

Chemical Abstracts 75: 88950s (1971), abstracting
French Patent No. 2,036,045, 12/24/70.
Merck Manual (1972), pp. 300-303.

Primary Examiner—Stanley J. Friedman
Assistant Examiner—Norman A. Drezin
Attorney, Agent, or Firm—Browdy and Neimark

[57] **ABSTRACT**

The medicine contains lysine pantothenate in suitable
form for re-establishing a normal figure of white blood
cells in leukopenic patients.

8 Claims, No Drawings

MEDICINE COMPRISING LYSINE DERIVATIVES

The present invention relates to a medicine based on derivatives of lysine, and especially the pantothenate of this essential amino-acid; these derivatives are utilized, according to the invention, as suitable pharmaceutical preparations; they are utilized to cause stimulation of different metabolic mechanisms, particularly of the ones related to the formation of leukocytes.

This invention takes advantage for therapeutic purposes of the property, not already known, of some derivatives of lysine to stimulate the production of leukocytes

According to another characteristic of the invention, the lysine salts which are utilized can be included into very different pharmaceutical recipes, allowing the proper utilization of the same for human therapeutic use.

The specific physiological activity of the lysine salts, claimed in the present invention, is exemplified by a group of experimental and clinical observations.

A. — TOXICO-PHARMACOLOGY

The lysine derivatives have no acute or lingering toxicity.

With respect to lysine pantothenate:

the L.D 50 is less than 10 g/kg by oral administration, and

the L.D 50 is less than 8 g/kg by parenteral administration.

The administration of the product to rats, during three months, has not caused any prejudicial phenomenon and anatomo-pathological examinations have not revealed any impairment of the main organic systems (muscles, nervous tissues, digestive and endocrine glands and excretion systems).

The leukopenia caused by various aggressive chemical and physical agents (medical poisons and radiations) are favorably influenced experimentally by the administration of lysine derivatives.

Particularly, the administration of lysine pantothenate to a rat made leukopenic through injection of cyclophosphamide (Endoxan) 40 mg/kg caused an alleviation of the poisonous effects. While the leukocyte numerations of the reference batch remain constant during the test, i.e., less than the initial value, the animals treated by the lysine derivatives have their number of leukocytes returning to normal and even become higher than the original value.

The following table shows an abstract of a pharmacological test.

PERCENTAGE OF VARIATION IN RELATION TO THE REFERENCE LEUKOCYTE NUMERATIONS

Batch No	4th day	6th day	11th day	13th day
Batch No 1				
Reference	-32.35	-40.5	-16.9	-11.67
Batch No 2				
Lysine	-49.6	-26.5	+26.2	+16.5
Pantothenate				

As non-restrictive examples, below are given formula designed for the treatment of syndromes under consideration.

1. Oral and digestive preparations

- A -		
Lysine pantothenate	0.60 g	
Aromatized excipient and		
Distilled water	Q.S.P. 5 ml	
1 to 3 ampules per day		
- B -		
Lysine pantothenate	0.25 g	
Excipient Q.S.P. 1 coated tablet		
2 to 5 tablets per day		
- C -		
Lysine pantothenate	0.40 g	
Excipient	Q.S.P. 1 suppository	
1 to 3 suppositories per day		
2. - Injectable preparations		
- D -		
Lysine pantothenate	0.20 g	
Twice-distilled water	Q.S.P. 5 ml	
for an injectable ampule through		
intra-muscular administration.		
1 to 2 ampules per day		

1 to 2 ampule per day.

The active product compositions of the above formulae can be, according to therapeutic needs, reduced up to 25 % or increased up to 50 % of the above mentioned quantities.

B — CLINICALLY

The administration of lysine pantothenate at suitable doses to patients having leukopenia of various etiologies, causes in a relatively short time, a return to normal of the leukocytary formula of the patients.

CASE No. 1

L. JOSEPHA — 68 years old

Physical and psychical asthenia with anorexia, loss of weight, poor general condition.

Treatment: lysine pantothenate 0.90 g per day for fifteen days.

Improvement of the general condition, psychical and physical.

	Leukocytes	
	before treatment	after treatment
Numeration	3000	8000
Polynuclears	38%	59%
Eosinophils	2%	3%
Lymphocytes	57%	34%
Monocytes	3%	4%

CASE No. 2

HAR. JULIA — 85 years old

Sequelae of a fractured femur, surgically treated.

Treatment: lysine pantothenate 0.60 g per day for ten days.

Slight clinical improvement.

	Leukocytes	
	before treatment	after treatment
Numeration	3600	6600
Polynuclears	33%	70%
Eosinophils	1%	2%
Lymphocytes	63%	25%
Monocytes	3%	3%

CASE No. 3

GAREL — 31 years old
Disseminated sclerosis with almost a total anorexia.
Treatment: lysine pantothenate 0.90 g per day for ten 5
days.
Decreased of the anorexia.

	Leukocytes	
	before treatment	after treatment
Numeration	3200	7600
Polynuclears	30%	70%
Eosinophils	4%	2%
Lymphocytes	62%	25%
Monocytes	4%	3%

CASE No. 4

ERM Robert — 78 years old
Sequelae of left hemiplegia (under treatment for reedu-
cation)
Treatment: 1.20 g of lysine pantothenate per day for
ten days.
Clinical improvement.

	Leukocytes	
	before treatment	after treatment
Numeration	6100	7100
Polynuclears	53%	64%
Eosinophils	0	1%
Lymphocytes	41%	23%
Monocytes	6%	12%

What is specifically claimed in this invention is as fol-
lows:

- a. the evidence of a property of lysine and of its deriv-
atives, and more especially of lysine pantothenate,
on the formation of white blood corpuscles,
- b. the utilization of this physiological activity for
therapeutical purposes and more particularly in the
treatment of leukopenia, and
- c. the utilization of the lysine derivatives in pharma-
ceutical preparations adapted to the considered
therapeutical uses.

I claim:

- 1. A method of increasing the number of leukocytes
in a patient having leukopenia which comprises admin-
istering to said patient, lysine pantothenate in an
amount effective to increase the leukocyte numeration
of said patient.
- 2. The method of claim 1 wherein said lysine panto-
thenate is administered orally.
- 3. The method of claim 1 wherein said lysine panto-
thenate is administered parenterally.
- 4. The method of claim 1 wherein said lysine panto-
thenate is administered rectally.
- 5. The method of claim 1 wherein said lysine panto-
thenate is in admixture with a pharmaceutically accept-
able carrier.
- 6. The method of claim 2 wherein said lysine panto-
thenate is administered in a daily dose of 0.5 to 1.8
gms.
- 7. The method of claim 3 wherein said lysine panto-
thenate is administered in a daily dose of 0.2 to 0.4
gms.
- 8. The method of claim 4 wherein said lysine panto-
thenate is administered in a daily dose of 0.4 to 1.2
gms.

* * * * *

40

45

50

55

60

65