United States Patent Office 3,830,926 Patented Aug. 20, 1974

3,830,926

ANTI-MICROBIAL COMPOSITIONS AND METHODS WITH 3-(5-NITRO-2-FURYL)-PYRAZOLES

Graham Arton Howarth, Wilmslow, and William Hoyle, Bramhall, England, assignors to Ciba-Geigy Corporation, Ardsley, N.Y.

No Drawing. Original application June 4, 1970, Ser. No. 43,585, now Patent No. 3,682,956. Divided and this application June 1, 1972, Ser. No. 258,704

Int. Cl. A61k *27/00*

U.S. Cl. 424—273 3 Claims

ABSTRACT OF THE DISCLOSURE

Compounds of the class of 5-amino-4-carbamoyl-3-(5-nitro-2-furyl)-pyrazole substituted in 1-position of the pyrazole ring by alkyl or hydroxyalkyl have anti-microbial properties; these compounds are active ingredients of pharmaceutical and feedstuff compositions; they are useful for the treatment of microbial infections and for protecting organic material against microbial attack; a typical embodiment is 5-amino-4-carbamoyl-1-methyl-3-(5-nitro-2-furyl)-pyrazole.

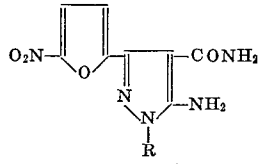
CROSS-REFERENCE TO RELATED APPLICATION

This is a division of Ser. No. 43,585, filed June 4, 1970, now U.S. Pat. No. 3,682,956.

DETAILED DESCRIPTION

The present invention relates to substituted 5-amino-4-carbamoyl-3-(5-nitro-2-furyl)-pyrazoles with anti-microbial activity. It further relates to pharmaceutical and feedstuff compositions as well as to methods for the treatment of microbial infections of mammals and to methods of protecting organic material against microbial attack.

More particularly, the present invention pertains to compounds of formula



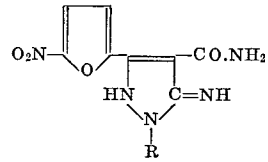
(I)

wherein R is alkyl having at most five carbon atoms or hydroxyalkyl having from two to five carbon atoms.

If R is alkyl, then it may be a straight- or branched-chain alkyl group. Preferably it will contain from one to three carbon atoms. Examples of alkyl groups are methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, tertiarylbutyl and n-pentyl groups. If R is hydroxyalkyl, then preferably it contains two or three carbon atoms.

Nitrofuryl-pyrazoles of formula I may form salts with organic and inorganic acids. Examples of suitable acids include hydrochloric, hydrobromic, sulphuric, phosphoric, methanesulphonic, ethanedisulphonic, acetic, trichloroacetic, oxalic, succinic, maleic, fumaric, malic, tartaric, citric and mandelic acids.

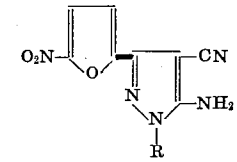
Although the compounds produced by the present invention have been ascribed by formula I above, they may also be represented by the following tautomeric formula IA,



(IA)

and any specified compound of the present invention may occur in either these tautomeric forms or as a mixture of both of them. In this specification, however, the compounds of the present invention are regarded for purposes of clarity as having the formula I and are thus described and exemplified as being 5-nitrofuryl-pyrazole derivatives.

Compounds of the present invention are produced according to a first process comprising hydrolysing a nitrofuryl-pyrazole derivative having formula II,

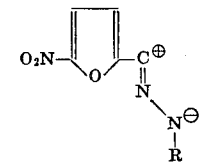


(II)

wherein R is as previously defined.

The process may be carried out under conventional hydrolytic conditions, preferably those conventionally used in the acidic hydrolysis of nitriles, for instance by treating with aqueous sulphuric acid within a temperature range of between 0 and 100° C. Preferably the hydrolysis is effected at a reaction temperature of between 90° and 100° C. Preferably, the compound of formula II is heated with a mixture of concentrated sulphuric acid and ethanol during a reaction time of from one to two hours, and at a temperature of from 90° to 100° C. The resulting reaction product may then advantageously be poured into an excess of water to precipitate the desired 5-nitrofuryl-pyrazole of formula I.

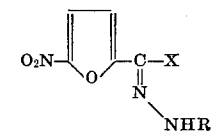
The starting compounds of formula II may be prepared by reacting the corresponding 5-nitrofuryl-nitrilimine, which in one of its mesomeric forms may be represented by the formula III,



(III)

with malononitrile.

The nitro-furyl-nitrilimine of formula III may conveniently be generated, during the course of the reaction with malononitrile, by treating the corresponding nitrofuryl-α-halo-hydrazone having the formula IV,



(IV)

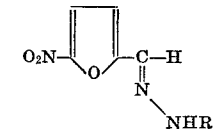
wherein

X is halogen, and

R is as defined before with a base.

The process may, if desired, be effected in the presence of a further conventional hydrogen halide acceptor. The halogen present in the halo-hydrazone of formula IV is preferably chlorine or bromine.

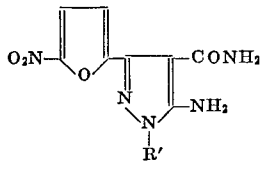
The nitrofuryl-α-halo-hydrazones of formula IV are new compounds. They may be produced, for example, by reacting the corresponding nitrofuryl-hydrazones having the formula V,



(V)

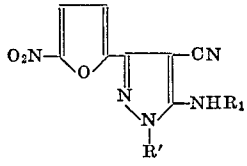
with an N-halo compound bearing the requisite halogen. Examples of N-halo compounds which may be used, are N-halo benzotriazoles and N-halo succinimides. Of the N-halo succinimides, the N-chloro compound may be used, but the N-bromo derivative is preferred.

According to a second process a compound falling under formula I, and having formula I',



(I')

wherein R' is alkyl containing at most five carbon atoms, is prepared by hydrolysing and deacylating a compound of formula VI,

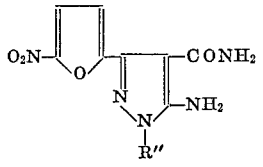


(VI)

wherein

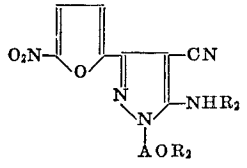
R_1 is alkyl, and

R' is as defined before by treating it with a protonating agent in a polar solvent, and then hydrolising the protonated intermediate.



(I'')

wherein R'' is hydroxyalkyl having from two to five carbon atoms, are prepared by hydrolysing and deacylating a compound having formula VII,



(VII)

wherein

R_2 is lower acyl, and

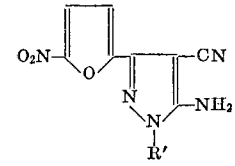
A is alkylene having from two to five carbon atoms, by treating it with a protonating agent in a polar solvent and then hydrolysing the protonated intermediate.

In the hydrolising and deacylating processes, the preferred protonating reagent is ethanolic hydrogen chloride, 40% w./w. being a suitable concentration. Other protonating agents, such as sulphuric acid in other polar solvents, may also be used.

The second and third processes according to the invention are essentially similar. The only difference is that in the second process the substituent R' as alkyl group is unchanged, whereas in the third process the substituent AOR_2 is itself deacylated to form a hydroxy alkyl group.

Normally both the second and third processes according to the invention will involve heating the starting material with a protonating agent such as ethanolic hydrogen chloride for a period of time sufficient to ensure reaction, then cooling the reaction mixture and either adding ice/water, or pouring the reaction mixture into ice/water to precipitate the desired product. The processes are carried out at temperatures between 0° C. and the boiling point of the polar solvent.

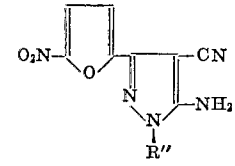
The starting materials of formula VI used for the second process according to the invention, may be prepared by acylating a compound of formula II',



(II')

wherein R' is alkyl having at most five carbon atoms with an acylating agent containing the acyl group R_1.

The starting materials of formula VII used in the third process according to the invention, are novel compounds and are found themselves to possess anti-microbial activity. These compounds of formula VII may be prepared by acylating with a suitable acylating agent compounds of formula II'',



(II'')

wherein R'' is hydroxy alkyl having from two to five carbon atoms, in order to introduce the acyl group R_2.

These compounds of formula II'' may be prepared by a similar series of reactions as described above, starting from a suitable substituted nitrofuryl nitrilimine.

The compounds of the present invention of formula I and formula VII have valuable anti-microbial properties, in particular have anti-bacterial, anthelminthic, anti-protozoal cocidiostatic, trypanocidal and anti-malarial activity of value in human or veterinary medicine. The compounds are particularly valuable in the treatment of infections of the intestinal and urinary tracts. The compounds may also be used to protect a high molecular weight hydrophobic or other organic material susceptible to bacterial or other microbial deterioration by contacting the organic material with, impregnating in, or otherwise treating with, the compounds. The compounds also find application as growth-promoting additives to animal feedstuffs.

The anti-microbial properties of the compounds of the invention are demonstrated in a variety of standard *in vitro* and *in vivo* tests. Thus, 5-amino-4-carbamoyl-1-methyl-3-(5-nitro-2-furyl)-pyrazole and 5-amino-4-carbamoyl-1-(2 - hydroxyethyl)-3-(5-nitro-2-furyl)-pyrazole have been found to have an excellent activity against Staphylococcus, *Escherichia coli,* Klebsiella, Salmonella and other bacteria.

The toxicity of the compounds of the invention as determined in mice on oral administration is of favourably low order.

For their internal use in mammals, the compounds of formula I are administered orally in daily dosages of from about 1 to about 50 mg./kg., although the exact dosage has to be adjusted to the type of infection, the age, weight and the particular condition of the host being treated.

The compounds of the present invention are administered advantageously in form of a pharmaceutical composition comprising an anti-microbially effective amount of a compound of formula I and a pharmaceutically acceptable carrier therefor.

The pharmaceutical compositions according to the invention contain at least one compound of formula I as active substance together with a conventional pharmaceutical carrier. The type of carrier actually used depends to a great extent on the intended application. For external application, for example in disinfecting healthy skin, disinfecting wounds and in treating dermatoses and infections of the mucous membranes caused by bacteria, oint-

ments, powders and tinctures are particularly useful. The ointment bases may be anhydrous, for instance they can consist of mixtures of wool fat and soft paraffin, or they can consist of aqueous emulsions in which the active substance is suspended. Suitable carriers for powders are for instance, rice starch and other starches; the bulk weight of the carriers may be made lighter, if desired, for example by adding highly dispersed silicic acid, or may be made heavier by adding talcum. The tinctures may contain at least one active ingredient of formula I in aqueous ethanol, in particular 45% to 75% ethanol, to which 10% to 20% of glycerol may be added, if desired. Solutions prepared from polyethylene glycol and other conventional solubility promoters, and also optionally, from emulsifying agents, may be used with particular advantage in disinfecting healthy skin.

The content of active ingredient in pharmaceutical compositions for external application is preferably in the range of from 0.1% to 5%.

Gargles or concentrates for their preparation, and tablets for slow dissolution in the mouth, are suitable for the disinfection of the mouth and throat. The former are preferably prepared from alcoholic solutions containing 1% to 5% of active substance to which glycerol or flavourings may be added. Lozenges, that is solid dosage units, preferably have a relatively high content of sugar or similar substances and a relatively low content of active substance, for instance 0.2% to 20% by weight, as well as the usual conventional additives, such as binding agents and flavourings.

Solid dosage units, in particular tablets, dragées (sugar coated tablets) and capsules, are convenient for use in intestinal disinfection and for the oral treatment of urinary tract infections. These units preferably contain from 10% to 90% of the compound of formula I, to enable the administration of daily dosages of from 0.1 to 2.5 grams to adults, or of suitably reduced doses to children. Tablets and dragée cores are produced by combining the compounds of formula I with solid, pulverulent carriers such as lactose, saccharose, sorbitol, maize starch, potato starch or amylopectin, cellulose derivatives or gelatines, preferably with the addition of lubricants such as magnesium or calcium stearate or polyethylene glycols of suitable molecular weight. Dragée cores may then be coated, for example with concentrated sugar solutions which can also contain gum arabic, talcum and/or titanium dioxide, or they may be coated with a lacquer dissolved in volatile organic solvents or a mixture of solvents. Dyestuffs can be added to these coatings, for instance to differentiate between varying dosages. Soft gelatine capsules consist, for example, of a mixture of gelatines and glycerol and may contain, for example, mixtures of the compound of formula I with polyethylene glycol. Hard gelatine capsules contain, for example, granulates of an active substance with solid pulverulent carriers, for instance lactose, saccharose, sorbitol, mannitol, starches (such as potato starch, maize starch or amylopectin), cellulose derivatives of gelatines, and magnesium stearate or stearic acid.

In all forms of administration, compounds of the formula I can be present as sole active ingredients or they can also be combined with other known pharmacologically active, and especially anti-bacterial and/or anti-mycotically or other anti-microbially active substances, for example to broaden the range of applications. They can be combined, for example, with 5,7-dichloro-2-methyl-8-quinolinol or other derivatives of 8-quinolinol, with sulfamerazine or sulfafurazole or other derivatives of sulfanilamide, with chloramphenicol or tetracycline or other antibiotics, with 3,4',5-tribromosalicylanilide or other halogenated salicylanilides, with halogenated carbanilides, with halogenated benzoxazoles or benzoxazolones, with polychloro-hydroxy-diphenylmethanes, with halogen-dihydroxy-diphenyl sulphides, with 4,4'-dichloro-2-hydroxy - diphenylether or 2',4,4'-trichloro-2-hydroxy-diphenylether or other polyhalogenhydroxy-diphenylethers, or with bactericidal quaternary compounds or with certain dithiocarbamic acid derivatives such as tetramethylthiuram disulphide. Also, carriers which themselves have favourable pharmacological properties may be used, for instance sulphur, as a powder base or zinc stearate as a component of ointment bases.

The invention also provides a method of protecting an organic material susceptible to bacterial or other microbial attack which comprises treating the material with a compound of formula I. The organic material may be, for instance, a natural or synthetic polymeric material, a proteinaceous or carbohydrate substance, or a natural or synthetic fibre or textile material formed therefrom.

The invention also provides an animal feedtuff composition comprising a compound of formula I, in an amount sufficient to promote the growth of the animal fed with the composition.

The following examples will serve to further typify the nature of the present invention, but they, in no way, should be construed as a limitation on the scope thereof. The temperatures are given in degrees Centigrade.

EXAMPLE 1

(a) To a prepared mixture of 40 ml. of concentrated sulphuric acid and 40 ml. of ethanol are added 20 g. of 5-amino-4-cyano-1-methyl - 3 - (5-nitro-2-furyl)-pyrazole and the resultant mixture is stirred on a steam bath at 90° to 100° C. for 90 minutes. The reaction mixture is then diluted with 500 ml. of water and stirring is continued until crystallisation is complete. The crude product was collected, washed with water and recrystallised from water.

The product is 5-amino - 4 - carbamoyl-1-methyl-3-(5-nitro-2-furyl)-pyrazole, having melting point 242° C. with decomposition.

(b) The starting material 5-amino-4-cyano-1-methyl-3-(5-nitro-2-furyl)-pyrazole is prepared as follows:

To a stirred solution of 16.9 g. of 5-nitro-2-furaldehyde N'-methylhydrazone dissolved in 100 ml. of dimethylformamide is slowly added 17.8 g. of N-bromosuccinimide at 20–30° C. After further stirring, the mixture is cooled to 10° C.

To the stirred mixture is then added 6.6 g. of malonitrile followed by the slow addition of a mixture of 10.1 g. of triethylamino and 25 ml. of dimethylformamide at 10–20° C.

After further stirring, the mixture is diluted with 500 ml. of iced water and the precipitate is collected, washed with water and dried. The dried solid is recrystallised from ethyl acetate.

The product is 5-amino-4-cyano-1-methyl-3-(5-nitro-2-furyl)-pyrazole having melting point 250° C. with decomposition.

In an analogous manner are prepared:

(c) 5-Amino-4-cyano-1-isopropyl-3-(5-nitro-2-furyl)-pyrazole;

(d) 5-Amino-4-cyano-1-(n-pentyl)-3-(5-nitro-2-furyl)-pyrazole;

(e) 5-Amino-4-cyano-1-(2-hydroxyethyl)-3-(5-nitro-2-furyl)-pyrazole, M.P. 216° C.;

(f) 5-Amino-4-cyano-1-ethyl-3-(5-nitro-2-furyl)-pyrazole, M.P. 189° C.;

(g) 5-Amino-4-cyano-1-n-propyl-3-(5-nitro-2-furyl)-pyrazole, M.P. 165° C.

EXAMPLE 2

The procedure described in Example 1(a) is carried out using 5-amino-4-cyano - 1 - isopropyl-3-(5-nitro-2-furyl)-pyrazole as starting material instead of 5-amino-4-cyano-1-methyl-3-(5-nitro-2-furyl)-pyrazole, the reaction conditions being the same.

The product is 5-amino-4-carbamoyl-1-isopropyl-2-(5-nitro-2-furyl)-pyrazole.

EXAMPLE 3

The procedure described in Example 1(a) is carried out using 5-amino - 4 - cyano-1-(n-pentyl)-3-(5-nitro-2-furyl)-pyrazole as starting material instead of 5-amino-4-cyano-1-methyl-3-(5-nitro-2-furyl)-pyrazole, the reaction conditions being the same.

The product is 5-amino-4-carbamoyl-1-(n-pentyl)-3-(5-nitro-2-furyl)-pyrazole.

EXAMPLE 4

The procedure described in Example 1(a) is carried out using 5 - amino - 4-cyano-1-(2-hydroxyethyl)-3-(5-nitro-2 - furyl)-pyrazole as starting material instead of 5-amino-4 - cyano - 1-methyl-3-(5-nitro-2-furyl)-pyrazole, the reaction conditions being the same.

The product is 5 - amino - 4-carbamoyl-1-(2-hydroxyethyl) - 3 - (5-nitro-2-furyl)-pyrazole, having melting point 202° C.

EXAMPLE 5

(a) A mixture of 10 g. of 5 - amino - 4-cyano-1-(2-hydroxyethyl)-3 - (5 - nitro - 2 - furyl) - pyrazole and 200 ml. of acetic anhydride is heated under reflux for 4.5 hours and then evaporated to dryness under reduced pressure. The solid residue on recrystallisation from aqueous dimethylformamide gives 5-acetamido-1-(2-acetoxyethyl)-4-cyano-3-(5-nitro-2-furyl)-pyrazole, M.P. 191° C.

(b) A mixture of 12.0 g. of 5-acetamido-1-(2-acetoxyethyl) - 4 - cyano-3-(5-nitro-2-furyl)-pyrazole and 50 ml. of ethanolic hydrogen chloride (40% w./w.) is heated under reflux for 15 minutes and cooled.

To the mixture is then added 100 ml. of ice/water and the precipitated solid is collected, recrystallised from water and dried. The product is 5-amino-4-carbamoyl-1-(2 - hydroxyethyl) - 3 - (5-nitro-2-furyl)-pyrazole having melting point 202° C.

EXAMPLE 6

To a solution of 23.3 g. of 5-amino-4-cyano-1-methyl-3-(5-nitro-2-furyl)-pyrazole dissolved in a mixture of 70 ml. dimethylformamide and 70 ml. pyridine is added 7.8 g. of acetyl chloride and the mixture is heated under reflux for 2 hours. After cooling, the mixture is diluted with 150 ml. of ice/water and 5 - acetamido-4-cyano-1-methyl-3-(5-nitro-2-furyl)-pyrazole which is precipitated, collected, washed with water and dried, M.P. 250° C.

The procedure described in Example 5 is repeated using the 5 - acetamido - 4 - cyano-1-methyl-3-(5-nitro-2-furyl)-pyrazole as the starting material instead of 5-acetamido-1-(2-acetoxyethyl)-4 - cyano-3-(5-nitro-2-furyl)-pyrazole, the reaction conditions being the same.

The product is 5 - amino - 4-carbamoyl-1-methyl-3-(5-nitro - 2 - furyl)-pyrazole, having melting point 245° C.

EXAMPLE 7

5 - Acetamido-4-cyano-3-(5-nitro-2-furyl)-1-(n-propyl)-pyrazole (M.P. 215° C.) is prepared in a similar manner to 5 - acetamido - 4-cyano - 1-methyl-3-(5-nitro-2-furyl)-pyrazole described in Example 6, starting from 5-amino-4 - cyano - 3-(5-nitro-2-furyl)-1-(n-propyl)-pyrazole.

The procedure described in Example 5 is carried out using the 5 - acetamido - 4-cyano-3-(5-nitro-2-furyl)-1-(n - propyl) - pyrazole as starting material instead of 5-acetamido - 1 - (2 - acetoxyethyl) - 4-cyano-3-(5-nitro-2-furyl)-pyrazole, the reaction conditions being the same.

The product is 5 - amino - 4-carbamoyl-3-(5-nitro-2-furyl) - 1 - (n-propyl)-pyrazole, having melting point 198° C.

EXAMPLE 8

5 - Acetamido - 4 - cyano-1-ethyl-3-(5-nitro-2-furyl)-pyrazole is prepared in a similar manner to 5 - acetamido-4 - cyano-1-methyl-3-(5-nitro-2-furyl)-pyrazole described in Example 6, starting from 5-amino-4-cyano-1-ethyl-3-(5-nitro-2-furyl)-pyrazole.

The procedure described in Example 5 is carried out using 5 - acetamido - 4-cyano-1-ethyl-3-(5-nitro-2-furyl)-pyrazole as starting material instead of 5-acetamido-1-(2 - acetoxyethyl) - 4-cyano-3-(5-nitro-2-furyl)-pyrazole, the reaction conditions being the same.

The product is 5-amino-4-carbamoyl-1-ethyl-3-(5-nitro-2-furyl)-pyrazole, having melting point 210° C.

EXAMPLE 9

The procedure described in Example 1 is carried out using 5 - amino - 4-cyano-1-ethyl-3-(5-nitro-2-furyl)-pyrazole as starting material instead of 5-amino-4-cyano-1-methyl-3-(5-nitro-2-furyl)-pyrazole, the reaction conditions being the same.

The product is 5 - amino - 4-carbamoyl-1-ethyl-3-(5-nitro-2-furyl)-pyrazole, having melting point 210° C.

EXAMPLE 10

The procedure described in Example 1 is carried out using 5 - amino-4-cyano-1-(n-propyl)-3-(5-nitro-2-furyl)-pyrazole as starting material instead of 5-amino-4-cyano-1-methyl - 3 - (5-nitro-2-furyl)-pyrazole, the reaction conditions being the same.

The product is 5-amino-4-carbamoyl-1-(n-propyl)-3-(5-nitro-2-furyl)-pyrazole, having melting point 198° C.

EXAMPLE 11

Preparation of Tablets

A mixture consisting of 100 g. of 5-amino-4-carbamoyl-1-methyl-3-(5-nitro-2-furyl)-pyrazole, 60.0 g. of maize starch and 35.0 g. of lactose is moistened with a solution of 5.0 g. of gelatin and 3.0 g. of glycerol in 70.0 g. of water and granulated through a sieve. The granulate is mixed with a mixture of 15.0 g. of talcum, 10.0 g. of maize starch and 2.0 g. of magnesium stearate. The resulting mixture is pressed into 1.000 tablets, each containing 100 mg. of active substance. If desired, the tablets can be grooved for better adaption of the dosage.

EXAMPLE 12

Preparation of Dragées

Composition for 1.000 dragées:

	G.
(I)	
5-Amino-4-carbamoyl-1-(2-hydroxyethyl)-3-(5-nitro-2-furyl)-pyrazole	100.0
Maize starch	27.0
Gelatin	8.0
(II)	
Glycerol	2.0
Distilled water q.s. ad 100 ml.	
Maize starch	10.0
(III)	
Talcum	7.0
Magnesium stearate	1.0
	155.0
(IV)	
White dragée coating:	
Shellac	2.0
Sugar	50.0
Talcum	38.0
Gum arabic	7.4
Colloidal silicon dioxide	2.2
Titanium dioxide	0.4

Composition I is granulated in the heat with composition II through a sieve of 1.2 mm. mesh diameter. The dried granulate is mixed with composition III and the resulting mixture is pressed into 1.000 dragée cores. These

are then coated with composition IV and dried. The dragées obtained weigh 255.0 mg. and contain 100 mg. of active substance.

EXAMPLE 13

Preparation of a Syrup

Composition:

	G.
5-Amino-4-carbamoyl-1-(2-hydroxyethyl)-3-(5-nitro-2-furyl)-pyrazole	100.0
Colloidal silicon dioxide	13.0
p-Hydroxybenzoic acid methyl ester	1.4
p-Hydroxybenzoic acid propyl ester	0.6
Citric acid	1.0
Sodium cyclamate	5.0
Distilled water	610.0
Glycerol	100.0
Sodium carboxylmethyl cellulose	4.0
Sugar	320.0
	1.155.0

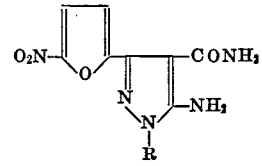
The active substance and the colloidal silicon dioxide are passed through a sieve of 1.2 mm. diameter (I).

The p-hydroxybenzoic acid esters, the citric and the sodium cyclamate are dissolved in the given amount of boiling distilled water; the glycerol is then added to this solution (II). The sodium carboxymethyl cellulose and the sugar are thoroughly mixed (III).

Composition III is then added at 75° C. to solution II under stirring until complete dissolution of III. The viscous, slightly turbid liquid is cooled to room temperature, filtered, if necessary, and mixed with composition I. Water is added to the resulting mixture up to the prescribed weight of 1.155.0 g., and the syrup obtained is homogenized.

What is claimed is:

1. A pharmaceutical composition comprising an antibacterially effective amount of a compound of the formula I

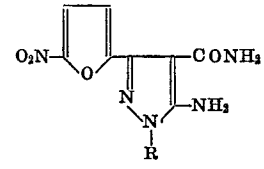


(I)

wherein R is alkyl having at most five carbon atoms or hydroxyalkyl having from two to five carbon atoms, and a pharmaceutically acceptable carrier therefor.

2. The method for the treatment of a mammal suffering from a bacterial infection selected from the group consisting of Staphylococcus, *Escherichia coli*, Klebsiella, and Salmonella, which method comprises administering to said mammal an antibacterially effective amount of the composition according to claim 1.

3. The method of protecting an organic material susceptible to bacterial attack, which comprises treating said material with an antibacterially effective amount of a compound of the formula I



(I)

wherein R is alkyl having at most five carbon atoms or hydroxyalkyl having from two to five carbon atoms.

References Cited

UNITED STATES PATENTS

3,660,425 5/1972 De Wald et al. ------ 424—273

SAM ROSEN, Primary Examiner

PO-1050
(5/69)

UNITED STATES PATENT OFFICE
CERTIFICATE OF CORRECTION

Patent No. 3,830,926 Dated August 20, 1974

Inventor(s) GRAHAM ARTON HOWARTH ET AL

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

Column 1, line 9, insert --- Claims priority, applications Great Britain, June 5, 1969, 28423/69; April 28, 1970, 20274/70 ---

Signed and sealed this 11th day of February 1975.

(SEAL)
Attest:

RUTH C. MASON
Attesting Officer

C. MARSHALL DANN
Commissioner of Patents
and Trademarks

aaa