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(54) ANTIPEPTIC ULCER COMPOSITION

(71) I, DU HONG-YUE, a citizen of Taiwan, of No. 10 Lane 48, Teh-Cheng St., Hsin-Chu Hsien, Taiwan, Formuja, do hereby hereby declare the invention, for which I pray that a patent may be granted to me, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention relates to an antipeptic ulcer composition. More particularly, it provides an antipeptic ulcer composition comprising ferrous sulfate, clove and optionally licorice herebelow referred to as agents A, B and C respectively.

The agent A, ferrous sulfate, is commonly known as a treatment for iron deficiency; the agent B, clove, is used as a carminative and a flavour; and the agent C, licorice, is considered to possess demulcent, expectorant and laxative properties and is used considerably as a flavouring agent.

In the recent years, the extracts of licorice with various solvents have been employed in treating peptic ulcers, such as carbenoxolone, glycyrrhetic acid (K2), FM100 FM100 is a licorice extract such as described in UK Patent Specification No. 1,182,179), etc.. The composition according to the present invention shows a great deal of difference from them. Besides, there has been no one using agent A or both A and B for antipeptic ulcer composition.

Research carried out on various compositions of agents A, B and C has shown no curative effect is obtained when merely use agents A and C. A composition using A and B, herebelow referred as CD, indeed has some curative effect. Most of all, a composition using A, B and C herebelow referred as CD1, shows excellent synergistic cooperative action in treating peptic ulcer. The mechanism in the curative action of said compositions CD or CD1 has not been clarified yet, but it seems to be very different from that of antacid or anticholinergic drug.

The curative test of CD1 as described below shows that CD1 is much more effective than antacid, antipeptic agent (carrageenin), and anticholinergic drug (atropine sulfate). The curative ratio of CD1 even exceeds that of the most effective drug FM100.

The antipeptic ulcer compositions of the present invention CD and CD1 are prepared by compounding agents A, B and A, B, C respectively. When compositions of the present invention are administered as antipeptic ulcer compositions, it is advantageous to administer them as tablets, powders capsules or granules. The pharmaceutically acceptable inactive carrier is which can be used for said purpose are corn starch, or starch paste.

The animal test procedures are like those in acetic acid ulcer (so-called intractible ulcer). The details of the experimental procedures can be obtained with reference to Jap. J. Pharmacology 19.418, 1969 by Takagi. K.,

In the experiments according to the present invention, male Wistar rats weighing 200-230 gm were laparatomized under ether anaesthesia; and 0.05 ml of 30% by weight acetic acid solution was injected into the subserosal layer in the glandular stomach. Then the abdomen was closed and the rats were fed normally.

CD1 or CD suspended in 0.5% by weight C.M.C. solution was administered orally twice a day. The control animals were treated with the vehicle alone. The animals were sacrificed 15 days after said operation to observe the curative ratio of the ulcers, and the results are summarized below as examples and tables.

Example I

A composition CD chosen in 88% by weight of agent A and 12% of agent B is tested as an example under procedures of acetic acid ulcer mentioned above. The results obtained are

shown herebelow in Table I.

Table I

Treatment (twice daily)	Administration time	No of rats	Ulcer Index ±SE (mm^2)	Curative ratio	P value
Control	15 days	10	16.2 ± 1.6		
CD: 80mg/kg	15 days	7	12.6 ± 2.3	22.4 %	>0.2
FM100:200mg/kg	15 days	10	9.5 ± 1.9	41.2%	<0.02

Remarks: The ulcer index is defined as the sum of the ulcer area which was calculated by multiplying the length by the width of each ulcer.

Example II

A composition CDI chosen in 68% by weight of agent A, 9% by weight of agent B and 23% by weight of agent C is tested as an example under procedures of acetic acid ulcer mentioned above. The results obtained are shown herebelow in Table II.

Table II

Treatment (twice daily)	Administration time	No of rats	Ulcer Index ±SE (mm^2)	Curative ratio	P value
Control	15 days	7	21.7 ± 2.0		
CD1: 100mg/kg	15 days	7	9.6 ± 1.7	55.7%	<0.001

For the purpose of comparison and reference, the curative ratio of several conventional drugs by 15 days administration were as follows:

No.	Drugs	Curative ratio
1.	Aluminium silicate (1000 mg/kg per o.s.)	11.4%
2.	Atropine Sulfate (20 mg/kg s.c.)	26.7%
3.	Chlorophyl Cu-Na (500 mg/kg per o.s.)	39.8%
4.	Glycyrrhetic acid (K_2) (700 mg/kg per o.s.)	33.7%

Remarks: Data from Jap. J. Pharmacol. 19.418 (1969)

Besides, a seasonal variation of experimental results in FM100 are listed in Table III.

Table III

Exp. No.	Administration time (twice daily)	Treatment	No. of rats	Ulcer Index ±SE (mm^2)	Curative ratio
1	10 days	Control	10	20.9 ± 3.7	
		FM100:400mg/kg	10	14.3 ± 2.0	32%
2	10 days	Control	11	19.2 ± 2.6	
		FM100:200mg/kg	12	11.8 ± 1.4	38%
3	10 days	Control	12	19.5 ± 3.1	
		FM100:200mg/kg	11	11.4 ± 1.9	41%
4	10 days	Control	8	33.1 ± 4.3	
		FM100:200mg/kg	10	15.1 ± 1.6	54%
		400mg/kg	10	16.6 ± 2.6	50%
5	15 days	Control	18	22.6 ± 4.0	
		FM100:400mg/kg	16	11.4 ± 2.6	50%

Remarks: Data from Jap. J. Pharmacol. 21.832(1971).

Therefore, it is concluded that CD1 has an excellent curative ratio in therapeutic effect on chronic peptic ulcer. Besides, it also has less side effects than other agents.

WHAT I CLAIM IS:—

1. An antipeptic ulcer composition comprising ferrous sulfate and clove.
2. An antipeptic ulcer composition as claimed in claim 1 further comprising licorice.
3. An antipeptic ulcer composition as claimed in claim 1 or 2 wherein the composition contains a pharmaceutically acceptable inactive carrier and is in the form of tablets.
4. An antipeptic ulcer composition as claimed in claim 1 and substantially as hereinbefore described.

shown herebelow in Table I.

Table I

Treatment (twice daily)	Administration time	No of rats	Ulcer Index ±SE (mm^2)	Curative ratio	P value
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A composition CDI chosen in 68% by weight of agent A, 9% by weight of agent B and 23% by weight of agent C is tested as an example under procedures of acetic acid ulcer mentioned above. The results obtained are shown herebelow in Table II.

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4	10 days	Control	8	33.1 ± 4.3	
		FM100:200mg/kg	10	15.1 ± 1.6	54%
		400mg/kg	10	16.6 ± 2.6	50%
5	15 days	Control	18	22.6 ± 4.0	
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4. An antipeptic ulcer composition as claimed in claim 1 and substantially as hereinbefore described.

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