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3,487,150

DEXTRAN SULPHATE TREATMENT OF PEPTIC ULCERS

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4 Claims

ABSTRACT OF THE DISCLOSURE

The use of dextran sulphate, preferably in the form of sodium or potassium dextran sulphate, containing at least 13% sulphur for oral administration in the treatment and inhibition of peptic ulcers in dosage units of 8–20 parts by weight per 60,000 parts by weight of the mammal is disclosed. Dextran sulphate has fully anti-peptic activity and surprisingly causes no side activity such as anti-coagulation of the blood. The anti-peptic activity is found in vivo to be higher than that of other sulphated polysaccharides.

The present invention relates to the treatment of peptic ulcers and, more particularly, to a composition including dextran sulphate and the oral administration of such composition in the treatment of peptic ulcers.

For many years it has been recognized that a component of gastric juice is an inhibitor of peptic activity. It has been generally assumed that the active components of the inhibitor of peptic activity found in gastric juice are degradation products of proteins, such as polypeptides, peptides or amino acids.

In 1960 it was reported that an inhibitor of peptic activity could be recovered by dialysis from gastric juice, the inhibitor being effective in acid environment (Redo et al.; "An Inhibitor of Peptic Activity Recoverable From Gastric Juice"; Surg. Forum, vol. 10, page 129; 1960). This inhibitory activity has also been found in saliva and urine. The study of such inhibitory fractions by chromatographic methods have shown several amino acids; however, when these and other amino acids are used singly or in various combination, they fail to reproduce the anti-peptic activity of the original fraction.

It has also been known that certain polysaccharides diminish the ulcerogenic activity of acid-pepsin combinations (e.g. Houck et al.; "The Inhibition of Pepsin and Peptic Ulcers"; Gastroenterology; vol. 39, page 196; 1960), such polysaccharides including heparin, chondroitin sulphate, and carrageenin. However, in spite of the knowledge that such materials which inhibit ulcerogenic activity, a more effective treatment for the prevention and inhibition of peptic ulcers has been desired.

It is therefore an object of the present invention to provide a more effective treatment for peptic ulcers.

It is another object of the present invention to provide a method and composition for the successful treatment of peptic ulcers.

It is another object of the present invention to provide a method and composition which will inhibit the formation of peptic ulcers.

These and other objects and the nature and advantages of the present invention will become apparent from the following description.

The present invention provides, generally, the oral ad-

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ministration of dextran sulphate, the dextran sulphate dissolving in the stomach to inhibit peptic activity.

Dextran sulphate has been used in the past as an anti-coagulant in which it has been administered intravenously or intramuscularly (The Merck Index; 7th Edition; 1960; page 331). Dextran sulphate has also been used, in smaller quantities, for the treatment of hyperipemia. In this latter connection, the patent of Morii et al., No. 3,126,320, shows that dextran sulphate may be administered orally, but only if provided with an enteric coating to prevent dissolving of the dextran sulphate in the stomach.

In the present invention, and directly contrary to the teaching of Morii et al., the dextran sulphate is provided so that it must dissolve in the stomach. Dextran sulphate may be administered orally to both treat ulcers already present and to inhibit the formation of ulcers in mammals when the mammals are subject to an ulcer causing environment, such as during the administration of corticosteroids, during the acute phase of extensive burns, with certain brain lesions, or in patients with a past history of ulcer subjected to special stress producing situations.

It is essential to the present invention that the dextran sulphate composition which is orally administered be capable of dissolving in the stomach where it may contact the peptic ulcer or mix with the ulcer producing material in contact with the ulcer forming areas. Gastric juice is generally recognized to be strongly acidic, the pH being generally below 3.0. It therefore follows that the dextran sulphate must be capable of dissolving at a pH below 3.0 (i.e., it is acid soluble). Similarly, the carrier for the dextran sulphate must also dissolve at a pH below 3.0 to prevent the carrier from surrounding the dextran sulphate and preventing dissolution thereof while in the stomach. Thus, any enteric carrier would not be suitable unless it were to act merely as a matrix from which the dextran sulphate could be leached while in the stomach. The dextran sulphate should preferably be used in the form of a water soluble alkali metal salt, such as sodium or potassium dextran sulphate.

The conventional tablet forming carriers such as starch, sucrose, dextrin, lactose, talc and/or glucose have been found to be successful carriers for dextran sulphate in the treatment of peptic ulcers. In addition, the dextran sulphate, preferably in the form of a water soluble salt, may be merely dissolved in water and administered orally as a liquid. The dextran sulphate may also be incorporated into chewing gum from which it will be leached by saliva and carried to the stomach or it may be enclosed in a suitable gelatin capsule along with powdered filler materials.

In the treatment of a 60 kg. mammal, it has been found that a dosage unit of from about 1 to 2 grams, taken three or four times daily will be effective in both preventing the formation of peptic ulcers and eliminating already formed peptic ulcers, although higher dosages may be desirable for the treatment of already formed ulcers. A daily dosage of 50 mg. for a 400 gram mammal has proven highly effective in preventing ulceration in an extreme situation. Therefore, the daily dosage should be about 8–10 parts by weight of the dextran sulphate per 60,000 parts by weight of the mammal.

The dextran sulphate used in the present invention may be prepared by known processes, for example, by using chlorosulphonic acid in pyridine or in formamide in the presence of pyridine. For reasons of processing, however, it has been found that the sulphate used is preferably that prepared in formamide using chlorosulphonic acid in the