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GLYCOCYAMINE AND METHYLATING AGENT IN VIVO CREATINE PRODUCING COMPOSITION

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3 Claims. (Cl. 167—55)

This invention relates to therapeutic compositions and to a method of administering the same.

This is a continuation-in-part application, based on our co-pending application, Serial Number 201,066, filed December 15, 1950, now abandoned, on Therapeutic Composition and Method.

One of the objects of this invention is to provide therapeutic compositions which are effective in the treatment of diseased and otherwise damaged and weak muscle tissues, and diseased and otherwise damaged and weak nerve tissues.

Another object of this invention is to provide therapeutic compositions for the treatment of muscular and nervous diseases and the like, which compositions are physiologically effective in the treatment of such conditions.

Other objects and advantages of this invention will be readily apparent from the following detailed description thereof.

It is well established that creatine in the form of phosphocreatine is a source of energy for the muscles and nerve cells of the human body. We have found that, by making available to the patient the physiological precursors of creatine, marked improvement has been obtained in the condition of the muscles. We have further found that in order to obtain this improvement it is necessary to furnish much greater amounts of creatine-producing material than are required by a healthy person.

We have found that glycocyamine may be methylated in vivo by compounds or methylating agents such as betaine, betaine hydrate, choline and dimethylthetin to form creatine. The creatine thus formed passes to all tissues of the body and is combined with physiologically available phosphate to form phosphocreatine, an available source of energy for the muscles and nerve tissues. During the course of our researches, we have also found that, while methionine is a methylating agent for glycocyamine, it is not suitable for use in human therapy, since in the amounts required methionine has a toxic effect on the human body.

The following examples are illustrative of preferred embodiments of our invention, but it is not intended to limit the invention thereto. The proportions given are by weight.

Example 1

	Parts
Glycocyamine	1
Betaine hydrate	4

It will be noted that the methylating agent, that is, betaine hydrate, is provided in excess of the order of 4–1 over that theoretically required to react with glycocyamine to form creatine. A molar excess of methylating agent is necessary in order to assure that substantially all of the glycocyamine is converted to creatine, since it has been found that the presence in the body of exogenous glycocyamine alone tends to cause liver disease (fatty infiltration), and prolonged ingestion of glycocyamine unaccompanied by a sufficient quantity of methylating agent to assure complete conversion of the glycocyamine

may lead to other toxic effects, particularly in patients suffering from cardio-renal limitations.

The daily dosage of glycocyamine may vary over a fairly wide range depending upon the particular conditions and the patient being treated. Ordinarily the amount of glycocyamine administered per day is roughly 2½ times that amount of glycocyamine normally formed within the human body through ingestion of a balanced diet. This excess amount of glycocyamine is equivalent to about 30 mg. per pound of body weight per day. Regardless of the amount of glycocyamine administered, it is to be understood that the above-mentioned ratio of methylating agent to glycocyamine is always maintained; that is, the methylating agent must be present in molar excess per mol of glycocyamine. On the basis of 30 mg. of glycocyamine per pound of body weight per day, the dosage of the composition set forth in Example 1 would be about 150 mg. per pound of body weight per day. This amount is given in divided doses, preferably four equal portions, taken at spaced intervals during the day.

We prefer to administer the medicament or composition by oral administration of the glycocyamine and methylating agent in combined form, either as a suspension of glycocyamine in an aqueous solution of the methylating agent, or in tablet form, but the composition may be administered in various other ways: the glycocyamine may be given orally in the form of tablets and immediately thereafter an aqueous solution of the methylating agent may be taken; the glycocyamine may be administered orally in the form of tablets or in suspension and immediately before or after, an aqueous solution of the methylating agent may be taken orally; tablets of glycocyamine and the methylating agent may be separately prepared and taken orally as such; or, if desired, the composition may be injected. It is important, however, that the glycocyamine and methylating agent be administered substantially simultaneously so that they are both present in the system of the patient at the same time to enable the methylation reaction to take place, and to avoid the toxic effects noted above. Moreover, it will be apparent to those skilled in the art that, regardless of the method of administration, the glycocyamine and methylating agent must be present in therapeutically effective concentrations. For example, in the case of the combined suspension, only sufficient water should be used to permit convenient ingestion by the patient of the relatively large daily doses which are required. Similarly, in the case of use of tablets, inert fillers or binders should be kept at a minimum to avoid the taking of prohibitively large, or a prohibitively large number of tablets.

Example 2

	Parts
Glycocyamine	1
Betaine hydrate	5

On the basis of 30 mg. of glycocyamine per pound of body weight per day, the dosage of the composition set forth in Example 2 is about 180 mg. per pound of body weight per day.

Example 3

	Parts
Glycocyamine	1
Betaine hydrate	3

On the basis of 30 mg. of glycocyamine per pound of body weight per day, the dosage of the composition set forth in Example 3 is about 120 mg. per pound of body weight per day.

A significant number of the patients treated with the composition of this invention have experienced a marked increase in the sense of well being and an increase in muscular energy output. The compositions of this invention have been administered in accordance with the

methods described above and have been found to be effective, in many cases when used as an adjunct to conventional and other therapeutic regimens, in the treatment of: cardio-vascular diseases, paresis resulting from poliomyelitis and multiple sclerosis. In 1954 other investigators published reports of alleged investigations on the use of the compositions in the treatment of the anxiety-tension-fatigue syndrome, sometimes referred to as the stress phenomenon, and alleged it to be of value as an adjunct to educative therapy. Such subsequent clinical investigators reported facilitated management of patients with anxiety-tension-fatigue problems and, additionally, other subsequent clinical investigators have reported many occurrences of relief from anginal pain, and improved articulation and ambulation of patients with neuro-muscular impairment.

While we have fully described a preferred embodiment of our invention, it is to be understood that we do not wish to be limited to the details herein set forth, but our invention is of the full scope of the appended claims.

We claim:

1. A therapeutic composition, which produces creatine in vivo in the human body, said composition being effective in the treatment of diseased and weak muscle tissues in a dosage of the essential therapeutically active ingredients including glycocyamine providing about 30 milligrams of glycocyamine per pound of body weight per day, said composition containing as essential therapeutically active ingredients glycocyamine and from about three to about five mols per mol of glycocyamine of a material

selected from the group consisting of betaine, betaine hydrate, choline and dimethylthetin, said glycocyamine being present in said composition predominantly as a solid, the concentration of said glycocyamine and said material in said composition being such that said composition can be therapeutically administered in the amount requisite to provide about 30 milligrams of glycocyamine per pound of body weight per day.

2. The composition of claim 1 wherein said material is betaine hydrate.

3. The composition of claim 1 in which the material is betaine hydrate present in the ratio of five mols per mol of glycocyamine.

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