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FATTY ACID SALTS

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This invention relates to new salts of organic bases and fatty acids. More particularly, this invention relates to novel salts of specific physiologically acceptable organic bases and hydrophilic straight chain fatty acids.

For a great many years it has been known that most of the nutritional requirements of an individual can be introduced by the use of parenteral techniques when necessary. Normally such nutriments are introduced into the vascular system. This method of introducing nutriments is characterized as parenteral alimentation. The science of parenteral alimentation has progressed to a point where water, electrolytes, carbohydrates and protein (in the form of protein hydrolysate) can be administered safely and routinely. These developments have contributed substantially to the reduction of surgical risks and the enhancement of healing processes.

In spite of the many advances in parenteral alimentation, a high caloric parenteral solution that can be administered safely and routinely is still desired. Carbohydrate materials have heretofore provided the only generally accepted source of parenterally introduced calories. In the average human more than three liters of fluid per day by the parenteral route will likely produce a water overload. The maximum sugar concentration that can be safely administered by the I.V. route without hypertonicity problems is 10%. Thus if one administers three liters of a 10% solution of a hexose (glucose, fructose and combinations thereof) only 1200 calories are provided. The minimal daily requirement for a normal healthy individual is about 1800 calories. Many surgical patients require an even higher daily caloric intake. It is readily observable, therefore, that carbohydrates alone cannot supply the requisite daily caloric requirements when parenteral alimentation is the sole source of nutriments, a situation which is not uncommon.

Fats, of course, are high in caloric value. Fats, however, are not soluble in water and must be introduced parenterally in the form of an emulsion. Fat emulsions are presently being employed on a limited scale for parenteral alimentation, but the manufacture and use of such emulsions pose a number of problems. Fat emulsions are difficult to manufacture, and the size of the fat particles in the emulsion is not easily controlled and maintained. Under manufacturing conditions, the emulsions which are obtained are often pyrogenic, i.e. they engender a febrile response when administered parenterally. Fat emulsions tend to have a poor shelf life, even when stored at refrigerator temperatures, thereby making commercial distribution through common marketing channels a difficult task. The new and novel compounds of this invention are non-hemolytic, non-toxic salts of certain physiologically acceptable organic bases and certain substantially hydrophilic fatty acids. These compositions provide a high caloric value and are suitable for parenteral alimentation.

The physiologically acceptable organic bases employed in the manufacture of the compositions of this invention are sufficiently basic in character that they will form salts with the weakly acidic fatty acids which provide the anionic moiety of the salt. Preferably, these organic bases provide some caloric value themselves. Examples of such organic bases are choline, lysine, arginine and ornithine.

The fatty acid which provides the anionic moiety of the

salts of the invention is a substantially hydrophilic straight chain fatty acid. Examples of such hydrophilic fatty acids are straight chain hydroxy alkanoic acids which contain from 8 to 20 carbon atoms and from 1 to 4 hydroxyl groups, there being at least one hydroxyl group per 4 to 6 carbon atoms; straight chain alkadienoic acids which contain from 6 to 8 carbon atoms; and straight chain dicarboxylic acids which contain from 8 to 14 carbon atoms. Specific examples of such substantially hydrophilic straight chain fatty acids are aleruitic acid (9, 10, 16-trihydroxypalmitic acid), sorbic acid 2, 4-hexodienoic acid), omega-hydroxycarprioic acid, tetrahydroxystearic acid and 10, 11-dihydroxyundecanoic acid.

The following are illustrative of the salts of this invention: arginine sorbate, 1-arginine aleuritate, 1-arginine tetrahydroxystearate, 1-lysine sorbate, 1-lysine aleuritate, 1-arginine 9, 10, 12-trihydroxystearate, 1-arginine 10, 11-dihydroxyundecanoate, 1-lysine-9, 10, 12-trihydroxystearate and 1-lysine-10, 11-dihydroxyundecanoate.

The salts of this invention are readily prepared in solution by combining molar equivalent amounts of the reactants, that is, the physiologically acceptable organic base and the substantially hydrophilic straight chain fatty acid, and by adjusting the pH, where necessary, to promote maximum solubility. The pH is, however, in a range such that the resulting salt solution is physiologically acceptable. In most instances the isolation of the salts as discreet solids is not practicable, since the fatty acids which are employed are diastereoisomers and their salts are difficult to crystallize. Furthermore, when these salts are employed for purposes of parenteral alimentation, it is not necessary that the salts be provided in the form of solids, since these salts are administered in solution.

The compositions of this invention are not restricted to the chemically bound reactants which comprise the salts. The compositions of this invention include mixtures of the chemically dissociated reactants which combine chemically to form salts. Such reactants in combination are also new and novel compositions.

The unique character of the compounds of this invention in providing high caloric value, and being at the same time suitable for parenteral alimentation, is believed to be attributable to the presence of the hydroxyl groups or the unsaturated linkages in the fatty acid moiety of the compositions. These hydroxyl groups and unsaturated linkages apparently alter the hydrophobic character of the fatty acid moiety and render this moiety sufficiently hydrophilic that the resultant salt is water soluble and substantially non surface active. When the conventional type of fatty acid is employed the resulting salt is not sufficiently water soluble and further, when introduced parenterally, a substantial degree of hemolysis results. It is believed that this hemolysis is the result of the surface active properties possessed by these conventional fatty acids in an environment such as that provided in the vascular system.

A more comprehensive understanding of this invention is obtained by reference to the following examples:

Example I

In the preparation of the 1-arginine aleuritate, 1-arginine (3.50 gm., 0.02 M) and aleuritic acid (6.10 gm., 0.02 M) were dissolved with warming in 50 ml. of 10% ethanol. The solution was quick-frozen in a Dry Ice-acetone bath and then lyophilized. Drying was completed in vacuo over phosphorous pentoxide at 57° C. The dry white powder thus obtained comprised 1-arginine aleuritate and was soluble at 20° C. in water to the extent of 10%.

Example II

In the preparation of 1-lysine aleuritate equimolar (0.02 M) amounts of 1-lysine and aleuritic acid were dissolved with warming in 50 ml. of 10% ethanol. The solution

was quick-frozen in a Dry Ice-acetone bath and then lyophilized. Drying was completed in vacuo over phosphorous pentoxide at 57° C. The dry white powder thus obtained comprised 1-lysine aleuritate and was soluble in water at 20° C. to the extent of 10%.

Example III

In the preparation of 1-arginine dithreo-9, 10, 12, 13-tetrahydroxystearate, equimolar (0.02 M) amounts of 1-arginine and dithreo-9, 10, 12, 13-tetrahydroxystearic acid were dissolved with warming in 50 ml. of 10% ethanol. The solution was quick-frozen in a Dry Ice-acetone bath and then lyophilized. Drying was completed in vacuo over phosphorous pentoxide at 57° C. The dry white powder thus obtained was soluble in water.

Example IV

In the preparation of di-1-arginine sebacate, equimolar amounts (0.02 M) of 1-arginine and sebacic acid were dissolved with warming in 50 ml. of 10% ethanol. The solution was quick-frozen in a Dry Ice-acetone bath and then lyophilized. Drying was completed in vacuo over phosphorous pentoxide at 57° C. The dry white powder thus obtained comprised di-1-arginine sebacate and was soluble in water at 20° C. to the extent of 20%.

While in the foregoing specification, a detailed description of embodiments of the invention has been set forth

for the purpose of understanding, it will be apparent to those skilled in the art that many modifications in the details thereof may be made without departing from the spirit and principles of the invention.

What is claimed is:

1. A salt of a physiologically acceptable organic base selected from the class consisting of lysine, arginine, and ornithine, and a fatty acid selected from the class consisting of aleuritic acid, sorbic acid, omega-hydroxycaproic acid, trihydroxystearic acid, tetra hydroxystearic acid and 10, 11 dihydroxyundecanoic acid.
2. Arginine sorbate.
3. Arginine aleuritate.
4. Lysine sorbate.
5. Lysine aleuritate.
6. Arginine trihydroxystearate.
7. Arginine 10, 11-dihydroxyundecanoate.
8. Lysine-9, 10, 12-trihydroxystearate.
9. Lysine-10, 11-dihydroxyundecanoate.
10. Arginine tetrahydroxystearate.

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