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3,773,946
**TRIGLYCERIDE-LOWERING COMPOSITIONS
 AND METHODS**

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 No Drawing. Continuation-in-part of abandoned applica-
 tion Ser. No. 854,756, Sept. 2, 1969. This application
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6 Claims

ABSTRACT OF THE DISCLOSURE

Pharmaceutical compositions comprising a pharmaceu-
 tical carrier and an $\alpha, \alpha, \alpha', \alpha'$ -tetramethylalkanedioic
 acid having a total of 14 to 18 carbon atoms, or a salt or
 alkyl ester of such an alkanedioic acid. Methods for the
 lowering of serum triglyceride levels by administering an
 $\alpha, \alpha, \alpha', \alpha'$ -tetramethylalkanedioic acid having a total of 14
 to 18 carbon atoms, or a salt or alkyl ester of such an
 alkanedioic acid.

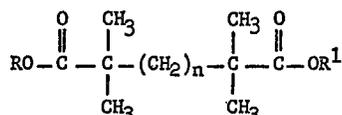
CROSS REFERENCE TO RELATED APPLICATION

This is a continuation-in-part of co-pending application
 Ser. No. 854,756, filed Sept. 2, 1969, now abandoned.

SUMMARY AND DETAILED DESCRIPTION

The present invention relates to pharmaceutical composi-
 tions possessing serum triglyceride-lowering activity,
 and to methods for lowering serum triglyceride levels, said
 compositions and methods employing certain alkanedioic
 acids and salts and alkyl esters thereof.

More particularly, the invention relates to pharmaceu-
 tical compositions and methods employing compounds
 which can be represented by the formula



in which n represents 6, 7, 8, 9, or 10; and each of R and
 R^1 represents hydrogen, a salt-forming cation, or a lower
 alkyl radical. The lower alkyl radicals are those containing
 not more than 8 carbon atoms. The salt-forming cations
 are preferably the pharmaceutically-acceptable cations
 of alkali metals, alkaline earth metals, ammonium, and
 substituted ammonium.

In accordance with the invention, pharmaceutical composi-
 tions are produced by formulating a compound of the
 foregoing formula (as an active ingredient) in dosage
 unit form with a pharmaceutical carrier. Some examples
 of dosage unit forms are tablets, capsules, lozenges, and
 pills; as well as powders and aqueous and non-aqueous
 solutions and suspensions packaged in containers con-
 taining either one or some larger number of dosage units
 and capable of being subdivided into individual doses
 by such means as measurement into a teaspoon or other
 standard container. Some examples of suitable pharmaceu-
 tical carriers, including pharmaceutical diluents, are
 gelatin capsules; sugars such as lactose and sucrose;
 starches such as corn starch and potato starch; cellulose
 derivatives such as sodium carboxymethyl cellulose, ethyl
 cellulose, methyl cellulose, and cellulose acetate phthalate;
 gelatin; talc; stearic acid; magnesium stearate; vegetable
 oils such as peanut oil, cottonseed oil, sesame oil, olive
 oil, corn oil, and oil of theobroma; propylene glycol;
 glycerine, sorbitol; polyethylene glycol; water; agar;
 alginate; isotonic saline; and phosphate buffer solu-
 tions; as well as other compatible substances normally
 used in pharmaceutical formulations. The compositions

of the invention can also contain other components such
 as coloring agents, flavoring agents, and/or preservatives.
 These materials, if present, are usually used in relatively
 small amounts. The compositions can, if desired, also con-
 tain other therapeutic agents.

The percentage of the active ingredient in the foregoing
 compositions can be varied within wide limits but for
 practical purposes it is preferably present in a concentra-
 tion of at least 10% in a solid composition and at least
 2% in a primarily liquid composition. The most satisfac-
 tory compositions are those in which a much higher pro-
 portion of the active ingredient is present. The composi-
 tions of the invention preferably contain from 20 to
 1,000 mg. of the active ingredient per dosage unit so that
 the entire amount to be administered during a day can
 be made up from a reasonable number of dosage units.

Also in accordance with the invention, the compounds
 of the foregoing formula are administered for the purpose
 of lowering serum triglyceride levels. The aforementioned
 compounds and compositions containing the same can be
 administered either orally or parenterally, in dosage unit
 form, with the dose adjusted to the needs and tolerances
 of the individual patient. Oral administration is preferred.
 The usual human dosage range is from 50 to 2,000 mg. per
 day, preferably 100 to 500 mg. per day, optionally in
 divided portions. Treatment is continued while satisfactory
 control of the serum triglyceride level is maintained with-
 out undesired side-effects.

The methods of the invention, as explained above, pro-
 duce a lowering of the serum triglyceride level. In many
 cases the aforementioned compounds and compositions,
 especially when they are administered at a relatively high
 dosage, also produce a lowering of the serum cholesterol
 level. The lowering of serum triglycerides is a charac-
 teristic feature of the invention and the lowering of serum
 cholesterol is an incidental feature.

The effectiveness of the aforementioned compounds and
 compositions in lowering serum triglycerides can be
 demonstrated by standard methods. For example, male
 rats weighing 200-250 g. are maintained on a normal
 pellet diet. Each animal in a treatment group is given a
 daily oral dose of a test compound for 7 days. An un-
 treated control group is also maintained. At the end of
 the 7-day test period the animals are weighed and sacri-
 ficed, and the serum cholesterol and serum triglycerides
 are determined from blood samples taken from the vena
 cava. The methods used are described in "Journal of
 Laboratory and Clinical Medicine," 50, 318 (1957) and
 "Journal of Laboratory and Clinical Medicine," 50, 152
 (1957). The test compound is considered to exhibit a
 side effect if the weight of the animals in the treatment
 group is significantly less than the weight of the animals
 in the control group. In a representative determination,
 2,2,9,9-tetramethyldecanedioic acid at 5 mg./kg. per day
 for 7 days produced a 44% reduction of serum tri-
 glycerides with no effect on serum cholesterol or weight
 of the animals, relative to the untreated control group.
 2,2,9,9-tetramethyldecanedioic acid, diethyl ester at 75
 mg./kg. per day for 7 days produced a 74% reduction
 of serum triglycerides with no effect on serum cholesterol
 or weight of the animals, relative to the untreated control
 group.

The preferred pharmaceutical compositions and methods
 of the invention are those employing an $\alpha, \alpha, \alpha', \alpha'$ -tetra-
 methylalkanedioic acid of the formula

