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(54) **CITRATE MAGNESIQUE DE L-CARNITINE**
(54) **L-CARNITINE MAGNESIUM CITRATE**

(57) The novel compound L-carnitine magnesium citrate is disclosed, together with a process for its production, by reaction of a magnesium compound, citric acid and L-carnitine. The product is useful as a combination preparation in sports nutrition or as a pharmacologically active ingredient.

ABSTRACT OF THE DISCLOSURE

The novel compound L-carnitine magnesium citrate is disclosed, together with a process for its production, by reaction of a magnesium compound, citric acid and L-carnitine. The product is useful as a combination preparation in sports nutrition or as a pharmacologically active ingredient.

This invention relates to L-carnitine magnesium citrate, which is present as a true complex salt, to a process for the production of this compound and to the use of this compound as a combination preparation of carnitine and magnesium for use in sports nutrition or as a pharmacologically active ingredient.

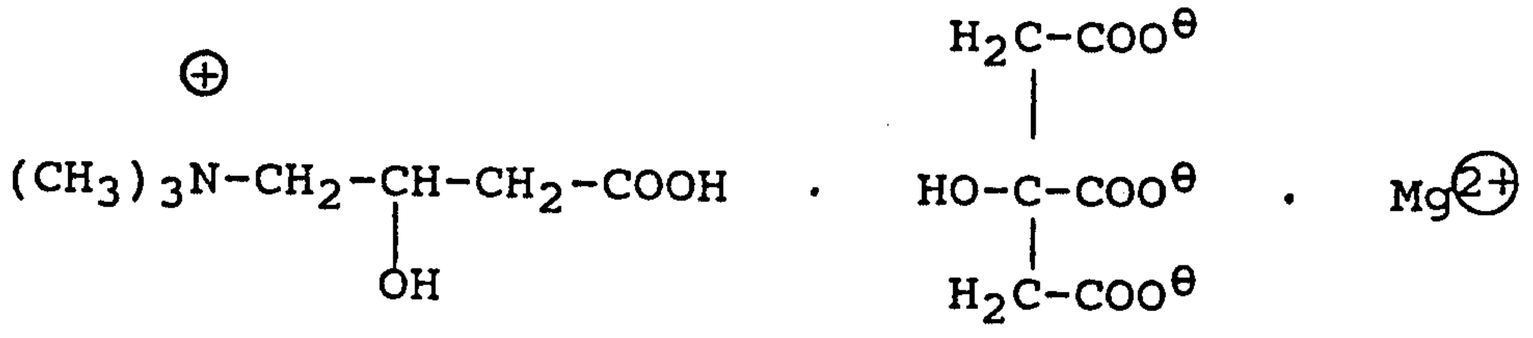
Both magnesium and L-carnitine are increasingly eliminated during physical training via perspiration or urine. These losses cause:

-- magnesium or L-carnitine deficiency phenomena
-- muscle cramps
-- reduction in efficiency of muscle performance
-- cardiac irregularities

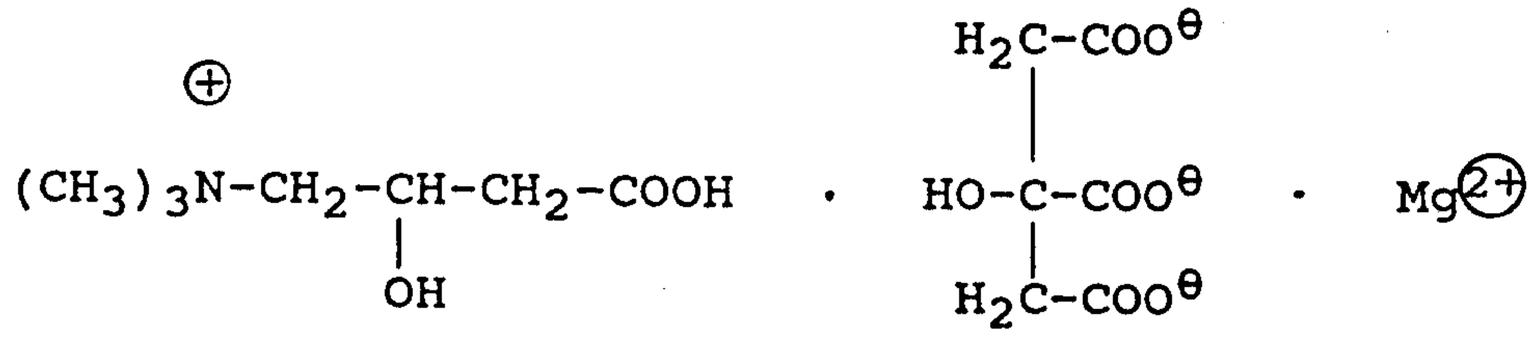
It is known that L-carnitine as well as magnesium salts, e.g., magnesium aspartate and magnesium orotate, exhibit high hygroscopicity.

The main object of the invention is to produce a new derivative of L-carnitine which exhibits only slight hygroscopicity and good thermal stability.

Accordingly, one aspect of the invention provides L-carnitine magnesium citrate having the following formula:



The invention also involves a process for the production of L-carnitine magnesium citrate of the formula:



which comprises reacting a magnesium compound, citric acid and L-carnitine in stoichiometric portions, in a suitable solvent and at a temperature in the range of 20 to 100°C, to form the corresponding L-carnitine magnesium citrate

and then recovering the L-carnitine magnesium citrate from the solution.

In a preferred embodiment of the process, magnesium citrate (in place of the magnesium compound and the citric acid) and L-carnitine in stoichiometric portions, in a suitable solvent, are converted to the corresponding L-carnitine magnesium citrate and then the L-carnitine magnesium citrate is recovered from the solution.

Water is preferably used as the solvent. Magnesium hydroxide, magnesium oxide or magnesium chloride is preferably used as the magnesium compound. Most preferably magnesium hydroxide is used as the magnesium compound.

The L-carnitine magnesium citrate is preferably recovered from the solution by evaporation to dryness. The solution is preferably concentrated by evaporation by spray drying. The solution is alternatively concentrated by evaporation on a rotary evaporator. After concentration by evaporation on a rotary evaporator, the L-carnitine magnesium citrate is preferably recrystallized in a mixture of a low-boiling alcohol with an aliphatic ketone.

The invention also involves the use of L-carnitine magnesium citrate as a combination preparation of carnitine and magnesium in the field of sports nutrition. The invention further involves the use of L-carnitine magnesium citrate as a pharmacologically active ingredient.

As indicated above, the production of L-carnitine magnesium citrate can be performed according to the process of the invention from stoichiometric portions of a magnesium compound, citric acid and L-carnitine, in a suitable solvent, such as water, methanol and ethanol. Preferably the reaction is performed in an aqueous medium. The reaction temperature is suitably from 20° to 100°C, preferably from 50° to 70°C. Magnesium hydroxide, magnesium oxide and magnesium chloride can be used, for instance, as the magnesium compound with magnesium hydroxide being preferred.

According to a preferred variation of the process according to the invention, L-carnitine magnesium citrate can be recovered from the reaction of magnesium citrate and L-carnitine.

The magnesium citrate salt may be obtained if the solution, after a certain reaction time, is either spray-dried, vacuum-dried, freeze-dried or concentrated by evaporation on a rotary evaporator. Preferably, the solution is concentrated by evaporation by spray drying. By spray drying, the desired product is obtained in the desired grain size. However, instead of spray drying, the solution can be concentrated by evaporation on a rotary evaporator and the resultant residue further treated by a purification treatment/scheme in a suitable solvent. The residue is suitably taken up in a mixture of a low-boiling alcohol with an aliphatic ketone. Methanol, ethanol, propanol and isopropanol are examples of suitable alcohols, with methanol preferably being used. Acetone and methyl ethyl ketone are examples of the ketone. Acetone is preferably used.

The compounds of the invention represent an ideal ratio of L-carnitine and magnesium. The muscle tissue of a healthy adult contains both 20 g of magnesium and 20 g of L-carnitine and can absorb 2 g of L-carnitine and about 300 mg of magnesium for optimal energy supply. A daily dose of 2 to 5 g of L-carnitine magnesium citrate supplies the body with 780 to 1950 mg of L-carnitine and 126 to 315 mg of magnesium. By the synergistic effect of magnesium and L-carnitine, the compound of the invention exhibits the following extraordinary, useful properties:

-- clearly higher performance and improved endurance in athletes as well as shorter rest periods

-- balancing of the increased magnesium and L-carnitine demand in competitive sports

-- delay of fatigue

-- strengthening of cardiac performance and prevention of cardiac irregularities

-- increased stress tolerance

-- less tendency to muscle and vascular spasms

-- improvement of muscular activity

-- increase of the activity of enzyme reactions in energy metabolism.

The following Example illustrates the invention.

Example

L-carnitine magnesium citrate

A mixture of citric acid (19.3 g, 0.1 mol), magnesium hydroxide (6.1 g , 0.1 mol) and L-carnitine (16.1 g, 0.1 mol) was dissolved in water (50 ml) and stirred for 1 hour at 60°C. Following spray drying, 36.0 g of a product in the form of a fine, light powder was obtained from the clear solution, corresponding to a yield of 95 percent (based on the L-carnitine used). The solution was concentrated by evaporation on a rotary evaporator. Then the residue was taken up in a mixture of acetone (100 ml) and methanol (100 ml), filtered and dried (12 hours at 60°C and 40 mbars). A coarser powder was obtained, corresponding to a yield of 95 percent (based on the L-carnitine used). Data for the product was as follows:

Melting point: over 250°C

Specific rotation: $[\alpha]_D^{25}$ [c = 1% in H_2O] - 12° (± 1°)

Solubility: over 50 g/100 ml of water

The structure was confirmed by IR, NMR and X-ray spectroscopy. The product also exhibited the following characteristics:

Thermal stability:

Externally unchanged after 24 hours exposure in air at 100°C

Weight loss: 5%

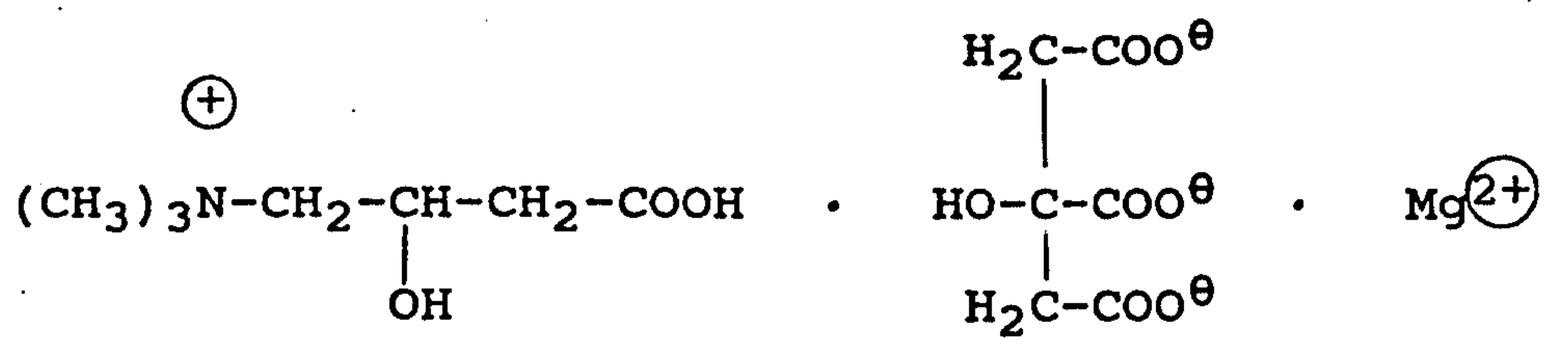
Hygroscopicity:

Air moisture (%)	32	44	56	66	73	80
Water absorption after 1 week (%)	8	15	21	29	35	46

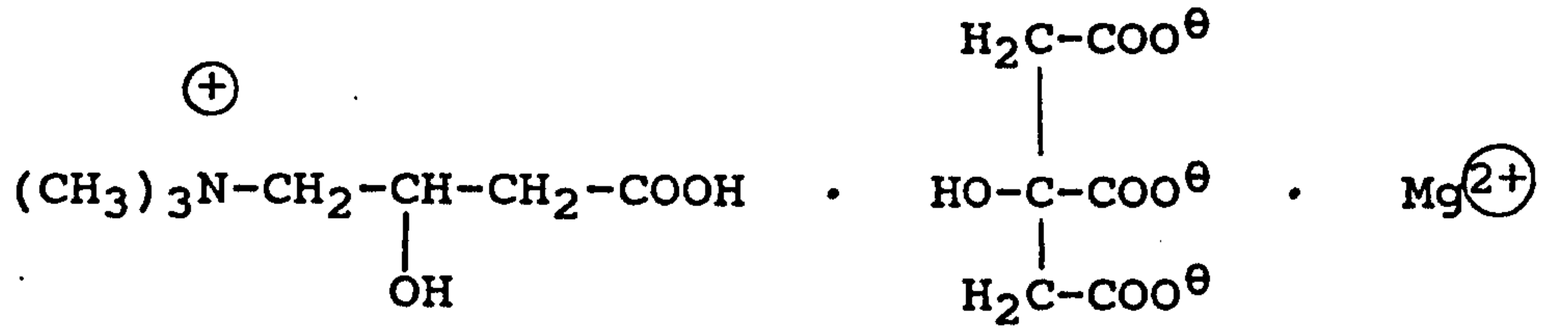
No deliquescence.

THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. L-carnitine magnesium citrate of the formula:



2. A process for the production of L-carnitine magnesium citrate of the formula:



which comprises reacting a magnesium compound, citric acid and L-carnitine in stoichiometric portions, in a suitable solvent and at a temperature in the range of 20 to 100°C, to form the corresponding L-carnitine magnesium citrate and recovering the L-carnitine magnesium citrate from the solution.

3. A process according to claim 2, wherein water is used as the solvent.

4. A process according to claim 2 or 3, wherein magnesium hydroxide, magnesium oxide or magnesium chloride is used as the magnesium compound.

5. A process according to claim 4, wherein magnesium hydroxide is used as the magnesium compound.

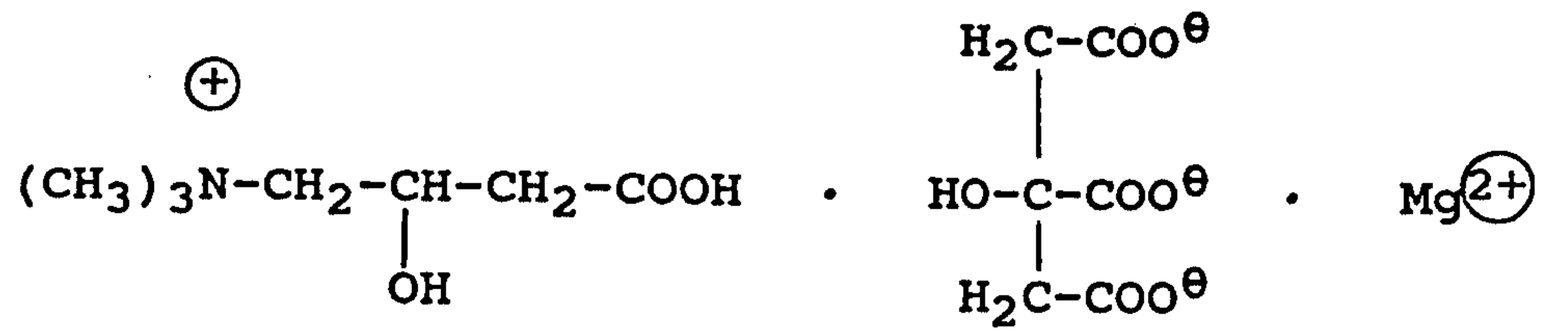
6. A process according to any one of claims 2 to 5, wherein the L-carnitine magnesium citrate is recovered from the solution by evaporation to dryness.

7. A process according to claim 6, wherein the solution is concentrated by evaporation by spray drying.

8. A process according to claim 6, wherein the solution is concentrated by evaporation on a rotary evaporator.

9. A process according to claim 8, wherein after concentration by evaporation on the rotary evaporator, L-carnitine magnesium citrate is recrystallized in a mixture of a low-boiling alkyl alcohol and an aliphatic ketone.

10. A process for the production of L-carnitine magnesium citrate of the formula:



which comprises reacting magnesium citrate and L-carnitine in stoichiometric portions, in a suitable solvent and at a temperature in the range of 20 to 100°C, to form the corresponding L-carnitine magnesium citrate and then recovering the L-carnitine magnesium citrate from the solution.

11. A process according to claim 10, wherein water is used as the solvent.

12. A process according to claim 10 or 11, wherein magnesium hydroxide, magnesium oxide or magnesium chloride is used as the magnesium compound.

13. A process according to claim 12, wherein magnesium hydroxide is used as the magnesium compound.

14. A process according to any one of claims 10 to 13, wherein the L-carnitine magnesium citrate is recovered from the solution by evaporation to dryness.

15. A process according to claim 14, wherein the solution is concentrated by evaporation by spray drying.

16. A process according to claim 14, wherein the solution is concentrated by evaporation on a rotary evaporator.

17. A process according to claim 16, wherein after concentration by evaporation on the rotary evaporator, L-carnitine magnesium citrate is recrystallized in a mixture of a low-boiling alkyl alcohol and an aliphatic ketone.