The invention relates to compositions containing L-carnitine for oral administration in the form of tablets, capsules or powders.

L-Carnitine plays an important role in fat metabolism, and it is mainly used in sport diets but also in the treatment of illnesses associated with a disturbed metabolism. In sport diet L-carnitine containing compositions are widely used because they contribute substantial energy for the muscles, enhancing the staying power. Such compositions are of great importance because they improve the muscle activity leading to an increased endurance and higher stress tolerance as well as a delayed tiring and a shorter recovery period.

The use of L-carnitine containing compositions, however, is not restricted to sport diets, but such compositions may also be used in geriatry and as general food additives.

Basically, the administration may be effected by enteral or parenteral route. For the preferred enteral, i.e. oral, administration the suitable application forms preferably are tablets or capsules, if desired, also powders or granulates. The preparation is effected by methods of pharmaceutical technology, independent of whether the dosage forms are intended for dietary or therapeutical purposes. In the past the preparation and handling of such dosage forms were substantially impaired by the high hygroscopicity of the L-carnitine. For example, tablets containing L-carnitine have to be prepared with exlusion of moisture and they have to be packed individually in airtight manner because they would disintegrate in a short period even at normal humidity. Furthermore, L-carnitine frequently contains traces of trimethyl amine which is repugnant for the user due to its fish-like odor.

It is therefore an object of the invention to provide a non-hygroscopic and odor-free form of L-carnitine which does not contain any physiologically objective additives and which is particularly well suited for the preparation of tablets or capsules.

This object is achieved according to patent claim 1 of the invention by using L-carnitine-L-tartrate. L-Carnitine-L-tartrate shall mean the salt of L-

carnitine with L-tartaric acid in a molar ratio of 2:1.

It was found that L-carnitine-L-tartrate is storage-stable at normal humidity (≤ 60 % of relative humdity) and may be processed without special caution. L-Carnitine-L-tartrate forms a crystalline powder which may be processed with ease and is particularly suited for the use in processes effected with fast moving machines because it neither tends to form lumps nor to become tacky. Furthermore it is completely odor-free having a refreshing, slightly acidic taste due to the bound tartaric acid.

Preferably, L-Carnitine is used alone or with further active substances, such as e.g. vitamins, amino acids, trace elements or mineral substances, as well as, if desired, auxiliarly substances usual in the respective dosage forms. In particular, such dosage forms include all types of tablets, namely those which are swallowed whole, chewable or sucking tablets, as well as those which are dissolved in a liquid before being taken. Included therein on the one hand are non-coated tablets and tablets in a mono- or a multilayer form or coated tablets and effervescent tablets and, on the other hand, coated tablets, such as film tablets or dragées. Also preferred dosage forms are capsules from soft or hard gelatine, hard gelatine capsules in the form of two piece capsules are particularly preferred. With advantage the L-carnitine-L-tartrate may also be used as a powder, e.g. with gas-forming additives as effervescent powders, or as a granulate. Auxiliarly substances, such as fillers, binders, lubricating and mold-release agents, flow control agents, and disintegrants, may be used in the preparation of tablets together with coloring and flavoring agents. Such auxiliary substances as well as their use in the preparation technology of the mentioned dosage forms are familiar to the expert.

The amount of the active substance per dosage unit is suitably between 50 mg and 1000 mg, preferably between 100 mg and 500 mg (calculated as L-carnitine).

As auxiliary substances necessary for the preparation of tablets there may be used:
fillers, such as lactose, sucrose, fructose, mannitol, other sugars, sugar

alcohols and starch;
binders, such as starch, gelatine, cellulose ethers, cellulose, carboxy methyl cellulose, polyvinyl pyrrolidone and other water-soluble polymers;
disintegrants, such as starch, starch ethers, alginates, cellulose esters, cellulose ethers and pectine derivatives;
lubricating and mold-release agents, such as talcum, stearate, highly dispersed silica and silicones, as well as optionally food dyestuffs, flavoring agents, vitamins, amino acids, mineral and trace elements, sweetening agents and sodium hydrogen carbonate in the case of effervescent tablets.

Preferably the portion of L-carnitine-L-tartrate (calculated as L-carnitine) is between 20 and 70 % of the overall weight of the tablet.

Powders for the use in capsules or for the direct oral administration consist of L-carnitine-L-tartrate and flow control agents, such as highly dispersed silica, talcum and stearates. Granulates for the use in capsules or for the direct oral administration consist of L-carnitine-L-tartrate and binders. The amounts of the flow control agent or the binder are reasonably within 0.1 and 10 weight-%, preferably between 0.5 and 5 weight%.

In the use of L-carnitine-L-tartrate according to the invention the amount of fillers and binders necessary for the preparation of solid oral compositions in general is substantially smaller than when L-carnitine is used. Thus, for instance, it is not possible to prepare storage-stable capsules from L-carnitine without the use of fillers.

The following examples illustrate the embodiments of the invention.

EXAMPLE 1

Preparation of L-carnitine-L-tartrate

L-Tartaric acid was dissolved in the necessary amount of hot 90 % aqueous ethanol, the calculated amount of L-carnitine was added, the salt was crystallized by cooling, filtered off and dried.
The product had the following charactistics:
colorless crystals
melting point: 169-175°C
$[\alpha]_D^{25}$: -10.9° ± 0.6° (25°C, c=1 % in water)

composition: molar ratio of carnitine:tartaric acid = 2:1 (^{1}H-NMR)
water solubility: about 73 g/100 g of solution

Water take-up at a humidity of 32 %:

after h	L-carnitine-tartrate; %	L-carnitine: %
1	0	1.9
2	0	3.6
4	0	6.3
8	0	8.6
24	0	12.3

Water take-up at a humidity of 66 %

after h	L-carnitine-L-tartrate; %	L-carnitine; %
1	0	6.0
2	0	9.6
4	0	21.6
8	0.1	45.2
24	0.1	67.7

EXAMPLE 2

Lozenges with orange flavor

Lozenges weighing 2 200 mg each were prepared according to the following recipe:

	mg
L-carnitine-L-tartrate	732
fructose	1089
orange flavor	30
quinoline-yellow lacquer	4
carboxy methyl cellulose	25
polyvinyl pyrrolidone	20
sucrose stearate	100
talcum	160
magnesium stearate	40

The fructose was blended with the carboxy methyl cellulose and three quarters of the lacquer dyestuff, then granulated with a solution of polyvinyl pyrrolidone in ethanol (85 %), dried and sieved. The orange flavor and the residual lacquer dyestuff were blended with 20 % of the L-carnitine-L-tartrate, sieved and then added to the remaining L-carnitine-L-tartrate. The

sucrose stearate was added, carefully blended in, and then the blend was sieved.

Finally the fructose granulate and then the talcum and magnesium stearate were added and each blended in homogenously.

Until tablets were formed the blend was stored in an air-tight container and then compressed to round biplanar tablets having bevelled edges. The tablet diameter was 20 mm, the tickness was about 5.4 mm.

For comparison similar lozenges were prepared containing 500 mg of L-carnitine and 232 mg of microcrystalline cellulose (for weight balance) instead of the L-carnitine-L-tartrate.

The water take-up under a constant relative humidity was determined with particulate tablets.

When stored under a relative humidity of 56 % the particulate tablets containing L-carnitine-L-tartrate did not take up any water within 10 days. In comparison to this, tablets containing L-carnitine took up 12 % of water under similar conditions. The use of L-carnitine-L-tartrate according to the invention results in tablets which are storage-stable even under extreme conditions.

EXAMPLE 3

Lozenges with peppermint flavor

Lozenges each weighing 2200 mg were prepared according to the following recipe:

	mg
L-carnitine-L-tartrate	732
mannitol	1100
aspartame	13
peppermint flavor	10
carboxy methyl cellulose	25
polyvinyl pyrrolidone	20
sucrose stearate	100
talcum	160
magnesium stearate	40

Mannitol was blended with the carboxy methyl cellulose and with the aspartame, then granulated with a solution of polyvinyl pyrrolidone in ethanol (80 %), dried and sieved.

The peppermint flavor was blended in with about 10 % of the L-carnitine-L-tartrate, sieved and then added to the remaining L-carnitine-L-tartrate. The sucrose stearate was added, blended carefully, and the blend was sieved.

Then the mannitol granulate and after this the talcum and the magnesium stearate were added, and intermixed homogenously. Until tabletting the mixture was stored in an air-tight container and then compressed to round biplanar tablets having bevelled edges. The tablet diameter was 20 mm, the thickness about 5.7 mm.

For comparison, the preparation of tablets was repeated with L-carnitine and microcrystalline cellulose as in example 2.

Also with these tablets the water take-up was determined as in example 2.

The use of L-carnitine-L-tartrate according to the invention resulted in stable tablets suitable for storage, while tablets on the basis of L-carnitine formed a tacky mass after one week storage due to the take-up of water.

EXAMPLE 4

Tablets to be swallowed

According to the following recipe 12 000 tablets each weighing 650 mg were prepared:

L-carnitine-L-tartrate	4.392 kg
lactose monohydrate	2.028 kg
wheat starch for direct tablet formation	420 g
cellulose, microcrystalline	360 g
silica (Aerosil® 200)	60 g
talcum	480 g
magnesium stearate	60 g

L-Carnitine-L-tartrate was blended homogenously with the wheat starch and the cellulose and then sieved. Lactose was added, blended in uniformly, and the blend was once more sieved. Talcum, magnesium stearate and silica were intimately blended, sieved and added to the blend of the active ingredient. The whole blend was once more blended thoroughly and kept in a tightly sealed container until the formation of tablets.

Circular tablets having bevelled edges and a diameter of 13 mm and a thickness of about 3.9 mm were compressed which had a compression strength of 60

to 70 N. They disintegrated in water of 20°C within 15 to 17 minutes.

EXAMPLE 5

Capsules to be used as food supplement

According to the following composition hard gelatine capsules were prepared with L-carnitine-L-tartrate:

L-carnitine-L-tartrate	366 mg
magnesium stearate	4 mg

Magnesium stearate was sieved with a sieve of 0.5 mm mesh width, L-carnitine-L-tartrate was added, and the two componentes were thoroughly blended for 15 minutes.

Then the blend was filled into CONI-SNAP®-capsules of size 1. This resulted in capsules which were storage-stable even under tropical conditions.

366 mg of L-carnitine-L-tartrate per capsule corresponded to 250 mg of L-carnitine.

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Patent Claims

1. Use of L-carnitine-L-tartrate for the preparation of L-carnitine containing compositions for oral administration.

2. Use of L-carnitine-L-tartrate for the preparation of L-carnitine containing tablets, capsules, powders or granulates.

3. L-carnitine containing pharmaceutical compositions, particularly for the enteral administration in the form of tablets, capsules, powders or granulates, characterised in that they contain L-carnitine-L-tartrate.

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