

the appended claims, are nevertheless hereby defined as equivalents of those specifically recited compounds and so are within the scope of the appended claims.

The KK-mice tests were carried out on db/db mice with spontaneous diabetes from the United Kingdom. The same correlating results could be obtained for this system as for the KK mice. This system too, is a suitable model for type-II diabetes.

The kidney tissue, taken from KK mice with diabetes-mellitus from the FRG, was studied by means of electron microscopy. Vascular (glomerulum) basal-lamina thickness was evaluated by means of morphometry, mesangium proliferation was measured, and the animals treated with L-arginine were compared to the untreated controls.

The panel of treated animals had significantly lower basal-lamina values and a significantly reduced mesangium proliferation.

In the accompanying drawings:

FIG. 1, as indicated above, is a display of the various reaction diagrams described;

FIG. 2 is an electron-microscopic presentation of a glomerulum without arginine treatment, taken from a KK mouse; and

FIG. 3 shows a glomerulum with the same enlargement factor, taken from a KK mouse treated with arginine.

A comparison shows that the basal lamina of FIG. 2 is thicker than in FIG. 3 and that the mesangium proliferation is lower in FIG. 2. FIG. 3 does not show any mesangium proliferation and a thinner glomerulum basal lamina.

The tests made with the free L-arginine base were also carried out with agmatine. The results obtained were comparable to the results obtained with the tests described above.

Tests made on animals with streptomycin-induced diabetes showed comparable results.

Tests on spontaneous diabetic BB rats showed also corresponding results.

The tests made using arginine or agmatine were also performed with spermidine and creatine. The tests showed results that were comparable to the results obtained with the above tests.

The types of animals used for the tests reflect the possibilities of treatment, in case of type-I and type-II diabetes.

Suitable pharmaceutical preparations, inhibiting collagen cross-linkage, are manufactured advantageously and in a simple manner by combining arginine, spermidine, creatine, agmatine, a salt or analogous product thereof, with pharmaceutically suitable, chemically inert fillers, carriers, stretching agents or excipients, as

they are generally used for the manufacture of medical preparations for oral or parenteral application, or for local injection, and as are generally and collectively referred to as "excipients" in the present specification and claims. The compounds according to the present invention may be compounded or formulated in the form of tablets, powders, capsules, suspensions, solutions, emulsions and similar dosage forms. The preparations may be manufactured by mixing arginine, spermidine, creatine, agmatine, an analogous product or salt thereof, preferably in water-soluble form, with the above conventional diluents or tableting additives, such as cellulose powder, corn starch, lactose, talcum, stearic acid, magnesium stearate, rubber or the like, in keeping with known and conventional manufacturing methods that have become established in the industry.

If the product is intended for parenteral application or local injection, the substances according to the present invention may preferably be combined in their non-toxic, water-soluble form with carriers such as water, salt solution, glucose solution or alike.

Effective amounts of any of the compounds according to the present invention may be administered to the body of a diabetes patient according to one of several methods, e.g. orally, i.e. by means of capsules or tablets, parenterally in the form of sterile solutions or suspensions, intravenously in sterile solutions, or locally in the form of sterile solutions or suspensions.

The daily dosage level for an adult human is 1 to 4 g/day, preferably about 3 g/day. Below about 1 g/day, the compounds of the present invention are not effective. Above about 4 g/day, the compounds are in substantial excess of the required amount and so are medically unjustifiable.

A typical dosage form is a tablet consisting of 0.5 g arginine in 4 g crushed linseed as an excipient, or a gelatine capsule containing 0.5 arginine, a typical dosage regimen being the oral administration of two such capsules or tablets three times a day.

What is claimed is:

1. A process for inhibiting glucose-mediated collagen cross-linking in diabetes patients, comprising administering to a diabetes patient in the need of same an amount from about 1 to about 4 g per day of a compound selected from the group consisting of arginine, creatine, agmatine and pharmaceutically acceptable salts thereof, thereby to inhibit glucose-mediated collagen cross-linking in diabetes patients.

2. A process as claimed in claim 1, in which said amount is about 3 per day.

3. A process as claimed in claim 1, in which said compound is administered orally.

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