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(54) Titre : MOYEN POUR AMELIORER ET MAINTENIR L'ACTIVITE INTESTINALE, ET SON PROCEDE DE PRODUCTION

(54) Title: METHOD FOR IMPROVING AND MAINTAINING BOWEL FUNCTION AS WELL AS A METHOD FOR THE PRODUCTION THEREOF

(57) Abrégé/Abstract:
The invention relates to an agent for improving and maintaining bowel function and/or for improving and/or normalizing defecation. Said agent contains a material which decomposes in the stomach and/or the short intestinal tract and is provided with a compound which dissolves first in the intestine and contains prophylactic or laxative active ingredients which are first predominantly or exclusively released in the intestine. The invention also relates to a method for the production of the agent and its utilization.

Abstract

The invention relates to an agent for improving and maintaining bowel function and/or for improving and/or normalizing defecation. Said agent contains a material which decomposes in the stomach and/or the short intestinal tract and is provided with a compound which dissolves first in the intestine and contains prophylactic or laxative active ingredients which are first predominantly or exclusively released in the intestine. The invention also relates to a method for the production of the agent and its utilization

Composition for improving and maintaining intestinal activity and process for its preparation

The present invention relates to a composition for improving and maintaining intestinal activity.

US 3,688,763 describes a method of collecting cellular material from the large intestine of humans. The patient swallows a capsule the outer coating of which together with the container situated beneath dissolves in the intestine and releases a compressed sponge which is then expelled via natural evacuation of the bowels. On its transport through the intestine, the sponge scrapes off outer cells of the intestinal lumen which are carried along to the outside. By this means, in a simple manner, intestinal cells are removed from the patient with the purposes of then studying these for tumors or cancer cells.

This system had the object of collecting intestinal cells for analytical purposes. However, targeted stimulation of intestinal activity is not achieved in this manner.

DE 4 025 912 discloses a composition for oral intake which consists of a receptacle which, in the stomach, can be dissolved and releases the contents. This receptacle is filled with a material which on being released in the stomach increases in volume and as a result induces in the person a feeling of satiation.

The disadvantage of this system is that it is directed solely toward filling the stomach. A stimulation of intestinal activity is thus not associated with it, however.

It is an object of the present invention to provide a composition comprising a material which is deformable

and, if appropriate, is form-reducible and/or reversibly compressible and which passes through the esophagus and the stomach and in the intestine releases a stimulating action on the intestinal activity.

This object is achieved by means of the fact that the composition comprises a material which, if it is degradable in the stomach and/or small intestine it is provided with a compound which does not dissolve until in the intestine and which is loaded with active compounds, for example for prophylaxis, or with laxatives, in such a manner that these are predominantly or exclusively not released until in the intestine.

Preferably, the material has three-dimensional polymeric networks. Particularly preferably, the material is present in the form of a sponge-like structure. In addition to such sponges, gels or gelatinous materials, for example, are also usable.

Sponge-like structures are taken to mean according to the invention foams which consist of gas-filled spherical/polyhedral cells which are limited by highly viscous or solid cell walls. It is possible to employ according to the invention both naturally occurring sponges and synthetically prepared sponge-like structures.

The sponge-like or spongy structures are prepared by methods known per se from the prior art. Depending on the starting material employed, in the simplest case a foam can be obtained by blowing, beating, shaking, spraying or stirring in the relevant gas atmosphere. In the case of polymers the foam structure is produced by chemical reactions. Thus polyurethanes are foamed by adding blowing agents which decompose at a defined temperature during processing with gas formation, or by adding liquid solvents during the polymerization.

Foaming takes place either on leaving the extrusion dye, that is to say following the extrusion or injection molding, or in open molds. Curing takes place under the conditions characteristic of the particular chemical compound of the material.

An essential prerequisite for the employability of the material is that it is compressible without breaking the cell walls. It is further essential for the selection of material and manner of foam formation that it remains swellable without the cell walls being destroyed.

Preferably, the material is designed in such a manner that it can be compressed to 1/2 to 1/100, preferably 1/4 to 1/50, particularly preferably 1/10 to 1/20, of its volume or its size. Under physiological conditions, the compressed material, after passage through the esophagus and the stomach, is to be able to expand preferably to two to hundred times, particularly preferably to four to fifty times, very particularly preferably to ten to twenty times, its volume in the intestine.

In order to prevent constipation of the intestine or, in the worst case, even an intestinal obstruction, the volume of the decompressed materials must be chosen appropriately. In order to achieve the desired stimulating effect on the intestinal activity even with relatively small embodiments of the inventive composition, a plurality of inventive compositions can be taken orally.

The material used according to the invention can have any desired shape in the decompressed state. However, preference is given to cuboid or rectangular or round embodiments.

The material for the embodiment preferred according to the invention to be used as sponge-like structure can be natural, semisynthetic or synthetic polymers.

Examples of suitable synthetic polymers are polyurethanes, polyacrylates, poly(meth)acrylic esters, homopolymers and copolymers of vinyl acetate. The natural and semisynthetic polymers include, inter alia, cellulose, cellulose ethers, diethylcellulose or cellulose esters, such as cellulose diacetate, cellulose triacetate, cellulose acetate propionate, cellulose acetate and cellulose butyrate. Those which are suitable according to the invention are, for example, cellulose derivatives, in particular corresponding ethers, for example methyl cellulose, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, or sodium carboxymethyl cellulose (preferably those compounds of high viscosity); natural (anionic) mucilages, for example xanthan gum, guar gum, tragacanth or alginic acid and salts thereof, and the like. In addition, the use of insoluble polysaccharides such as chitin or chitin derivatives or microcrystalline cellulose is also conceivable. Particular preference is given according to the invention to unbranched high-molecular-weight polymers. In particular, those polymers can be employed according to the invention which have a fibrous structure. Examples of such materials are the scleroproteins such as keratins, conchagens, fibroin, elastins and collagen.

Also, polymers which are crosslinked in a stable manner come into consideration. In particular, uronic-acid-containing polysaccharides or their salts are conceivable here that are crosslinked to one another by ionic bonds and are crosslinked in a stable manner by additional covalent bonds, for example by ester bonds catalyzed by mineral acids.

In a particular embodiment of the invention the polymers can decompress not only in the intestine, but as early as in the stomach, and then in this state pass into the intestine and pass through this. The materials which come into consideration here, in particular, are those which are scarcely observably, to not at all, degradable or absorbable in gastrointestinal fluids.

The material present in the inventive composition alone can thus already exert an action in the intestine which is comparable with that of a dietary fiber and owing to which it stimulates the intestinal activity and/or contributes to the improvement and maintenance of intestinal activity. In addition, the material, according to the invention, is loaded with active compounds or laxatives, more precisely in such a manner that the active compounds or laxatives are released predominantly or exclusively in the intestine.

In a preferred embodiment of the present invention, the material is provided with a compound which dissolves exclusively in the intestine. This is necessary in particular if the material used is degradable as early as in the stomach or small intestine.

The dissolution of the compound is affected by various parameters, in part also prevailing simultaneously in the intestine, for example pH, pressure, redox potential and enzymatic dissolution via the intestinal flora. In addition, the residence time of the composition in the intestine also affects the rate at which the compound dissolves.

For preference, the compound dissolves at a pH between 5 and 10, preferably between 7 and 9, particularly preferably between 5.5 and 8.5. Dissolution in the pH environment of the intestine at a pH between 6.4 ± 0.6 and 7.0 ± 0.7 is extremely prefered.

The compound is applied to the material according to the invention preferably in the form of a coating which, if appropriate, can also be made up of a plurality of layers. The minimum layer thickness here can vary considerably and is dependent on the film-former used and its composition. Osterwald H. et al. (Acta Pharm Technol, 1980, 26: 201-209) describes, for example, a minimum layer thickness of 46 µm for the preparation of a film-former in organic solvents, preparation with an ammonium salt solution requires a layer thickness of 161 µm, as an emulsion 46 µm and as a latex dispersion 52 µm. According to the invention, the layer thickness is from 10 µm to several millimeters, preferably from 15 µm to 3 mm.

However, instead of a coating applied directly to the material, the material can be introduced into a container which dissolves under the above-described conditions. That is to say the container is stable in the stomach, but dissolves in the intestine.

In another variant of the invention, the compound can be introduced into the material. This may be achieved, for example, by mixing the material with the compound as early as when the inventive composition is prepared. Preferably, this may also be achieved by impregnating the material in a solution of the compound. Obviously, such a, for example impregnated composition can also be provided with a coating of the compound. Likewise, the impregnated material can also be introduced into the above-described container. In addition, the material can be introduced into a container which itself is coated or impregnated with the compound or into which the compound is introduced.

The time and location of the dissolution of the compound may be influenced by the selection and combination of the compounds, which achieves targeted release of the material in the intestine and, in

particular, in the various intestinal sections, such as the jejunum, ileum and colon. The solubility of the compounds can depend on one or more factors, for example pH, time of exposure, redox potential of the intestine, enzymatic activities of the intestinal flora, or pressure which is produced by intestinal peristalsis. The various possibilities for controlling the release of active compounds are described extensively. The pH-dependent solubility is described, for example, in *Marvola et al.*, Eur J Pharm Sci, 1999, 7:259-267 and *Khan ZI et al.*, J Controlled Release, 1999, 58:215-222. *Pozzi F. et al.*, J Controlled Release, 1994, 31:99-108; *Wilding IR et al.*, Pharmacol Ther, 1994, 62:97-124; *Niwa K. et al.*, J Drug Target, 1995, 3:83-89 and US-4871549 disclose systems which release the active compounds as a function of time. Examples of systems having a combined pH and time dependency are described in *Rodriguez M. et al.*, J Controlled Release, 1998, 55:67-77 and *Gazzinga A. et al.*, STP Pharm Sci, 1995, 5:83-88. The dissolution of compounds due to a changed redox potential in the intestine is dealt with by *Bronsted H. et al.*, Pharm Res 1992, 9:1540-1545; *Yeh PY et al.*, J Controlled Release, 1995, 36:109-124; *Shanta KL et al.*, Biomaterials, 1995, 16:1313-1318 and *Kimura Y et al.*, Polymer, 1992, 33:5294-5299. Examples of systems which are released by the enzymes of the intestinal flora are described in *Ashford M et al.*, J Controlled Release, 1994, 30:225-232; *Fernandez-Hervas MJ et al.*, Int J Pharm, 1998, 169:115-119; *EP-0460921; US-4432966* and *Milojevic S et al.*, J Controlled Release, 1996, 38:75-84. The dissolution of systems due to the pressure of intestinal peristalsis is covered in *Muraoka M et al.*, J Controlled Release, 1998, 52:119-129.

Preference is given according to the invention to the following compounds and their combinations which are, however, in no way limiting for the present invention:

hydroxypropyl methyl cellulose phthalate (HPMCP 55), hydroxypropyl methyl cellulose acetate succinate (Aqoat AS-MF, Aqoat AS-HF), 1:1 copolymer of methacrylic acid and ethyl acrylate (Eudragit®L), copolymer of vinyl acetate and crotonic acid (Coating CE 5142), cellulose acetate phthalate (CAP, Aquateric), methacrylate copolymers (Eudragit®S), shellac, Time Clock System®, carnauba wax, hydroxypropyl methyl cellulose (TC-5), Pulsincap®, polyethylene glycol, crosslinked polyethylene glycol, ethyl cellulose, ethyl cellulose/ethanol mixture, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, glycerol monostearate, Eudragit®E. In addition, hydrogels from azo compounds are possible, for example N-substituted methacrylamide, N-tert-butylacrylamide, acrylic acid in the presence of 4,4'-bis(methacryloylamino)azobenzenes, 4,4'-bis(N-methacryloyl-6-aminohexanoylamino)azobenzene or 3,3',5,5'-tetrabromo-4,4,4'4'-tetra(methacryloylamino)azobenzene. Examples of other compounds are unbranched polymer precursors, for example containing N,N-dimethylacrylamide, N-tert-butylacrylamide, acrylic acid, N-methacryloylglycylglycine p-nitrophenyl ester, crosslinked by suitable crosslinkers, for example N,N'-(ω-aminocaproyl)-4,4'-diaminoazobenzene and polymers containing azo compounds, for example 2-hydroxyethyl methacrylate, 4-(methacryloyloxy)azobenzene, N-(2-hydroxypropyl)methacrylamide copolymers, copolymers containing styrene and 2-hydroxyethyl methacrylate crosslinked by, for example, 4,4'-divinylazobenzene or N,N'-bis(β-sterylsulfonyl)-4,4'-diaminoazobenzene. Also, poly(ether-ester)azo polymers can also be used according to the invention, for example copolymers containing 4-[4-[(6-hydroxyhexyl)-oxy]phenyl]azobenzoic acid and 16-hydroxyhexadecanoic acid, copolymers containing 4-[2-[2-(2-hydrdoxy-ethoxy)ethoxy]ethoxy]benzoic acid, 4-[4-[2-[2-(2-hydroxyethoxy)ethoxy]ethoxy]phenyl]azobenzoic acid and 16-hydroxyhexadecanoic acid or 12-hydroxydodecanoic acid and segmented polyurethanes containing m-xylene

diisocyanate, 3,3'-dihydroxyazobenzene, polyethylene glycol or 1,2-propanediol. In addition, usable compounds are azo-compound-containing polyamides or copolymers of 4-[4-(chlorocarbonyl)phenyl)]azobenzoyl chloride and α,ω-bis(aminopropyl) poly(tetramethylene oxide) and copolymers of 4-[4-chlorocarbonyl)-phenyl]azobenzoyl chloride and Jeffamine ED-600.

In addition, pectins are used, which can be additionally coated or embedded in a matrix, for example, methoxy pectin, amidated pectin, calcium pectate, pectin in combination with ethylcellulose (Aquacoat, Surelease), acrylic ester polymers (Eudragit RS30D, Eudragit NE30D). In addition, combinations of pectins with other dietary fibers are used. Examples of dietary fibers are guar (galactomannan) or chitosan, the dietary fibers themselves in turn being able to be coated or a constituent of a matrix. In this case the following substances are used as film-formers: polymethacrylate solutions, copolymers containing polyurethane and di-, oligo- or polysaccharides (galactomannans) and ethyl-galactomannans or acetylgalactomannans. In addition, cyanoacrylate, inulin, inulin suspensions containing Eudragit-RS, methacrylated inulin, chondroitin sulfate, chondroitin polymers containing 1,12-diaminododecane and dicyclohexylcarbodiimide, amorphous amylose or amorphous amylose together with other film-forming polymers are used as film-former. In addition, dextrans can be used which can be crosslinked in various ways, for example with diisocyanates, fatty acid esters, for example lauryl acid, glutaraldehyde. Conjugates of biphenylacetic acid and β-cyclodextrin, copolymers of β-cyclodextrins with methacrylic acid copolymers or acrylic acid polymers with disaccharide side groups are also used according to the invention.

The choice of compounds and their many possible combinations make possible targeted release of the material in the intestine with regards to time and

location. The compound can here also already comprise active compounds and/or laxatives.

The material present in the inventive composition can be loaded with active compounds or laxatives in this case in a manner comparable to that which has already been described in the loading of the material with a compound. The active compounds or laxatives or combinations thereof can be introduced/applied into/onto the material. This can preferably take place in the form of a coating, in which case the coating, if appropriate, can also be made up of a plurality of layers. In another variant of the invention, the active compounds and/or laxatives can be introduced into the material. This may be achieved, for example, by direct mixing of the material with the active compounds and/or laxatives during the preparation of the inventive composition. Preferably, this can also be achieved by impregnating the material in a solution of the active compounds and/or laxatives. Obviously, such a material, for example impregnated material, can additionally also be provided with a coating of the active compounds and/or laxatives. In addition, the material can be encased by the active compounds and/or laxatives in the form of a container. In addition, the material can be introduced into a container, for example made of the abovementioned compounds which is itself coated or impregnated with the active compounds and/or laxatives or into which the active compounds and/or laxatives are introduced.

In one embodiment of the present invention, the material which is thus loaded with the active compounds and/or laxatives can be compressed and in addition be provided with a compound of the above-described type and in the previously described manner. The dissolution of the compound in the intestine leads to the decompression in the intestine of the material

obtained, together with release of the active compounds and/or laxatives.

In another embodiment of the invention, the active compounds and/or laxatives can themselves be provided with the compounds of the above-described type and in the manner described above. The material can then be loaded with the resulting active compounds and/or laxatives in the manner described. The material which is loaded with the active compounds and/or laxatives is then compressed and if appropriate additionally provided with a compound which does not dissolve until in the intestine. The dissolution of the compound causes the release of the active compounds and/or the laxatives.

For the purposes of the invention, active compounds are all substances having a pharmaceutical or biological action. Examples are betamethasone, thioetic acid, sotalol, salbutamol, norfenefrine, solymarin, dihydroergotamine, buflumedil, etofibrate, indometacin, oxazepam, beta-acetyldigoxim, piroxicam, haloperidol, ISMN, amitirptyline, diclofenac, nifedipine, verapamil, pyritinol, nitrendipine, doxycycline, bromhexine, methylprednisolone, clonidine, fenofibrate, allopurinol, pirenzepine, levothyroxine, tamoxifen, metildigoxin, o-(beta-hydroxyethyl)rutoside, propicillin, aciclovir mononitrate, paracetamol, naftidrofuryl, pentoxyfylline, propafenone, acebutolol, L-thyroxine, tramadol, bromocriptine, loperamide, ketotifen, fenoterol, Ca dobelisate, propranolol, minocycline, nicergoline, ambroxol, metoprolol, beta-sitosterol, enalapril hydrogen maleate, bezafibrate, ISDN, gallopamil, xanthinol nicotinate, digitoxin, flunitrazepan, bencyclane, dexapanthenol, pindolol, lorazepam, diltiazem, piracetam, phenoxymethylpenicillin, furosemide, bromazepam, flunarizine, erythromycin, metoclopramide, acemetacin, ranitidine, biperiden, metamizole, doxepin, dipotassium chlorazepate,

tetrazepam, estramustine phosphate, terbutaline, captopril, maprotiline, prazosin, atenolol, glibenclamide, cefaclor, etilefrine, cimetidine, theophylline, hydromirphone, ibuprofen, primidone, clobazam, oxaceprol, medroxyprogresterone, flecainide, Mg pridoxal 5-phosphate glutamate, hymecromone, etofylline clofibrate, vincamine, cinarizine, diazepam, ketoprofen, flupentixol, molsidomine, glibornuide, dimetindene, melperone, soquinolol, dibydrocodeine, clomethiazole, clemastine, glisoxepide, kallidinogenase, oxyfedrine, baclofen, carboxymethylcysteine, thiorodecine, betathistine, L-tryptophan, myrtol, bromalains, prenylamine, salazosulfapyridine, astemizole, sulpiride, benzerazide, dibenzepin, acetylsalicylic acid, miconazole, nystatin, ketoconazole, Na picosulfate, cholestyramine, gemifibrocil, rifampicin, fluorocortolone, mexiletine, amoxicillin, terfenadrine, mucopolysaccharide polysulfates, triazolam, mianserin, tiaprofenic acid, amezinium methyl sulfate, mefloquine, probucol, quinidine, carbamepine, Mg L-aspartate, penbutolol, piretanide, amitriptyline, cyproterone, Na valproate, mebeverine, bisacodyl, 5-aminosalicylic acid, dihydralazine, magaldrate, phenprocoumon, amantadine, naproxen, cartelol, famotidine, methyldopa, auranofin, estriol, nadolol, levomepromazine, doxorubicin, medofenoxate, azathioprine, flutamide, norfloxacin, fendiline, prajmalium bitartrate, escin.

Further examples are the following active substances: acetaminophen (= paracetamol), acetohexamide, acetyldigoxim, acetylsalicylic acid, acromycin, anipamil, benzocaine, beta-carotene, chloramphenicol, chlordiazepoxide, chlormadino acetate, chlorthiazide, cinnarizine, clonazepam, codeine, decamethasone, diazepam, dicumarol, digitoxin, digoxin, dihydroergotamine, drotaverine, flunitrazepam, furosemide, gramicidin, griseofluvin, hexobarbital, hydrochlorothiazide, hydrocortisone, hydroflumethazig, indimethazine, ketoprofen, lonetil, medazepam, mefruside,

methandrostenolone, methylprednisolone, methylsulfadiazine (= sulfaperin), nalidixic acid, nifedipine, nitrazepam, nitrofurantoin, nystatin, estradiol, papaverine, phenacetin, phenobarbital, phenylbutazone, phenytoin, prednisone, reserpine, spironolactone, streptomycin, sulfadimidine (= sulfamethazine), sulfamethizole, sulfamethoxazole, (= sulfameter), sulfaperin, sulfathiazole, sulfisoxazole, testosterone, tolazamide, tolbutamide, trimethoprim, tyrothricin, vitamins, minerals.

Active compounds which also come into consideration are those having prophylactic action, for example in the field of tumor therapy.

In addition, for the purposes of the invention active compounds are also to be taken to mean laxatives.

The inventive composition can comprise, in addition to pharmaceutically active materials and/or biologically active materials foodstuffs or food supplements, for example vitamins, dietary fibers, proteins, minerals and other food constituents, taste and stimulant substances or flavorings.

In addition to said substances, it is also possible to add other ancillary substances to the material. These may also be, for example, antioxidants, preservatives, pigments or sweeteners. Inter alia, release-slowing substances may additionally be suitable in the case where pharmaceutically active substances are used.

In addition, the compositions according to the present invention can additionally contain fillers, disintegrants, binders and lubricants and also excipients.

Release-slowing ancillary substances which can be used are essentially water-insoluble ancillary substances or mixtures thereof, such as lipids, inter alia fatty

alcohols, for example cetyl alcohol, stearyl alcohol and cetostearyl alcohol; glycerides, for example glycerol monostearate or mixtures of mono-, di- and triglycerides of vegetable oils; hydrogenated oils, such as hydrogenated castor oil or hydrogenated cottonseed oil; waxes, for example beeswax or carnauba wax; solid hydrocarbons, for example paraffin or earth wax; fatty acids, for example stearic acid; certain cellulose derivatives, for example ethyl cellulose or acetyl cellulose; polymers or copolymers, such as polyalkylenes, for example polyethylene, polyvinyl compounds, for example polyvinyl chloride or polyvinyl acetate, and also vinyl chloride-vinyl acetate copolymers and copolymers with crotonic acid, or polymers and copolymers of acrylates and methacrylates, for example copolymers of acrylates and methyl methacrylates.

In addition, the present invention relates to a composition for use for improving and maintaining intestinal activity and for improving and/or normalizing bowel movements, which composition comprises a material which, if it is degradable in the stomach and/or small intestine it is provided with a compound which does not dissolve until in the intestine and which is loaded with active compounds, for example for prophylaxis, or with laxatives, in such a manner that these are predominantly or exclusively not released until in the intestine.

In addition, the present invention also relates to a process for preparing the above-described composition.

In this process, in principle, a suspension of the material is first prepared and is then freeze-dried. If appropriate, the material is comminuted in advance and/or is subjected to an alkaline and/or an acidic pretreatment. The freeze-drying is preferably carried out at -80 to +50°C, in particular -30 to +40°C.

In an embodiment of the inventive process in which the material is present in the form of a sponge-like structure, soluble collagen from the hides of young cattle or pigs (animals), for example, can be used. This is because the contents of soluble collagen in the hide of animals become increasingly lower with increasing age of the organism, since the collagen forms an insoluble three-dimensional network by intermolecular crosslinking. The crosslinking points are stable chemical bonds between individual collagen molecules.

Therefore, in the preparation of the required collagen suspensions for sponge preparation, the hides must originate from animals (bulls) which are one to two years old. Even here, the collagen is already forming an insoluble network. A strongly alkaline and acidic pretreatment of the hide, and mechanical forces during the preparation of the sponge suspension can cause individual chemical and physical crosslinking points in the collagen to be disrupted.

When the sponge is dried by freeze-drying and subsequent heating at 90°C to 130°C, preferably 120°C, new crosslinking points are introduced back into the sponge material by the relatively high temperatures. This causes the long-lasting insolubility of the sponge body in gastrointestinal fluids and/or water. This relative insolubility is a prerequisite for a relatively strong and stable structure which triggers a lasting stimulating effect and thus already a first laxative (purgative) action in the intestine, which is comparable with the action of dietary fibers in general. This action can be supported by the loading with active compounds and/or laxatives.

In a particularly preferred embodiment of the present invention, stably crosslinked polyuronic-acid-

containing polysaccharides are used, in particular alginates or their salts.

Particularly preferably, the inventive composition is prepared as follows: a suspension of the material is first prepared and from this suspension, using methods known per se, a sponge- or foam-like structure is prepared. The material is then reversibly compressed. Before, during or after the preparation of the sponge-like structure, the material is loaded with active compounds, for example for prophylaxis, or with laxatives in such a manner that these are predominantly or exclusively not released until in the intestine. If appropriate, a compound is applied to the material as prepared and/or a compound is introduced into the material and/or this material is encased with such a compound, with this compound not dissolving until in the intestine.

Before, during or after the preparation of the sponge-like or foam-like structure, the material can in addition be loaded with the abovementioned compounds, pharmaceutically and/or biologically active substances, nutrients and food supplements, foodstuffs, taste and stimulant substances, flavorings, ancillary substances or release-slowing substances.

All customary methods come into consideration in this regard. In the simplest case this can be carried out during the sponge material preparation phase by mixing the material and the corresponding substances. Also, impregnating the material with a solution of the substances is conceivable. In addition, the abovementioned substances can be applied directly to the surface of the material. This can be achieved, for example, by dipping, spraying, coating or similar methods.

The resultant material is then reversibly compressed. This can be performed by pressing, rolling or

comparable methods. In a particular embodiment of the invention, the material can also be compressed by chewing movements during oral intake of the material.

The compressed material thus prepared can, in a preferred embodiment of the invention, be encased with the above-described compound. That is to say either a container, for example a capsule casing, is produced from the compound and the material is introduced into this, or the compound is directly applied to the material, for instance by dipping, spraying, coating or similar methods. In another embodiment of the invention, the compound is introduced into the material. This can be achieved by impregnation, for example.

The invention is not limited to the described processes, but also applies to all other processes in which sponges, sponge-like structures or gels are prepared which, due to the relative insolubility in water and/or gastrointestinal fluids, are to or can, achieve long-lasting stimulation of the intestinal activity, if appropriate mediated by appropriately suitable compounds.

A purpose of the inventive process is to obtain a composition that develops a long-lasting stimulating action in the intestine and at the same time is suitable for targeted release of active compounds in the intestine, in particular for prophylaxis, or of laxatives. This purpose is achieved by said process steps.

The inventive composition is taken orally. The solid, compressed sponge body or solid foam body passes through the mouth, throat, esophagus and stomach by addition of beverage and gentle chewing or swallowing movements and swells in the intestine, preferably back

to its original volume. If appropriate, the volume can also be greater than or less than the original volume.

In contrast to other food/food supplements/dietetic or medicinal products which are rapidly decomposed in the intestine or pass into the intestine already in a comminuted state, the material which is prepared in the described manner and consists of natural, semisynthetic or synthetic polymers and also stably crosslinked polymers, in particular in the form of a solid sponge body or foam body, owing to its predominantly three-dimensional polymeric network and the only slight solubility in the intestine, retains its original solid and mechanically stable structure over a period of several hours. In this case the inventive composition is present in sufficiently compressed form on passage through the esophagus and during passage through the stomach or small intestine in order to decompress in the intestine, in particular in the large intestine, and to develop the desired stimulating action.

In a particular embodiment of the invention the composition, however, can also decompress as early as in the stomach and in this state can pass into the intestine and pass through this. This applies in particular to materials which can also pass through the stomach and small intestine in decompressed form without being degraded.

For the particular case that the material, however, should already begin to degrade in the stomach or small intestine, appropriate protection from premature degradation must take place. Such a protection can be achieved by providing the material with a compound which dissolves exclusively in the intestine. In this case this compound can be incorporated/applied into/onto the material in the manner mentioned above or coated therewith.

Otherwise, it is, however, perfectly conceivable that the inventive composition can be provided, so to speak optionally, with an above-described compound.

A compound which may be applied/introduced onto/into the structure, or a casing of the compound offers the possibility of firstly protecting the material from premature degradation and secondly to affect the location of decompression of the material. The same applies to active compounds or laxatives with which the material is loaded.

Oral intake of the inventive composition and decompression in the intestine produce an excitation of the stretch receptors of the intestinal wall, which themselves initiate intestinal contractions. As a result, long-lasting excitation of intestinal activity may be achieved, resulting in a shortening of the transit time of the intestinal contents and, in association with an improved water binding capacity of the stools, followed by more favorable growth conditions for the intestinal flora, as a result of which, ultimately, intestinal secretion and intestinal blood circulation are stimulated. The intestinal activity can in addition be improved and maintained by the release of the active compounds or laxatives. However, in addition, active compounds can also be released in the intestine which develop their action at a site other than the intestine.

In addition, the present invention relates to the use of the inventive composition for preparing compositions for improving and maintaining intestinal activity and for improving and/or normalizing bowel movements and for preparing pharmaceutically active compositions and/or nutrients and/or food supplements and/or (dietetic) foods. Also, the inventive composition itself can be used for improving and maintaining intestinal activity and for improving and/or

normalizing bowel movements and/or for reducing the transit time of chyme in the intestine, combined with a prophylactic or laxative action. In addition, use of the inventive composition is conceivable in the fields of pharmacy and/or health and/or for nutrition and/or food supplementation. For this purpose the composition comprises the above-described active compounds or nutrients, food supplements, foods, taste and stimulant substances, flavorings or other ancillary substances.

Patent Claims:

1. A composition for improving and maintaining intestinal activity and/or for improving and/or normalizing bowel movements, characterized in that it comprises a material which, if it is degradable in the stomach and/or small intestine, is provided with a compound which does not dissolve until in the intestine, and is loaded with active compounds, for example for prophylaxis, or with laxatives in such a manner that these are predominantly or exclusively not released until in the intestine.

2. The composition as claimed in claim 1, characterized in that the material has three-dimensional polymeric networks.

3. The composition as claimed in either of claims 1 or 2, characterized in that the material is in the form of a sponge-like structure.

4. The composition as claimed in one of claims 1 to 3, characterized in that the material is coated with the compound.

5. The composition as claimed in one of claims 1 to 4, characterized in that the material is introduced into a container which consists of a compound which is exclusively soluble in the intestine.

6. The composition as claimed in one of claims 1 to 5, characterized in that the compound is introduced into the material.

7. The composition as claimed in one of claims 1 to 6, characterized in that the compound is soluble in liquid having a pH from 5 to 10.

8. The composition as claimed in one of claims 1 to 7, characterized in that the compound is soluble in liquids having a pH from 5.5 to 8.5.

9. The composition as claimed in one of claims 1 to 8, characterized in that the compound is soluble in liquids having a pH from 6.4 ± 0.6 to 7.0 ± 0.7.

10. The composition as claimed in one of claims 1 to 9, characterized in that the material comprises natural, semisynthetic or synthetic polymers and also stably crosslinked bodies or combinations thereof.

11. The composition as claimed in one of claims 1 to 10, characterized in that the material comprises collagen, cellulose or alginate.

12. The composition as claimed in one of claims 1 to 11, characterized in that the material is compressible to one half to one hundredth, preferably one quarter to one fiftieth, particularly preferably one tenth to one twentieth of its original size.

13. The composition as claimed in one of the preceding claims 1 to 12, characterized in that the material can be decompressed in the intestine to two to one hundred times, preferably four to fifty times, particularly preferably ten to twenty times, its size in the compressed state.

14. The composition as claimed in one of the preceding claims 1 to 13, characterized in that it comprises

pharmaceutically and/or biologically active substances, laxatives, nutrients or food supplements, foodstuffs, taste or stimulant substances, flavorings or other ancillary substances.

15. The composition as claimed in one of claims 1 to 14 for use for improving and maintaining intestinal activity and for improving and/or normalizing bowel movements, characterized in that it comprises a material which, if it is degradable in the stomach and/or small intestine, is provided with a compound which does not dissolve until in the intestine and is loaded with active compounds, for example for prophylaxis, or with laxatives in such a manner that these are predominantly or exclusively not released until in the intestine.

16. A process for preparing a composition for improving and maintaining intestinal activity as claimed in one of claims 1 to 15, characterized in that

a) a suspension of the material is prepared,
b) from this suspension a sponge-like or foam-like structure is prepared by methods known per se,
c) the material is then reversibly compressed,
d) before, during or after step b) the material is loaded with active compounds, for example for prophylaxis, or with laxatives in such a manner that these are predominantly or exclusively not released until in the intestine and
e) if appropriate a compound is applied to this material and/or a compound is introduced into the material and/or this material is encased with such a compound, with this compound not dissolving until in the intestine.

17. The use of the composition as claimed in one of the preceding claims for preparing compositions for improving and maintaining intestinal activity and for improving and/or normalizing bowel movements.

18. The use of the composition as claimed in one of the preceding claims for preparing pharmaceutically active compositions and/or nutrients and/or food supplements and/or (dietetic) foods.

19. The use of the composition as claimed in one of the preceding claims for improving and maintaining intestinal activity and for improving and/or normalizing bowel movements and/or for reducing the transit time of the chyme in the intestine, combined with a prophylactic or laxative action.

20. The use of the composition as claimed in one of the preceding claims in the fields of pharmacy and/or health and/or for nutrition and/or food supplementation.