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(54) **Title:** PACKAGING CONTAINING SOFT CAPSULES

(54) **Bezeichnung:** PACKUNG ENTHALTEND WEICHKAPSELN

(57) **Abstract:** The invention relates to a packaging containing a packing means and soft capsules, a method for stabilising soft capsules and a method for producing the packaging.

(57) **Zusammenfassung:** Die Erfindung betrifft eine Packung umfassend ein Packmittel und Weichkapseln, ein Verfahren zur Stabilisierung von Weichkapseln sowie ein Verfahren zur Herstellung der Packung.

PACK CONTAINING SOFT CAPSULES

The invention relates to a pack comprising a packaging material and soft capsules, to a process for the stabilisation of soft capsules, and to a process for the production of the pack.

Soft capsules are capsules which, owing to additions of softeners, such as, for example, glycerol, sorbitol, maltitol and polyethylene glycols, present in the capsule shell, have a certain elasticity and softness and are employed for the administration of various substances, such as, for example, medicaments, food supplements and/or functional ingredients. Soft capsules can be produced, for example, on the basis of gelatine or starch. Gelatine-based soft capsules have long been known as soft gelatine capsules and are commercially available from various suppliers. Starch-based soft capsules are a relatively new development, an example thereof are soft capsules marketed by Swiss Caps, Switzerland, under the trade name Vega-Gels®.

If liquid or semi-solid substances are to be administered by means of the soft capsules, they can be encapsulated directly, solids are first dissolved or suspended in liquid or semi-solid bases, such as, for example, fats, oils, wax mixtures or polyethylene glycols, possibly in combination with emulsifiers. Depending on the method of administration, such as, for example, orally, rectally or vaginally, soft capsules can have various shapes, they can be, for example, round, oval, oblong or torpedo-shaped. Soft capsules can be produced by the processes known in the prior art, such as, for example, by the Scherer process, the Accogel process or the droplet or blowing process.

The softening action of the softener component present in the shells of soft capsules is essentially based on the hygroscopicity thereof and the associated inclusion of water the capsule shell. At room temperature (22°C / 45 to 65% RH (RH = relative humidity)), soft capsules have a water content of

about 7 to 8% by weight. If the water content is significantly below this, for example due to excessively dry storage or drying, this results in embrittlement of the capsule shell, with the consequence of increased fragility of the capsule wall and the formation of cracks. If the water content is significantly above this, for example due to excessively moist storage, swelling of the capsule shell and sticking together of the soft capsules occur. Both excessively dry and also excessively moist storage also result in unpredictable effects on the substances to be administered and any further auxiliaries present, meaning that the supply with the substances present therein that is intended with the taking of soft capsules can no longer be ensured. Varying environmental influences result in totally incalculable influences on the stability of soft capsules, meaning that their shelf life, i.e. the period over which the soft capsules are within the respective specifications applying to them which have to be met in order that they can be taken as intended, can no longer be predicted with the requisite certainty. This is unacceptable, in particular also for safety reasons.

In one embodiment the present invention relates to finding a simple and inexpensive way of avoiding the losses in quality arising both with embrittlement of the capsule shell and also due to swelling and sticking together and significantly increasing the shelf life of soft capsules at high dryness, high atmospheric humidity, possibly also together with high temperatures, as prevail, for example, in climatic zones III and IV, and also in the case of strongly varying atmospheric humidity.

Disclosed herein is the introduction of soft capsules
into a packaging material in the inside wall(s) of which an absorbent and at least one channel former is embedded, at least over part of the area. The invention thus relates to a pack comprising a resealable container in/on the inside wall(s) of which at least one channel former is embedded, at least over part of the area, together with at least one absorbent, and at least one soft capsule, where the soft capsule(s) is (are) present in the container.

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A first aspect of the invention provides a pack comprising a resealable container, wherein in or on at least one inside wall of the container at least one channel former is embedded, at least over part of the area, together with at least one absorbent, and at least one soft capsule, wherein the at least one soft capsule is present in the container.

A second aspect of the invention provides a process for the production of a pack as defined in the first aspect, comprising introducing at least one soft capsule into a resealable container, wherein in or on at least one inside wall of the container at least one channel former is embedded, at least over part of the area, together with at least one absorbent; and then sealing the container.

A third aspect of the invention provides a process for increasing the shelf life of soft capsules comprising introducing the soft capsules into a resealable container, wherein in or on at least one inside wall of the container at least one channel former is embedded, at least over part of the area, together with at least one absorbent; and then sealing the container.

Surprisingly, the storage of the soft capsules results in an increase in the shelf life, although the container with an absorbent an agent is present which results in a drying action. This is because drying of soft capsules results, via the removal of water, precisely in embrittlement and fragility of the capsule shell or even cracking, i.e. precisely the state that is avoided by the invention.

According to an advantageous embodiment, the pack according to the invention contains soft gelatine capsules as soft capsules. The invention therefore relates to a pack which is characterised in that the soft capsule(s) present therein is (are) (a) soft gelatine capsule(s).

According to a further advantageous embodiment, the pack according to the invention contains as starch-based soft capsules. The invention therefore relates to a pack which is characterised in that the soft capsule(s) present therein is (are) (a) starch-based soft capsule(s).

The container is resealable and can have any spatial shape, such as, for example, that of a cylinder or cuboid, provided that it is sufficiently large to accommodate the soft capsules inside.

Resealable means that the container can be opened and re-closed repeatedly, i.e. at least once, preferably a number of times, particularly preferably at least as often as corresponds to the number of soft capsules present in the container. The container is so tightly sealed after each opening and closing operation that ingress of moisture and gases into the interior of the container is effectively prevented.

Opening and sealing of the container is carried out by a tightly sealing closure matched to the container. All types of closures can be employed so long as they ensure that gases and/or moisture cannot penetrate into the interior of the container in the closed state, or can only do so in extremely small amounts, even after repeated opening and closing of the container.

According to an embodiment of the invention, lids are used as closure. Examples of lids are screw caps, caps which are inverted over the upper edge of the vessels, or introduced into the interior of the vessel. In the case of spatial shapes which have corners, such as, for example, cuboids, the corners of the opening and the matching lid may also be slightly rounded in order to increase the tightness of the container against gases and moisture.

According to a preferred embodiment, the container has a cuboid-shaped spatial shape, rounded corners and is readily stackable. An embodiment of this type is depicted by way of example in Figure 1. The container comprises walls (2) whose inward-facing sides contain, at least over part of the area, at least one channel former together with at least one absorbent, has rounded corners (7) and has a lid (1) as closure.

The absorbents and channel formers present in the container may jointly either be present directly in the inside wall(s) of the polymer forming the container or be applied as a layer to the inside wall(s) of the polymeric container. Likewise, absorbents and channel formers may be embedded in an inlay, which is introduced into the container as insert, so that at least part of the inside walls of the container are lined thereby.

Inside wall(s) is taken to mean the inward-facing surface of the wall/walls of the container, i.e. the surface(s) of the container which is (are) in contact with the soft capsule(s) present therein.

Suitable materials for the container are polymers. Polymers, which can be employed in a mixture with absorbents and channel formers, are, in particular, thermoplastics, such as, for example, polyolefins, such as polyethylene and/or polypropylenes, polyisoprenes, polybutadienes, polybutenes, polysiloxanes, polyamides, ethylene-vinyl acetate copolymers, ethylene-methacrylate copolymers, polystyrenes, polyesters, polyanhydrides, polyacrylate nitriles, polysulfonates, polyester amides, polyacrylate esters, propylene-maleic anhydride, polyethylene-maleic anhydride, polyethylene-urethanes, polyethylene-ethyl-vinyl alcohols, polyethylene-nylon and/or polyurethanes. The walls provided

with absorbents and channel formers on their inside surface have, based on the total weight of the mixture of polymer, channel formers and absorbents, a content of polymer of 10 - 90% by weight.

Absorbents which may be present are in principle any type of desiccants, i.e. moisture-binding binders. Three groups of desiccants come into consideration:

The first group contains chemical substances which form hydrates with water. Examples of chemical substances of this type are anhydrous salts, which tend to absorb water or moisture, and form a stable hydrate in the process. The moisture is bound, and liberation thereof is prevented by a chemical reaction.

The second group of desiccants contains substances which are reactive. The substances react with water or moisture by forming a new substance. The newly formed substances are normally stable at low temperatures, which is only reversible with expenditure of high energy. Desiccants of this type are used principally for drying solvents and as water-absorbent material in polymers which themselves have to remain in a moisture-reduced state.

The third group of desiccants binds the moisture by physical adsorption. The desiccant contains particles having fine capillaries into which the moisture is drawn. The pore size of the capillaries and the density thereof in the desiccant determine the absorption properties. Examples of desiccants of this type are molecular sieves, silica gels, certain synthetic polymers, such as, for example, those which are used in babies' nappies, and starches. Desiccants from the third group are preferably present in the container since they are substantially inert and water-insoluble. Particular preference is given here to molecular sieves having a pore size of 3 to 15 Ångström and/or silica gels having a pore size of 24 Ångström.

Suitable channel formers are hydrophilic substances, such as, for example, polyglycols, ethylvinyl alcols, glycerol, polyvinyl alcohols, polyvinylpyrrolidone,

vinylpyrrolidone, N-methylpyrrolidone, polysaccharides, saccharides and/or sugar alcohols. Preferred polyglycols are polyethylene glycol and/or polypropylene glycol. Saccharides which can be used are, for example, glucose, mannose, galactose and/or fructose. Suitable sugar alcohols are, for example, mannitol, sorbitol, hexitol, dulcitol, xylitol, ribitol and/or erythrol. Polysaccharides are taken to mean, for example, dextrins and/or hydrolysed starch.

In the inside walls provided with absorbents and channel formers, the channel formers can have a proportion of 10 - 40% by weight, based on the total weight of the mixture of polymer, channel formers and absorbents.

Absorbents and channel formers are embedded over part of the surface or over the entire area in the inside wall(s) of the container. Over part of the area means that at least part of the total area of the container forming the inside wall(s) comprises absorbents and channel formers.

Over the entire area means that the entire area of the container forming the inside walls comprises absorbents and channel formers. According to an advantageous embodiment, absorbents and channel formers are present in at least 10%, preferably in at least 50%, particularly preferably in at least 90%, of the inside walls, based on the total inside surface area of the container.

Containers made from polymers which comprise absorbents and channel formers and which are suitable as container for the pack according to the invention are known in the prior art and are described, for example, in WO 97/32663 A1, EP 1000873 A2 and WO 03/086900 A1, EP 1421991 A1. Containers which can be employed in the pack according to the invention are commercially available and are available, for example, from Capitol Specialty Plastics Inc., 2039 McMillan Street Auburn, Alabama, USA, under the trade name Activ-Vial or from Süd Chemie, Ostenrieder Str. 15, 85368 Moosburg, Germany, under the trade name 2 AP Multipolymer.

The pack according to the invention is produced by dispensing the soft capsule(s) into a resealable container in/on the inside wall(s) of which at least one channel former is embedded, at least over part of the area, together with at least one absorbent, and subsequently sealing the container. The present invention therefore also relates to a process for the production of a pack, which is characterised in that the soft capsule(s) is (are) introduced into a resealable container in/on the inside wall(s) of which at least one channel former is embedded, at least over part of the area, together with at least one absorbent, and the container is subsequently sealed.

The pack according to the invention results in an increase in the shelf life of the soft capsules present therein. The invention therefore also relates to a process for increasing the shelf life of soft capsules, which is characterised in that they are introduced into a resealable container in/on the inside wall(s) of which at least one channel former is embedded, at least over part of the area, together with at least one absorbent, and the container is subsequently sealed.

The stabilising action of the pack according to the invention is based on the influence of the container on the in soft capsule(s), which can consequently be made available with a long shelf life. Achievement of the action according to the invention thus requires that the soft capsule(s) is (are) present in the container, i.e. the soft capsule(s) and container are together in the form of a pack.

Besides the stabilising action on the soft capsule shell, in the pack according to the invention also results in stabilisation of the active compounds and/or auxiliaries present therein, i.e. the entire formulation. This applies, in particular, if the active compounds and/or auxiliaries present are sensitive to moisture. Examples of moisture-sensitive active compounds which are thus preferably present in the soft capsules in the pack are many pharmaceutical active compounds, such as hormones or proteins, vitamins, cells, such as, for example, probiotic cultures.

The examples explain the invention without being restricted thereto.

Example 1

Investigation of the stability of soft capsules in the pack according to the invention compared with soft capsules in conventional packaging materials

Multivitamin soft capsules (active-compound composition and capsule shell as described below) are introduced individually into a thermoformed cavity film made from PVC 250 µm + 40 g/m^2 of PVDC and heat-sealed with aluminium foil (20 µm) and into a resealable container in/on the inside wall(s) of which at least one channel former is embedded, at least over part of the area, together with at least one absorbent (type: M-3006-16 Activ-Vial) in the inside walls of which a molecular sieve having a capacity of 1.92 g is embedded.

The blisters and containers containing the multivitamin soft capsules are stored at 40°C and 75% relative humidity (RH), removed from storage after predetermined times, assessed visually with respect to their appearance and investigated analytically with respect to the amounts of active compound present. The results are compiled in Tables 1 and 2.

Product	Multivitamin soft capsule*			
Batch	9018401			
Packaging material	PVC/PVDC-aluminium blister			
Storage condition	40°C/75% RH			
Storage duration	Start		3 months	
Parameter	mg/capsule	%	mg/capsule	%
Ascorbic acid	209	100	159	76
Dexpanthenol	13.5	100	9.7	72
Thiamine*HCL	19.7	100	17.1	87
Cyanocobalamine	0.199	100	0.171	86
Folic acid	0.62	100	0.57	92

Table 1

* Composition of the soft capsule shell: gelatine 209.76 mg, glycerol 85%

65.83 mg, sorbitol solution 70% 44.21 mg, black iron oxide 1.22 mg, red iron oxide 3.89 mg.

Product	Multivitamin soft capsule*			
Batch	9018802			
Packaging material	Container in the inside walls of which a channel former and an absorbent are embedded			
Storage condition	40°C/75%RH			
Storage duration	Start		6 months	
Parameter	mg/capsule	%	mg/capsule	%
Ascorbic acid	213	100	210	99
Dexpanthenol	13.3	100	12.8	96
Thiamine*HCL	19.6	100	19.3	98
Cyanocobalamine	0.21	100	0.173	82
Folic acid	0.60	100	0.520	87

Table 2

* Composition of the soft capsule shell: gelatine 209.76 mg, glycerol 85% 65.83 mg, sorbitol solution 70% 44.21 mg, black iron oxide 1.22 mg, red iron oxide 3.89 mg.

Example 2

Investigation of the stability of soft capsules in the pack according to the invention

Multivitamin soft capsules (active-compound composition and capsule shell as described below) are introduced into a resealable container in/on the inside wall(s) of which at least one channel former is embedded, at least over part of the area, together with at least one absorbent (type: M-3006-16 Activ-Vial) in the inside walls of which a molecular sieve having a capacity of 1.92 g is embedded.

The the multivitamin soft capsules are stored at 30°C and 65% relative humidity (RH), removed from storage after predetermined times, assessed

visually with respect to their appearance and investigated analytically with respect to the amounts of active compound present. The results are compiled in Table 3.

Product	Multivitamin soft capsule*			
Batch	GD 06 0045			
Packaging material	Container in the inside walls of which a channel former and an absorbent are embedded			
Storage condition	30°C/65%RH			
Storage duration	Start		6 months	
Parameter	mg/capsule	%	mg/capsule	%
ß-Carotene	2.3	100	2.0	87
Thiamine nitrate	2.40	100	2.37	99
Riboflavin	2.09	100	2.23	107
Nicotinamide	20.6	100	20.1	98
Pyridoxine*HCL	3.60	100	3.39	94
Ascorbic acid	120.5	100	115.0	95
Tocopherol acetate	20.0	100	19.8	99
Folic acid	0.581	100	0.603	104
Biotin	0.176	100	0.185	105
Cyanocobalamine	0.0163	100	0.0158	97
Calcium panthotenate	15.6	100	14.9	96

Table 3

* Composition of the soft capsule shell: gelatine, glycerol 98-100%, sorbitol solution 70%, water

Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", and variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps.

The reference in this specification to any prior publication (or information derived from it), or to any matter which is known, is not, and should not be taken as, an acknowledgement or admission or any form of suggestion that that prior publication (or information derived from it) or known matter forms part of the common general knowledge in the field of endeavour to which this specification relates.

The claims defining the invention are as follows:

1. Pack comprising a resealable container, wherein in or on at least one inside wall of the container at least one channel former is embedded, at least over part of the area, together with at least one absorbent, and at least one soft capsule, wherein the at least one soft capsule is present in the container.

2. Pack according to Claim 1, wherein the at least one soft capsule is a soft gelatine capsule.

3. Pack according to Claim 1, wherein the at least one soft capsule is a starch-based soft capsule.

4. Pack according to any one of Claims 1 to 3, wherein the container has a cuboid-shaped basic shape.

5. Pack according to any one of Claims 1 to 4, wherein the at least one absorbent is a desiccant which binds moisture by physical adsorption.

6. Pack according to Claim 5, wherein the desiccant is a molecular sieve or silica gel.

7. Process for the production of a pack according to any one of Claims 1 to 6, comprising introducing at least one soft capsule into a resealable container, wherein in or on at least one inside wall of the container at least one channel former is embedded, at least over part of the area, together with at least one absorbent; and then sealing the container.

8. Process for increasing the shelf life of soft capsules comprising introducing the soft capsules into a resealable container, wherein in or on at least one inside wall of the container at least one channel former is embedded, at least over part of the area, together with at least one absorbent; and then sealing the container.

9. Pack as defined in Claim 1, substantially as hereinbefore described with reference to the Examples and/or the Drawing.

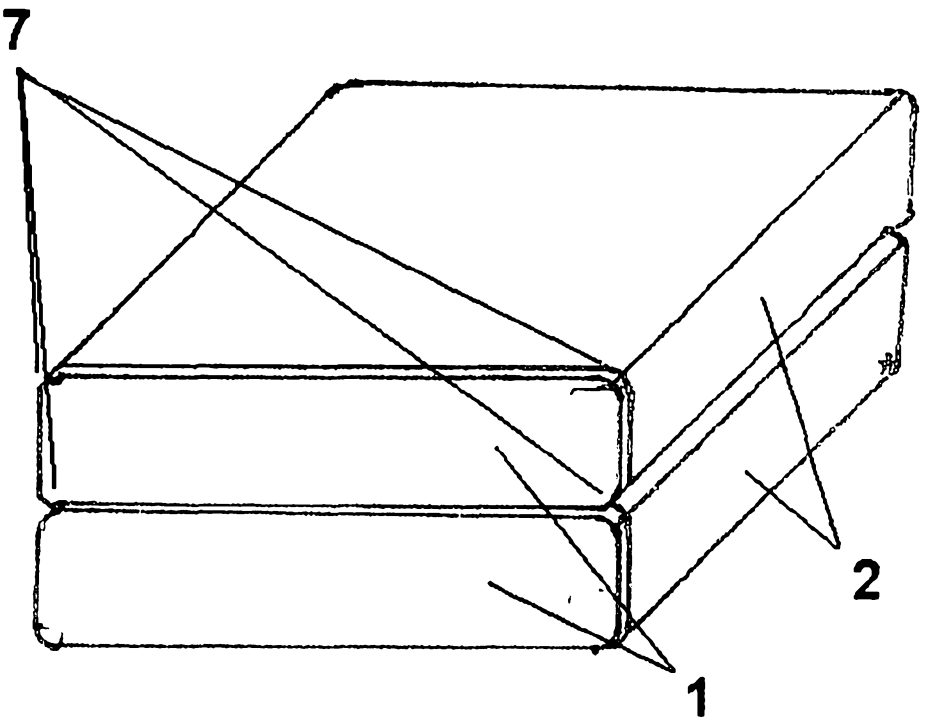

Figure 1