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ENTERIC GELATIN CAPSULE SHELL OR ENVELOPE

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4 Claims. (Cl. 167—82)

This invention relates to an improved gelatin envelope or protective enclosure for medicaments or other substances which envelope or enclosure is enteric.

This improvement is herein described as particularly relating to an enteric capsule shell but it may be embodied in an envelope or enclosure surrounding a tablet or medicament in any suitable dosage form.

Heretofore, medicaments intended for intestinal dispersion and having individual dosages in tablet, pill, or capsule form have been coated with various types of enteric coatings. Gelatin is the commonly used capsule shell material and gelatin capsule shells have been so coated but so far as is known there has not been available a gelatin or other sheet of enteric character which possessed the necessary physical characteristics for use as capsule shell material.

One form of enteric coating used was a phthalic acid ester of cellulose. Such material was applied as were other enteric coating materials as a coating to the outer surface of the medicament which might be in the form of a pill or tablet, or applied as a coating to the outer surface of a capsule shell. Such enteric material was always applied as a coating to an otherwise self contained medicament dosage. If the medicament was in fluid form it was first capsulated as within a gelatin shell and the enteric material was applied as a coating to the capsule shell. Such coating materials lacked the elasticity and flexibility of gelatin and were not suitable for use in sheet form as capsule shells. Such coating material possessed the disadvantage under certain circumstances of breaking down through development of cracks or fissures therein. They were particularly unsuitable when used as a coating upon a gelatin capsule shell not only for the above reasons but for the further reason that due to change in size and shape of the capsule shell as a result of accidental deformation or temperature variations, the coating film tended to rupture and break.

This invention is directed toward the provision of an improved gelatin envelope or sheet material which may be used in the formation of an envelope or capsule shell and which will protect the medicament from the action of the stomach secretions upon passage of the medicament therethrough but which will break down upon exposure to the intestinal secretions, releasing the medicament therein. We have discovered that when a suitable cellulose derivative, which is water soluble, such as the sodium salt of cellulose acetate phthalate, is added in relatively small percentage such as five to ten per cent to a suitably plasticized commercial gelatin solution, and such solution used to form a capsule shell or envelope for a medicament, and when such capsule shell is subjected to a suitable tanning treatment that the capsule so formed will pass through the stomach without release of its contained medicament but will break down in the intestines sufficiently to release the medicament. The gelatin solution may be the conventional one of one-third gelatin, one-third water and one-third glycerin, or it may be a relatively harder gelatin mixture wherein the glycerin content is reduced.

For example, we have found that a suitable gelatin mixture may be prepared as follows:

Materials

Gelatin (coarse or medium ground, 200–225 bloom)	pounds	10
Water	do	13
Glycerin	do	4½
Cellulose acetate hydrogen phthalate (ground fine)	pounds	1½
Sodium acid carbonate	grams	160

Procedure

Grind the cellulose acetate hydrogen phthalate on a micro pulverizer or otherwise suitably pulverize the same. Determine the theoretical amount of sodium acid carbonate required to neutralize and dissolve the cellulose acetate phthalate which commercially varies in degree of esterification. Mix the required amount of sodium bicarbonate with the phthalate as by dry mixing in a Hobart mixer for 10–15 minutes. Add 8 lbs. of 80° C. water to the mixture and mix until all phthalate has gone into solution. Allow to stand overnight to permit complete reaction and evolution of all gas. Add 4½ lbs. glycerin to 5 lbs. water; add gelatin with mixing. Allow to soak overnight. Next morning add the phthalate solution to the soaked gelatin with stirring. Break up all large aggregates of gelatin. Put in gel tank and melt at 60° C. Maintain on heat until air and CO_2 free. Such a gelatin solution should be free from undissolved phthalate. The pH should not exceed 7–7.5.

Such a gelatin solution will form a suitable band or sheet capable of use in a capsulating machine and may be used to form a capsule shell enclosing a suitable medicament or to form other enveloping enclosures.

A suitable tanning treatment is to formalize

the capsule shell thus prepared in a 1% formaldehyde solution for forty-five or sixty seconds followed by washing in water and drying. The tanning may be accomplished in other suitable ways such as through the employment of chromic acid salts, solutions of tannic acid and the like.

Alkalies and alkali salts other than sodium bicarbonate may be used to produce the water soluble cellulose derivative. For example, sodium carbonate, potassium carbonate, potassium bicarbonate or the like may be used in the correct amount necessary to neutralize and dissolve the cellulose acetate phthalate.

The tanning treatment renders the gelatin constituent of the shell resistant to solution in the stomach and the cellulose derivative fraction of the shell is resistant to attack by the stomach juices whereby the capsule passes through the stomach without release of its content. When the capsule enters into the intestines however, the shell breaks down sufficiently to release the content material. It is believed that while the tanned gelatin is still resistant to solution, because of its tanning, that the cellulose derivative fraction of the shell responds to the intestinal secretions and the phthalate reverts to the soluble alkali salt providing openings through the shell which cause it to break down and release its content material.

It is understood that the water soluble form of the cellulose derivative changes to the water insoluble form in the stomach due to the relatively high acid environment found there.

What we claim:

1. A content material surrounded by a tanned gelatin envelope which has dispersed throughout a sufficient amount of an alkali metal salt of cellulose acetate phthalate to render the envelope responsive to the action of the intestinal secretions to release the content substance while resisting dissolution in the acid stomach secretions.

2. A medicament surrounded by a tanned gelatin envelope which envelope contains in dispersed admixture with a gelatin 5% to 10% by weight of an alkali metal salt of cellulose acetate phthalate.

3. A medicament surrounded by a tanned gelatin envelope which envelope contains in dispersed admixture with the gelatin a small percentage of sodium salt of cellulose acetate phthalate in sufficient amount to cause the envelope to release the medicament in response to intestinal secretions.

4. An enteric capsule shell consisting of a tanned gelatin envelope which contains in dispersed admixture with a gelatin an alkali metal salt of cellulose acetate phthalate.

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