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SOFT ELASTIC CAPSULES AND PROCESS FOR PRODUCING

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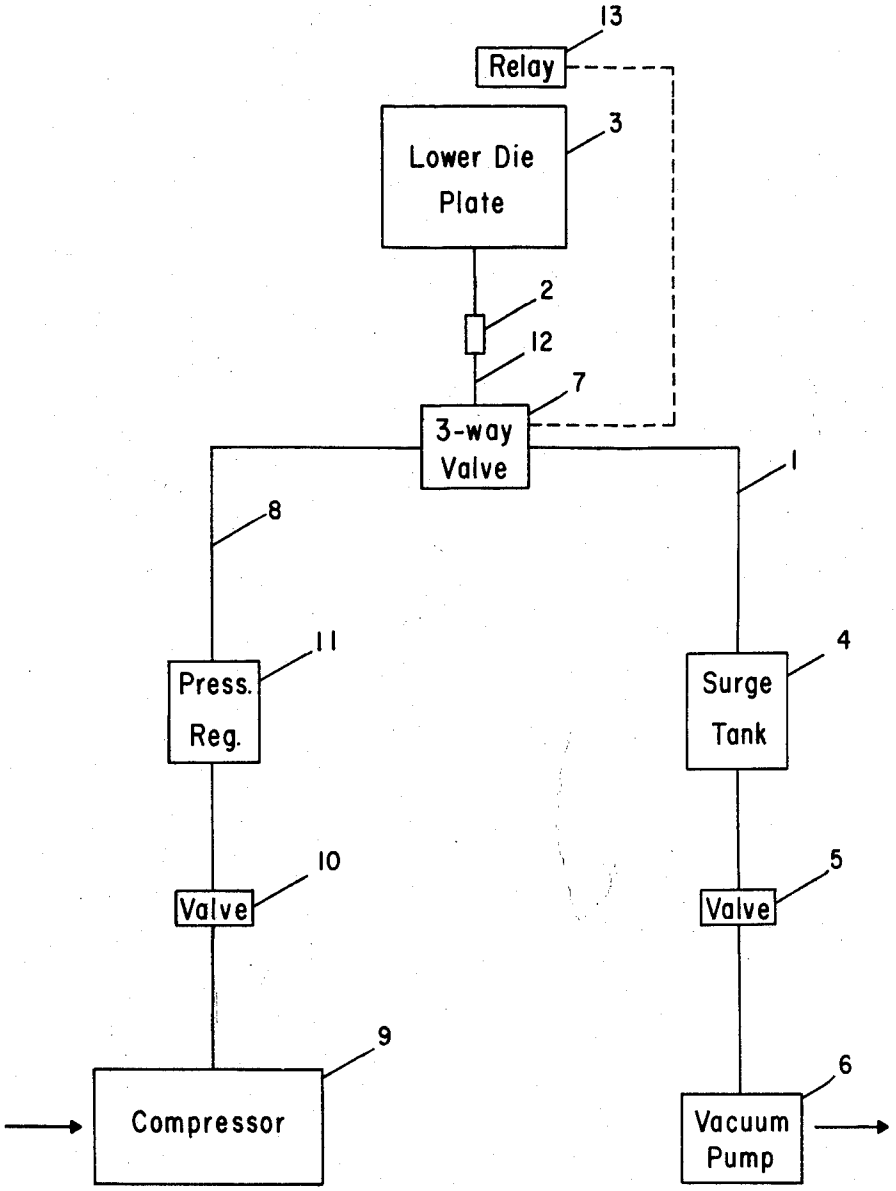

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SOFT ELASTIC CAPSULES AND PROCESS FOR PRODUCING

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This invention relates to a process for producing substantially filled soft elastic capsules and to capsules produced thereby.

The process of this invention can be embodied in any soft elastic capsule manufacturing equipment in which the capsule fill is introduced prior to formation of the completed capsule. In its essentials the novel process comprises (1) closing the capsule sufficiently to permit escape of air but not capsule fill from the volume to be enclosed, (2) inwardly deforming the surface of the said capsule to expel air therefrom, and (3) while maintaining said inward deformation, completing closure of said capsule.

The soft elastic capsule has long been regarded as an advantageous form of medication because of its shape, appearance and resistance to tampering and accidental separation. In addition, such capsules offer the most suitable pharmaceutical form in which to present liquids, such as the oil-soluble vitamins, which cannot be conveniently or economically reduced to powders for filling into conventional hard gelatin capsules. Heretofore a common problem associated with this pharmaceutical form has been the unavoidable retention of air pockets in the filled capsule, thereby giving to the capsule the appearance of less than a complete fill where the color of the capsule permits visualization of the contents.

Recently it has become of increasing interest to produce soft elastic capsules containing dry solids, such dosage forms having use, for example, in affording sustained release of the enclosed medication. The problem is aggravated in this type of product, particularly where the solids are in granular form, and more particularly in the case of pilules and spherical granules. Here the conventional soft elastic capsule filling techniques have proved less than satisfactory in manufacture because of the significant volume of air entrapped in the capsule on closure. Thus when the granules are charged into the mold cavity they do not assume their most compact orientation and tend to occupy a greater volume than is desired. To accommodate the excess volume it has been necessary to provide mold cavities of larger size than would otherwise be employed. The completed capsule containing such granules therefore gives the appearance of substantially less than a complete fill and is not only unattractive but raises the prospect in the mind of the user that less than a full dose has been provided.

Various solutions to this problem have been explored. The mold or filling head or both have been vibrated during filling. An electric needle has been used for puncturing the formed capsules to release excess air and reseal the capsules. Capsules have been pricked to permit escape of entrapped air. Hollow tubes, such as hypodermic needles, have been employed to withdraw air from the capsules. These approaches, however, have all been found inadequate as an adjunct to regular manufacturing procedures.

The process of this invention alleviates the prior difficulties to give a novel capsule in which the contained material has no degrees of freedom and which, therefore, in actuality and appearance, is substantially filled. By "no degrees of freedom" and "substantially filled" are meant a capsule fill in which there is little or no perceptible movement of the liquid or of the solid particles enclosed therein. Using this method, for example, transparent soft elastic capsules containing discrete solid particles, such as spherical solids (e.g., pilules), in particular those measuring at least about 0.04 in. in diameter, can be prepared which heretofore have necessitated the use of an opaque capsule or else the toleration of an inelegant capsule having the appearance of being only partially filled. Thus where a feature of a pharmaceutical product lies in its presentation in the form of numerous small discrete particles, such as pilules, which, on release in the body, disperse to areas of different arbsorbability to give a true sustained release effect, the increased patient acceptance of such a product through visualization of the contents of the capsule provides a significant advantage.

The term "'capsule portion" as employed herein refers to the preformed capsule segment into which the capsule fill is deposited in capsule-making processes characterized by the provision of horizontally disposed die plates (e.g., as in machines manufactured by the Arthur Colton Company), the cavities thereof forming the molds for the said capsule segments or "'capsule portions." The term "capsule body" refers to the partially formed capsule into which the capsule fill is injected or deposited in capsule-making processes utilizing vertically disposed die plates (e.g., as in machines manufactured by the R. P. Scherer Corporation).

Deformation of the capsule portion or capsule body with consequent displacement of internal volume and expulsion of a corresponding volume of air can be accomplished either mechanically or pneumatically, depending on the characteristics of the basic machine being adapted in accord herewith. Thus, in the context hereof, "inwardly deforming" and terms of like import refer to the action of a localized pressure resulting from (1) application of a positive gas pressure or relief of existing vacuum to a localized area of the capsule body or capsule portion, or (2) application of a localized mechanical pressure, as through a fixed or reciprocating rod of such length and cross section as to produce a reversible inward deformation of the capsule body or capsule portion at the contact area. It is, of course, necessary that the pressure, by whatever means applied, be so controlled and directed as to avoid puncturing the capsule wall or otherwise causing permanent injury thereto.

As described, the inward deformation of the capsule body or capsule portion causes the expulsion of air from the volume to be enclosed. However, the capsule fill must be retained within said volume. Thus the deformation is initiated after bringing together the capsule portions, where the capsule is formed from separate bodies, as in the horizontal or vertical die plate process, or the partial closing of a capsule formed by the rotary die process, in both cases closing being carried to the point at which air but not capsule fill will escape through the available clearance.

By way of exemplifying the preferred embodiment of this invention, particular reference will be made to the production of soft elastic capsules by a modified horizontal die plate machine of a type long known in the art and manufactured by the Arthur Colton Company. In this machine the capsules are formed between horizontally positioned upper and lower die plates having oppositely disposed cavities. A sheet of gelatin is placed over the bottom die plate and drawn into the cavities of the said plate by vacuum applied through openings in the said cavities, the gelatin thereby lining the interior surface of the cavities to form the lower portion of the capsules. The fill is charged into the thus formed lower capsule portions in the usual manner and a second sheet of gelatin laid thereover. In the usual operation of the process the

upper and lower die plates are at this point pressed together to unite the capsule portions and form the completed capsule, the said die plates separated, the vacuum relieved on the lower die plate, and the completed capsules removed therefrom.

In the preferred embodiment of this process, the same steps are followed through filling the lower capsule portions. Then, however, instead of immediately pressing together the upper and lower die plates to unite the capsule portions, the said plates are brought into such proximity that air will pass from the volume to be enclosed but the capsule fill will be retained therein. At this point the vacuum on the lower die plate is broken and a brief surge of air creating a positive pressure is admitted through the vacuum line to the said lower die plate and thence to the lower capsule portions contained therein. The pressure thus applied causes a reversible inward deformation of the lower capsule portion with expulsion of a corresponding volume of air from the volume which would otherwise be enclosed. While the positive pressure is being applied and the lower capsule portion inwardly deformed as described, the two die plates are pressed together in the usual manner to unite the respective capsule portions and form the completed capsules. Suitable vacuum is then re-established to assure retention of the completed capsules in the lower die plate, and normal operation of the machine and process thereof is resumed, the die plates being separated, the vacuum again broken and the capsules removed from the said lower die plate.

The foregoing embodiment is illustrated in the accompanying drawing, and reference will now be made thereto in conjunction with the mechanical modifications introduced in a conventional machine of the type described to carry out the process of this invention. In the operation of the machine without the present modification, vacuum line **1** is connected directly, through flexible connector **2**, to lower die plate **3**. Vacuum is thus drawn from lower die plate **3** through surge tank **4** and shut-off valve **5** by vacuum pump **6**. As presently modified, three-way valve **7** is inserted in vacuum line **1**. Also connected to three-way valve **7** is compressed air line **8**. With said three-way valve **7** in the pressurizing position, air is delivered to lower die plate **3** by compressor **9** through shut-off valve **10** and pressure regulator valve **11**. Thus line **12** between three-way valve **7** and lower die plate **3**, containing flexible connector **2**, serves alternately to exhaust air from and deliver air to said lower die plate **3**. Three-way valve **7** is responsive to time-delay relay **13** actuated by the press (not shown), said relay **13** causing three-way valve **7** to admit positive air pressure through line **12** to lower die plate **3** when upper and lower die plates are in pressing position but prior to actual pressing. During the period of air pressurization the press brings the die plates together to unite the upper and lower capsule portions, whereupon time-delay relay **13** actuates three-way valve **7** to the vacuum position, and vacuum is re-established. The die plates are then separated, the vacuum broken by disconnecting line **12** at flexible connector **2**, and the completed capsules are removed from lower die plate **3**.

It will be apparent that the optimum pressure and the period of pressurization depend on the thickness of the gelatin sheets, the size of the die cavity (i.e., the size of the capsule being produced), and the size of the particles or viscosity of the fluid being encapsulated. Accordingly, no critical range of pressures can be specified, although satisfactory conditions are readily determinable by routine testing. The setting of the time-delay relay to actuate the three-way valve will vary, primarily, with the size of the particles or viscosity of the fluid in the capsules, i.e., the clearance necessary between the capsule portions. In the embodiment illustrated it was found that solidly filled soft elastic capsules containing 2 mg. granules each approximating 0.050 in. in diameter could be satisfactorily produced with an air pressure of 4–12 p.s.i. (preferably 8 p.s.i.) from a 100 p.s.i. air source and a vacuum of 7–23 in. water. The period of application of air pressure is immaterial so long as pressurization is maintained until closure of the capsule is complete.

Reference has been made above to pressurization as a means for accomplishing the inward deformation of the capsule portion in the lower die plate. It will be understood, however, that other means can be employed to this end. Thus, instead of applying a positive pressure the reversible deformation can be induced by relieving the vacuum to atmospheric pressure to obtain a relative pressurization. Also, instead of utilizing a time delay relay, the three-way valve can be actuated from contact points on the press travel, said contact points being so placed as to actuate the valve when the die plates are pressed to a predetermined clearance and again when capsule closure (corresponding to the lowest point in press travel) is complete. From the foregoing description one skilled in the art can readily modify other existing soft elastic capsule machines, such as those of the vertical die plate or rotary die types, to operate in accord with this invention.

What is claimed is:

1. In a process for producing a substantially filled soft elastic capsule, with solid particles the capsule fill being charged into the capsule prior to complete closure thereof, the improvement which comprises: (1) closing the capsule sufficiently to permit escape of air but not capsule fill from the volume to be enclosed, (2) inwardly deforming the surface thereof; (3) completing the closure of said capsule while maintaining said inward deformation, and (4) removing said inward deformation.

2. In a process for producing a substantially filled soft elastic capsules, with solid particles said capsules being formed by the union of two capsule portions, the capsule fill being charged into one capsule portion prior to union of said two capsule portions, the improvement which comprises: (1) filling one capsule portion, (2) bringing the capsule portions into such proximity as to permit the escape of air but not capsule fill from the volume to be enclosed, (3) inwardly deforming the surface of at least one capsule portion, (4) uniting said capsule portions while maintaining said inward deformation, (5) completing the union of said capsule portions to form the completed capsule, and (6) removing said inward deformation.

3. In a process for producing a substantially filled soft elastic capsule with solid particles, said capsule being formed by the union of two capsule portions, the capsule fill being charged into one capsule portion prior to complete closure, the improvement which comprises: (1) filling one capsule portion, (2) uniting the two capsule portions sufficiently to permit escape of air but not capsule fill from the volume to be enclosed, (3) directing a localized pressure against the surface of at least one capsule portion to inwardly deform the surface thereof and expel air but not capsule fill from the volume to be enclosed, (4) uniting said capsule portions to form the completed capsule while maintaining said localized pressure, and (5) withdrawing said localized pressure from the surface of said capsule portion.

4. In a process for producing a soft elastic capsule substantially filled with solid particles, utilizing a horizontal die plate machine, said capsule being formed by the union of two capsule portions, one capsule portion being retained in the lower die cavity by vacuum applied to the under surface of said cavity, the capsule fill being charged into said lower capsule portion prior to the union of two capsule portions by pressure on the upper die plate containing opposing cavities, the improvement which comprises: (1) filling the lower capsule portions retained by vacuum in the die cavity, (2) bringing the two capsule portions into such proximity as to permit escape of air but not capsule fill from the volume to be enclosed, (3) replacing the vacuum with a positive pressure to inwardly deform the lower capsule portions and expel air from

the volume to be enclosed, (4) completing the closure of the two capsule portions while maintaining the positive pressure, (5) re-establishing the vacuum on the lower capsule portions, (6) separating the upper and lower die plates, (7) breaking the vacuum on capsules retained in the lower die plate, and (8) removing the completed capsules from the lower die-plate cavities.

5. Filled soft elastic capsules made according to the process of claim 1.

6. Filled soft elastic capsules made according to the process of claim 2.

7. Filled soft elastic capsules made according to the process of claim 3.

8. Filled soft elastic capsules made according to the process of claim 4.

9. Soft elastic capsules filled with spherical solids having no degrees of freedom therein.

10. Transparent soft elastic capsules filled with spherical solids having no degrees of freedom therein.

11. Transparent soft elastic capsules filled with spherical solids measuring at least about 0.04 in. in diameter and having no degrees of freedom therein.

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