

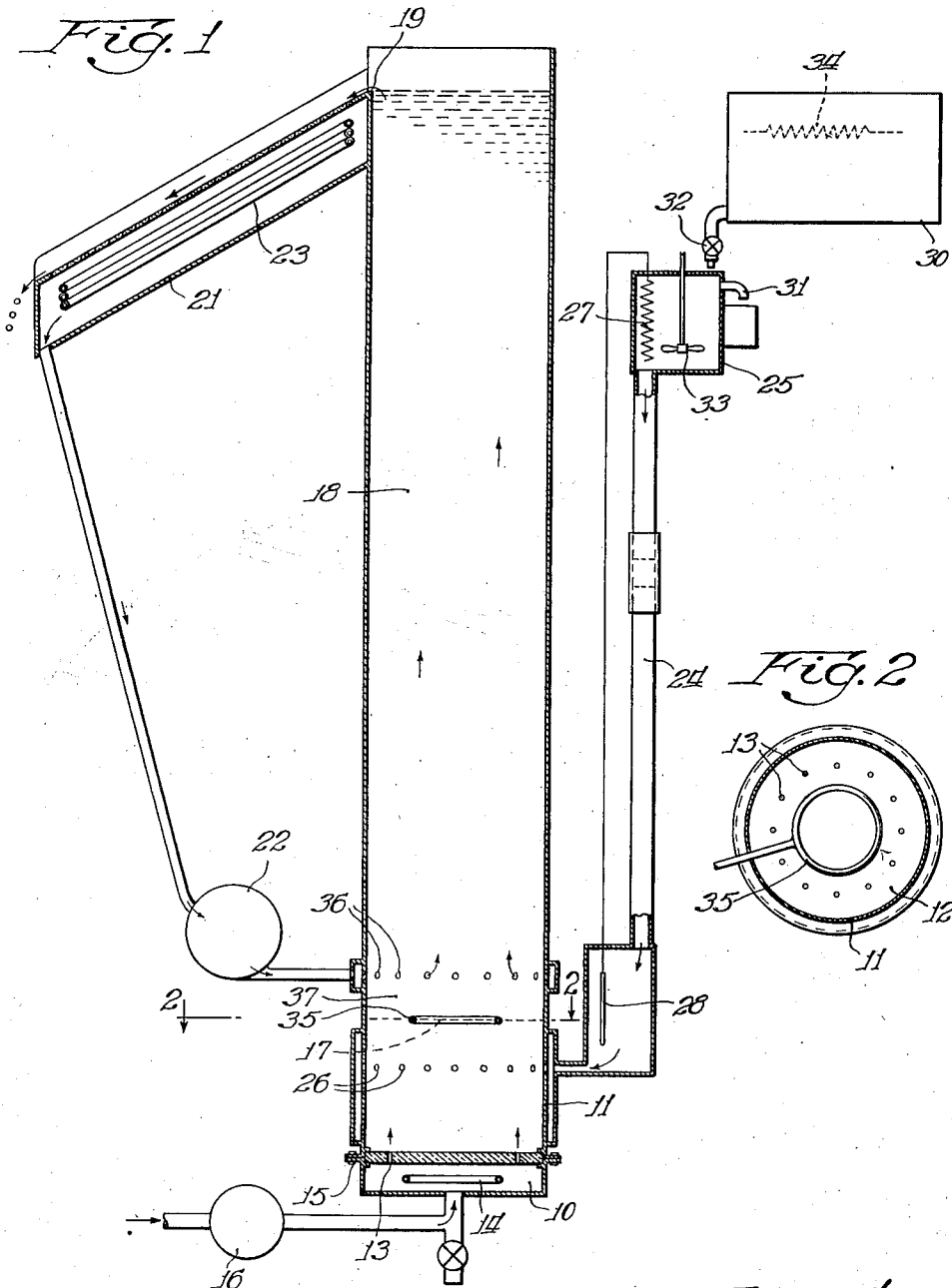
Feb. 29, 1944.

R. W. GUNNELL

2,342,661

MANUFACTURE OF CAPSULES

Filed Jan. 28, 1942



Inventor:
Robert W. Gunnell
By: Roland E. Ehm
Att'y.

UNITED STATES PATENT OFFICE

2,342,661

MANUFACTURE OF CAPSULES

Robert W. Gunnell, Hammond, Ind.

Application January 28, 1942, Serial No. 428,575

20 Claims. (Cl. 117-113)

This invention relates to the manufacture of capsules, and among other objects aims to provide an improved method and apparatus for producing capsules containing medicaments or other substances.

The nature of the invention may be readily understood by reference to one method and apparatus embodying the invention and shown in the accompanying drawing.

In said drawing:

Fig. 1 is an elevation in diagrammatic form of a method and apparatus for producing capsules.

Fig. 2 is a plan section on the plane 2-2 of Fig. 1.

According to the illustrative method, the medicament or other substances to be capsulated is formed into globules or pellets comprising a measured or predetermined volume and covered with a capsule-forming film such as gelatin. For simplicity and convenience the term "medicament" will be employed in a general sense to include whatever substance is capsulated whether or not it is strictly a medicament. The medicament may advantageously be in liquid form and released in liquid globules or drops which naturally form into spherical shape, and on which a capsule is created by solidifying or otherwise setting thereon a retaining film of coating liquid. The expression "drops" is used in a general sense and not to define a specific amount of medicament. In the present case, the globules are introduced into a coating liquid (such as a gelatin sol, that is, a liquid containing gelatin) comprising the capsule-forming material. The latter preferably has a specific gravity greater than that of the medicament so that the globules will rise in the liquid. For capsulating with a thermo-plastic coating material, the globules of medicament are preferably chilled before introduction into the coating liquid and the latter is maintained at such temperature that a coating of the liquid will congeal on the globules as they rise. The temperature differences between that of the globules and the coating liquid depends upon the amount of cooling necessary to congeal an adequate film of coating on the globules.

The coated globules are removed from the capsulating material before the latter has an opportunity to affect or impair the coating, and thereupon the coating is conditioned, in this case by cooling or chilling, so as to set or harden it sufficiently for handling. The resultant capsules are seamless and, therefore, cannot develop leaks as in the seamed capsules heretofore on the market.

In the illustrative apparatus the medicament is advantageously introduced at the lower portion 10 of a receptacle 11 containing in its lower portion a body of coating liquid, such as liquid containing gelatin. Below the body of coating liquid is a diaphragm 12 through which globules of medicament are introduced into the coating liquid. In the present instance the medicament being in liquid condition, the globules are advantageously formed by ejecting fixed charges of medicament through orifices 13 in the diaphragm. A temperature regulating device including a cooling coil 14 serves to cool the medicament to the proper temperature and to maintain it at such temperature upon introduction of the medicament in globule form into the coating liquid. The diaphragm advantageously incorporates insulation to prevent chilling of the capsule-forming liquid by the cool medicament below it. The lower portion 10 of the receptacle and the diaphragm 12 are removable from the superposed receptacle to permit easy substitution of diaphragms to change orifice size. For that purpose the upper and lower receptacles are flanged as at 15 and the joint between them is sealed by a gasket.

As shown in Fig. 2, the orifices 13 are arranged in a circular series. The orifice diameter cooperates in determining the size of the drops released. Their size and rate of release is advantageously controlled by a measuring pump 16 or other means, which periodically forces a predetermined volume of medicament through the orifices 13. If necessary, in order to secure discharge of uniform globules from each of the orifices, the measuring pump may be provided with a separate measuring chamber and line for each orifice. Generally this is not necessary since with uniform temperatures and orifices, uniform globules will be discharged from each of the orifices.

The depth of the coating liquid is adjusted to what is necessary to congeal an adequate film of the globules, but is not great enough to remelt or otherwise impair the coating as the globules rise through the coating liquid. In the present case the upper lever of the coating liquid terminates at dotted line 17. The capsule or film congealed on the globules should be sufficiently thick and strong safely to retain the contents of the globules and to withstand usual handling. The thickness of the film will vary in case of a thermo-plastic coating with the temperature difference between the coating liquid and globule, with the size of the globule (that is, its heat absorbing capacity), and with the time of immer-

sion in the coating liquid. For gelatin coatings, the range of variation in coating liquid may be from .005 of an inch to .030 of an inch. When the coated globules rise to the surface of the coating liquid, they pass into a conditioning zone in which the coating is set or hardened. Such conditioning zone is, in this case, represented by a supernatant layer 18 of liquid chilled substantially below the melting point of the coating and whose specific gravity is less than that of the coating liquid by virtue of which the conditioning liquid floats as a layer upon the coating liquid. The conditioning liquid is of such character as not to dissolve or otherwise impair the gelatin or other coating or to be easily miscible with or soluble in or a solvent of the coating liquid. One form of conditioning liquid for a gelatin coating is a mixture of naphtha and carbon tetrachloride. The latter is relatively heavy and serves to adjust the specific gravity of the conditioning liquid to exceed that of the coated globules so that the latter will rise through the conditioning liquid. The adjusted specific gravity of the liquid is less than that of the coating liquid. Neither naphtha nor carbon tetrachloride react with either the gelatin or the gelatin sol.

The nature of the coating liquid determines the character of the conditioning liquid 18 whose function is to treat or condition the coating for handling. In the present case, the coating is conditioned merely by cooling.

The depth of the column of conditioning liquid is substantial as compared with that of the coating liquid so as adequately to harden or toughen the coating for handling.

When the coated globules reach the surface of the conditioning liquid, they may be either manually or mechanically removed. In the present instance they flow over a weir 19 and roll down an inclined perforated drain board to drain off any adhering cooling liquid into a receptacle 21. A circulating pump 22 advantageously maintains a circulation or upward current of the cooling liquid both to maintain the column of cooling liquid at the desired low temperature and also to carry the capsules over the weir. A temperature-regulating coil 23 located in the receptacle 21 re-cools the cooling liquid to a predetermined temperature.

Coating liquid is supplied through conduit 24 from a constant level reservoir 25. Conduit 24 leads to a header having a series of orifices 26 around the space 11 so that fresh coating liquid will enter the space 11 without causing undue turbulence. The header may advantageously act as a jacket around the coating liquid to prevent loss of heat through the sides of the receptable. The coating liquid is heated by heating element 27 controlled by thermostat 28 located adjacent the entry of the coating liquid into the receptacle. In normal operation, temperature conditioned coating liquid is supplied at such uniform rate and distribution as to maintain sufficiently uniform temperature conditions in the body of coating liquid in receptable 11.

In the present case, the rate of supply of coating liquid is controlled hydrostatically; that is, the level of reservoir 25 is adjusted by means of a telescoping sleeve in the conduit 24 so that the column of coating liquid balances the combined head of coating liquid and conditioning liquid in receptacle 11. Since the volume of the latter is maintained constant, a reduction of the coating liquid in receptacle 11 results in flow of coating liquid from conduit 24 into receptacle 11. Coat-

ing liquid is supplied to reservoir 25 from storage tank 30. The level of the reservoir 25 is maintained constant by the overflow 31 and by adjusting the valve 32 from tank 30 to feed coating liquid at a rate sufficient to keep reservoir filled to overflowing. A stirring device 33 circulates the liquid around the heating element 27. Tank 30 is preferably supplied with a heater 34 to prevent congealing of the coating.

To prevent undue cooling or congealing of the coating liquid at the inter-face 17 between the coating liquid and the cooling liquid, heating means in the form of an electric heater coil 35 is advantageously located at the inter-face and serves to prevent the cooling liquid from unduly lowering the temperature of the coating liquid at the inter-face. The coating liquid is maintained in such fluid condition at the inter-face that rising of the coated globules through the inter-face is not restrained and appendages or tails of coating material are not dragged along with the globules. The heating coil is supported by its lead-in conduit and is preferably positioned out of the vertical lines of travel of the globules (see Fig. 2).

Cooling liquid adjusted to the proper temperature is re-introduced through orifices 36 located sufficiently above the heater 35 so as not to neutralize its action. Preferably the latter orifices are directed slightly upward so that the incoming conditioning liquid has an upward movement which assists in moving the coated globules upwardly and also prevents material interference with the intermediate heated zone 37 above the inter-face.

One illustrative coating material for forming a gelatin capsule comprises by weight:

	Percent
Gelatin of 150 to 250 Bloom	25
Glycerine	15
Water	60

A depth of about two inches of such liquid in receptacle 11 at about 100 degrees Fahrenheit will develop a satisfactory gelatin coating on three minim globules of cod liver oil introduced at a temperature of about 12 degrees Fahrenheit. The glycerine functions as a so-called plasticizer to prevent the capsule from becoming too brittle. Gelatin of a wide range of quality may be used. However, the poorer the quality the higher the gelatin concentration required in the sol and the poorer the quality of coating. Superior results are obtained by the use of gelatin of from 150 to 300 Bloom. The temperature of the gelatin sol in the receptacle should be from 90 to 100 degrees Fahrenheit and that of the conditioning liquid for gelatin capsules of from 40 to 60 degrees Fahrenheit.

It will be understood that various types of coating and conditioning liquid may be used. Preferably, they should have the following properties.

1. The coating liquid should be heavier than the medicament and should form a coating thereon as the globules of medicament rise through it.
2. The conditioning liquid should:
 - a. Properly condition the coating to toughen it;
 - b. Be lighter in weight than the coating liquid but heavier than the medicament;
 - c. Not dissolve or otherwise impair the coating nor should it be miscible with or readily soluble in the coating liquid.

For some uses the coating or capsule formed need not be soluble. Gelatin is the most commonly used capsulating material if solubility of the capsule be essential.

Obviously, the invention is not limited to the details of the illustrative method or apparatus since these may be variously modified. Moreover, it is not indispensable that all features of the invention be used conjointly since various features of the invention may be used to advantage in different combinations and sub-combinations.

Having described my invention, I claim:

1. The method of forming capsules or the like which comprises introducing a globule of material to be capsulized into a body of coating liquid, collecting a coating therefrom on said globule, and then treating the globule to harden the coating.

2. The method of forming capsules or the like which comprises introducing a globule of liquid to be capsulized into a body of coating liquid, maintaining the latter in liquid form, passing the globule therethrough and during such passage collecting a coating of said coating liquid on said globule, and then cooling the coated globule to harden the coating.

3. The method of coating capsules or the like which comprises introducing into a body of coating liquid a globule of material substantially cooler than the coating liquid, maintaining the body of the latter in liquid condition, causing the coating only of the liquid to congeal on said globule and removing the coated globule from the liquid and hardening the coating.

4. The method of forming capsules or the like which comprises introducing into the lower portion of a body of coating liquid a globule of material of lower specific gravity than the liquid, allowing the globule to rise through the liquid so as to be coated thereby, then removing the globule from the liquid and hardening the coating.

5. The method of forming capsules or the like which comprises introducing into the lower portion of a body of coating liquid a globule of liquid to be coated of lower specific gravity than the coating liquid, allowing the globule to rise through the coating liquid so as to be coated thereby, then removing the globule from the liquid and hardening the coating.

6. The method of forming capsules or the like which comprises introducing into a body of coating liquid a globule of liquid to be coated of lower specific gravity than the coating liquid and substantially cooler than the coating liquid and allowing said globule to rise through the coating liquid and to congeal a film of coating liquid thereon, and then hardening the coating.

7. The method of forming capsules or the like which comprises introducing into a body of coating liquid a globule of material to be coated, causing the globule to rise through the coating liquid and then pass into a body of cooling liquid to harden the coating.

8. The method of forming capsules or the like which comprises introducing into a body of coating liquid a globule of material to be coated, causing the globule to rise through the coating liquid to receive a coating, then to pass into a superposed layer of cooling liquid for hardening the coating.

9. The method of forming capsules or the like which comprises introducing into a body of coating liquid a globule of material of less specific gravity than the coating liquid so that the globule

rises through the coating liquid and receives a coating, then allowing the globule to rise through a superposed layer of cooling liquid of less specific gravity than the coating liquid but greater specific gravity than the globule.

10. The method of forming capsules or the like which comprises introducing into the lower portion of superposed layers of coating and cooling liquids a globule of material cooler than the coating liquid causing the globule to rise through the coating liquid so as to congeal a film of coating thereon and then allowing the globule to rise into the cooling liquid to harden the coating.

11. The method of forming capsules or the like which comprises introducing into the lower portion of superposed layers of coating and cooling liquids a globule of liquid cooler than the coating liquid and of lower specific gravity than said cooling liquid, allowing the globule to rise through the coating liquid to congeal a film of coating thereon and then allowing the coated globule to rise through the coating liquid to harden the coating.

12. The method of forming capsules or the like which comprises introducing into a body of thermo-plastic coating liquid having superposed thereon a body of cooling liquid a globule of lower specific gravity than the coating liquid, allowing the globule to rise first through the coating liquid to receive a coating thereof and then through the cooling liquid to harden the coating, and maintaining the temperature of the cooling liquid adjacent the upper surface of the coating liquid at such temperature as will maintain the liquidity of the coating liquid at its upper surface.

13. The method of forming capsules or the like which comprises introducing into the lower portion of a body of gelatin in liquid form a globule of liquid cooler and of lower specific gravity than the gelatin liquid, allowing the globule to rise through the coating liquid and congeal a film of coating thereon, and then introducing the globule into a body of cooling liquid to harden the coating.

14. The method of forming capsules or the like which comprises introducing into a body of gelatin in liquid form having a superposed layer of cooling liquid above the same a globule of liquid cooler and of lower specific gravity than said gelatin, allowing said globule to rise through the gelatin to congeal a film thereon and then allowing the coated globule to rise through the cooling liquid to harden the coating.

15. Apparatus for forming capsules comprising in combination a receptacle having therein a body of liquid coating solution and a superposed layer of cooling liquid, an orifice adjacent the lower portion of the coating liquid and means at the inter-face between the coating liquid and the cooling liquid for elevating the temperature of the cooling liquid adjacent said inter-face to prevent congealing of the gelatin at the inter-face, and means for cooling the upper portion of the cooling liquid.

16. Apparatus for forming capsules comprising in combination a receptacle having therein a body of liquid coating solution and a superposed layer of cooling liquid, an orifice adjacent the lower portion of the coating liquid, means for introducing small quantities of liquid periodically through said orifice and means at the inter-face between the coating liquid and the cooling liquid for elevating the temperature of the cooling

liquid adjacent said inter-face to prevent congealing at the inter-face, and means for cooling the upper portion of the cooling liquid.

17. Apparatus for forming capsules comprising in combination a receptacle having therein a body of liquid coating solution and a superposed layer of cooling liquid, an orifice adjacent the lower portion of the coating liquid, means for introducing small quantities of liquid periodically through said orifice and means at the inter-face between the coating liquid and the cooling liquid for elevating the temperature of the cooling liquid adjacent said inter-face to prevent congealing at the inter-face, and means for circulating and cooling the upper portion of said cooling liquid.

18. Apparatus for forming capsules comprising in combination a receptacle having therein a body of liquid coating solution and a superposed layer of cooling liquid, an orifice adjacent the lower portion of the coating liquid, means for introducing small quantities of liquid periodically through said orifice and means at the inter-face between the coating liquid and the cooling liquid for elevating the temperature of the cooling liquid adjacent said inter-face to prevent congealing at the inter-face, and means for regulating the temperature of the coating liquid to maintain it in liquid condition.

19. Apparatus for forming capsules comprising in combination a receptacle having therein a body of liquid coating solution and a superposed layer of cooling liquid, an orifice adjacent the lower portion of the coating liquid, means for introducing small quantities of liquid periodically through said orifice and means at the inter-face between the coating liquid and the cooling liquid for elevating the temperature of the cooling liquid adjacent said inter-face to prevent congealing at the inter-face, means for regulating the temperature of the coating liquid to maintain it in liquid condition, and means for circulating and cooling the upper portion of said cooling liquid.

20. Apparatus for forming capsules or the like comprising in combination a receptacle having therein a body of liquid coating solution and a superposed layer of liquid for conditioning the coating, means adjacent the lower end of the receptacle for introducing predetermined amounts of liquid to be capsulized, and means at the top of the conditioning liquid for removing the capsules.

ROBERT W. GUNNELL.