

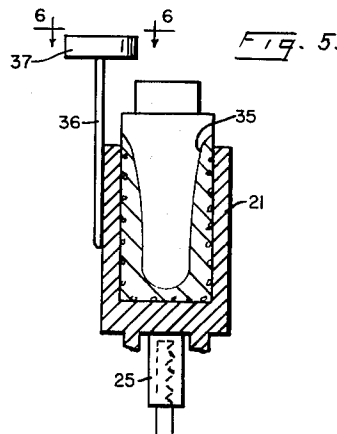
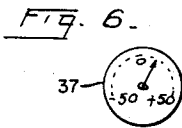
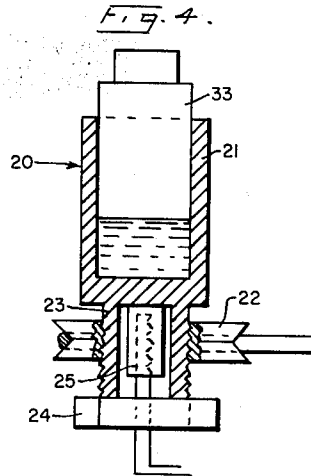
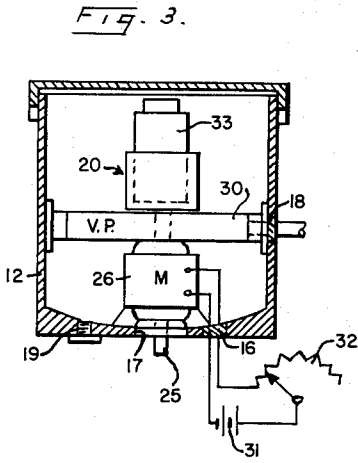
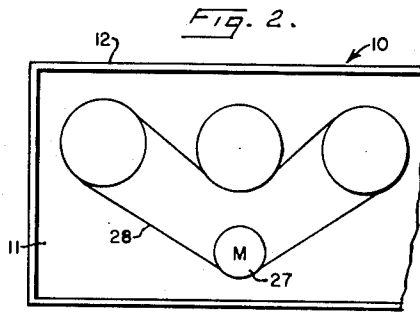
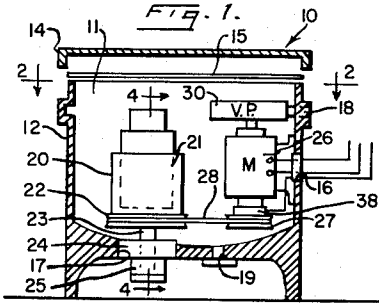
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S. M. BROADWIN

3,203,108

CENTRIFUGAL FREEZE DRYING APPARATUS

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INVENTOR
SAMUEL M. BROADWIN

BY
Howard T. Jeanneret

AGENT

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CENTRIFUGAL FREEZE DRYING APPARATUS

Samuel M. Broadwin, 345 E. 81st St., New York, N.Y.

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1 Claim. (Cl. 34—58)

This invention relates to my pending application Ser. No. 121,912 filed July 5, 1961, for Automatic Shell Freezing of Heat Sensitive Materials, which is now abandoned.

This invention relates to the method of freeze drying of materials and more particularly to a method of vacuum dehydration of heat sensitive liquids containing living cells without the use of refrigerants for storage and maximum survival of the cells.

The pharmaceutical industries usually receive these products in a liquid state. However they must be prepared and solidified in situ in such various treatments as cooling, dehydration in vacuo and for successive thermal treatment involving gradual heating.

More particularly the liquids that are to be considered under the method of treatment according to this invention are heat sensitive liquids such as enzymes and serums containing living cells and the particular method of treatment of these liquids includes apparatus comprised of a vacuum chamber containing heating and cooling means therein and a centrifuge with supports for the small bottles or the like which hold the material or liquid to be treated. In this apparatus and according to the method of treatment, the bottle containing the liquid is maintained in an upright position during treatment. Such position due to the centrifugal force produced by the centrifuge results in a spread of the liquid mass over most of the entire internal surface of the bottle to produce a shell form that is in turn frozen during the cooling produced by the evacuation of air from the vacuum chamber.

The apparatus according to the present invention includes a vacuum chamber in which there is supported a rotatable shaft and in which the shaft in turn supports means for receiving and holding small bottles containing the material or liquid to be treated. In operation the shaft is rotated and hence the supports and bottles revolvable in a vertical position causing the liquid contained in the bottle to be disposed along the side walls as well as the bottom surface of the bottle thereby increasing the free surface area of the liquid and more readily permitting the necessary cooling or heating during the treatment of the heat sensitive liquid.

In this particular invention the centrifuge is contained within a vacuum chamber and the cooling of the bottles and their contents is provided by the evacuation of the air from the chamber and the dehydration of the heat sensitive liquid within the bottle is provided in two stages, that is, the liquid within the bottle is first formed into a shell shaped form within each container by the centrifuge and is frozen in this form while being partially dehydrated by the vacuum. The degree of freezing of the shell formed liquid is controlled to a -15° to prevent damage to the living cells in the heat sensitive liquid. The process is stopped at this point and the frozen shells

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may then be treated without centrifuge by heating elements within the vacuum chamber in which the heat is applied by conduction directly to the bottles to evaporate any of the liquid that has not been frozen and due to the vacuum maintained, the frozen shell may be completely dehydrated in a second step reducing the temperature to -50° without injuring the living cells in the heat sensitive liquid. The arrangement as described above permits the process or method to be performed without removing the bottles from their supporting means during the operation of the apparatus. However the second stage of drying may be produced by removing the bottles from the centrifuge and storing in a drying device at a lower temperature to produce a complete dehydration.

It is an object of this invention to provide a method of vacuum dehydration of a heat sensitive liquid containing living cells without the use of refrigerants to permit storing said liquids and to insure a maximum survival of the living cells.

A further object of this invention is to provide a method of vacuum dehydration of an enzyme without the use of refrigerants to permit storing said serum and to insure a maximum survival of the living cells.

A still further object of this invention is to provide a method of vacuum dehydration of a serum without the use of refrigerants to permit storing said serum and to insure a maximum survival of the living cells.

Other objects of this invention shall be apparent by reference to the accompanying detailed description and the drawing in which

FIG. 1 is a cross sectional view of a vacuum chamber and centrifuge according to this invention,

FIG. 2 is a plan view taken on line 2—2 of FIG. 1,

FIG. 3 is a cross sectional view of a further embodiment of this invention,

FIG. 4 is a cross sectional view taken on line 4—4 of FIG. 1,

FIG. 5 is a cross sectional view similar to FIG. 4 illustrating a further embodiment of this invention, and

FIG. 6 is a plan view taken on line 6—6 of FIG. 5.

Referring to the drawings and particularly FIGS. 1 and 2 there is illustrated a device 10 for shell freezing and dehydrating heat sensitive materials. The device 10 includes a vacuum type chamber 11 provided by a boxlike structure 12 that is sealed by a cover 14 and the cover 14 is provided with a rubber gasket 15. The cover 14 is preferably a transparent cover to permit inspection of the device during its operation. The box-like structure 12 is provided with a port 16 for wiring or controls and a port 17 for introduction of the heater element and a port 18 for the vacuum pump and a port 19 for a vacuum break. Revolvably mounted within the chamber 11 is a centrifuge element 20 which comprises a bottle holder 21 affixed to a pulley 22 and centrally supported by a shaft 23 which is mounted in a bearing 24. Shaft 23 and bearing 24 are provided with a hollow center to permit the introduction of a heater element 25. Also mounted within chamber 11 is a motor 26 operated through its wired terminals passing through port 16 to an exterior control. Motor 26 is provided with a pulley 27 at one end to drive pulley 22 by means of a belt 28. Motor 26 at its opposite end is connected to a vacuum pump 30.

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The chamber 11 may have one or more centrifuges as shown in FIG. 2 and they will all be driven in the same fashion by pulley 27 and a single belt 28 as the direction of rotation is of no consequence.

Referring to FIG. 3 there is illustrated a further embodiment of this invention in which a device 10A is provided being a boxlike structure 12 similar to the prior embodiment with a vacuum chamber 11 and containing a centrifuge 20, a motor 26 and a vacuum pump 30 and provided with similar ports 16, 17, 18 and 19. However in this embodiment there is a single shaft that is the axial extension of the motor shaft so that motor 26 rests upon the bottom surface of the structure 12 and the vacuum pump 30 is fitted adjacent the motor 26 and driven by the motor shaft 23 and the centrifuge 20 is positioned above the vacuum pump 30 and also supported and driven by shaft 23. Motor 26 may be connected to a power source 31 and a rheostat 32 so that its r.p.m. may be controlled thus providing the desired degree of centrifugal force in the centrifuge 20.

Referring to FIG. 4 there is illustrated a cross sectional view of the centrifuge 20 which is comprised of a bottle holder 21 that is mounted on a hollow shaft 23 which is supported by the bearing 24. The pulley 22 is rigidly affixed to the hollow shaft 23 to drive the centrifuge. The bottle support 21 retains the bottle 33 as illustrated and the bottle 33 will retain a predetermined quantity of the heat sensitive liquid that is to be treated. Thus in operation the vacuum chamber 11 is first evacuated by the vacuum pump 30 to a reading of about 2 mm. In reducing the vacuum in this chamber to this degree, it produces a drop in temperature which starts the initial freezing of the liquid contained in bottle 33. At this time the initial freezing is clearly visible due to the transparent cover and open ended bottle 33. Thus the centrifuge or rather the motor may be started to produce a spinning of the bottle 33 and the spreading of the heat sensitive liquid within bottle 33 to its shell-like form while the freezing continues until the temperature has dropped to -15° and there is a complete frozen shell within the bottle 33. The centrifuge or rather motor controlling the centrifuge may be stopped as the centrifugal force for dispersing the liquid is no longer necessary. However the bottle 33 may either be removed from the vacuum chamber for storage under a still lower temperature and slow dehydration or the motor may be operated to drive the vacuum pump only while the bottle remains in the vacuum chamber 11 to drop the temperature to -50° so that the dehydration will continue.

Referring to FIG. 5 it is apparent that with the initial freezing of the heat sensitive liquid into a shell like form as illustrated there is only a 10% dehydration. Thus there is still fluid trapped within the frozen shell 35. To drive this fluid out of the frozen shell it is necessary to induce heat into the shell. This is provided by the heater 17 which bears against the bottom of the centrifuge 20 to thus provide heat by conduction through the holder 21 about the complete frozen shell causing the fluid to evaporate while the vacuum chamber 11 is still maintained at a low temperature to insure maintaining the frozen shell as already formed. Thus by controlling the degree of heat supplied all of the unfrozen fluid may be evaporated and the shell 35 completely dehydrated. During this process of dehydration it becomes necessary to know what temperature is attained and is being maintained within the vacuum chamber 11. Thus a simple contact thermometer 36 with a circular visual indicating dial 37 has been utilized as illustrated in FIGS. 5 and 6 by affixing the contact element to the exterior surface of the bottle holder 21. The rotation of 21, although producing considerable centrifugal force, does not damage this type of thermometer and a reading of the thermometer may be made at any time by stopping the rotation of the centrifuge. Thus when the vacuum pump is first operated the thermometer will show the drop of tempera-

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ture and at a freezing temperature the centrifuge is started, and when the temperature drops to -15° the centrifuge is stopped for the second stage of dehydration. Although motor 26 has been indicated as the single driving means for the centrifuge and the vacuum pump, it is necessary to provide a control so that motor 26 may drive the vacuum pump 30 alone during the initial stage of evacuating chamber 11 and a control to activate pulley 27 either by a slip clutch 38 or by dividing the motor shaft into two driving shafts one at either end. Thus the centrifuge 20 may be started at the desired time and similarly when a temperature reading of -15° has been reached, the rotation of the centrifuge 20 may be stopped while the vacuum pump is continued dropping the temperature still lower for dehydration of the frozen shell as illustrated in FIG. 5. The heater 17 may also be used to provide an even distribution of heat by conduction and to reduce the rate of freezing. That is, although the vacuum pump will evacuate the air and produce about 20% dehydration of the contents of each bottle 33, it also produces a drop in temperature within the vacuum chamber 11. If this drop is rapid the freeze of the material or heat sensitive liquid will also be rapid and this is harmful in the treatment by dehydration of the fluids containing living cells. It has been found that the rapid freezing produced by centrifuges in the past, where the temperature has been dropped in one stage to -50° , resulted in a recovery of only about 15% of the living cells in enzymes and serums. In developing a two stage method of dehydration wherein the temperature drop has been slowed and stopped at -15° and then the dehydration continued at a slowed rate while dropping the temperature to a desired -50° for storage, the recovery of living cells in the dehydrated material is as high as 80%. Enzymes and serums containing living cells can not be simply frozen to preserve cell survival although blood is treated by simply freezing and the cell survival does suffer by this treatment. The method of controlling the temperature drop according to this invention may be (1) by varying the vacuum trap temperature, that is as the vacuum pump draws air from the vacuum chamber it must be drawn through a trap, the trap in turn is surrounded by a heating element to permit controlling the trap temperature. (2) by varying the vacuum pressure, the evacuation from atmospheric pressure to about 2 mm. also produces a sharp drop in temperature. (3) By using heaters (conduction type) to induce heat directly to the heat sensitive liquid to slow the temperature drop, thus a slowed rate of freezing and temperature drop during dehydration may be maintained to promote cell survival during this method of treatment. By providing visual control, that is, with a transparent cover the material being treated may be continually observed and by providing a thermometer affixed to the material holder a direct reading may be made at any time, thus the method of two stage treatment may be accurately carried out.

Although we have illustrated a simplified form of apparatus to carry out the necessary steps according to the method of this invention, the apparatus may be enlarged, may be duplicated or the number of centrifuges may be multiplied or the components may be combined in a different order without departing from the spirit of this invention and this invention shall be limited only by the appended claim.

What is claimed is:

Apparatus for freeze drying a heat sensitive liquid containing living cells comprising a self-contained unit consisting of a cabinet having a vacuum chamber that is closed, sealed and evacuated to 2 mm. and maintained at this reduced vacuum, said vacuum chamber comprising a bottom wall, a plurality of vertically disposed shafts rotatably mounted on said bottom wall, a bottle holder mounted on each of said shafts for retaining a small bottle containing said heat-sensitive liquid and constitut-

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ing a plurality of vertical centrifuges within said vacuum chamber, a motor positioned within said chamber and connected through pulleys to drive said centrifuges as a unit, a vacuum pump disposed within said chamber and driven by said motor for evacuating said chamber, said holder having a hollow bottom portion, a heater arranged in said hollow portion of each of said bottle holders to provide an equal distribution of heat by conduction to said heat sensitive liquid, said pulleys being arranged about said hollow bottom portion, a thermometer connected to each of said centrifuges to indicate the temperature within each centrifuge at all times, a rheostat electrically connected to said motor for varying the rotational speed of the motor and said vacuum pump to control the

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rapidity of freezing of the heat sensitive liquid in said centrifuges.

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15 NORMAN YUDKOFF, *Primary Examiner*.