Aug. 27, 1957 S. CERLETTI 2,803,888

APPARATUS FOR LYOPHILISING PRODUCTS CONTAINED IN SMALL BOTTLES

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Fig. 1

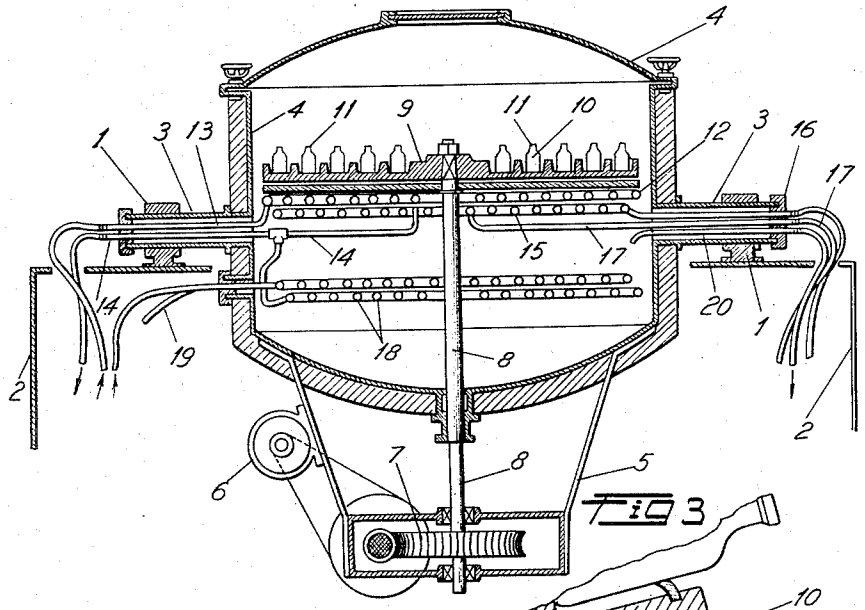


Fig 3

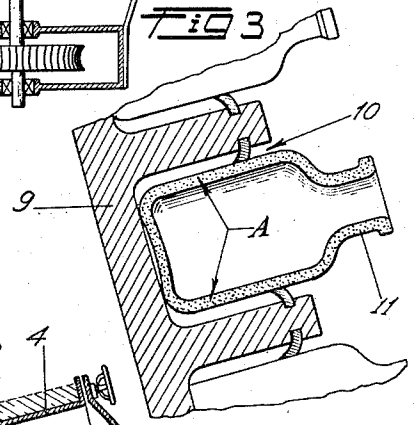
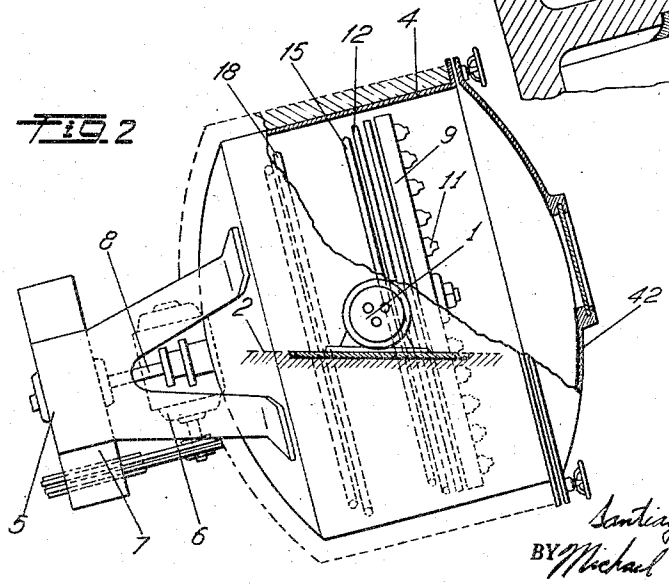


Fig 2



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APPARATUS FOR LYOPHILISING PRODUCTS CONTAINED IN SMALL BOTTLES

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3 Claims. (Cl. 34—62)

The present invention relates to a process for lyophilizing products contained in small bottles or the like, and an apparatus for effecting said process.

The chemical and pharmaceutical industries usually deal with products in a solid state which are contained in small bottles or the like. These products are usually received by these industries in the liquid state, however, and must be prepared and solidified in situ through such various treatments as cooling, dehydration in vacuo and/or successive thermal treatment involving gradual heating. In general, the treatments which may be necessary to produce the applicable product are vacuum, cooling, dehydration and sublimation processes.

More particularly, such treatments are performed in apparatuses called lyophilizers which are comprised of vacuum chambers containing heating and cooling means therein as well as supports for the small bottles or the like which hold the material to be treated. In these apparatuses, and according to such processes, the bottle containing the material, is maintained in upright position during treatment, such position necessarily resulting in a limited free surface area which may be exposed to treatment. Conversely, if the free surface area of the material contained in the bottle were to be increased, the treatment could be carried out much more efficiently inasmuch as the mass of the product would be spread out over a wider area, and the surface exposed to treatment thereby increased.

Such an object has been accomplished by the process and apparatus of the present invention wherein the above-mentioned results are accomplished in the most satisfactory manner and in a shorter time than could be accomplished with the lyophilizers heretofore used.

The apparatus, according to the present invention, includes a vacuum chamber supporting a shaft therein, the shaft rotatable within the chamber and being capable of supporting a supporting means for receiving and holding small bottles containing the material to be treated. The vacuum chamber, and hence the shaft supported thereby, may be angularly displaced so that the bottles revolve from a vertical to a horizontal position preparatory to the solidification process. This angular displacement causes the liquid contained in the bottle to be disposed along the side walls as well as the bottom surface of the bottles, thereby increasing the free surface area of the material and more readily permitting the necessary treatment. Also included in the chamber are a heating and cooling means for performing the applicable treating processes on the product.

The shaft carrying the bottle supporting means may also be rotated either within, or together with, the vacuum chamber. Furthermore, the angular displacement which the vacuum chamber is capable of moving through indicates a loading position when the chamber is in a vertical position and an operating position when the chamber has been angularly displaced to a substantially horizontal position. The bottles may therefore be placed into the chamber in an upright position while the

apparatus is in the loading position and be tilted to a substantially horizontal position when the apparatus is in the operation position. While the solidification process is taking place, the axis of the shaft does not vary from this substantially horizontal position but may be rotated as the process requires.

More particularly, the apparatus comprises a vacuum chamber angularly displaceable around a horizontal axis such displacement being approximately 90°. In its interior, the vacuum chamber is provided with a shaft which, in turn, is provided with suitable supporting means for the small bottles holding the material to be treated. The shaft is rotatable either in conjunction with, or independently of, the chamber.

The vacuum chamber also includes cooling and heating means which may be controlled from the exterior of the chamber and which effectuate the thermal treatments necessary for the applicable process.

Thus, by angularly displacing the vacuum chamber until the axis of rotation of the shaft as well as the axes of the bottles themselves are brought to a substantially horizontal position, and then rotating the shaft, the condition is reached whereby the liquid material contained in the bottles is distributed evenly upon the side walls of the bottle. This material gradually solidifies, while so distributed, thereby forming a substantially cylindrical and tubular shape whose free surface is greater than if the material were held in an upright bottle.

The heating and the cooling means consist preferably of coils suitably disposed in the vacuum chamber in relation to the position of the bottle supports. The supply of heating and cooling fluids in the coils is adjusted by controls located outside the chamber so as to effectuate any thermal variation necessary to perform the process without having to resort to the opening of the vacuum chamber. More particularly, there is at least one cooling coil and at least one heating coil located facing, and preferably under, a plate which forms part of the bottle supporting means. These coils are located in close proximity to each other and provide for the heating and the cooling of the bottle. Another cooling coil or element may also be provided and spaced from the other coils to act as a condenser for condensing and solidifying any substances that might develop during the thermal treatments and in vacuo of the material to be treated.

The arrangement as described above permits the applicable processes to be performed without removing the bottles from the supporting means or in any way dislodging them during the operation of the apparatus.

The novel features which are considered as characteristic for the invention are set forth in particular in the appended claims. The invention itself, however, both as to its construction and its method of operation, together with additional objects and advantages thereof, will be best understood from the following description of a specific embodiment when read in connection with the accompanying drawing, in which:

Fig. 1 shows the apparatus in a vertical rest position;

Fig. 2 shows the apparatus in a substantially horizontal operating position, with some parts in section; and

Fig. 3 is an enlarged view of a particular portion of Fig. 2.

Referring now to the drawing, and particularly to Fig. 1, hollow trunnions 3 are journalled on supports 1 which comprise part of the machine frame 2. The vacuum chamber 4 is mounted on the trunnions 3 and are closed by a lid *4a* which is suitably coated with an insulating material or the like. The vacuum chamber 4 is supported for turning movement about the horizontal axis of the trunnion 3. A structure 5 is secured to the vacuum chamber 4, the structure 5 comprising a motor 6 which

drives, through a speed reducer 7, a shaft 8 penetrating the chamber 4. The axis of shaft 8 is perpendicular to the axis of the trunnion 3 and therefore vertical when the apparatus is in the rest position. A plate 9, integral with the supports 10 for the small bottle 11 or the like containing the material to be treated, is mounted on one end of the shaft 8. The shaft 8 and therefore the plate 9 is slowly rotated by the motor 6.

A cooling coil 12, which may be for example spiral-shaped, is placed under plate 9. This coil 12 is located adjacent the supports for the bottles 11 and is connected to inlet duct 13 and exhaust duct 14 which pass through one of the hollow trunnions 3. Immediately under the coil 12, a heating coil 15, also preferably spiral-shaped, is provided which is connected to ducts 16 and 17 which pass through the other of the trunnions 3. A second cooling coil 18 is provided beneath and spaced from the coils 13 and 14 and which acts as a condenser. Coil 18 is connected to supply duct 19 and exhaust duct 14.

The small bottles containing the liquid material are put in their respective supports 10 while the apparatus is in the rest position shown in Fig. 1. When the solidification operation of the process is to be effected, the apparatus is angularly displaced, as indicated in Fig. 2, until the axis of the shaft 8 is placed in a substantially horizontal position. Thus, the bottles 11 or the like also take a position wherein their axes are substantially horizontal. Therefore, by angularly displacing the shaft 8, the liquid material contained in the bottles is spread out along the cylindrical side walls of the bottles and by rotating the shaft 8 the liquid is distributed along the entire wall surface of the bottles. With the material so distributed within the bottles, the solidification process can be accomplished much more efficiently inasmuch as the liquid will be spread out evenly along the entire periphery of the bottle. The thickness A (see Fig. 3) of the material will be much less than if the bottles were held vertically and the free surface area of the product exposed for treatment will be much greater. This greater surface area over which the material is distributed facilitates more rapid treatment of the material and hence a more efficient operation of the apparatus may be maintained.

The several steps of the operation may be carried out most efficiently by first establishing a vacuum in the chamber 4 through the duct 20 and by then heating and cooling the region wherein the bottles are located in a manner required by the applicable treatment. The coil 18 may act as a condenser for substances which are volatilized due to either the vacuum or the heating to which the product is subjected.

It will be understood that each of the elements described above, or two or more together, may also find a useful application in other types of lyophilizers differing from the types described above.

While the invention has been illustrated and described as embodied in a process for lyophilizing products contained in small bottles etc. and an apparatus for accomplishing the same, it is not intended to be limited to the details shown, since various modifications and structural changes may be made without departing in any way from the spirit of the present invention.

Without further analysis, the foregoing will so fully reveal the gist of the present invention that others can by applying current knowledge readily adapt it for various applications without omitting features that, from the standpoint of prior art, fairly constitute essential characteristics of the generic or specific aspects of this invention and, therefore, such adaptations should and are intended to be comprehended within the meaning and range of equivalence of the following claims.

What is claimed as new and desired to be secured by Letters Patent is:

1. In a lyophilizing apparatus, in combination, a support; a housing having a pair of trunnions aligned on a first axis and projecting in opposite directions laterally

therefrom, said housing having a second axis normal to said first axis and being mounted on said support for movement between an inoperative position wherein said second axis is substantially vertical and an operative position wherein said second axis is substantially horizontal; support plate means adapted to receive at least one receptacle having a continuous tubular side wall in such a manner that the receptacle is substantially immovable relative to said support plate means and in a position wherein the side wall is normal to said support plate means; mounting means for mounting said support plate means in said housing for rotation about said second axis in a plane normal thereto so that when said housing is in its inoperative position said support plate means is in a substantially horizontal position and when said housing is in its operative position said support plate means is in a substantially vertical position; and rotating means mounted on said housing for tilting movement therewith and including a motor and speed reduction means for rotating said support plate means at slow speed about said second axis whereby when said housing is in its inoperative position a receptacle having a continuous tubular side wall may be placed onto said support plate means and be received thereby and when said housing is in its operative position and said rotating means continuously rotates said support plate means about said second axis the receptacle is rotated about a substantially horizontal axis parallel to the side wall thereof so that different points of the side wall are displaced vertically relative to each other so that consequently a substance in the receptacle which tends to solidify will line the entire inner surface of the side wall of the receptacle.

2. A lyophilizing apparatus comprising, in combination, an airtight housing having an axis and mounted for movement between an inoperative position wherein said axis is substantially vertical and an operative position wherein said axis is substantially horizontal; support plate means adapted to receive at least one receptacle having a continuous tubular side wall in such a manner that the receptacle is substantially immovable relative to said support plate means and in a position wherein the side wall is normal to said support plate means; mounting means for mounting said support plate means in said housing for rotation about said axis in a plane normal thereto so that when said housing is in its inoperative position said support plate means is in a substantially horizontal position and when said housing is in its operative position said support plate means is in a substantially vertical position; rotating means for rotating said support plate means at slow speed about said axis at least when said housing is in its operative position; temperature controlling means in said housing for controlling the temperature therein; and pressure controlling means in said housing for controlling the pressure therein whereby when said housing is in its inoperative position a receptacle having a continuous tubular side wall may be placed onto said support plate means and be received thereby and when said housing is in its operative position and said rotating means continuously rotates said support plate means about said axis the receptacle is rotated about a substantially horizontal axis parallel to the side wall thereof so that different points of the side wall are displaced vertically relative to each other so that consequently a substance in the receptacle which tends to solidify will line the entire inner surface of the side wall of the receptacle while being subjected to a predetermined temperature and to a predetermined pressure.

3. A lyophilizing apparatus comprising, in combination, a support; an airtight housing having a pair of trunnions aligned on a first axis projecting in opposite directions lateral therefrom, said housing having a second axis normal to said first axis and being mounted on said support for tilting movement between an inoperative position wherein said second axis is substantially vertical and an operative position wherein said second axis is substantially

horizontal; support plate means adapted to receive at least one receptacle having a continuous tubular side wall in such a manner that the receptacle is substantially immovable relative to said support plate means and in a position wherein the side wall is normal to said support plate means; mounting means for mounting said support plate means in said housing for rotation about said second axis in a plane normal thereto so that when said housing is in its inoperative position said support plate means is in a substantially horizontal position and when said housing is in its operative position said support plate means is in a substantially vertical position; rotating means mounted on said housing for tilting movement therewith and including a motor and speed reduction means for rotating said support plate means at slow speed about said second axis; temperature controlling means in said housing for controlling the temperature therein; and pressure controlling means in said housing for controlling the pressure therein, whereby when said housing is in its inoperative position a receptacle having a continuous tubular side wall may be placed onto said support plate means and be received thereby and when said housing is in its operative position and said rotating means continuously rotates said support plate means about said second axis the receptacle

is rotated about a substantially horizontal axis parallel to the side walls thereof so that different points of the side wall are displaced vertically relative to each other so that a substance in the receptacle which tends to solidify will line the entire inner surface of the side wall of the receptacle while being subjected to a predetermined temperature and pressure.

References Cited in the file of this patent

UNITED STATES PATENTS

1,377,591	Kuhlemeier et al.	May 10, 1921
1,646,715	Taylor	Oct. 25, 1927
2,153,184	Hagen	Apr. 4, 1939
2,178,419	Clark et al.	Oct. 31, 1939
2,373,806	Barnes et al.	Apr. 17, 1945
2,445,120	Levinson et al.	July 13, 1948

OTHER REFERENCES

"Freeze Drying," by E. W. Flosdorf, copyright 1949 by Reinhold Publishing Corp., 330 West 42nd St., New York 18, New York, pages 167, 170–173 and 191 relied on.

Friedgood et al.: Science, vol. 105, 1947, pp. 99 and 100.