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PROCESS FOR STERILIZING BIOLOGICAL LIQUIDS

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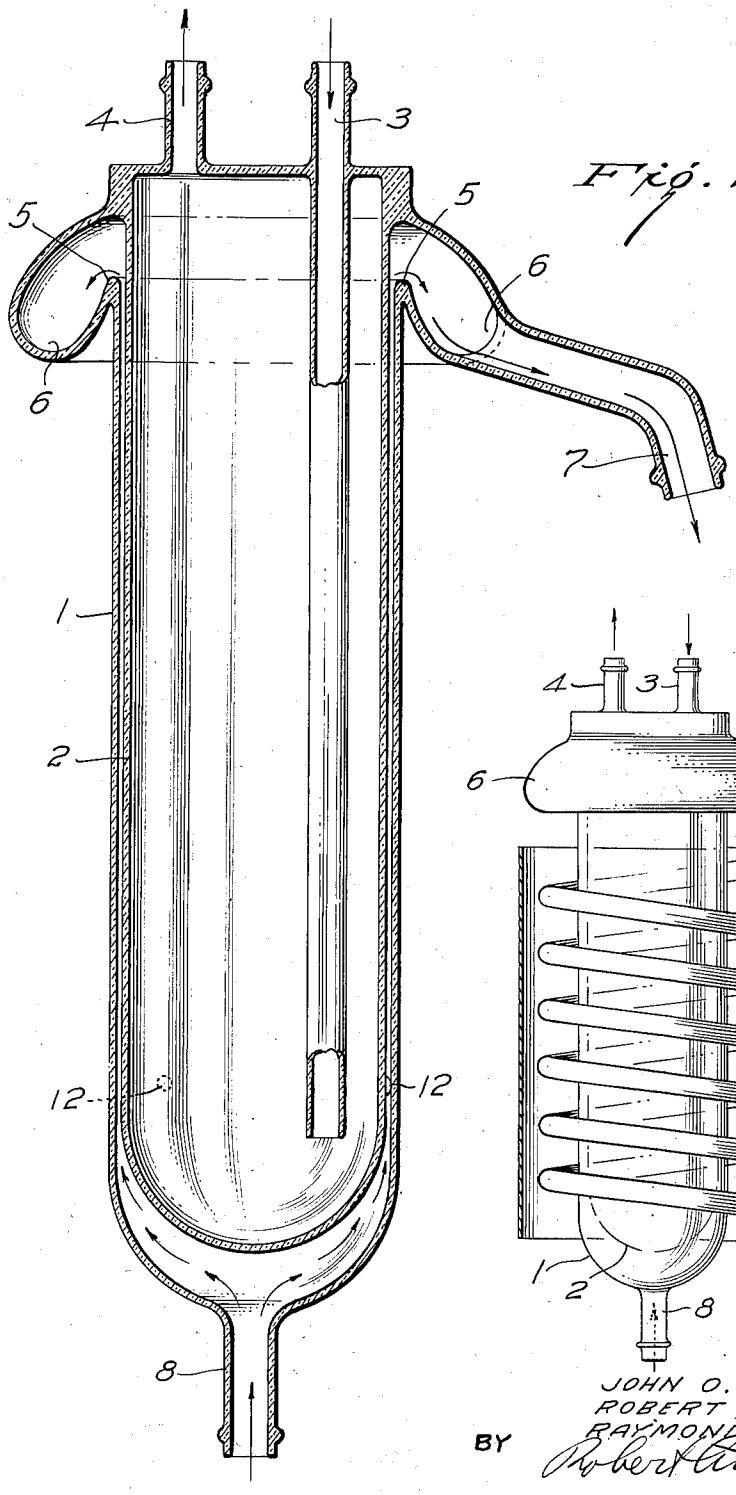

Fig. 2.

Fig. 1.

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PROCESS FOR STERILIZING BIOLOGICAL LIQUIDS

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4 Claims. (Cl. 250—49)

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This invention relates to a process of irradiating biological dispersions to effect differential killing of a component of the dispersion.

It has been found that various radiations such as ultraviolet and X-ray are capable of destroying or killing certain components of biological dispersions. Thus, for example, dispersions of pathogenic microorganisms or viruses may be irradiated sufficiently to kill the pathogenic components or to inactivate them without destroying other components such as antigens which may be present. It is thus possible to prepare sterile vaccines, and other biological products. The radiation treatment offers certain marked advantages over other methods of killing or inactivating pathogenic components such as treating with chemical compounds, for instance, formaldehyde, phenol, and the like, or the use of heat. No contamination due to added chemicals results nor is there any danger of decomposition by reason of higher temperatures. However, in the past the use of radiation for the treatment of biological dispersions has suffered from a number of disadvantages. In the first place it is necessary to regulate the radiation with extreme precision. If any portions of the dispersion receive inadequate radiation, pathogenic organisms or molecules may remain alive or activated. If, on the other hand, in the interests of safety, sufficient radiation is employed to assure that no portion of the dispersion is insufficiently radiated, then certain portions may receive too much radiation which results in a destruction of antigens or other radiation-unstable, desired components. Another factor which has been a problem is adequate output and maintenance of predetermined temperatures. Maximum utilization of radiant energy is also a factor although somewhat less serious than those mentioned above.

Continuous radiation treatments of materials containing provitamins in order to produce vitamins have achieved considerable commercial success. In most of these processes a moderately thin film of the liquid or dispersion is caused to flow through a beam of radiant energy such as, for example, ultraviolet light. These processes present only one of the major problems which are encountered in the killing or inactivation of pathogenic components for the production of vaccines or other biological preparations. This is the attainment of adequate output. The problem of irradiation of materials containing provitamins is purely one of obtaining sufficient average radiation because if a small portion of the material irradiated receives deficient radiation, this only reduces to a small degree the total

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amount of vitamin produced. In the case of biological preparations containing pathogenic organisms or components, however, under-irradiation of even a small portion may be fatal if it fails to kill the pathogenic material. This, as pointed out above, constitutes the real problem to which the present invention presents a simple solution.

According to the present invention a thin, perfectly uniform, essentially annular film of material to be irradiated is subjected to constant pressure against a constant hydrostatic head and the flow path length is maintained the same. As a result a perfectly uniform flow of a thin layer of uniform thickness is obtainable and the rate of flow through the beam of radiation is the same at all points, and as the path length is the same the total irradiation remains constant. The use of a constant hydrostatic head to provide back pressure prevents nonuniformity of flow and minimizes any change in rate with fluctuations of applied pressure. It is thus possible to determine the proper degree of irradiation for complete killing or inactivation of pathogenic components without any danger of over-irradiation. At the same time a continuous process of high output is made possible, although, of course, the output level which is obtainable with relatively thicker and less accurately controlled films in the production of vitamins will normally not be reached because the present invention requires a liquid layer thickness very much less than that which is possible in vitamin irradiation because it is necessary that all portions of the film receive substantially the same amount of radiation, and with a thick film the outer layers of the film will tend to reduce the transmission to the inner layers.

Another advantage of the present invention which is obtainable in one of its preferred modifications is that the annular film permits application of radiation to one side while cooling the other side. It is possible to position the radiator on the inside of the annular layer or surround it on the outside. The latter is preferred because with suitable radiators and reflectors an extremely uniform level of radiation may be obtained with good efficiency. This is in marked contrast to processes such as the irradiation of provitamins to form vitamins where the most important factor is effective utilization of the radiant energy, and radiators completely surrounded by the films to be irradiated present advantages in energy utilization whereas in the process of the present invention where extreme uniformity is the most important factor, external radiation and internal cooling are preferred.

An essentially annular film of material to be

irradiated has been referred to above. In practice the simplest form is a true annulus, that is, a space between concentric cylindrical surfaces. However, where the film is of uniform cross section and path length against constant hydrostatic head it is perfectly possible to use films which are contained between concentric surfaces other than cylinders. For instance, they may be elliptical or even polygonal. For practical operation true circular annuli present so many structural advantages that they are preferred.

It has been found that the ultraviolet radiation is particularly effective in certain ranges, the most important band being about 2537 A° and 2650 A°. Shorter wave lengths also have killing power but the selectivity is less because these very short wave lengths also have destructive effects on the cells which reduces their effectiveness in producing antibodies. It is therefore preferable to use radiation sources which have a good portion of their energy in the most effective range. Therefore, while the invention is not limited to the use of any particular radiation source, we prefer to use low pressure mercury vapor tubes, the pressure being kept at a sufficiently low point so that a large portion of the energy is radiated at the wave length of the mercury line of about 2537 A°. These tubes can be arranged in helical coils or similar shapes to surround the layer of liquid to be irradiated, and high utilization of the energy is thus possible. However, the present invention is not concerned with the use of any particular shape or design of radiator. It is also possible to use radiations of extremely short wave length, for example, X-rays or even penetrating high-speed electron beams.

While it is not necessary to use any particular type of constant hydrostatic head on the moving annular film the one which is simplest and in operation the most reliable involves a gravity hydrostatic head which is readily obtained by the provision of a circular overflow weir providing an overflow at constant level into a space such as a launder of sufficient cross-section so that the hydrostatic head on the moving annular film is determined by weir height alone.

The invention will be described in greater detail in connection with a preferred type of apparatus which is illustrative of one of many types in which the process of the present invention may be carried out. The specific description will be made in conjunction with the drawing in which;

Fig. 1 is a vertical section through an irradiation cell; and

Fig. 2 is a side elevation on a somewhat smaller scale and including radiation means and reflector.

Fig. 1 shows an irradiation cell of suitable ultraviolet transparent glass or quartz. The cell consists of an outer jacket 1 and a closed-end inner jacket 2. These jackets are cylindrical and concentric and form an annular space which may, for example, be about 1.5 mm. wide. The alignment of the jackets is maintained by the three spacers 12. The inner jacket 2 is provided with a cooling water inlet tube 3 and outlet tube 4. These are connected to a suitable source of cooling water (not shown). The upper end of the outer jacket terminates in a circular weir 5 of uniform height onto which is sealed a glass launder 6 provided with a discharge outlet 7. The upper edge of the launder in turn is sealed to the top of the inner jacket so as to protect the contents of the launder from the atmosphere. The bottom of the outer jacket is provided with an inlet pipe 8.

Around the outer jacket 1 there is coiled a helical mercury vapor discharge tube 9 provided with wires 10, its ends connected to a conventional source, (not shown), of alternating current of suitable voltage. Around the mercury vapor tube 9 there is mounted a concentric reflector 11 which may be of polished aluminum. The tube illustrated is a low pressure quartz mercury vapor discharge tube of the type sold by the Hanovia Company under their designation Sc2537.

In operation a biological liquid, for example, a rabies vaccine to be sterilized, is introduced into inlet 8 at constant pressure from a source of constant liquid pressure, (not shown), which may be of conventional design, for example, of the constant hydrostatic head type. The flow of the vaccine up through the narrow annular space between the two jackets proceeds at a perfectly uniform rate as the path length and annular cross-section is constant and the hydrostatic head, against which the film flows, is likewise constant and determined by the height of the overflow weir 5. The irradiated material overflowing does not completely fill the launder 6 and flows off through the outlet 7. Flow rates and radiation intensities are adjusted to assure a killing of any living pathogenic organisms. At the same time decomposition of the desired active constituents of the vaccine is minimized by the accurately determined radiation and the low temperature which is maintained by the cooling water in the inner jacket 2. A typical flow rate is one which will give an exposure time of from 20 to 25 seconds with the radiation intensity obtainable with the lamp illustrated.

The process is continuous and automatic, not requiring constant supervision and a relatively very large output is obtained while at the same time the inactivation of the vaccine is perfect at all times.

The process of the present invention in a preferred type of equipment has been described in conjunction with the treatment of a biological liquid, in which pathogenic organisms or components are to be killed or inactivated. This is the purpose for which the process of the present invention is primarily designed. It should be understood that the process may be used if desired for the irradiation of materials containing provitamins. Here, however, the absolute accuracy of radiation control is not required and the output is decreased by the thinness of the flowing film. In other words, for vitamin production the process of the present invention is operative but is less efficient than the irradiation processes currently used. It is, therefore, not suitable economically for large scale production in this field.

We claim:

1. A process of inactivating pathogenic components of biological liquids which comprises flowing under constant pressure an accurately uniform, essentially annular film against a constant hydrostatic head, the flow being substantially parallel to the axis of the annulus and all portions of the film traversing paths of substantially equal length, the film being sufficiently thin so that the rate of flow is not materially affected by minor pressure variations on the liquid and subjecting the moving film to a uniform radiation of wave length suitable for an inactivation of the pathogenic components, the rate of flow and radiation intensity being adjusted to assure complete inactivation of the pathogenic components.

2. A process of inactivating pathogenic components of biological liquids which comprises flowing under constant pressure an accurately

uniform, essentially annular film against a constant hydrostatic head, the flow being substantially parallel to the axis of the annulus and all portions of the film traversing paths of substantially equal length, the film being sufficiently thin so that rate of flow is not materially affected by minor pressure variations on the liquid and subjecting the moving film to a uniform radiation of ultraviolet light having a large portion of energy radiated in the 2537 and 2650 A bands, the rate of flow and radiation intensity being adjusted to assure complete inactivation of pathogenic components.

3. A process according to claim 1 in which the flowing film of biological liquid is subjected to indirect cooling on its inner surface and irradiation on its outer surface.

4. A process according to claim 2 in which the

flowing film of biological liquid is subjected to indirect cooling on its inner surface and irradiation on its outer surface.

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