Identifying doses in commercial liquid drugs sterilized by ionizing radiation

Drug sterilization with ionizing radiation, such as gamma-radiation using doses up to 25 kGy is a well-established technology, which can adequately eliminate bacteria by breaking down their DNA. This method is gaining ground due to its numerous advantages. It exhibits a high penetrating power that allows the heat-free sterilization of heat-sensitive pharmaceutical preparations in their final packaging.

Establishment of a method to identify irradiated drugs and determine the administered dose (post-sterilization dosimetry) would be useful for both the consumers and the manufacturers. The former would become aware of the potential degradation of the pharmaceutical preparation due to its exposure to ionizing radiation, while the latter would be able to evaluate in-situ the actual dose absorbed by the products and verify that it conforms to the minimum sterilization doses dictated by current legislation. It would also interest a government agency whose role would be to certify that drugs have indeed been sterilized with the minimum dose.

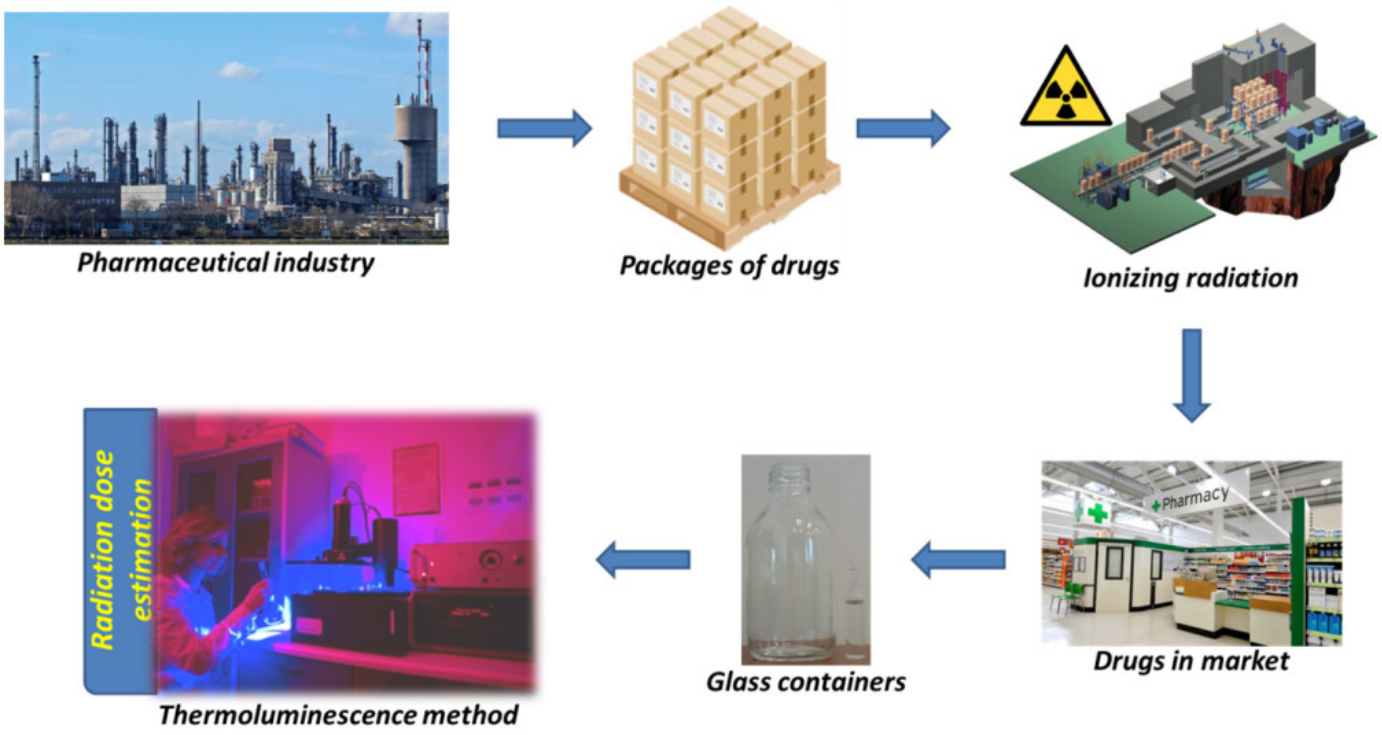

Fig. 1. From the manufacture of liquid drugs to the dose estimation flowchart

Thermoluminescence (*TL*) is a well-known dosimetric method, which could be used for this

purpose. When a *solid* poly-crystalline material is exposed to ionizing radiation, electron-hole pairs are produced, their number being proportional to the absorbed dose. The electrons and holes move freely in the lattice until they recombine or being trapped at certain active sites in the crystalline matrix. These traps are actually impurities or defects in the lattice that, from an energy point of view, exist between the conduction and valance band of the crystal. Electrons remain in these traps until they acquire sufficient energy to escape, which can be provided by an external triggering event such as heating. When this happens, the released electrons can recombine with free holes and in the process light is emitted. The intensity of the emitted light is proportional to the population of the trapped electrons and since their number is proportional to the absorbed dose of radiation, the detection and measurement of the emitted light as the temperature increases (glow curve) gives a measure of the dose the material has received. It should be noted that in some materials release of trapped electrons and recombination with holes can also take place spontaneously in room temperature. This phenomenon, called fading, is an undesirable effect for dosimetric purposes.

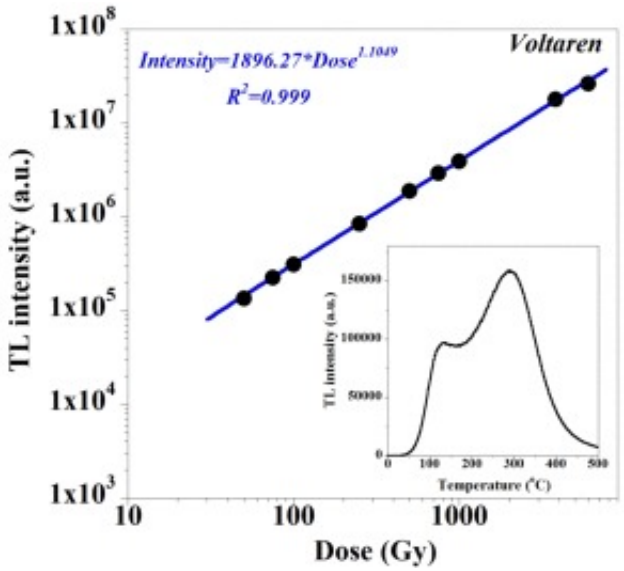

Fig. 2. Dose response (log-log scale) for the second peak counts for the Voltaren glass container (185-450 ^{o}C); the solid lines represent the regression lines derived from the equation given in the charts (of the form Y=a*Dk). The inset illustrates the glow curve for the same glass container after a beta-dose of 6 kGy

Following the above, it is clear that the estimation of the sterilization dose is more feasible and direct in the case of *solid* drugs (tablets, powder). However, this could also be accomplished in the case of *liquid-state* drugs implicitly, by investigating the luminescence behavior of their *glass* (in most cases) *containers*, since they are equally and jointly exposed to the ionizing radiation during the sterilization process (Fig. 1).

In the present study, preliminary thermoluminescence experiments with high beta-doses (up to 6 kGy) were conducted on two different types (bottle, ampoule) of glass containers of two commonly used commercial liquid drugs, Hexalen® and Voltaren®, to investigate their potential luminescent properties, which would allow the detection and retrospective evaluation of the radiation dose used in the sterilization process of the *liquid* drugs.

Results show that both glass containers exhibit interesting luminescent/dosimetric properties. More specifically, they present a linear TL dose response (light emitted per unit of absorbed dose) for doses up to 6 kGy (Fig. 2) with a stable behavior through time (absence of significant fading), while no significant sensitization (increased light emission after repeated irradiations) of the main peaks is observed. Thus, preliminary findings are very promising towards the post-sterilization dosimetry of commercial liquid drugs, using the Thermoluminescence response of their glass containers. In this respect, further analysis and experiments are required, and are currently in progress, employing even higher radiation doses.

Publication

Preliminary thermoluminescence investigation of commercial pharmaceutical glass containers towards the sterilization dosimetry of liquid drugs.
Kazakis NA, Tsirliganis NC, Kitis G
Appl Radiat Isot. 2015 Nov