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A detailed investigation of the TL and OSL trap properties and signal stability of commercial pharmaceutical glass containers towards their use as post-sterilization dosimeters of liquid drugs

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ABSTRACT

Drug sterilization with ionizing radiation is a well-established technology, which allows the adequate sterilization of heat-sensitive pharmaceutical preparations. However, the effects of irradiated drugs on the consumer when they are introduced in the human body are still unknown. Moreover, appropriate methods and protocols for the detection of irradiated drugs have not been established yet.

In two previous studies, the possibility to identify irradiated liquid-state drugs by means of TL and OSL measurements on their glass containers was explored with very promising findings. The present work complements the previous works, conducting a detailed investigation of the TL and OSL trap properties and signal stability on two types of glass containers of liquid pharmaceutical preparations.

Both the TL and OSL signals are composed by several components with linear dose response up to several kGy, while their stability with time is good, since an appreciable signal remains unaffected even 6 months post irradiation in both containers.

The new findings are very supportive and point towards the efficient use of the glass containers of commercial liquid drugs as probes for the post-sterilization dosimetry and accidental dosimetry of these drugs.

1. Introduction

Sterilization with ionizing irradiation, mainly gamma radiation, has been established as an acceptable method applied to several fields, such as foods and drugs. This sterilization method is preferred over other methods since its high penetrating power allows the easy, efficient, residueless, chemical-free and almost heat-free sterilization of heat-sensitive pharmaceutical preparations while being packed in their final product package [1,21,52].

When radiation passes through a drug system (or food), it interacts with water and other biological molecules and several chemical reactions are initiated resulting in the formation of radiolytic products [25]. Further degradation of the drug also can be caused, such as biological and physical changes (e.g. odor, color, texture, flavor, pH) on the drug and loss of its activity (e.g. [1,9,28,52]).

The above changes could put in risk the health and safety of the consumer [45,9], since drugs (solid or liquid) are introduced in the human body interacting with it with various ways and through multiple mechanisms. For example, the free radicals are highly reactive chemicals which can harm cells and at high concentrations, they can be hazardous to the body and damage all major components of cells, including DNA, proteins and cell membranes, contributing to the development of malignancies or other health conditions [44].

The above, in conjunction with the fact that the drug irradiation policies vary from country to country and that radiosterilization is permitted in some countries and not in others (e.g. [21]) leads to the necessity for a method to detect irradiated samples (post-sterilization dosimetry). Consequently, the development of drug irradiation detection methods, useful for regulatory compliance purposes, is an active area of investigation.

Towards this respect, several studies have been conducted with solid-state drugs (e.g. [45,49,4,48,16,17,26,30,46,8]). However, all of them use the electron paramagnetic resonance (EPR) spectroscopy for the detection of the irradiated drugs. Less than a handful researches focus on the TL (e.g. [54,49]) or the OSL [32,41] behavior of irradiated solid-state drugs.

However, all the above studies are limited to the dosimetric properties of solid drugs, while in many cases the doses applied are too low compared to those used during the ionizing sterilization. For this purpose, Author and his colleagues [33,34] extended the above methods

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(TL and OSL) to the post-sterilization dosimetry of liquid-state drugs as well. The above was accomplished exploring the TL and OSL behavior of two commercial liquid-drug glass containers for doses up to 30 kGy, since they are equally and jointly exposed to the ionizing radiation during the sterilization process. Results were encouraging towards the adequacy of drugs' glass containers as appropriate probes for the post-sterilization dosimetry of commercial liquid drugs.

In this respect, the present work is an extension of the previous studies [33,34] in order to gain an insight into the trap properties and signal time-stability of the glass containers. The above is accomplished by means of a computerized curve deconvolution analysis (CCDA) of both TL and OSL signals for doses up to 30 kGy and a long-term fading study in order to further assess the suitability of commercial pharmaceutical glass containers for the post-sterilization dosimetry of liquid drugs and for accidental dosimetry.

2. Experimental procedure

2.1. Drug selection and sample preparation

The glass containers studied were the same with those of the previous works [33,34], namely Hexalen® bottle and Voltaren® ampoules, corresponding to two of the most commonly used glass container types of liquid pharmaceutical preparations.

All drugs were supplied from a pharmacy in sealed boxes and before their expiration date as suggested by the manufacturer. Please note, from here on, unless otherwise stated, the terms Hexalen and Voltaren refer to the respective glass containers rather than the pharmaceutical substance.

More details about the selection of the drugs, the cleaning of the glass containers and the preparation of the samples can be found in the previous works. Glass grains of size 75–150 μm were selected for the TL and OSL measurements.

2.2. Instruments and methods

For the TL and OSL measurements a Riso TL/OSL reader (model TL/OSL-DA-15) was used, equipped with a $^{90}Sr/^{90}Y$ beta particle source. The system is also equipped with blue LEDs emitting at 470 nm arranged in six clusters each containing seven individual LEDs (maximum total power ~40 mW cm^{-2} at the sample) [11]. A 9235QA photomultiplier tube, combined with a Hoya U-340 and a heat absorbing Pilkington HA-3 filters, was used for light detection.

All TL measurements were performed in a nitrogen atmosphere with a low constant heating rate of 2 °C·s^{-1} up to a maximum temperature of 500 °C·s^{-1}. In addition, in all Continuous Wave Blue OSL measurements the stimulation time was 1500 s, while the power of the blue LEDs was kept constant at 85% of its maximum. In the OSL fading study the stimulation time was 2000 s. It must also be noted that in all cases a background signal was also acquired, which was subsequently subtracted from the original signal of the main measurement for the various dose-response calculations.

Beta-doses from 50 up to 30000 Gy were applied in aliquots of about 10.0 mg, while several measurements were conducted in two different samples for each glass container, in order to ensure the repeatability of the results. The above dose range was selected in order to explore the suitability of the glass containers in all possible dosimetric uses (accidental and post-sterilization).

3. Results and discussion

3.1. CW-OSL features

Fig. 1 illustrates typical CW-OSL decay curves (semi-log scale) recorded immediately after exposure to 1.0 kGy for both glass containers. An initial quickly decaying part in the first seconds of stimulation is observed in both cases, while stimulation time of 1500 s is not enough for the signal to reach the background level indicating the involvement of slow and hard-to-bleach components.

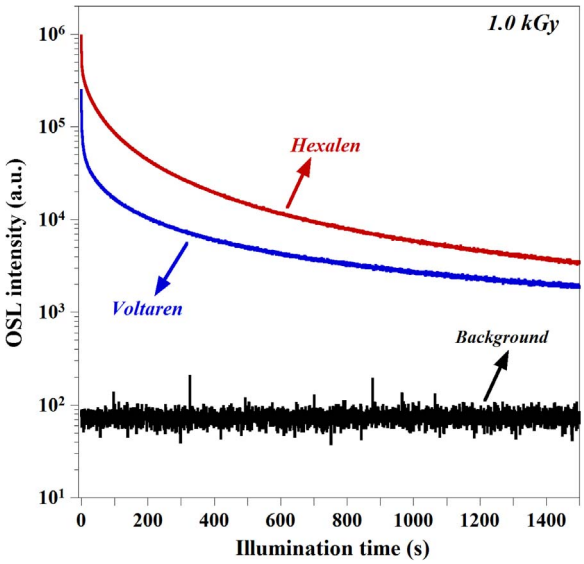

Fig. 1. Typical OSL decay curves for both glass containers; dose 1.0 kGy.

Very few studies have been conducted using OSL on glasses (e.g. [22,24,23,55,51]) thus few data are available regarding the shape and the components of such decay curves, especially at high doses. Yet, Galli et al. [24], studying the effective application of OSL to dating of mosaic glass, state that the observed decay curves were not a single exponential, indicative of the involvement of different electron traps, while a fast component was also prominent.

3.2. TL features

Fig. 2 presents typical TL glow curves for both glass containers after exposure to a low (50 Gy) and a high dose (3.8 kGy). In the low-dose glow curves (Fig. 2***a***) it is obvious that both glass containers have at least three overlapping peaks, one at low temperature (~90–100 °C), one broader centered at ~180–200 °C (for Hexalen) and ~290–300 °C (for Voltaren) and a smaller one at higher temperature, i.e., ~310 °C (for Hexalen) and ~390 °C (for Voltaren).

As the dose is further increased (Fig. 2***b***) the second peak becomes much broader and the glow curve tends to become single-peaked (especially in the case of Hexalen), which was also observed by Engin et al. [20] and Balogun et al. [6] studying window glass and sodalime glass respectively.

This broad peak has a full width at half maximum (FWHM) of about 150 °C for both glass containers. Such broad continuum TL peaks in glasses have been observed by most of the investigators exploring the TL properties of glasses (e.g. [5–7,18,20,50,51]). Such peaks in most cases are expected in amorphous materials.

On the other hand, several researchers working with various glasses recorded TL glow curves with well-defined peaks also present (e.g. [47,51,22,24,14,15]) besides the broad continuum peak, as in the present study. In most cases, the well-established "110 °C" peak of quartz is readily distinguishable, observed in the range 80–120 °C, while a discrete peak around 300 °C may also be present (e.g. [24]). The present glow curves of both glass containers resemble this structure with distinct peaks, typical for quartz, along with a broad peak. Moreover, Galli et al. [22] state that the existence of well-defined peaks is probably related to the presence of crystalline inclusions in the amorphous vitreous matrix. Based on the above, the presence of a highly fired crystalline silica oxide phase [55] seems also to be the case in the present study.