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PHOTOCATALYTIC DEGRADATION OF DRUGS UNDER LIGHT IRRADIATION

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Abstract: *Pharmaceuticals released in the environment represent a major concern to the entire world. These pharmaceutically active compounds have been detected in several public water systems in Europe, Australia and USA. For this reason, it's crucial to find solutions to destroy or inactivate this class of substances. In our study, we investigated the degradation kinetics of vinblastine, vincristine, docetaxel and epirubicin hydrochloride under light irradiation. Because of the urgent need to eliminate these compounds from hospital, zinc oxide particles dispersed into styrene butadiene styrene thin films (SBS_ZnO) was tested to reach better removal.*

Key words: *cytostatics, photocatalytic degradation, drug waste, emerging pollutants.*

1. Introduction

Pharmaceuticals have been consumed over the world for many decades, and their release in the aqueous environment from the last few years has described them as being one of the emerging contaminants. It has been reported that pharmaceutically active compounds have been detected in several public water systems in Europe, Australia and USA [3, 5]. Therefore, it is crucial to monitor their presence in the environment and to destroy or inactivate this class of substances in surface and underground water. There are several abnormal processes that affect the people when these pharmaceutically active compounds are found in nature, such as increased incidence of cancer, potential increased toxicity or development of antibiotic-resistant bacteria [1, 5, 6].

One of the most important classes of pharmaceuticals, mostly due to their cytotoxicity and the rate of administration, are anticancer drugs. These drugs are used in chemotherapy and help patients to fight with cancer, by destroying cancer cells. Chemotherapy is one of the most used methods to treat cancer, and therefore this is one of the reasons that make them one of the emerging contaminants [11, 7, 12].

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Globally, the most widely administered anticancer drugs and the most investigated in the aquatic environment have been 5-fluorouracil, methotrexate and doxorubicin [8], whereas other anti-cancer drugs such as vinblastine, vincristine, docetaxel, and epirubicin hydrochloride have received less attention. Vincristine (an antitumor vinca alkaloid) [15] and vinblastine (a vinca alkaloid antineoplastic agent) [14] are classified as non-biodegradable, while docetaxel (an antineoplastic agent) [10] and epirubicin hydrochloride (an antineoplastic agent derived from doxorubicin) [4] are readily biodegradable [2]. The chemical structures of the studied drugs are listed in Figure 1.

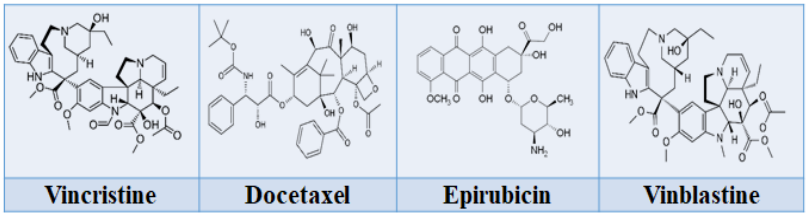

Fig. 1. *Chemical structures of the studied cytostatics*

2. Objectives

This study aims to investigate the degradation kinetics of vinblastine, vincristine, docetaxel and epirubicin hydrochloride under light irradiation. Because of the urgent need to eliminate these compounds from the environment, zinc oxide particles dispersed into styrene-butadiene-styrene thin films (SBS_ZnO) was also tested to reach better removal.

3. Materials and Method

2% zinc oxide was dispersed in the styrene-butadiene block-copolymer (with a star structure, 32% polystyrene and 196,000 g/mole) and carried out by spin casting in a 20% SBS solution in toluene, allowing the obtaining of 100x300 mm rectangular films (Figure 2). The dissolution was performed by external heating with an infrared lamp at a temperature that not exceeded 60 °C, avoiding thus the thermo-oxidative degradation of the styrene-butadiene block-copolymer.

Fig. 2. *SBS_ZnO film obtained by spin casting*

The irradiation experiments were carried out in a photochemical reactor filled with the drug solution (Figure 3) with or without the thin film (SBS_ZnO 1:10). The drug solutions (1.1*10-4M) were subjected to different irradiation times (from 0 to 4800 seconds), using a medium pressure Hg polychromatic lamp (275 W). The temperature reached during irradiation was 25 °C. Samples were collected at different irradiation times in quartz cuvettes (1 mm) and the entire content of each cuvette was analysed.

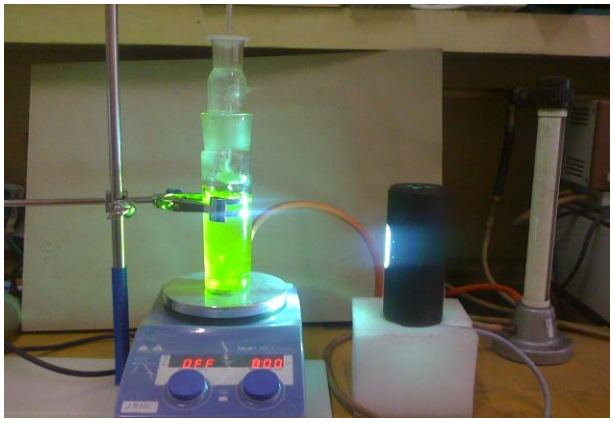

Fig. 3. *Photochemical reactor filled with the drug solution*

A M400 Carl Zeiss Jena spectrophotometer (range 200-900 nm) with double beam and microprocessor was used to measure the drug solution absorbance at the specific wavelength of each component. The chosen absorption value (λ max) was 295 nm for vincristine, 268 nm for vinblastine, 235 nm and 255 nm for epirubicin hydrochloride and for docetaxel 202 nm and 228 nm.

The FTIR samples spectra have been recorded with a Perkin Elmer Spectrum GX spectrometer, in the following conditions: range 4000 cm^{-1} to 600 cm^{-1}, 32 scan, resolution 4 cm^{-1}.

4. Results and Discussion

The results of vinblastine and vincristine degradation as a function of irradiation time were highlighted by the decreases of UV-Vis absorption bands (Figure 4). It can be observed that vincristine presents a fast degradation compared to vinblastine.

Fifty percent of vincristine degraded after 15 seconds of irradiation, while vinblastine reaches a degradation of 20% after 3250 seconds.

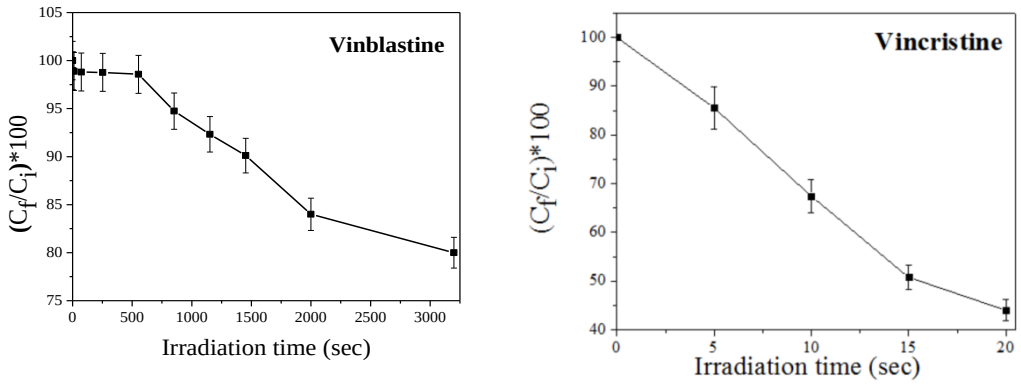

Fig. 4. *Degradation of vinblastine (left) and vincristine (right) depending on the irradiation time*

The SBS_ZnO film was used for irradiation in the heterogeneous environment with ZnO embedded in the polymer matrix, to avoiding several drawbacks, such as the turbidity that would be generated by the ZnO particles dispersed in the solution, their deposition on the bottom of the reactor and the concentration errors thus resulted. When SBS_ZnO film was used to cover the internal walls of the photoreactor, it was observed that the kinetics of disappearance of vinblastine was significantly accelerated (Figure 5). It can be reported that ZnO appears to be a best catalyst, 20% of the cytostatic degradation is obtained after 420 seconds of irradiation.

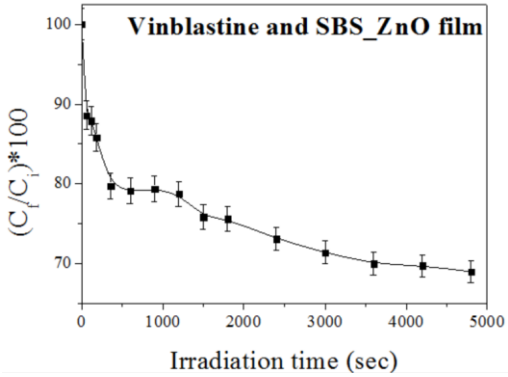

Fig. 5. *Degradation of vinblastine in the presence of SBS_ZnO film depending on the irradiation time*

The degradation of some readily biodegradable drugs, such as docetaxel and epirubicin hydrochloride was also investigated. It can be observed, that in comparison with the non-biodegradable tested drugs, the kinetics of disappearance degradation of epirubicin hydrochloride (Figure 6 - left) and docetaxel (Figure 6 - right) was significantly accelerated. Also, docetaxel presents a better degradation rate, 60% of the drug degraded after only 500 seconds of irradiation.

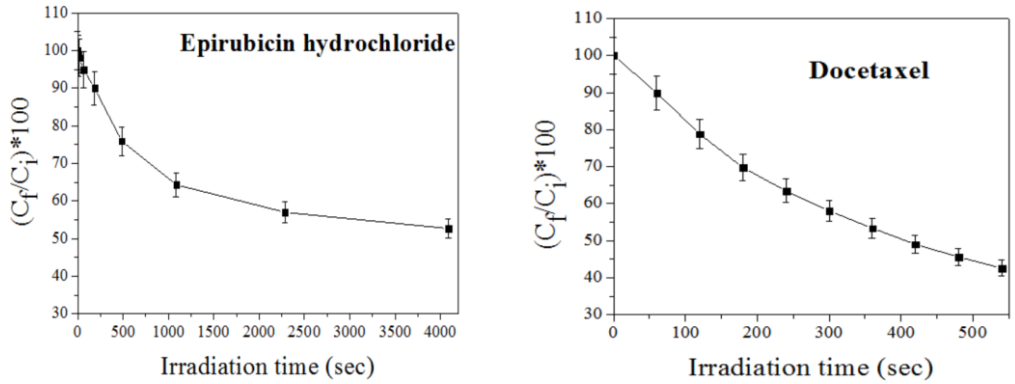

Fig. 6. *Degradation rate of epirubicin hydrochloride (left) and doctaxel (right)*

The photo-oxidation process of the drugs by FTIR analysis was studied in order to identify the changes of the characteristic bands before and after the irradiation process. In the case of vinblastine, it can be observed that the photo-oxidation process leads to the modification of specific absorption bands in the region between 1800 cm^{-1} and 1200 cm^{-1} (Figure 7 - left). Characteristic C=C ring stretch bands are observed before irradiation at 1615, and 1460 cm^{-1}, peaks which during irradiation of vinblastine disappear.

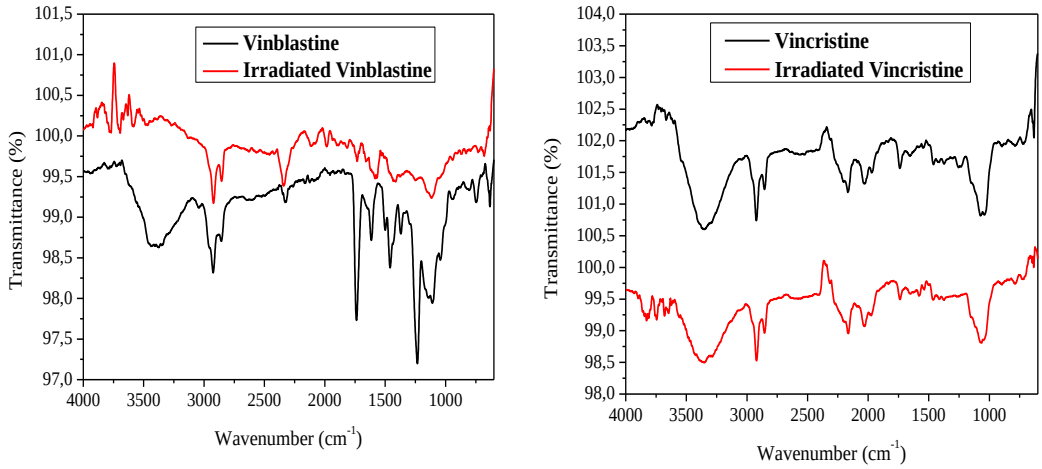

Fig. 7. *Photo-oxidation process of vinblastine (left) and vincristine (right) by FTIR spectroscopy*

As well, for non-irradiated vinblastine, at 3500 cm-1 O-H stretch band is present in the structure, but disappears after irradiation [16]. For vincristine, it can be observed that the degradative photo-oxidation processes could be quantified through the changes of the specific FTIR absorption bands in the region between 1200 cm^{-1} and 1800 cm^{-1}, and almost all the peaks after irradiation are decreased in intensity (Figure 7 - right) [13].

In the case of epirubicin hydrochloride, an intensity decrease of peaks in can be remarked after the irradiation of the cytostatic drug (Figure 8 - top). Also, there are some changes in the region between 1250 cm^{-1} and 2500 cm^{-1}.

Several changes occur in docetaxel spectrum after irradiation (Figure 8 - down).

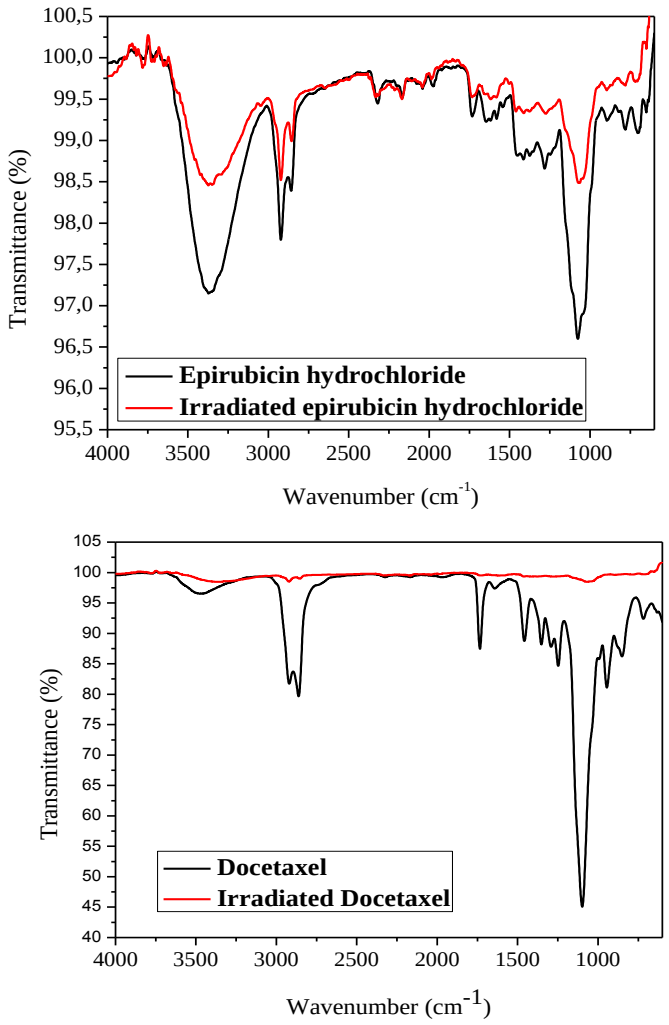

Fig. 8. *Photo-oxidation process of epirubicin hydrochloride (top) and docetaxel (down) by FTIR spectroscopy*

It can be observed that after degradation, only a few significant peaks remained at 2863 cm^{-1} (due to stretching of the C-H bond) and 1112 cm^{-1} (due to stretching of the C-O bond), which confirms the rapid degradation rate observed by the kinetics of degradation of docetaxel (Figure 6 - right) [9].

5. Conclusions

This study evidences that the degradation rate depends on the structure of the compound and the type of functional groups. Following the obtained results, it can be reported that vinblastine presented the lowest rate of degradation (20%), and this rate

has improved (30%) in the presence of the SBS_ZnO film. The other tested drugs presented a better degradation rate, 56% for vincristine, 47% for epirubicin hydrochloride and 57% for docetaxel. Also, this study demonstrated that the photocatalytic process plays a key role in the cytostatic drugs degradation and that the kinetics of degradation of the drugs can be significantly accelerated by using catalysts, such as ZnO. The SBS_ZnO film was used for irradiation in the heterogeneous environment with ZnO embedded in the polymer matrix, to avoiding several drawbacks, such as the turbidity that would be generated by the ZnO particles dispersed in the solution, their deposition on the bottom of the reactor and the concentration errors thus resulted.

Acknowledgements

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