IOCPS 2025 Conference
The 3rd International Online Conference on Polymer Science
19–21 November 2025 | Online
MDPI

E-Beam Radiation Processing of Semisolid Hydrogel for Doxorubicin Drug Delivery

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INTRODUCTION & AIM

Hydrogels used as local delivery systems are a viable alternative for the local administration of anti-tumour medications to overcome the side effects of oral or intravenous administration induced by chemotherapeutics. Hydrogels are considered to be the best alternative for cancer treatment because they allow non-invasive release, effectively support local and gradual release of anticancer drugs, increase drug solubility and bioavailability, offer high stability and controlled drug release, and may also help reduce the total dose required.

Herein, we designed and developed a novel semisolid hydrogel composed of collagen gel (calfskin), sodium carboxymethylcellulose (CMC), polyvinylpyrrolidone (PVP), and polyethylene oxide (PEO), using as crosslinking method the e-beam irradiation. The semisolid hydrogel can be used as an absorbent material with regenerative properties and as a biocompatible polymeric matrix for the progressive delivery of DOX, a broad-spectrum anticancer drug.

METHOD – hydrogel synthesis / DOX loading

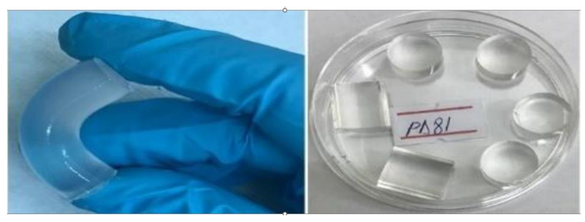
Hydrogel synthesis

The crosslinking of the polymer blends was performed at the ALID-7 linear electron accelerator (6 MeV) - National Institute for Laser, Plasma and Radiation Physics (INFLPR). The optimal irradiation dose was **25 kGy**, dose rate of **4 kGy/min**.

Hydrogel formulation:

- *0.3% Collagen gel*
- *0.2 % PEO*
- *0.6% CMC*
- *3.1% PVP (Mw=1300 kDa)*
- *95.8% Purified water*

Free of cross-linking agents



Hydrogels obtained after crosslinking by e-beam irradiation.

DOX-loading

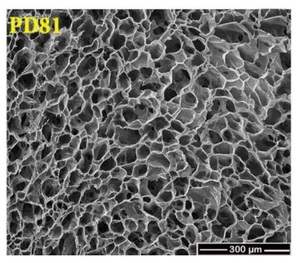
- ✓ ***Samples*** → Dry hydrogels (mass: 295 ± 0.0014 mg);
- ✓ ***Drug solution*** → 5 mL of DOX solution (200 ng/mL), sealed borosilicate glass containers;
- ✓ ***Conditions*** → Magnetic stirring at 500 rpm, 12 h, in the dark, at 20 °C;
- ✓ ***Post-loading treatment*** → Hydrogel treated with buffer solutions (pH 6.4 and 7.4) to remove residual surface DOX.

Drug loading - efficiency and release

- ***DOX quantification*** → LC - HPLC Agilent 1260 Infinity II;
- ***Detection*** → DAD (UV) + **FLD (*fluorescence*)** → 480 nm and 560 nm;
- ***HPLC column*** → Eclipse **C18** Plus (150 × 3 mm, 3.5 µm), 30 °C;
- ***Mobile phase*** → ACN/H_2O (25:75 v/v) + 0.1% formic acid, 0.6 mL/min;
- ***Gradient*** → 25% → 50% ACN, 7 min, Injection volume → 30 µL;
- ***Calibration curve***: (3.125 – 200) ng/mL doxorubicin.

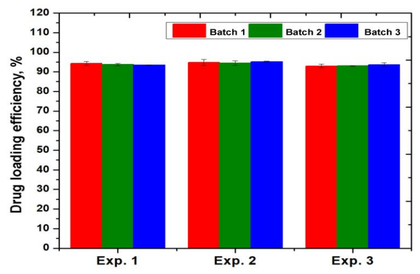
RESULTS & DISCUSSION

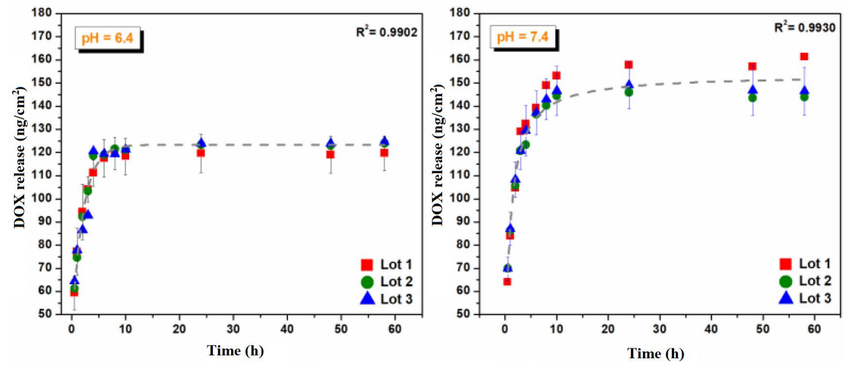
According to experimental results of loading and *in vitro* release, the semisolid hydrogel loaded **1145 ± 1%** ng of doxorubicin (DOX) and released different amounts of DOX, such as **120 ± 0.5%** ng/cm^2 at pH 6.4 and **150 ± 0.2%** ng/cm^2 at pH 7.4, for a period of 0.5 to 60 hours. In addition to the progressive release of DOX, the hydrogel retains its structure, is transparent, allows observation of the affected tissue, and has elastic properties unique to hydrogel-type systems.



SEM image.

Vertical diffusion cell system (HDT 1000).





Amount of DOX released (ng/cm^2) (Hydrogels Batch 1, Batch 2, and Batch 3 at pH 6.4 (*tumor medium*) and pH 7.4 (*physiological medium*).

$$Released\ equation\ t_n = \frac{A_U}{A_S} \times C_S \times \frac{V_C}{A_O} + \sum_{i=1}^{n-1} \left(AR_{t_{n-1}} \times \frac{V_S}{V_C} \right)$$

Where: A_U= sample surface area; A_R= amount of drug released (ng/cm^2); A_U= response (peak area) from the analysed sample solution; A_S = average response (peak area) from the standard solution; C_S = concentration of the standard solution (ng/mL); V_C= volume of the diffusion cell (7 mL); A_0= area of the hydrogel sample (cm^2); V_S= sample volume extracted at time t (1.5 mL).

CONCLUSION

- The hydrogel can function as an absorbent material across pH 5.4–9.4 and supports cell regeneration through topical application.
- The hydrogel maintains stability while releasing DOX for 60 hours at pH 6.4 and 7.4.
- The hydrogel is transparent and elastic, providing tissue monitoring.
- The hydrogel can be manufactured in various sizes depending on the size of the affected tissue.

FUTURE WORK / REFERENCES

Translating the results of *in vitro* studies (controlled release of DOX at different pHs) into *in vivo* models. This will demonstrate the efficacy of local therapy and the ability to reduce systemic side effects.

The efficacy of preclinical investigations will validate the transition to human clinical trials. This will illustrate effectiveness of localized treatments the hydrogel as a feasible alternative for patients unable to tolerate and its capacity to reduce systemic adverse effects.

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Acknowledgements:

- The Romanian Ministry of Education and Research under the National Nucleus Program LAPLAS VII under Contract No. 30N/2023.
- PN-III-P1-1.1-PD-2021-0552 (PD 20/2022 - 2024): Multicomponent hydrogel with hybrid structure obtained in situ by irradiation technology for the malignant melanoma therapy (**HYDRO-CAN**).