The 8th International Electronic Conference on Medicinal Chemistry (ECMC 2022)
01–30 NOVEMBER 2022 | ONLINE

Cyclodextrin based sponges for controlled drug delivery

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pharmaceuticals MDPI

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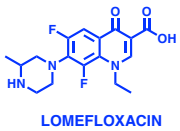
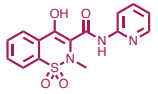
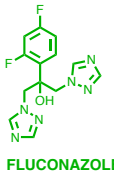
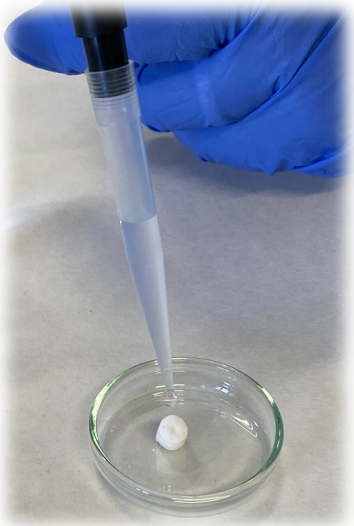
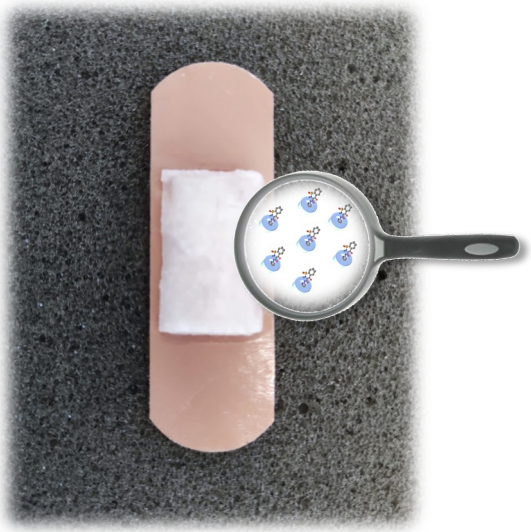
Cyclodextrin-Based Cryogels for Controlled Drug Delivery









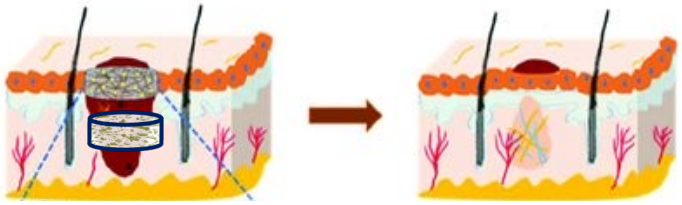


- ✓ high load capacity
- ✓ superabsorbent property
- ✓ high oxygen permeability
- ✓ excellent drug protection

Abstract: New drug delivery systems for wound healing application based on functionalized cyclodextrins monomers with acrylic or styrilic moieties have been synthesized and co-polymerized with 2-hydroxyethyl methacrylate (HEMA) via cryo-technique.
The carriers were successfully tested for the controlled release of antibiotics, anti-inflammatory, and antifungal drugs in the skin for wound healing. For this purpose, the cryogels were loaded with lomefloxacin, piroxicam, and fluconazole drugs with a drug loading efficiency (DLE) up to 78%. The release of the drugs was efficiently performed in the saline buffer (pH = 7.4), and acidic solution (pH = 3) showing efficiencies ranging from 23-95%. All theh new materials have been successfully tested for their biocompatibility over human fibroblast. The system has several advantages: it is low cost and environmentally friendly, and it has high stability and great versatility since it could be applied to several drugs.

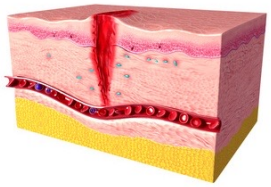
Keywords: macroporous cryogels, cyclodextrins, drug delivery, wound healyng, polymerization

Introduction



The **healing process** includes different phases:

- Inflammatory phase
- Proliferative phase
- Remodeling or maturation phase

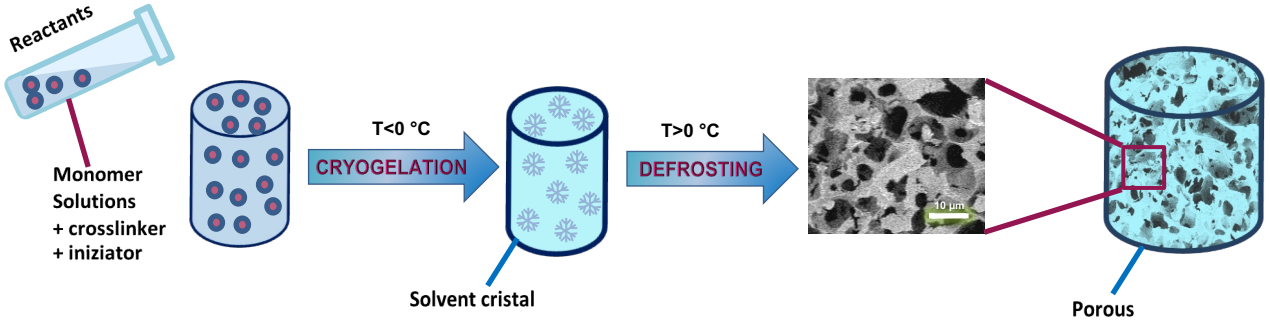


The ideal wound dressing should:

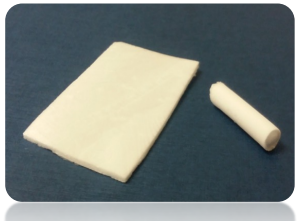
- ✓ create the optimum environment for healing
- ✓ promote wound debridement and cleansing
- ✓ control bleeding
- ✓ Protect the wound
- ✓ remove excess exudate
- ✓ release the drugs

Introduction

CRYO-POLYMERIZATION



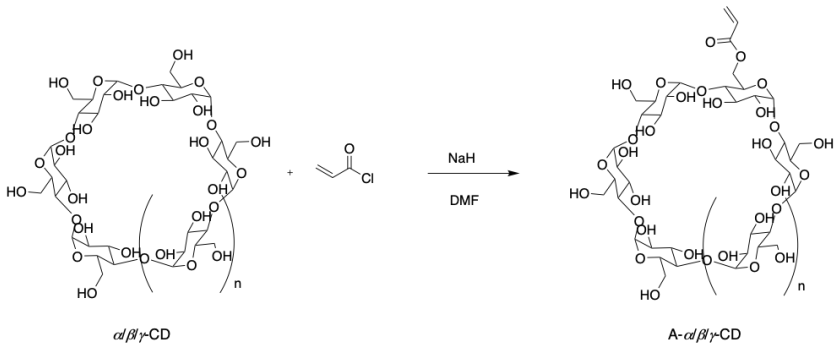
Schematic diagram of cryogels synthetic procedure



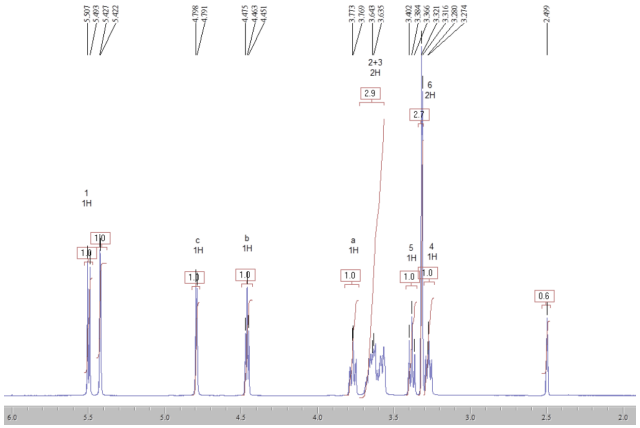
Cryogels are macroporous materials with pore diameter ranging from of 1 to 300 µm, synthesized by a radical cryopolimerization. Shape of cryogels could be modulate by changing reactors.

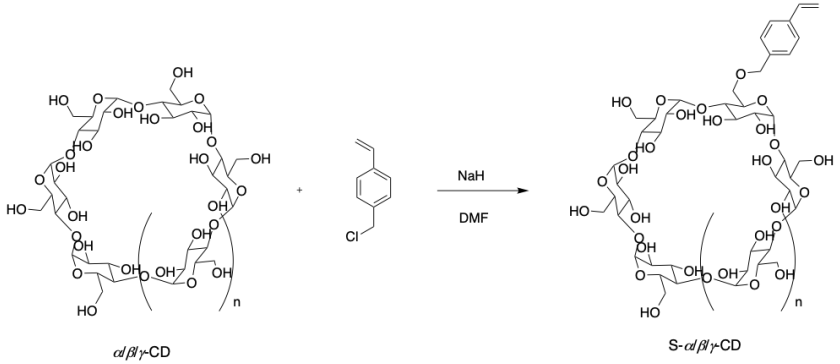
Results and discussion

Synthesis of Acr- Styr- α,β,γ-CDs

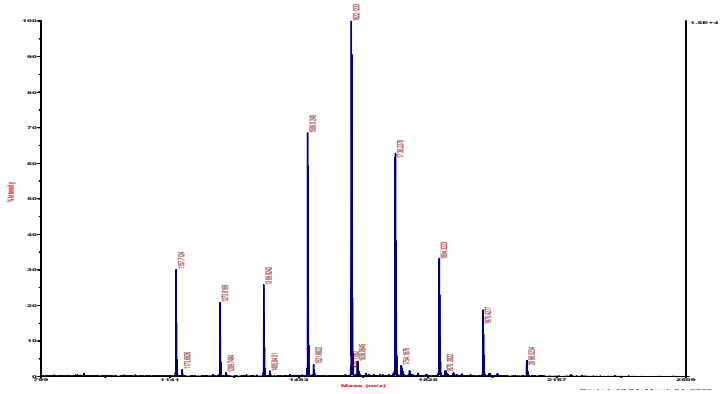


Acr-CD	n
α	1
β	2
γ	3





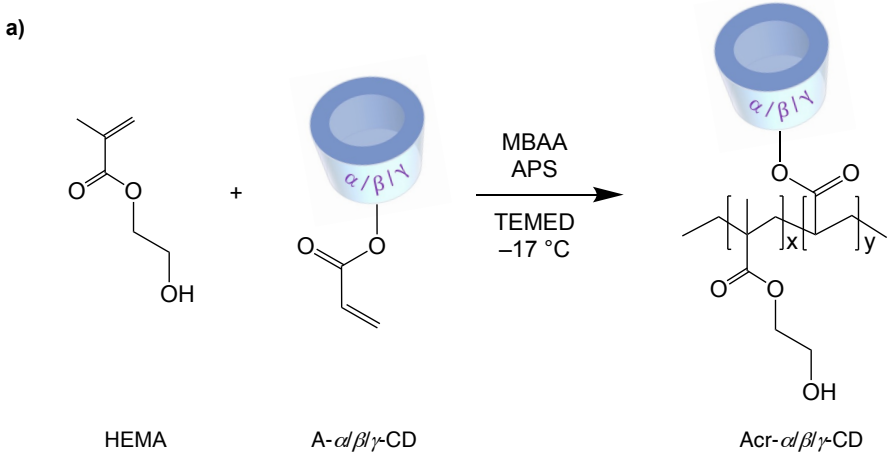
Styr-CD	n
α	1
β	2
γ	3

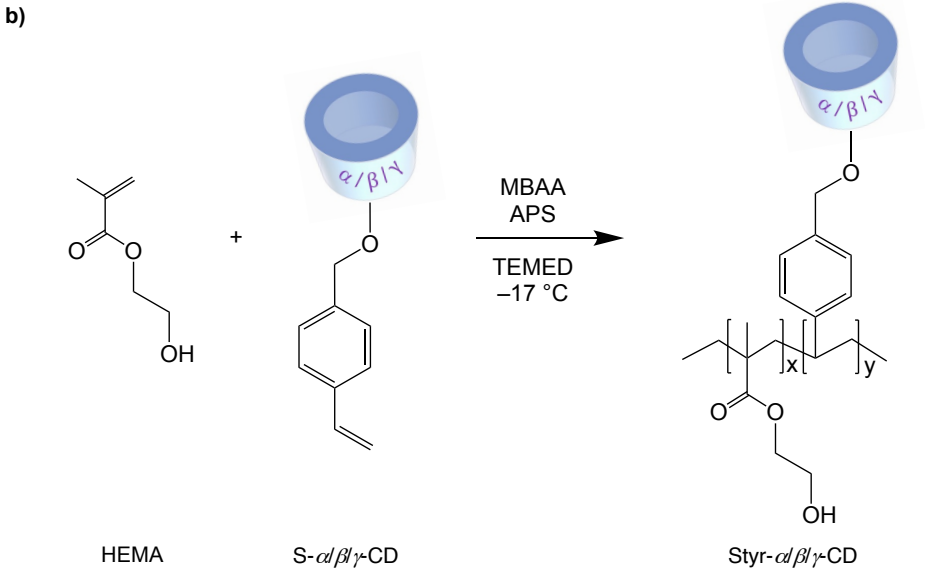


Results and discussion

Synthesis of HEMA/α,β,γ-CDs

cryogels



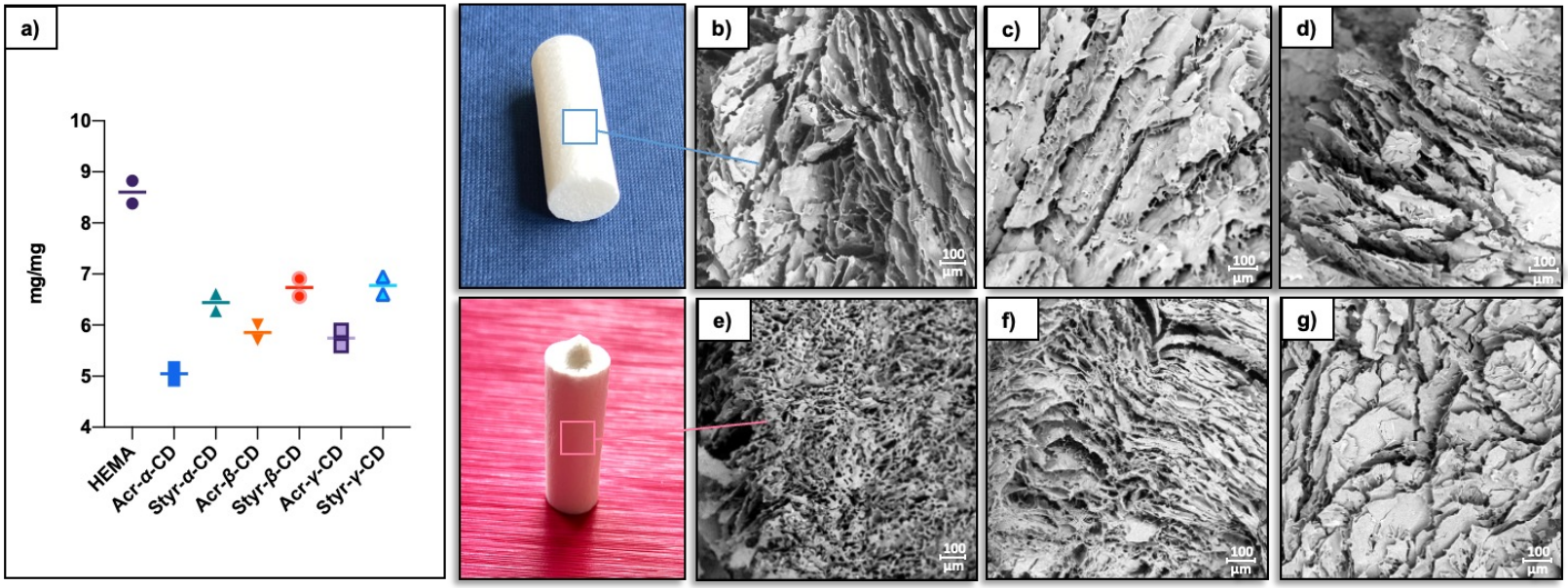


Results and discussion

a) Swelling ratio of HEMA-CD cryogels. All the new synthesized sponges shows swelling degree inferior to the HEMA reference.

SEM micrographs of synthesized cryogels confirmed the presence of a macroporous structure.

SEM images of (a) HEMA-αCDacr; (b) HEMA-βCDacr; (c) HEMA-γCDacr; (d) HEMA-αCDbenz; (e) HEMA-βCDbenz; (f) HEMA-γCDbenz. Scale bars are 100 µm.



Results and discussion

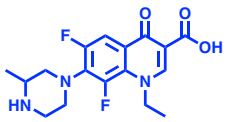
TGA analysis. All samples are characterized by an initial weight loss in the 80–140 °C range, most likely due to dehydration of CD and cryogels. Thermal degradation of HEMA-CD cryogels started from 270 to 480 °C.

Sample	T_5 (°C)	T_{max} (°C)	Weight residue (wt%)
Acr–α–CD	122.23	427.97	2.38
Acr–β–CD	121.54	436.74	1.14
Acr–γ–CD	157.18	438.02	2.58
Styr–α–CD	95.21	440.17	3.48
Styr–β–CD	95.12	434.52	3.71
Styr–γ–CD	79.40	436.73	2.28

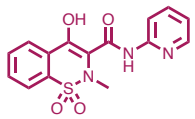
Results and discussion

Drugs loading efficiency (DLE) of HEMA, Acryl and Benzyl α/β/γ-CD cryogels.

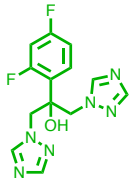
Piroxicam, Lomefloxacin, and Fluconazole, in a single and dual formulation, were loaded into cryogels with DLE up to 78%, with the best results gained from γ-CD cryogels.



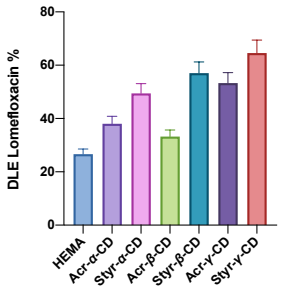
LOMEFLOXACIN

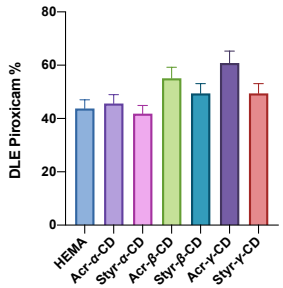


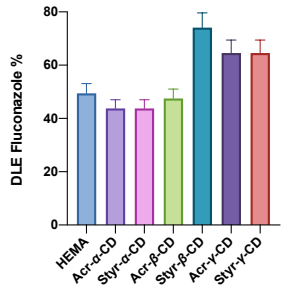
PIROXICAM

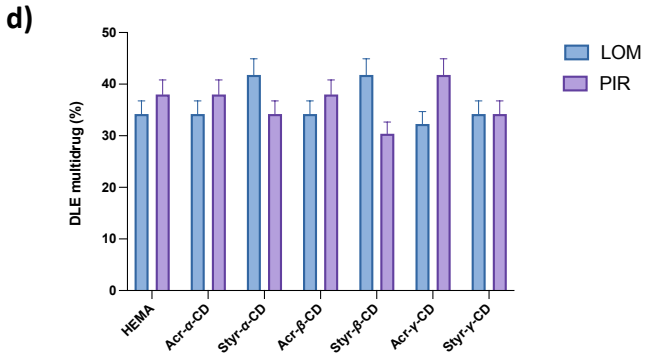


FLUCONAZOLE

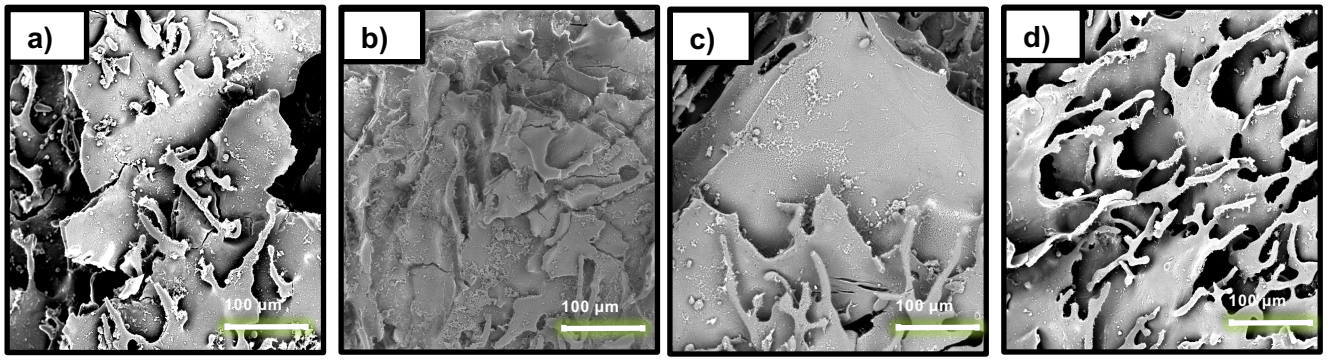








Results and discussion



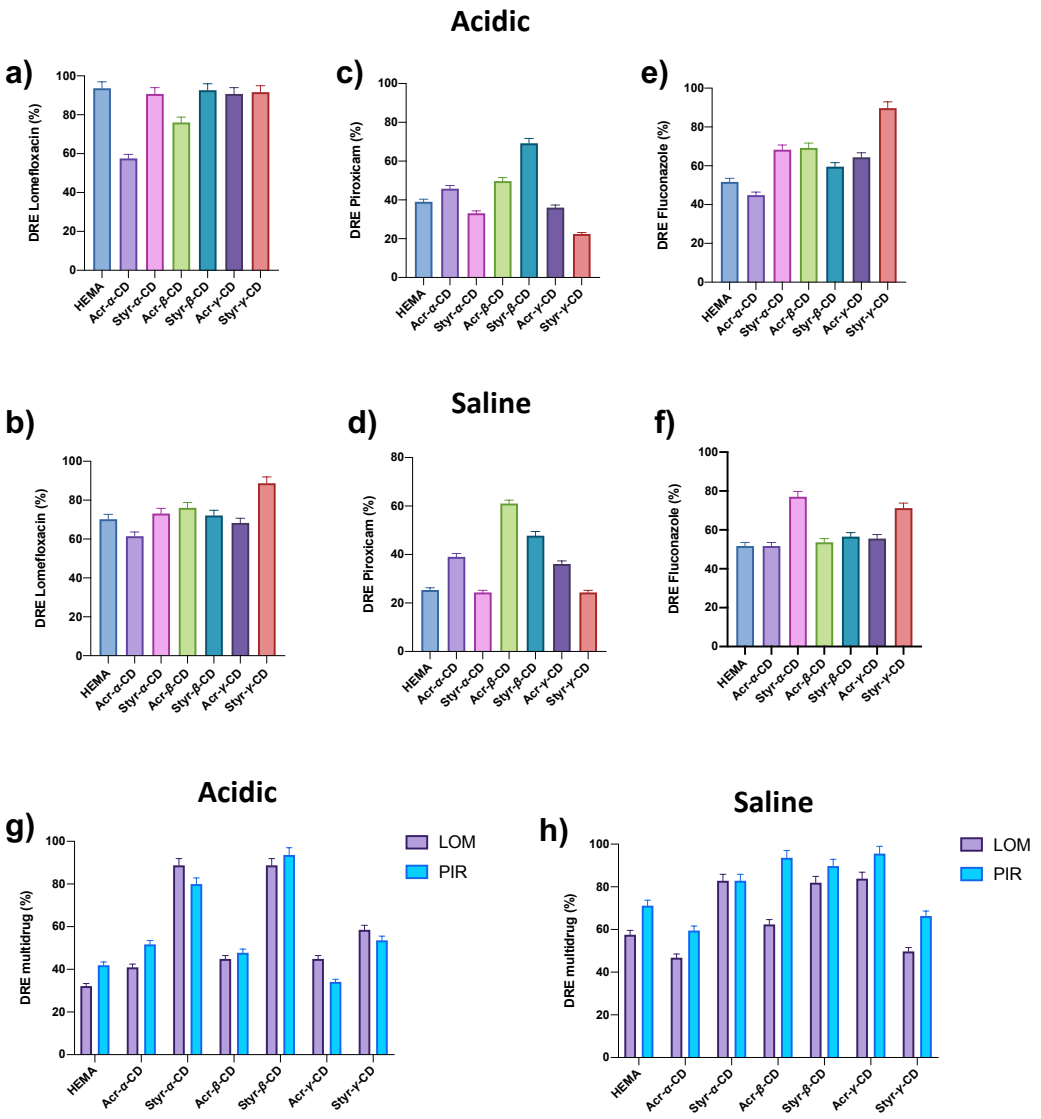
Element Symbol	Atomic Conc.	Weight Conc.
C	51.44	44.91
O	32.83	38.18
N	15.06	15.34
S	0.67	1.56

SEM of Acr-α-CD cryogel with LOM (a), PIR (b), FLU (c), and multidrug (d) shows the presence of the drugs in the sponges (up). EDX derived atom percentage of Acr-α-CD cryogel loaded with PIR (down) confirmed the successful of loading.

Results and discussion

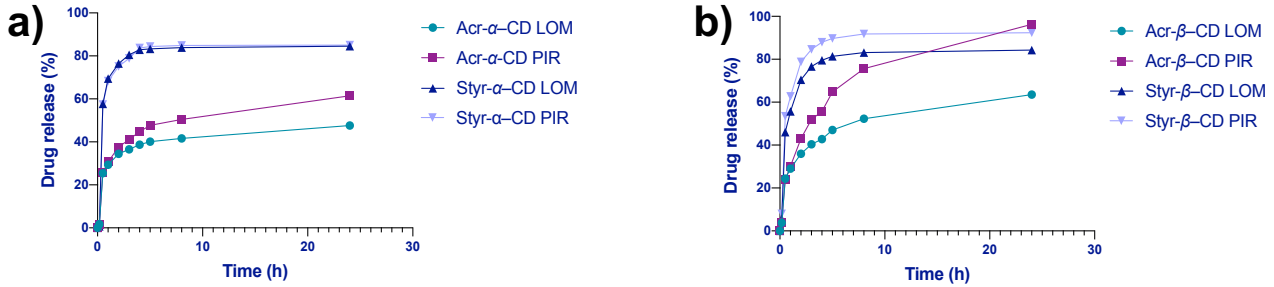
DRE in acidic solution (pH = 3) and saline buffer (pH = 7.4) of LOM (a, b), PIR (c, d), and FLU (e, f). DRE of LOM and PIR in a multidrug system in acidic (g) and saline (h) solutions.

The release of selected pharmaceutical was achieved by changing pH and salinity reaching value up to 95%.

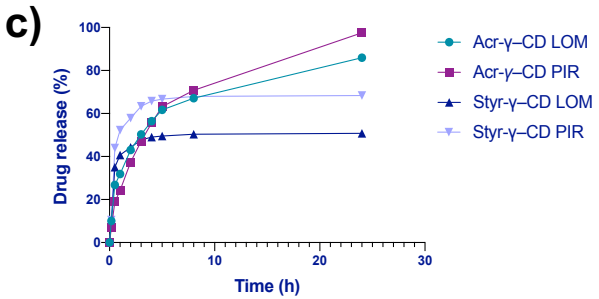


Results and discussion

Multidrug system (Piroxicam and Lomefloxacin loaded into the same cryogel): simultaneously drug release of Piroxicam and Lomefloxacin from CD cryogels in saline buffer.

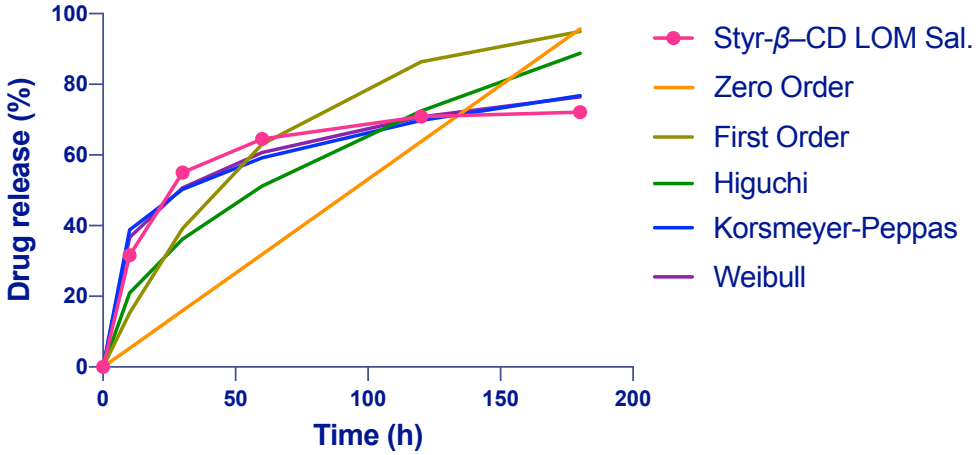


For all systems it was observed a burst effect occurring in the first 3–5 hours probably due to drugs adsorption on material surfaces. In addition, the drug release of the molecules embedded into the hydrophobic CD cavities within 24 hours ensures a treatment's continuity.

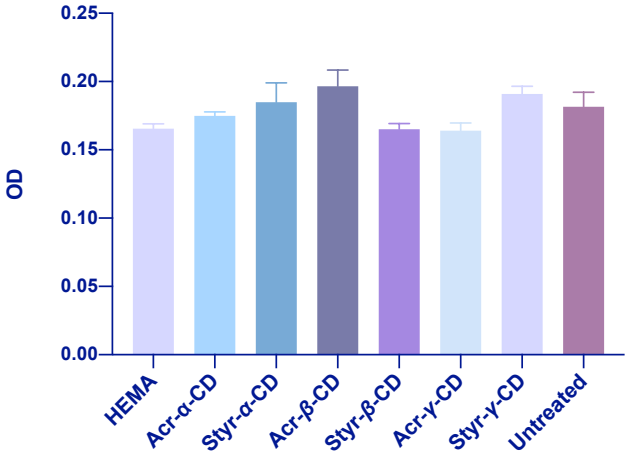


Results and discussion

Kinetic release fitting for Styr-β-CD with LOM in saline buffer.
The burst effect of our system is well described by Weibull and Korsmeyar-Peppas models (R^2 = 0.984).



No toxic effects were observed on HDF viability with all the tested compounds.



Conclusions

- ✓ As a proof of concept new cyclodextrin based cryogels have been produced for application in wound healing.
- ✓ The new systems are suitable for drug delivery and wound repair.
- ✓ The new materials are able to incorporate the drugs and release them under certain conditions.
- ✓ The materials are biocompatible and can be potentially used to deliver different drugs.