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# PERSPECTIVES OF NOVEL POLY(*D,L*-LACTIDE-*CO*- GLYCOLIDE)/HYDROXYAPATITE CORE-SHELL NANOPARTICLES AS CARRIERS OF ANTIBIOTICS

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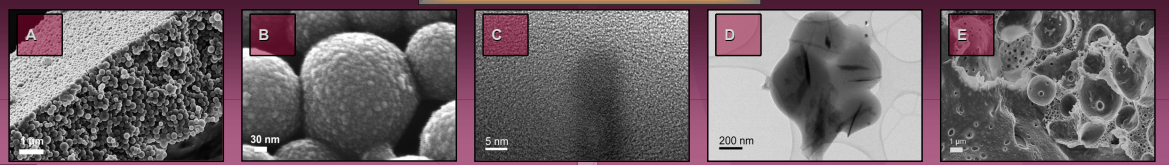
## INTRODUCTION

Local drug delivery for the treatment of infectious bone tissue diseases is a high-importance topic in the field of biomedicine for a last two decades. In general, some of the main problems related to controlled drug delivery of antibiotics are: (i) high initial burst effect with toxic outcome and (ii) low concentration of released drug during extended period of time with possibility for development of resistant spaces. There are some examples suggesting that core-shell particles applied as carriers of drug are able to provide high control over the process of drug release and to prevent burst effect.

## AIM

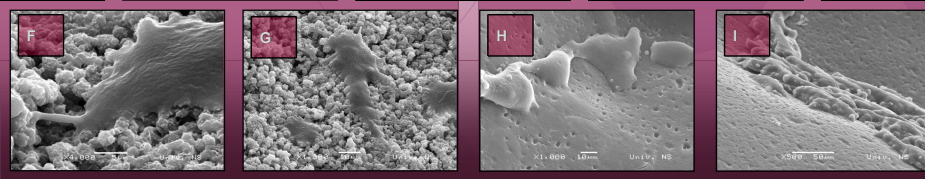
In this work, properties of PLGA/HAp composite, loaded with clindamycin in the form of active base and proactive phosphate, were analyzed. The main goals were: (i) investigation of the surface properties of material obtained during *in vitro* degradation, (i) analysis of material's cytocompatibility with fibroblast cells and (iii) estimation of the correlation between material's surface properties and cellular response.

## MORPHOLOGY and STRUCTURE




Morphology and structure of PLGA/HAp with clindamyicin before degradation (A, B, C and D)

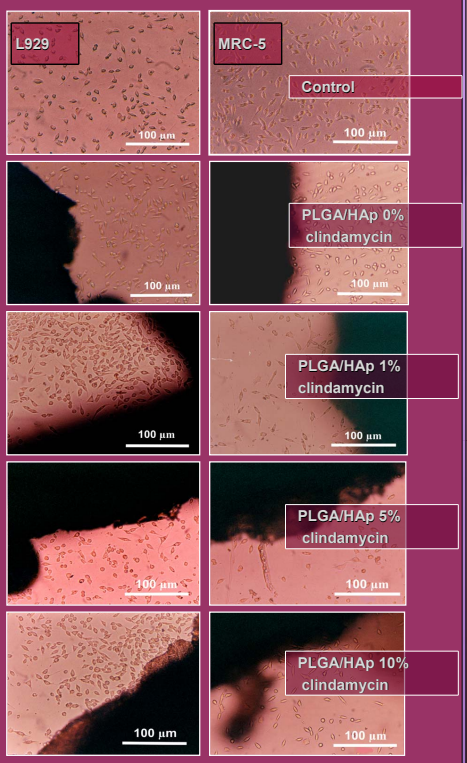
Morphology of PLGA/HAp with clindamycin after degradation (E)

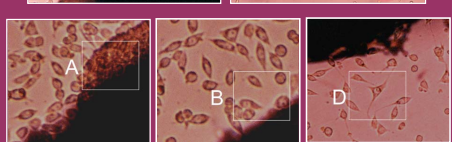



MRC-5 cells onto the surface of PLGA/HAp with clindamycin (F, G)

L929 cells onto the surface of PLGA/HAp with clindamycin (H, I)

## CELLULAR RESPONCE




## RESULTS and DISCUSSION

PLGA/HAp particles with loaded antibiotic showed morphology of nanostructured core-shells with planar organization. These structures were able to provide controlled release of the drug without initial burst effect. During the process of *in vitro* degradation, sphere-like morphology turned into the porous. Surface properties were continuously changed along degradation process showing increased wettability and surface area after 30 days of agging in PBS medium. Characteristics of the material's surface provided attachment of MRC-5 and L929 cells onto the material. Histological analyses showed absence of the changes in the shape and texture of vital cells and they had high affinity for interaction with material. According to the tests based on the mitochondrial activity (MTT) and compactness of the cells' membrane (DET), after cells interactions with PLGA/HAp with different contents of antibiotic during first 24h, high percents of survival were obtained. Agar test showed no detectable zone of decoloration around the samples and no observable signs of cell lysis indicating 0/0 cell response meaning absence or very low cytotoxicity effect .

## CONCLUSIONS

PLGA/HAp core-shells gave satisfied outcome during their interaction with human-like MRC-5 and L929 mouse fibroblast cells showing high level of compatibility and bioactivity of material which opened interesting field for the future *in vivo* research. Concerning that biodegradable PLGA shell is able to control process of drug release and that osteoconductive HAp core is able to promote bone reparation process, PLGA/HAp material shows promising properties for delivery of antibiotics.

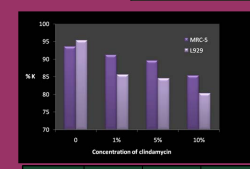
## EXPERIMENTAL PART

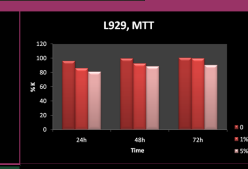
Degradation conditions:

- pH value: 7.4
- Degradation medium: PBS
- Temperature: 37 °C
- Shaking rate: 60 rpm
- Replacement of the buffer: every day

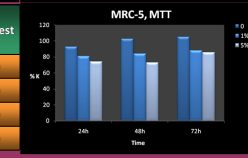
*Shaking water bath*

## CYTOTOXCISITY

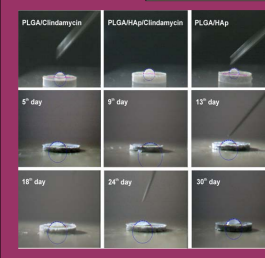



| Antibiotic (wt. %) | MTT (survival %) | DET (survival %) | Agar test |
|---|---|---|---|
| 0 | 92.9±1.2 | 93.6±2.3 | 0/0 |
| 1 | 80.9±0.3 | 91.2±5.0 | 0/0 |
| 5 | 74.1±2.9 | 89.6±2.8 | 0/0 |
| 10 | 68.8±1.4 | 85.3±2.4 | 0/0 |




## SURFACE PROPERTIES




| Degradation time (days) | Contact angle (°) |
|---|---|
| 0 | 89 |
| 5 | 56 |
| 9 | 40 |
| 13 | 52 |
| 18 | 57 |
| 24 | 58 |
| 30 | 64 |

| Degradation time (days) | Surface area ($m^2/g$) |
|---|---|
| 0 | 8.9 |
| 5 | 0.3 |
| 7 | No signal |
| 13 | No signal |
| 18 | No signal |
| 21 | 26.6 |
| 30 | 70.9 |

## DRUG RELEASE