# CIPROFLOXACIN RELEASE FROM POLYMERIC FILMS. MODELING AND PHARMACEUTICAL PARAMETERS DETERMINATION

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## INTRODUCTION

The Ciprofloxacin (Cipro) is a broad spectrum antibiotic, commonly used for infections of the urinary tract, intestinal, among others. Due to its very short biological half-life, approximately 4 to 5 hours, and its limited absorption efficiency, in conventional form, prompted the development of new delivery systems. Transdermal systems have numerous advantages, such as application in a specific site, painless, less frequent replacement and greater dosage flexibility. Sodium alginate (SA) is an anionic polysaccharide, derived mainly from brown algae and bacteria. On the other hand, recombinant elastin-type protein polymers (rELPs) are self-gelling, biodegradable and biocompatible polymers, tailored designed for different applications in human medicine. The aim of this work was to evaluate the feasibility of developing films based on rELP and SA for the controlled release of Cipro. The data obtained were analyzed using the "Lumped" model, which allowed determining the initial release rate and parameters of pharmaceutical relevance, in order to compare the different formulations developed.

## EXPERIMENTS

The **materials** used were rELP, designed and synthesized by the BIOFORGE group - University of Valladolid (Spain), SA purchased from Tododroga (Córdoba, Argentina) and the Cipro hydrochloride from Parafarm® (Buenos Aires, Argentina).

### rELP and SA films preparation

The procedings for rELP films preparation is showed in Figure 1 and for SA is showed in Figure 2

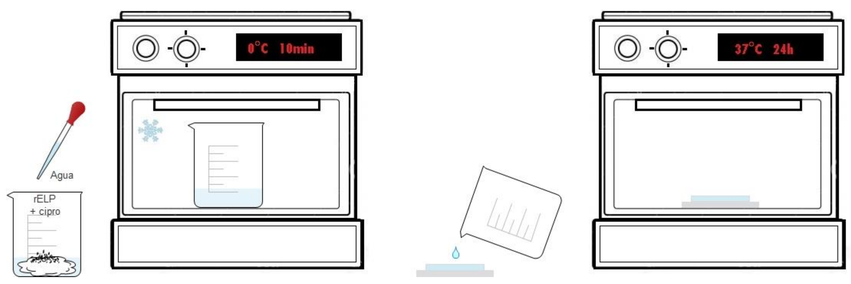


**Figure 1.** rELP-Cipro systems preparation.

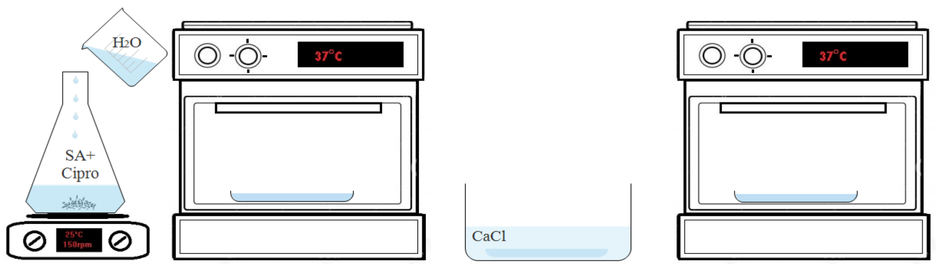


**Figure 2.** SA-Cipro system preparation..

rELP films were prepared with polymer concentrations of 16.6% w/w and with 10 mg of Cipro in 10 g of polymeric solution. SA films were prepared with concentrations of 1.5% w/w of polymer and 100 mg of Cipro in 30 ml of polymer solution.

### *In vitro drug* release tests

1x1 $cm^2$ samples were cut from the different films and their weights and thicknesses were determined

The samples were placed in test tubes containing 3 ml of physiological solution at 37 °C and with orbital shaking at 90 rpm.

At pre-established time, samples were taken by complete removal of the release medium, replacing the same volume with fresh medium

The Cipro concentration was quantified for each sample by UV spectrophotometry at 276 nm

### Data analysis

The data obtained were analyzed using a second-order kinetic model, called the Lumped model, developed and validated by our research group. Polymath 6.0 program was used to perform the regression.

$$M_t(\%) = \frac{a * t}{[1 + b * t]}$$

$M_t(\%)$ is the cumulative percentage amount of drug released at the moment $t$. Equation parameters $a$ (%/min) and $b$ ($min^{-1}$) can be obtained graphically.

Parameters of pharmaceutical relevance were calculated: the mean dissolution time (*MDT*), the time to release 80% of the drug ($t_{80\%}$) and the dissolution efficiency (*DE*).

## RESULTS

### Cipro release profile

Figure 3 show a high initial rate of drug release due to the transfer phenomenon that occurs because of the presence of the drug on the surface of films. Subsequently, a moving front of solvent occurs through the polymeric film, which allows the Cipro to diffuse towards the surface face so that it is available for dissolution in the release medium. As the distance between the surface and the advance of the moving front increases with time, the release speed decreases.

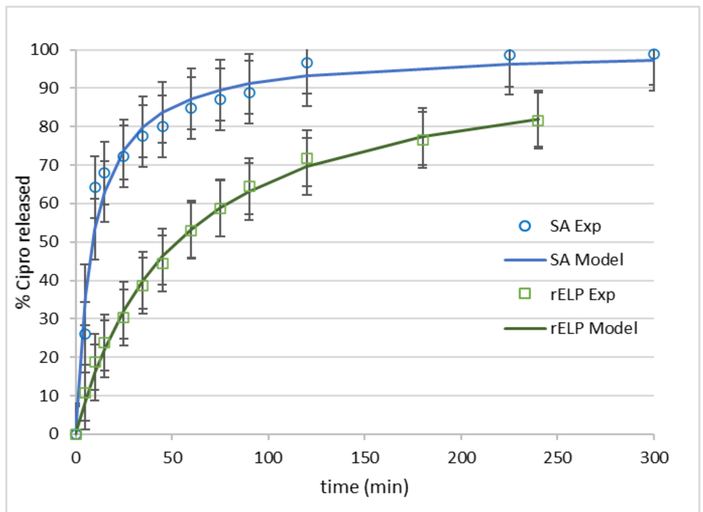


***Figure 3.*** Cipro release porfiles from rELP and SA films. The solid line represents the fit made using the Lumped mathematical model

### Data analysis

It is observed that SA systems has an initial rate of about 6 times higher than that of rELP systems. Furthermore, the $t_{80\%}$ parameter, is 35 min for the SA films. The pharmacopeia states that if this parameter is lower than 45 min, the release can be considered immediate, as in the case of SA platforms. In a system that modulates the dissolution of a drug, it is desirable a $t_{80\%}$ high value, as is the case with the rELP films, which would indicate a delay or control in the release process. The *DE* values are very close for both systems. Finally, the *MDT* value is a widely used pharmaceutical parameter to characterize the release rate of drugs from a specific dosage form that provides information about the ability to delay the release of the active ingredient from the polymer platform. A high *MDT* value indicates a greater ability to delay release. In this case, the behavior of $MDT_{80\%}$ is correlated with that presented by $t_{80\%}$, showing a value about 6 times higher for rELP systems than for SA ones.

**Table 1.** Lumped model parameters and parameters $t_{80\%}$, *MDT* and *DE* for the release curves of films with different polymer.

| Platform polymer | Model Lumped Parameters | | | Pharmaceutical relevant parameters | | |
|---|---|---|---|---|---|---|
| | a±sd* | b±sd* | M∞ | $t_{80\%}$ (min) | $MDT_{80\%}$ (min) | $DE_{200min}$ (%) |
| SA | 11.396±3.245 | 0.114±0.0375 | 0.2709 | 35.10 | 8.88 | 66.63 |
| rELP | 1.907±0.165 | 0.019±0,002 | 0.5605 | 209.76 | 53.06 | 58.79 |

*sd: standard deviation

## CONCLUSION

Platforms based on rELP polymer have a greater ability to release the drug gradually, while the systems based on SA would be useful for topical applications where rapid delivery of the drug is needed, providing high concentrations in a short time. Therefore it can be concluded that it is possible to modulate the release rate of Cipro through the films developed based on both polymers, with characteristics suitable for different applications. Consequently, both systems are promising strategies for the topical application of Cipro