**In vitro** permeation of gel formulations containing local anesthetics associated with poly-ε-caprolactone nanocapsules across pig oral mucosa.

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**Abstract**

The ideal topical anesthetic in Dentistry is not yet available. Thus, the objective of the present study was to evaluate *in vitro* the performance of different gel formulations containing 2.5% lidocaine and 2.5% prilocaine associated or not with poly-ε-caprolactone nanocapsules to cross pig buccal epithelium as a good indicative of efficient topical anesthesia *in vivo*. Permeation study was conducted in Franz type vertical diffusion cells during 5 h. In general, all the formulations tested presented good permeation and are good candidates for *in vivo* evaluation.

*Key words:* Oral mucosa, Topical anesthesia, Topical anesthetics, Dentistry.

### Introduction

Topical anesthesia is a common procedure performed in Dentistry prior to local anesthesia to reduce pain from needle insertion and anesthetic injection at the oral cavity. However, hardly even its success is reached. Lidocaine (LDC) is an amine–amide local anesthetic widely used in topical anesthesia. Nevertheless, its commercially available formulations fails to reduce pain in common dental procedures. Our research group demonstrated an improved anesthetic efficacy of local anesthetics encapsulated in polymeric nanocapsules in regional anesthesia (sciatic nerve blockade) in animal models. Therefore, the objective of the present study was to evaluate *in vitro* permeation of gel formulations of Carbopol or Aristoflex containing 2.5% lidocaine and 2.5% prilocaine associated or not with poly-ε-caprolactone nanocapsules (NC) in comparison to a commercial formulation across pig oral mucosa.

### Results and Discussion

*In vitro* permeation profile were evaluated as the cumulative amount of local anesthetics (LA) transported across pig buccal epithelium plotted as a function of time from the following formulations:
- Aristoflex gel + LDC + PLC free (ALP)
- Aristoflex gel + LDC + PLC in NC (ANLP)
- Carbopol gel + LDC + PLC free (CLP)
- Carbopol gel + LDC + PLC in NC (CNLP)
- Positive control: EMLA® (AstraZeneca)

The steady-state flux (Jss, in mg.cm⁻².h⁻¹) was obtained from the slope of the linear portion of the curve, and the lag time (h) was obtained from the intercept of this straight line on the x-axis (Chart 1).

**Chart 1.** Mean values (±SD) of the steady state flux (Jss) and lag time for permeation of LA across pig buccal epithelium (n=6).

<table>
<thead>
<tr>
<th>LA</th>
<th>Formulation</th>
<th>Jss</th>
<th>Lag time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ANLP</td>
<td>238.50±18.03ᵃ</td>
<td>4.71±0.70ᵃ</td>
</tr>
<tr>
<td></td>
<td>ALP</td>
<td>236.45±32.16ᵃ</td>
<td>3.29±1.18ᵃ</td>
</tr>
<tr>
<td>LDC</td>
<td>CNLP</td>
<td>160.88±31.20ᵇ</td>
<td>1.82±0.35ᵇ</td>
</tr>
<tr>
<td></td>
<td>CLP</td>
<td>248.03±14.60ᵃ</td>
<td>3.79±1.94ᵃ</td>
</tr>
<tr>
<td></td>
<td>EMLA</td>
<td>280.32±44.43ᵃ</td>
<td>13.23±4.90ᵇ</td>
</tr>
<tr>
<td>PLC</td>
<td>CNLP</td>
<td>172.24±20.99ᵇ</td>
<td>2.10±0.54ᵈ</td>
</tr>
<tr>
<td></td>
<td>CLP</td>
<td>168.14±20.40ᶜ</td>
<td>3.94±1.61ᵈ</td>
</tr>
<tr>
<td></td>
<td>EMLA</td>
<td>283.27±43.46ᶜ</td>
<td>4.68±2.98ᵈ</td>
</tr>
</tbody>
</table>

ANOVA/Tukey-Kramer. Different letters indicate statistically significant difference among the formulations into the permeation parameter for each LA (p<0.05). Each permeation parameter was analyzed separately.

**Conclusions**

In general, all formulations tested presented good permeation and are good candidates for *in vivo* evaluation.

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