

***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 testes 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 ever its success is reached¹. 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 procedures²⁻⁵. Our research group demonstrated an improved anesthetic efficacy of local anesthetics encapsulated in polymeric nanocapsules in regional anesthesia (sciatic nerve blockade) in animal models^{6,7}. 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 (J_{ss} , in $\text{mg}\cdot\text{cm}^{-2}\cdot\text{h}^{-1}$) 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 (\pm SD) of the steady state flux (J_{ss}) and lag time for permeation of LA across pig buccal epithelium (n=6).

LA	Formulation	J_{ss}	Lag time
LDC	ANLP	238.50 \pm 18.03 ^a	4.71 \pm 0.70 ^a
	ALP	236.45 \pm 32.16 ^a	3.29 \pm 1.18 ^a
	CNLP	160.88 \pm 31.20 ^b	1.82 \pm 0.35 ^a
	CLP	248.03 \pm 14.60 ^a	3.79 \pm 1.94 ^a
PLC	EMLA	280.32 \pm 44.43 ^a	13.23 \pm 4.90 ^b
	ANLP	211.09 \pm 25.91 ^c	6.26 \pm 0.63 ^c
	ALP	223.89 \pm 27.37 ^c	3.40 \pm 0.95 ^{cd}
	CNLP	172.24 \pm 20.99 ^c	2.10 \pm 0.54 ^d
	CLP	168.14 \pm 20.40 ^c	3.94 \pm 1.61 ^{cd}
	EMLA	283.27 \pm 43.46 ^d	4.68 \pm 2.98 ^{cd}

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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