ABSTRACT SUMMARY
Permeation of nicotine through porcine buccal mucosa and the effects of pH on buccal permeation of nicotine were evaluated in Franz diffusion cell model. Stratum corneum stripped skin and silicone membrane were also evaluated as alternative models for porcine buccal mucosa to evaluate permeation of nicotine. Study showed that pH had significant effect on the permeation of nicotine due to ionization of nicotine at lower pH. Results also demonstrated that silicone membrane and stripped skin could be useful alternative to porcine buccal mucosa.

EXPERIMENTAL METHODS
The effect of pH on permeation of nicotine through buccal mucosa was carried out using Franz diffusion cell. Porcine buccal mucosa surgically separated from the porcine cheek was mounted on the Franz cell. The donor compartment was filled with 500 µl of 1% (w/v) solution of nicotine hydrogen tartrate in phosphate buffer 0.1 M at pH 5.8 and 7.4. Receptor compartment was filled with PBS, pH 7.4 and was maintained at 37°C using thermostatic water pump. Receptor samples (0.5 mL) were taken at time interval of 0.5, 1, 1.5, 2, 2.5, 3, 3.5 and 4 h and replenished at each time point with equal volume of fresh buffer solution. The samples were analyzed by HPLC assay.

The purpose of the present study was to evaluate the permeation of nicotine through porcine buccal mucosa (BM) and to determine the effect of pH on nicotine permeation. Model membranes like silicone membrane (SM) and stratum corneum-stripped skin (SS) were also used to simulate the permeation of nicotine through buccal mucosa.
Receptor samples (0.5 mL) were collected at time interval of 0.5, 1, 1.5, 2, 2.5, 3, 3.5 and 4 h.

RESULTS AND DISCUSSION

The ionization of nicotine at lower pH resulted in poor permeation of nicotine. The cumulative amount of nicotine permeated at pH 5.8 was 10.297 ± 6.32 µg/sq.cm compared to the 148.90 ± 53.38 µg/sq.cm at pH 7.4 depicted in Fig. 1, as only 0.4% of the nicotine is present in un-ionized form at pH 5.8 compared to 24.2% at pH 7.4.

![Fig. 1. Effect of pH on nicotine permeation profile through buccal mucosa](image1)

**Fig. 1.** Effect of pH on nicotine permeation profile through buccal mucosa

Tape stripping was done to obtain the stratum corneum-stripped skin. The average cumulative amount of nicotine permeated through buccal mucosa and stripped skin at pH 8.0 was found to be 197.69 ± 75.89 and 152.71 ± 99.13 µg/sq.cm respectively, while the amount of nicotine permeated at pH 5.8 was found to be 15.22 ± 10.06 and 53.22 ± 15.59 µg/sq.cm (Fig.2).

![Fig. 2. Permeation profile of nicotine bitartrate through buccal mucosa and stripped skin](image2)

**Fig. 2.** Permeation profile of nicotine bitartrate through buccal mucosa and stripped skin

The cumulative amount of nicotine permeated through silicone membrane at pH 8.0 and 7.4 were found to be 170.87 ± 5.41 µg/sq.cm and 49.68 ± 2.93 µg/sq.cm, respectively. At pH 5.8 no permeation of nicotine was observed (Fig. 3). These results demonstrated that both stripped skin and silicone membrane show similar qualitative pH-permeation profile for nicotine and thus can serve as alternative models. Variability observed with silicone membrane is significantly lower compared to both the biological membranes. However, silicone membrane lacks the hydrophilic component of the biological membrane and thus no permeation was detectable at pH 5.8 where nicotine is predominantly in ionized state. Considering most formulations that are intended to deliver nicotine via buccal mucosa will target the pH>7.4 and thus the evaluation of nicotine permeation in silicone membrane is considered valid at a biologically relevant pH.

![Fig. 3. Effect of pH on permeation of nicotine bitartrate through silicone membrane](image3)

**Fig. 3.** Effect of pH on permeation of nicotine bitartrate through silicone membrane

CONCLUSION

This study showed that pH had an important role in the permeation of nicotine due to greater ionization of nicotine at pH below 6.0 resulting in poor permeation of nicotine through buccal mucosa and alternative membranes like stratum corneum-stripped skin and silicone membrane. Permeation studies also showed that alternative models like silicone membrane and stripped skin could be used to simulate drug delivery through porcine buccal mucosa.

REFERENCES


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