Conscious and Anesthetised Gottingen Minipigs as an In Vivo Model for Buccal Absorption—pH Dependent Absorption of Metoprolol

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Purpose

The potential of buccal mucosa as a site for systemic absorption has attracted increased attention in recent years creating a need for new predictive in vivo models. The aim of this study was to evaluate the pH dependent absorption of metoprolol by administering bioadhesive tablets to the buccal mucosa in Göttingen minipigs. Furthermore, the performance in an anesthetised and a conscious animal model was compared.

Methods

Buccal tablets buffered to pH 6.2 and 8.9, oral solution and intravenous injection were tested in four conscious and anaesthetised Göttingen minipigs in a non-randomised cross-over study. Blood samples were collected and processed before analysis by ultra performance liquid chromatography and a mass spectrometer. An ex vivo flow retention model was applied to study dissolution and retention of the bioadhesive buccal tablets.

Results

T_{max} obtained from the two buccal conscious groups (55±5 and 35±5 min) were significantly different to the buccal anesthetised groups (120±0 and 165±15 min). Also, the absolute bioavailability from the buccal tablet pH 8.9 (6.6±0.4 and 20.7±4.0%) was significantly different to the buccal tablet pH 6.2 (4.3±1.0 and 4.3±1.6%) for the conscious and anesthetised groups, respectively. The ex vivo flow retention model showed slower release from the buccal tablets with the resulting pH of 8.9 compared to buccal tablets pH 6.2, and the observed increase in bioavailability from this formulation can therefore be explained by an increase in permeability.

Conclusion

In conclusion, this study showed a pH dependent absolute bioavailability of metoprolol when administrated as bioadhesive buccal tablets to conscious and anesthetised minipigs. Also, anaesthesia was found to delay the time to reach maximal concentration as compared to the conscious pig model when administrated as buccal tablets.