INTRODUCTION

The interest in alternative routes of drug administration as well as new formulation techniques for pediatric medicines is steadily growing (1). A so-called "Composite Drug Dosage Form" for lidocaine hydrochloride (LC-HCl) of drug loaded minitablets (MT) and a placebo bilayered mucoadhesive buccal film (MBF) has already been successfully developed. The bilayered film, which consists of a mucoadhesive layer and an insoluble backing layer, is necessary to obtain precise treatment at the injured area by avoiding drug release into the oral cavity (2). Due to the hardness of the MTs this formulation could have an unpleasant mouthfeel and, consequently, a negative impact on the patient's compliance. For this reason, a 3D printing technique should be used to create a dosage form with a lower hardness. The aim of this study was to print film doses of LC-HCl with a comparable immediate release behavior to those of the already developed mucoadhesive composite drug dosage forms. Furthermore, the dissolution profile should be compared with produced composite drug dosage forms containing compressed MTs.

MATERIALS AND METHODS

MTs, with 2 mm diameter, were compressed using rotary tablet press (IMA Kilian). Bilayered MBFs containing ethylcellulose as backing layer and chitosan as mucoadhesive layer were produced using solvent casting method. Composites containing MTs were manufactured by direct incorporation during solvent casting as well as glued onto the dried films. A modified formulation of El Aita et al. (3) containing Lidocaine Hydrochloride 7.9 %, Kollicoat IR 39.5 %, distilled water ad 100.0 % was printed by an extrusion based 3D Bioplotter (EnvisionTec). The parameters for the printing process were: 2.7 bar pressure, 10 mm/s speed, 27 °C, needle diameter of 0.4 mm. Scanning electron microscope (Phnom G2 pro) was used to examine the surface morphology of produced dosage forms. In vitro dissolution studies were performed using USP apparatus I at 50 rpm rotation speed, 37.5 ± 0.5 °C in 900 ml phosphate buffer (pH 5.5). Drug release was quantified using UV – photometer (Shimadzu) at a wavelength of 203 nm. Water activity was measured by using a water activity sensor Aw – C2 (Rotronic).

RESULTS AND DISCUSSION

Composite drug dosage forms containing LC-HCl have been produced. Figure 1 shows the MT MBF – Combination produced by solvent casting (directly incorporated (A)) and the printing MBF – Combination (B). The water activity measurement shows that after 60 minutes an equilibrium state was observed [Fig. 2]. In addition, it could be shown that after a drying time of already 20 minutes, a water activity below 0.6 could be achieved, which prevents the bacterial growth in the dosage forms [4]. Both, the Composite drug dosage forms [Fig. 1 (B)], as well as the MBF, was stored in a vacuum drying oven with a set temperature of 30 °C during the water activity measurement.

Comparing the dissolution profiles of the printed formulation with isolated MT and the composite drug dosage form (glued with Carboxymethylcellulose (CMC)), no differences in drug release can be observed [Fig. 3]. Only the directly incorporated formulation shows a faster dissolution which can be explained by its different morphology shown by SEM images [Fig. 4].

CONCLUSION

The development of a printable formulation with LC-HCl was feasible. The printed composite formulation shows comparable dissolution profile to the glued MT composite. Due to the advantage of lower hardness, the printed composite formulation represents a promising optimization concerning this composite dosage forms. Further investigations will focus on potential differences in transmucosal permeation profiles.

References: