カードランの放出制御製剤への応用. II. テオフィリン含有カードラン錠のin vitroおよびin vivoでの評価

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Application of curdlan to controlled drug delivery. II. In vitro and in vivo drug release studies of theophylline -containing curdlan tablets

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ABSTRACT Tablets having two different surface areas were prepared from spray-dried particles of curdlan/theophylline. Drug release from the tablets was studied in vitro and in vivo. The in vitro drug release from a tablet with a larger surface area (Tab L)was faster than that with a smaller one(Tab S). The water uptake of Tab L was larger than that of Tab S, probably due to the difference in tablet's surface areas. However, the water uptake was not a rate-determining step for the drug release from curdlan tablets containing a large amount of theophylline. A straight line was obtained when release % was plotted vs. time. The slope of each curve was calculated as 0.59 for Tab L and 0.58 for Tab S. This indicates that the release mechanism is non-Fickian diffusion controlled. In addition, the curdlan tablets or theophylline powder was administered orally to 5 healthy volunteers, and saliva concentrations of theophylline were determined. Each saliva concentration was converted to plasma concentration using the saliva to plasma ratio of the drug in each subject. The AUC of Tab L was nearly the same as that of powder, while the AUC of Tab S was smaller than that of powder. The mean residence times(MRTs) of theophylline powder, Tab S and Tab L were 11.1 ± 1.5, 25.4 ± 6.3 and 17.1 ± 1.5 h,respectively. The mean dissolution times(MDTs) of Tab L in

vivo and Tab S in vivo were 5.0 ± 2.1 and 13.9 ± 5.4 h, respectively. On the other hand, the MDTs of Tab L in vitro and Tab S in vitro were 4.8 and 11.2 h, respectively. In vivo drug release was very similar to in vitro drug release in both tablets. The lower bioavailability of Tab S suggested that the drug release had not been completed during the gastrointestinal transit period. Tab L would thus be a better controlled release form than Tab S.

抄録 天然の多糖類カードランとテオフィリンの噴霧乾燥微粉末から錠剤を作成した。錠剤からの薬物放出は表面積に比例したが、その機構はnon-Fickianであった。また、錠剤への水分の浸透過程は薬物放出の律速段階ではなかった。

表面積の異なる2種のカードラン錠からのテオフィリン放出性についてin vitro及びin vivoで検討した。In vitroの平均溶出時間（MDT）とin vivoのMDTは相関していた。錠剤の表面積の違いにより、生物学的利用性（BA）が異なることが明らかとなった。今回作成した小さい方の錠剤（直径1.0cm）のBAが低かったのは、消化管内での薬物放出が不完全なためだと考えられた。大きい方の錠剤（直径1.3 cm）ではBAはほぼ100%であり、徐放性製剤として有用であった。