フィブロインを用いた放出制御型テオフィリン錠剤の調製

片山博和、一色美緒、吉富博則

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Application of Fibroin in Controlled Release Tablets Containing Theophylline

Hirokazu Katayama, Mio Issiki, and Hironori Yoshitomi

ABSTRACT: The applicability of fibroin, a major silk protein, to controlled release type dosage tablets was investigated *in vitro* and *in vivo*. Fibroin tablets containing theophylline were easily prepared by a direct compression method without additives. Five types of fibroin tablets with the same surface area and different amounts of theophylline were prepared. In an *in vitro* drug study, the drug release from the tablets was not affected by the pH of the release medium. The greater the fibroin content in the tablets, the lower the percentage released at time t. The Higuchi plots of the release data showed a linear release profile, indicating that the drug release from the fibroin tablets was diffusion-controlled through the matrix. Theophylline powder or a TF-41 tablet (theophylline: fibroin=4:1), or a commercial tablet, Uniphyl (once-a-day type) was administered to 5 healthy volunteers. The areas under the saliva theophylline concentration-time curve (*AUC*) of Uniphyl and TF-41 to that of powder were 85 % and 70 %, respectively (fasted). Conversely, the mean residence time and mean absorption time of TF-41 were long compared to Uniphyl (fasted). Therefore, the reduction of bioavailability in TF-41 was due to the delayed release from the tablets *in vivo*. Taken after a meal, the *AUCs* of TF-41 and Uniphyl increased and the absorption was completed. This suggested that the drug release from TF-41 may increase due to the stimulation of food on TF-41 itself and due to movement of the gastro-intestinal tract. In conclusion, fibroin could be used as the matrix in controlled-release tablets.

抄録　絹の主要タンパク質であるフィブロインを放出制御型錠剤のマトリックスとして応用可能かどうか検討した。

*In vitro*でのフィブロイン錠（F錠）からのテオフィリン放出は、溶出液のpHの影響を受けず、薬物含量を変えることにより調節可能であった。F錠からのテオフィリン放出機構は、マトリックス内の薬物拡散であることが明らかとなった。

市販のテオフィリン徐放錠と同等の放出パターンを示すF錠を5人の健常人に投与した。空腹時投与ではF錠のbioavailabilityは市販品に比べ低かったが、食後投与では同等であった。