膵リパーゼ感受性腸溶性製剤としての トリグリセリド小球体の作製と評価

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薬剤学 *YAKUZAIGAKU* **50** (2), 156－165 (1990).

Preparation and Evaluation of Triglyceride Spheres as an Enteric Release Dosage Form Sensitive to Pancreatic Lipase

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ABSTRACT A new enteric release system was designed and formulated by using various triglycerides (TG), which was given as spheres with an average size of about 700 μm. The release of an incorporated drug from these spheres was expected to be generated by lipid digestion of bile and pancreatic lipase in the intestine.

The spheres were prepared by using saturated fatty acid TG and sulfamethizole (SMZ) was incorportd as a model durg.

The influence of each kind of TG on the release behavior of SMZ from spheres in the 2nd fluid of JP XI with (JP－2－GL) or without (JP－2) gall powder and lipase was investigated. It was concluded that TG spheres, which were prepared with a kind of TG, were not applicable to be an enteric dosage form.

The amount of SMZ released from double coated TG spheres (DCTS), which were prepared with tristearin and trilaurin, was found to be small in the 1 st fluid (JP－1) of JP XI, JP－2, JP－2 with Tween 80 (0.1%) and JP－2 with gall powder, while all of SMZ in DCTS was released in JP－2－GL within 2 h.

Urinary excretion profiles of SMZ powder and DCTS were obtained in humans. The lag time of SMZ urinary excretion after administration of DCTS was found longer than that of SMZ powder. This result suggested that SMZ could be released from DCTS in the small intestine, but not in the stomach. The bioavailability of DCTS after meal was almost the same as that of SMZ powder.

抄録 トリグリセリド（TG）を材料とした小球体による新しい腸溶性製剤の開発を試みた。包含薬物の放出は，腸管内のリパーゼの脂質消化作用により起こることが期待できる。モデ

ル薬物としてのSulfamethizole（SMZ）と各種飽和脂肪酸TG単独で作成した小球体は，腸溶性製剤として有用ではなかった。トリラウリンとトリステアリンによる二重被覆小球体（DCTS）では，リパーゼ含有試験液中でのみ，SMZを速やかに放出した。このDCTSを人に経口投与後の尿中排泄を検討した結果，SMZ原末投与と比べて，尿中排泄開始時間の遅れが認められ，腸溶性の発現が示唆された。生物学的利用率にも問題はなかった。

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