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Gastrointestinal Transit of a Magnetically Marked Capsule Monitored Using a 37-Channel SQUID-Magnetometer

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Abstract. The gastrointestinal transit of magnetically marked solid pharmaceutical drug dosage forms can be monitored using biomagnetic measurement equipment. The presented study shows that using a 37-channel SQUID-magnetometer the investigation of the gastrointestinal transit of an ingested magnetically marked capsule becomes feasible with a temporal resolution in the order of milliseconds and a spatial resolution in the millimeter range.

1. INTRODUCTION

A prerequisite for the development of oral drug dosage forms is the knowledge about their gastrointestinal transit [1]. In particular, the transit times through the different parts of the gastrointestinal tract [2] and the location of dissolution or drug release [3] are of major importance. Usually, drug dosage forms labelled with γ -emitting radioisotopes are detected by scintillation cameras (γ -scintigraphy) [4]. γ -Scintigraphy provides sufficient information, but its applicability is limited by the use of radioactive isotopes. Therefore, there is need for alternative methods for the investigation of the gastrointestinal transit of drug dosage forms.

In this study an ingested solid oral drug dosage form is magnetically marked by ferrimagnetic iron oxide and is localized by means of biomagnetic measuring procedures. This includes the use of Superconducting Quantum Interference Devices (SQUIDS) as magnetic field detectors. In former studies we showed that the detection of magnetically marked oral drug dosage forms is possible [5, 6]. We could furthermore show that the high motility of the gastric organs produces rapid marker dislocations that complicate its localization if the measuring device is a 7-channel SQUID. Sequential measurements that simulate a 21-channel detector are sufficient for the localization of the marker at locations with low motility. At about 24 hours after ingestion the localization of an ingested steel ball has already been shown to be possible even using a 1-channel SQUID [7]. This is probably due to phases of strongly reduced motility in the colon. Here we show that a 37-channel SQUID-magnetometer is sufficient for the localization of an ingested magnetically marked capsule even throughout motility phases of the gut.

2. MATERIALS AND METHODS

0.5 g poly(methyl methacrylic acid) were dissolved in 7.6 g acetone and 1.9 g isopropylalcohol. 2.7 g of powdered magnetite were dispersed in this solution by agitation with ultrasound for 5 minutes. The dispersion was sprayed onto 50 g of sucrose pellets (diameter 0.8 - 1.0 mm) in a pelletiser. By this procedure about 50 μ g magnetite were added to each pellet. Thereafter a solution prepared of 0.5 g poly(methyl methacrylic acid), 0.1 g dibutylphthalate, 0.9 g isopropylalcohol and 3.6 g acetone was additionally sprayed onto the pellets. The pellets were proven to be insoluble in water, 0.1 M hydrochloric acid, and phosphate buffer pH 6.9 for at least 48 h. In order to simulate a solid unit oral drug dosage form this pellet was enclosed in a cylindrical capsule (length 16.1 mm, diameter 5.7 mm) of silicone rubber. Finally the capsule was magnetized in a short solenoid.

The measurements were performed in the Berlin Magnetically Shielded Room (BMSR) [8]. The z-component of the magnetic field (B_z) of the marker was recorded by a 37-channel SQUID-magnetometer [9], connected to a data acquisition system with a sampling frequency of 250 Hz.

A male volunteer who was in the fasted state for at least twelve hours was positioned under the SQUID-magnetometer in such a way that the x-y-plane of the SQUID-sensors was parallel to the volunteers chest. After starting the signal acquisition the volunteer ingested the magnetically marked capsule together with 50 ml water. After 30 minutes recording time the volunteer was allowed to leave the BMSR. 30 minutes later the next signal acquisition of 10 minutes duration was started. Such signal

acquisitions of 10 minutes duration were repeated several times. The latest time point of signal acquisition was performed six hours after ingestion.

3. RESULTS

The magnetic dipole moment of the marker was determined as $6.24 \mu\text{Am}^2$. From the B_z -values measured simultaneously at 37 positions and the given dipole moment of the marker its x , y , z position coordinates and its orientation were calculated as previously described [10] for each sampled time point. The data obtained with the 37-channel SQUID-magnetometer were sufficient for successful determinations of the marker positions. As an example figure 1 shows the marker positions in the x -, y -, and z -direction starting 10 s after ingestion for the following 2 minutes. They represent the passage of the marker from the esophagus into the stomach. Figure 2 shows a 3D-view of the marker positions.

Figure 1: Marker positions calculated for the first 2 minutes after ingestion. *a*, Movement in x -direction. *b*, Movement in y -direction. *c*, Movement in z -direction. The origin of the coordinate system is set to the first localization of the marker 10 s after ingestion.

Figure 2: 3D-view of marker positions calculated for the first 2 minutes after ingestion. The chest of the volunteer is orientated in the x - y -plane.

4. CONCLUSIONS

The use of a 37-channel SQUID-magnetometer allows the localization of solid oral dosage forms that are labelled with remanent ferromagnetic or ferrimagnetic substances within the gut. A sampling frequency of 250 Hz provides a temporal resolution of the motion in the millisecond range. The presented method avoids the currently necessary use of x-rays or radionuclides. Further studies using markers that are soluble in the gastrointestinal tract might enable the *in vivo* determination of the time course and localization of the disintegration of solid oral dosage forms.

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