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Notes

Gastrointestinal transit studies in the rat using ^{19}F-NMR

Sylvia J. Anie [1], John T. Fell [1], Roger D. Waigh [1] and Brian Wood [2]

[1] *Department of Pharmacy and* [2] *Biomedical NMR Unit (Stopford Building), University of Manchester, Manchester M13 9PL (U.K.)*

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Summary

^{19}F-NMR has been used to assess the movement of a non-disintegrating pellet containing a fluorinated derivative of pentaerythritol in the gastrointestinal tract of a rat. The data were treated using computer graphics to provide a three-dimensional representation of the movement of the pellet.

The behaviour and transit of solid oral dosage forms in the gastrointestinal tract are related to drug absorption. NMR imaging is a potentially valuable method of obtaining such data and may have advantages over gamma scintigraphy, the current method of choice.

Previous studies have shown that ^{19}F-NMR imaging may be used in conjunction with ^{1}H-NMR imaging to observe and locate a pellet in vivo (Anie et al., 1989; Anie, 1990). A significant problem encountered is the time associated with the acquisition of the images. Due to the rapid movement of the pellet in the gastrointestinal tract of the rat, a faster method of assessment would be useful. In view of this, ^{19}F-NMR has been investigated for this application without the requirement for the generation of images.

Studies utilised 200 g sedated (diazepam; intraperitoneal; 2.5 mg/kg) or anaesthetised (urethane; intraperitoneal; 5% in saline; 0.6 ml/100 g) Sprague-Dawley male rats, in an 18 h starved state. Hollow capsule-shaped pellets were filled with a fluorinated derivative of pentaerythritol (0.006 g) (Anie et al., 1991) and sealed to prevent leakage. A single pellet was orally admin-

Correspondence: J.T. Fell, Dept of Pharmacy, University of Manchester, Manchester M13 9PL, U.K.

istered into the stomach. A reference pellet containing the derivative was fixed to the dorsal region of the rat. The sedated or anaesthetised rat was placed in a perspex restraint cage, positioned in a birdcage coil and finally into the magnet. Each rat was killed and dissected on completion of the study to ascertain the position of the pellet in the gastrointestinal tract and to correlate this position with the NMR data.

Data acquisition was commenced 15 min after the administration of the pellet to the rat. The instrument used was an ORS/Bruker biospectrometer. The experiment was performed at 4.7 T with the birdcage coil tuned and matched to 188 MHz. Pulses of 90 and 180° were applied for 275 and 550 μs, respectively. The sequence repetition time (TR) was 2031 ms and the excitation pulse to echo duration (TE) was 24.8 ms. A one-dimensional experiment in each of the three gradients x, y and z allows rapid location of the centre of the pellets with a precision of roughly 0.5 mm. Field gradients used in the x, y and z directions were 2558, 2408 and 2257 Hz/cm, respectively. To increase the signal-to-noise ratio, each signal was acquired repeatedly, i.e. averaged. Signal averages were obtained approximately every 2 min for 5 h.

In each experiment, ^{19}F-NMR signals originating from the two pellets were obtained. Measurements made relative to the reference pellet (R) provided information as to the pellet mobility. Fig. 1 shows a selected portion of the Z profile acquired from a sedated rat. Each field map consists of 22 ^{19}F spectra and shows two peaks, one corresponding to the reference and the other to the pellet in the gastrointestinal tract. A three-dimensional pattern of movement relative to the reference pellet can thus be obtained. A greater movement of the pellet was obtained when the rats were sedated as opposed to being anaesthetised by urethane. This was confirmed on dissection.

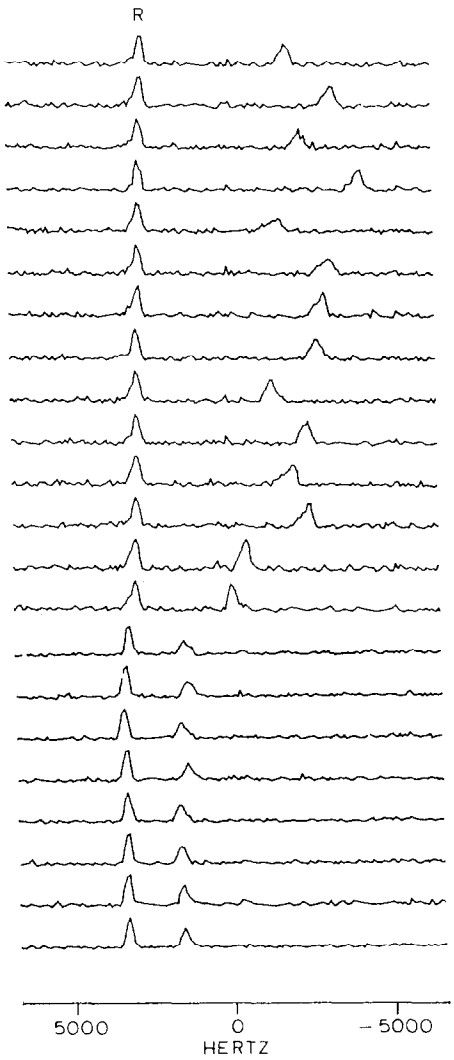

Fig. 1. The Z profile of a pellet in a sedated rat (scale: 1000 units = 0.44 cm).

The data can be treated using computer graphics to give a visual representation of the pellet movement. Typical displays are shown in Fig. 2a and b for anaesthetised and sedated rats depicting greater movement after sedation. The x, y and z co-ordinates are displayed to show the viewing plane. The plots can be rotated to obtain the three-dimensional image.

These studies coupled with previous work (Anie et al., 1991) demonstrate the non-invasive feature and potential of NMR methods for gastrointestinal transit studies. Linking NMR spec-

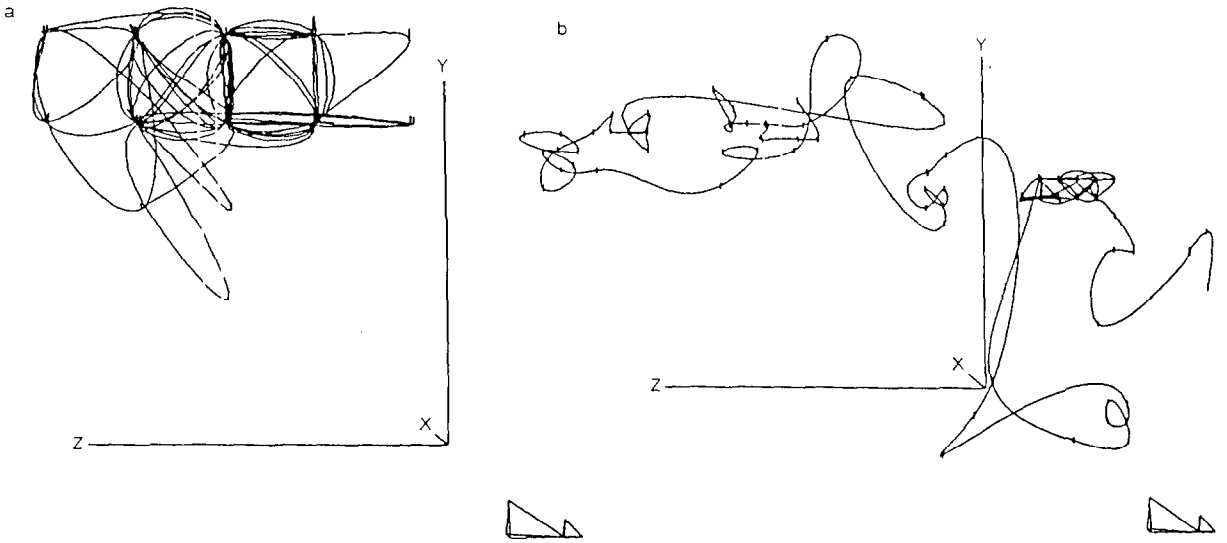

Fig. 2. (a) A three-dimensional plot of the pathway of a pellet acquired with an anaesthetised rat. (b) A three-dimensional plot of the pathway of a pellet acquired with a sedated rat.

troscopy with computer graphics allows rapid data acquisition and a visual representation of transit.

References

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