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ScienceDirect
Journal of Fluorine Chemistry 129 (2008) 137–138
JOURNAL OF FLUORINE CHEMISTRY
www.elsevier.com/locate/fluor

Short communication

^{19}F magnetic resonance imaging using vesicles of sucrose octaoleate-F_{104}

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Received 6 June 2007; received in revised form 19 October 2007; accepted 19 October 2007
Available online 12 November 2007

Abstract

A spin–echo technique is employed to produce high quality *in vitro* ^{19}F magnetic resonance images using vesicles of a highly fluorinated sucrose octaester. The results hold promise for *in vivo* imaging of the gastrointestinal tract.

Keyword : Highly fluorinated sucrose polyester

1. Introduction

It is known [1] that the human lipase enzyme cannot metabolize sucrose polyesters in which more than five of the eight OH groups have been esterified with long-chain fatty acids. Indeed, the commercial non-caloric fat substitute OLESTRA is a mixture of hexa-, hepta- and octaesters of sucrose with a variety of unsaturated and saturated fatty acids [2]. Although no *in vivo* experiments have been done to prove the point, it is very likely that the corresponding fluorinated fatty acid esters will also pass unchanged through the human gastrointestinal tract. Hence these materials may have application in biocompatible delivery systems for magnetic resonance imaging (MRI) of gastrointestinal disorders.

Recently [3], we have synthesized sucrose octaoleate-F_{104} and used it in an emulsion containing egg yolk phospholipid (EYP) to encapsulate hyperpolarized xenon gas. In this work, we explored the possible use of this system *in vitro* as part of an eventual biocompatible *in vivo* delivery systems for hyperpolarized xenon in functional ^{129}Xe MRI [4,5]. The success of hyperpolarized xenon imaging will depend ultimately on the rate of the xenon depolarization, hence long ^{129}Xe spin lattice relaxation times (T_1) are of critical importance. The observed T_1 value in above-mentioned EYP emulsion was 15 s [3], which would appear to present a substantial impediment for the eventual use of such a method for MRI applications.

However, the high fluorine content of sucrose octaoleate-F_{104} and its likely physiological inertness make it an attractive candidate for use as a ^{19}F imaging agent, provided that a biocompatible delivery system can be devised. ^{19}F MRI has been reported previously, in particular the use of perfluorononane as a contrast agent for gastrointestinal imaging has been demonstrated [6]. There is, nevertheless, merit in examining other inert fluorinated imaging agents, since image resolution and sensitivity will depend on the agent employed. A number of vesicles of fat-like molecules have been approved for consumption, namely Intralipid (Pharmacia) in which aqueous suspensions of lipid vesicles of approximately 0.1 μm in diameter can be tolerated by humans and are used clinically as nutrient supplements.

In this work, we have prepared aqueous suspensions of lipid vesicles containing sucrose octaoleate-F_{104} and employed these vesicles to obtain high quality ^{19}F magnetic resonance images *in vitro* in time frames of the order of a few seconds.

Fig. 1 shows a typical image obtained from four scans using the spin–echo method with an echo delay of 6 ms and a repetition time of 1.2 s. The internal diameter of the NMR tube containing the vesicles and the inner glass capillary can be estimated from the dimension bar on the right hand side of the image. With such an intense image and very high planar resolution, it should be possible to employ much smaller concentrations of the imaging agent when working *in vivo*.

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0022-1139/$ – see front matter
doi:10.1016/j.jfluchem.2007.10.008

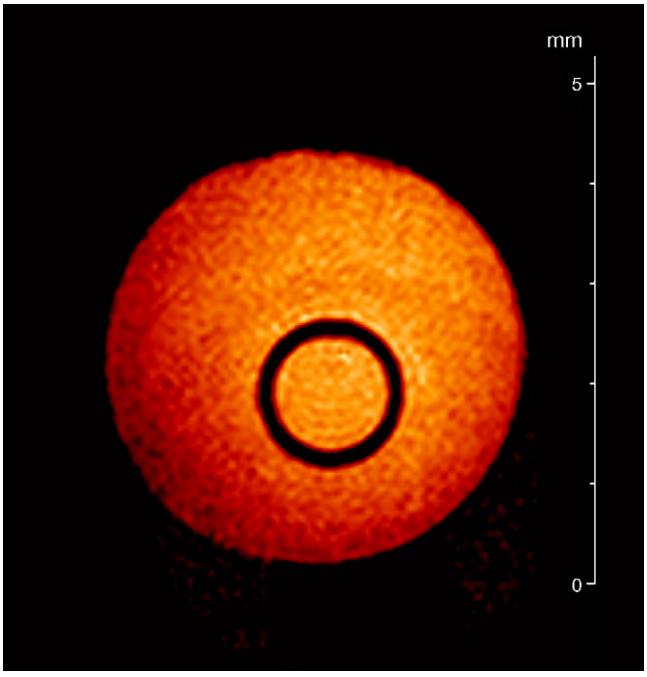

Fig. 1. ^{19}F NMR image of vesicles of sucrose octaoleate-F_{104}, obtained from four scans using the spin–echo technique with echo delay of 6 ms and repetition time of 1.2 s. The internal diameter of the 5 mm NMR tube and the 1 mm capillary tube can be estimated from the dimension bar on the right hand side of the image.

Assuming a density of 1 g/mL for sucrose octaoleate-F_{104} (MW = 4329) its molar concentration in the 1:1 (v/v) aqueous vesicles is approximately 0.12. However, the molar concentration of ^{19}F atoms in the sample is 104 times that, ie.12.5 M. Considering that 1 mm × 1 mm resolution is more than adequate for biological imaging, concentrations which are at least 50 times more dilute than employed in these experiments should be feasible, given the observed signal to noise ratio of 20 in these images. The relatively short spin–lattice relaxation times (T_1 = 0.4–0.5 s) also bode well for potential *in vivo* applications.

2. Experimental

^{19}F images were obtained at a frequency of 376.66 MHz using a Bruker DSX 400 NMR spectrometer equipped with a Micro 2.5 microimaging probe and a 5 mm solenoid coil. A single slice spin–echo sequence with a slice-selective 1 ms gauss-shaped 90° pulse [7] was employed. The frequency was set to the signal of the CF_3 groups which is 81.3 ppm downfield from $CFCl_3$ and is deshielded by *ca*. 25 ppm relative to the nearest CF_2 resonance [8]. Due to the relatively narrow excitation band of the pulse, only minor artifacts from other ^{19}F signals were observed. Echo time and repetition time were 6 ms and 1.2 s, respectively. The images were acquired in a field of view of 10 mm × 10 mm in a matrix of 160 × 160 pixels expanded during Fourier transformation to 256 × 256 pixels. The slice thickness was set to 1 mm with a slice selection gradient of 4.8 G/cm. The in-plane resolution was about 63 mkm with a read-out gradient of 31 G/cm and phase gradient changing between −62 and +62 G/cm. Images were acquired either from a single echo (in this case four accumulations were made) or from multiple echoes (in this case four echoes were added together and only one accumulation was made).

Vesicles of sucrose octaoleate-F_{104} were prepared by sonication of a 1:1 (v/v) mixture of the fluorinated ester and distilled water using a Branson 2510 model sonicator at a temperature of 300 K for 1 h. The vesicles were transferred via syringe to a 5 mm o.d. NMR tube, containing an inner 1 mm o.d. glass capillary. Vesicles were stable for a period of approximately 3 days at 300 K after preparation.

Acknowledgements

GWB thanks the Natural Sciences and Engineering Research Council of Canada (NSERC) for continuing financial support via a Discovery Grant.

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