Behaviour of Calcium Gelled Alginate Beads in Simulated Gastrointestinal Conditions

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INTRODUCTION

Alginates are extremely versatile biopolymers with a wide range of applications used by the food industry for their ability to retain water and for their gelling, viscosifying and stabilising properties (1). More recently the use of alginates and alginate/alginate-chitosan beads controlling release of macromolecules in gastrointestinal environments has been investigated (2, 3, 4, 5). Previous MRI studies have used such beads to investigate antral grinding (6), but they could also provide a model system for studying intestinal grinding. This study aims to investigate the behaviour of gelled alginate beads in physiologically simulated GI conditions, measuring T_2 relaxation, swell ratio, solution pH and tensile strength and records of TEM images and MRI intensity profiles of control and gastric and intestinal phases of simulated digestion.

METHODS Bead Manufacturing: 1.5% alginate DMB powder was added to de-ionised water. Alginate solution was then dripped into 0.37% calcium chloride solution. Solid alginate beads were stored at 5ºC in calcium chloride. Liquid centre beads were made by dripping alginate into calcium chloride solution and leaving for 5 minutes before being washed and stored in 0.05M sodium chloride solution. **Experiments:** 10 grams of alginate beads were placed in 200ml physiological simulated gastric solution (7) for 2 hours with pH being reduced to pH 2 after 15 minutes. The alginate beads were then removed and placed in 200ml simulated intestinal solution (7) for 3 hours. **Swell ratio (SR):** The alginate beads were sieved and weighed every 15 minutes and the SR calculated using $SR = \left(\left(m_f - m_i\right)/m_i\right) \times 100$ where m_i is initial control mass and m_f is final mass. **T_2 Measurements:** T_2 relaxation measurements were recorded every 15 minutes using a 0.252T bench top scanner and a CPMG sequence with 12 refocusing pulses. **Young's Modulus:** The Young's Modulus was calculated using a texture analyser (TA) and modulus calculations (8). **TEM:** Beads were fixed using 0.1% ruthenium tetroxide and epoxy resin and stained using 1% aq. uranyl acetate. 100nm sections, stained in lead citrate were examined using a Jeol 1200 TEM at 100kV. **Bead Profiling:** T_2 maps were acquired on a 3.0T Philips Intera Achieva MR scanner using a TSE sequence with echo spacing 15ms, echo train length 18, double echo sequence TE_1=45, TE_2=240 ms, TR=3000ms, reconstructed matrix 512x512 and slice thickness 1mm. Profiles were calculated using a program written in IDL®. **In Vivo Images**: were obtained using a coronal RARE sequence with 7mm slice thickness, 0.78mm in plane and 320 x 512 acquired matrix reconstructed at 512 x 512.

RESULTS

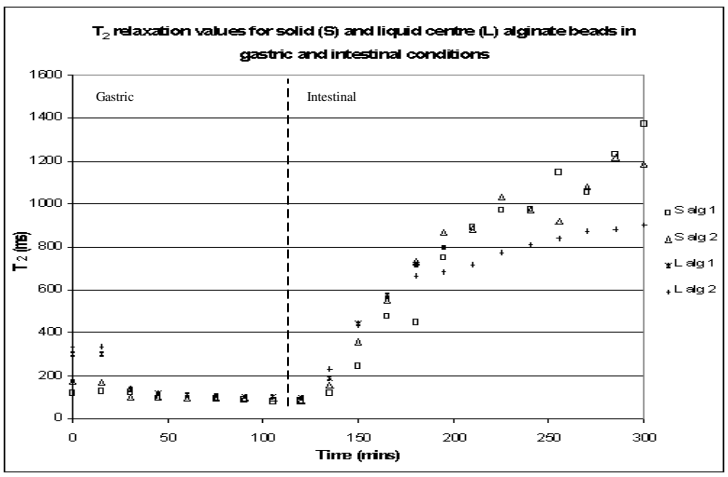

Figure 1. T_2 values

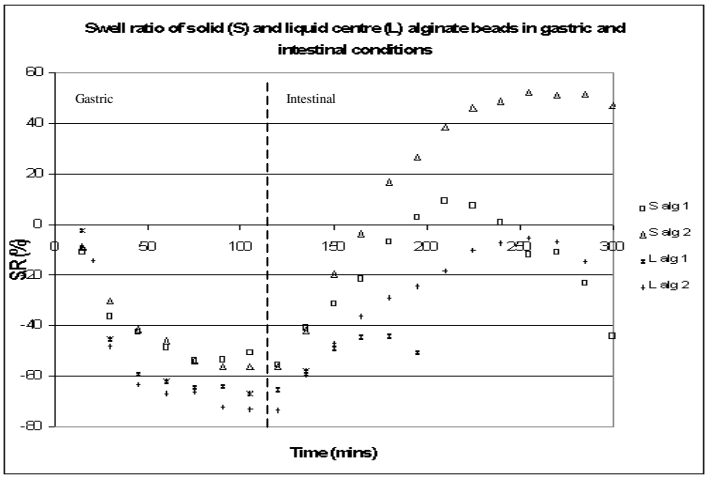

Figure 2. Swell ratios

DISCUSSION AND CONCLUSION

During the gastric phase the both solid and liquid centre alginate beads shrank in size and showed a decreased T_2. TA measurements showed the beads increased in strength as they shrank. When the beads were transferred to intestinal solution they increased in size considerably with increased T_2 due to absorption of the surrounding solution. The solid alginate beads remained intact, but the liquid centre beads started de-gelling during the intestinal phase.. TA results showed the alginate beads became weaker as size increased. TEM images show a closer gel network after the gastric phase and a more open network after the intestinal phase compared to control samples and MRI profiling shows a lower T_2 after the gastric phase and a higher T_2 after the intestinal phase compared to control samples. In conclusion, this study has successfully monitored bead behaviour in vitro using MRI. Figure 3 demonstrates that it will be possible to visualise beads in vivo and hence use the MR proposed to characterise them. Based on this work, future studies will evaluate the use of MRI to determine bead intra-intestinal behaviour in vivo with a view to observing intestinal activities.

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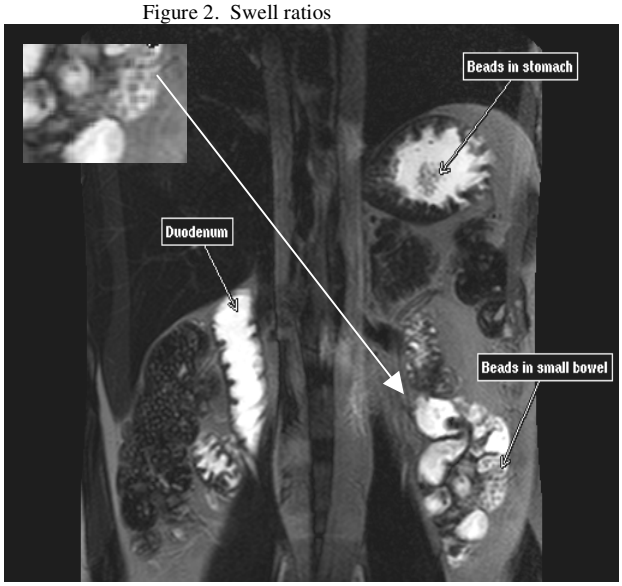

Figure 3. Alginate beads in vivo.