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Biological activity of alginate and its effect on pancreatic lipase inhibition as a potential treatment for obesity

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ABSTRACT

Alginates are classed as a dietary fibre and have been shown to inhibit digestive enzymes *in vitro*, and therefore could be used as an obesity treatment. The current study aims to assess whether alginate in a bread vehicle maintains its inhibition properties despite cooking and digestion, and may therefore be used as a potential treatment for obesity. After 180 min in a model gut that replicates digestion in the mouth, stomach and small intestines alginate bread (AB), control bread (CB), CB with Manucol® DM alginate, free DM alginate and model gut solution were collected. DM, LFR 5/60 and SF200 were heated at 37 °C and 200 °C, with DM also heated at 50, 100 and 150 °C. Samples from the model gut and heated alginate were assessed for molecular size and inhibition properties using viscosity, gel filtration and a lipase turbidity assay. AB does not significantly increase viscosity in the model gut. Viscosity of alginate reduces beyond 100 °C, although alginate retains its inhibition properties up to 150 °C. Cooking into the bread does not reduce the molecular size of the alginate or affect its inhibition properties. These data demonstrate the robustness of alginates lipase inhibition despite the cooking process and digestion. Therefore adding alginate to a bread vehicle may have the potential in the treatment for obesity.

1. Introduction

The World Health Organisation (WHO) recognised obesity as a global epidemic in 1997, and predict that the number of people who are obese and overweight is set to continue to rise (FAO/WHO, 2003). Although the most recognised form of maintaining a healthy weight is to consume a healthy diet and exercise, this is rarely achieved with adherence rates as low as 15% (Ayyad & Andersen, 2000). Alternative weight loss treatments such as pharmaceutical agents and surgery are available, however these treatments are associated with side effects and are not cost effective (Finer, James, Kopelman, Lean, & Williams, 2000; Hadvary, Lengsfeld, & Wolfer, 1988; Pi-Sunyer, 2006; Rich, Rubin, Walker, Schneeweiss, & Abenhaim, 2000).

An alternative treatment which has received considerable interest is dietary fibre, specifically alginate as a potential weight loss treatment (Strugala, Kennington, Campbell, Skjak-Braek, & Dettmar, 2005; Sunderland, Dettmar, & Pearson, 2000; Wilcox, Brownlee, Richardson, Dettmar, & Pearson, 2014). Alginates are present as a matrix polysaccharide in the cell walls of brown algae and consist of (Grasdalen, Larsen, & Smidsrod, 1977). These residues can combine to form G rich (G blocks), M rich (M blocks) or a mixture of G and M. The pattern of residues determines the physicochemical properties of alginate. They are widely used in industry, including adding to foods or beverages as thickening and stabilising agents as reviewed by Brownlee et al. (2005). An additional benefit of alginate is that it is able to form both ionic and acidic gels. This may be a possible mechanism for a reduction in the digestibility of macronutrients and a reduction in hunger seen after consumption of alginates in mixed diets partially because of the viscosity increase caused by gel formation in the stomach at low pH (Draget, Skjåk Bræka, & Stokke, 2005; Ellis, Apling, Leeds, & Bolster, 1981; Seal & Mathers, 2001; Wolf et al., 2002).

Abbreviations: WHO, World Health Organisation; GI, gastrointestinal tract; MO, methyl orange; DB, dextran blue; AB, alginate bread; CB, control bread.

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Previous research using alginate as a potential weight loss treatment added it to a beverage or cereal bar. The benefits reported in these studies include increased satiety, reduced calories consumed, reduced blood glucose and insulin, reduced fat digestion and weight loss. These beneficial physiological effects are countered by a number of problems including poor palatability, products being returned, burping, nausea, flatulence, stomach ache and subjects preferring the control products (Georg Jensen, Kristensen, & Astrup, 2012; Sandberg et al., 1994; Torsdottir, Alpsten, Holm, Sandberg, & Tolli, 1991; Williams et al., 2004). Poor palatability of these products may be due to gel formation and a slimy mouth feel (Ellis et al., 1981). The current study developed alginate-enriched bread in an attempt to overcome these adverse side effects, although the cooking process where temperatures may exceed 180 °C (Hasatani et al., 1991) may alter alginate properties, and in doing so reduce the ability of the alginate to alter the digestion process and inhibit digestive enzymes in the upper gastrointestinal tract (GI).

There are limited data on the properties of the alginate once it has been exposed to heat above 37 °C. McDowell (1977) and Leo, McLoughlin, and Malone (1990) suggested that when polymers are heated at temperatures above 100 °C the alginate structure may depolymerise. McDowell (1977) also indicated that at extreme temperatures in excess of 200 °C complete breakdown of the alginate and a rapid evolution of CO_2 from the uronic acid groups occurs. If these changes occurred during the cooking process the alginates may not retain their inhibitory properties in the upper GI tract. The aim of the current study was to assess whether alginate incorporated into bread retained its viscosity and inhibitory properties after baking. The study used a model gut to digest alginate-enriched bread and assess the physiochemical properties of the digesta and to determine if isolated alginate retained its inhibitory properties.

2. Methods

2.1. Materials

Sepharose 2B, methyl orange (MO), dextran blue (DB), sodium chloride, sodium azide, Tris, methanol, acetone, colipase from porcine pancreas ≥ 95% protein (Prod No: C3028), lipase from porcine pancreas type II 100–500 units/mg protein using olive oil as a substrate (Product No: L3126) and orlistat (tetrahydrolipstatin) were purchased from Sigma–Aldrich (Poole, UK). Aluminium oxide was purchased from Fisher Scientific (Loughborough, UK), and olive oil was purchased from Co-operative Foods (Manchester, UK). Deoxycholic acid sodium salt and taurodeoxycholic acid sodium salt were purchased from Fluka (Buchs, Switzerland). Alginates LFR 5/60 which is a low viscosity and low molecular weight (40,000) sodium alginate rich in guluronate F_g 0.64, SF200 which is a high viscosity and high molecular weight (380,000) sodium alginate rich in guluronate F_g 0.69 and Manucol® DM which is a high viscosity sodium alginate with a molecular weight ranging from 250,000 to 320,000 were a gift from FMC BioPolymer AS, Drammen, Norway and were stored at 4 °C in tightly-sealed containers and all alginate weights were corrected for water content. The control bread (CB) and alginate bread (AB) were produced by Greggs Plc and ingredients are presented in Table 1. The AB was 4% alginate MANUCOL® DM (w/w) wet dough as this made the most palatable bread.

2.2. Model gut procedure

The model gut replicates digestion in the mouth, stomach and the duodenum, which is consistent with criteria set out by Wickham, Faulks, and Mills (2009). In summary 5.2 g of the alginate bread (AB) and control bread (CB) were broken into crumbs ranging between 2 and 4 cm as this amount of bread and conditions that simulates the amount of bread consumed in an individual bite and mastication in the mouth. Samples were then placed into water bath two and mixed at 75 revolutions (rpm)/min for 30 s 50 ml of synthetic gastric juice was added to each sample and mixing continued for 60 min. Following this 25 ml of porcine bile was added and synthetic pancreatic juice was pumped in whilst mixing continued for an additional 120 min. Water baths, enzymes, synthetic solutions and bile were all added fresh and were set at 37 °C throughout the whole process. To ensure the model gut was replicating the pH of in-vivo digestion the pH was monitored throughout the process as previously described (Houghton et al., 2014).

The following experiments carried out:

i) 5.2 g Alginate bread (AB)
ii) 5.2 g Control bread (CB)
iii) 208 mg of MANUCOL DM alginate
iv) 5.2 g CB and 208 mg MANUCOL DM alginate

Model gut solution alone from 180 min was used as a control for all samples. 208 mg of alginate was used as this represents the total amount of alginate contained in 5.2 g of AB.

Table 1
Greggs Plc bread ingredients with or without Manucol® DM alginate at 4% per 100 g.

Regular bread	BF0003-5	
Nutrients per		**100 g**
Energy (kcal)		247
Energy (kJ)		1046
Protein (g)		10.2
Carbohydrates (g)		46.2
	Sugars	1.1
	Starch	45
Fat (g)		1.7
	Saturates	0.5
	Monosaturates	0.3
	Polyunsaturates	0.6
	Trans	0
Dietary fibre (AOAC) (g)		3
Sodium (g)		0.4 (374 mg)
Water (g)		36.8

2.3. Viscosity measurements

Samples i–iv were added at the start of the model gut and the solutions were removed at the end of the model gut (180 min). Samples v was model gut solution from 180 min with 208 mg of Manucol® DM and sample vi was the same solution taken from condition ii from 180 min with 208 mg of Manucol® DM. In samples v and vi the alginate was added upon completion of the model gut procedure. All conditions were compared with model gut solution alone as a control. The heated alginates were measured at 2 mg/ml in distilled H_2O, compared to distilled H_2O alone.

Viscosity was measured using a Contraves low shear 30 viscometer at room temperature over the speed range of 10^{-2}–10^{2} min^{-1}, as previously described (Pearson & Roberts, 2001). Results were expressed as specific viscosity (without units as it was derived from viscosity of the sample divided by the viscosity of the solvent).

2.4. Heating of alginate

5 g of three sodium alginates (LFR 5/60, DM and SF200) with a molecular weight range of 40–380 kDa and a mannuronate:guluronate ratio of 0.44–1.38:1 were heated in pyrex tubes at 37, 100 and 200 °C for 30 min before being cooled to room