THE EFFECTS OF INCREASED BUTYRATE DELIVERED AS BUTYRYLATED STARCH ON LARGE BOWEL PHYSIOLOGY IN THE RAT.

A thesis submitted for the degree of

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by

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Abstract:

Introduction: Short chain fatty acids (SCFA) are produced by large bowel fermentation of dietary carbohydrates including resistant starch (RS) and non-starch polysaccharides (NSP). SCFA (particularly butyrate) play a major role in maintaining large bowel function and may reduce the incidence of colonic disease. Butyrate is the preferred metabolic substrate of colonocytes and is believed to play a key role in modulating epithelial cell cycle, mucosal immune response and gut motility. Increasing large bowel butyrate supply requires intakes of NSP or (RS) much higher than those currently consumed in western diets. Recent studies have shown large bowel butyrate is increased by the ingestion of butyrylated starch but the characteristics and physiological effects of its ingestion in animal models of colonic disease have not yet been investigated.

Aims and Methods: The experiments in *in vitro* and in rats described in this thesis examined: the effects of production techniques and cooking on the capacity of butyrylated starch to deliver butyrate to the large bowel. They investigated the effects of increased butyrate levels on large bowel function in: (i) normal rats, (ii) the dextran sulphate sodium (DSS) rat model of ulcerative colitis (UC) and (iii) the high dietary protein rat model of colonocyte genetic damage.

Results: Starch type, pre-treatment and the degree of butyrylation influenced the *in vitro* digestion and fermentation characteristics of butyrylated starch before and after cooking. Butyrylated starch was less susceptible to small intestinal digestion RS as than high amylose maize starch (HAMS) *in vitro.* Feeding diets containing 10% cooked butyrylated starch delivered significantly greater amounts of butyrate to the large bowel of rats than 10% raw or cooked HAMS. Butyrate did not influence

colonocyte proliferation throughout the large bowel of the rat but increased distal colonic IL-18 concentrations and decreased longitudinal smooth muscle contractility. Feeding HAMS or butyrylated HAMS (HAMSB) to rats during DSS induced UC and during 7 days of recovery resulted in increased mucosal damage compared to low amylose maize starch (LAMS) fed rats. When rats were fed HAMS or HAMSB during the 7 days of recovery only, there was no significant difference in mucosal damage. Genetic damage, as measured by the comet assay, was 2 fold higher in rats fed high protein diet compared with those fed a low protein diet. Concurrent feeding of high protein and either HAMS or HAMSB resulted in significantly less genetic damage. Genetic damage in rats fed 20% HAMSB was half the levels of the 20% HAMS group, and was the same as the low protein diet.

Conclusions: Butyrylated starch delivered butyrate to the large bowel in rats effectively, was less susceptible to small intestinal digestion and had greater stability following cooking than the unmodified base starch. Increased digesta butyrate did not affect large bowel function or colonocyte proliferation in the normal rat; the effects on mucosal damage in the DSS rat model of ulcerative colitis were inconclusive. Increased luminal butyrate prevented high-protein induced colonocyte genetic damage. Butyrylated starches have potential to assist with the maintenance of bowel health and to contribute to reduced risk of colonic disease in the community.

Declaration:

This work contains no material that has been accepted for the award of any degree or diploma in any university or tertiary institution. To the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference has been made in the text.

I give consent for my thesis, when deposited in the library of the University of Adelaide to be available for loan and photocopying.

Balázs Hendrik Bajka

List of Publications:

Peer reviewed publications

Balázs H Bajka, David L Topping, Lynne Cobiac and Julie M Clarke. Butyrylated starch is less susceptible to enzymic hydrolysis and increases large bowel butyrate more than high amylose maize starch in the rat**. British Journal of Nutrition: 2006; 96, 276-282**

Balázs H Bajka, David L Topping, Lynne Cobiac and Julie M Clarke. Acylated Resistant Starches and the Influence of Cooking on Amylolysis *In Vitro* and Short Chain Fatty Acids *In Vivo.* Ed; Hannu Salovaara, Fred Gates and Maija Tenkanen. In **Dietary Fibre – Components & Functions, Wageningen Academic publishers.**

Conference presentations

Balázs H Bajka, David L Topping, Lynne Cobiac and Julie M Clarke. Differential *in vitro* Amylolysis and *in vivo* short-chain fatty acids production of raw and processed resistant starches*.* **Dietary Fibre 2006. Helsinki, June 12-14 2006.**

Balázs H Bajka, David L Topping, Lynne Cobiac and Julie M Clarke. Butyrylated High Amylose Starch Is More Effective Than High Amylose Starch in Preventing Dietary Protein-Induced Colonocyte Genetic Damage in Rats**. 10th European nutrition conference, July 10-14 2007. Ann Nutr Metab 2007;51(Supplement: Suppl. 1):162**.

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