

**Project number:** 6792  
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## Satiety; can cheese play a role?



### Key external stakeholders:

Dairy industry, Cheese producers, Diet Industry, Consumer

### Practical implications for stakeholders:

Healthy foods that increase our feeling of fullness may reduce our food intake and therefore help us manage our weight over time.

- Nine out of ten commercial Irish cheddar cheese significantly increased levels of the satiety hormone, GLP-1, from specialised gut cells cultured in the lab.
- 32 Volunteers who consumed Irish cheddar cheese, as a snack, had increased levels of GLP-1 in their blood.
- Regular consumption of cheese as a snack may increase our feeling of fullness

### Main results:

The key results were:

- At 4, 6, 8, and 10 months ripening, 9 Irish cheddar cheese samples increased levels of the satiety hormone, GLP-1, from specialised gut cells.
- The most potent cheese sample (>50 fold increase in GLP-1), when fed to mice reduced the amount of food they ate compared to those who received a control cheese.
- This bioactivity was not due to amino acids or flavour compounds.
- A follow up human trial found that volunteers who consumed this cheese as a snack, had higher GLP-1 levels circulating in their blood than those who consumed a scone or egg snack.

### Opportunity / Benefit:

Cheddar cheese consumed as a snack may increase the feeling of fullness and thus offers industry a new marketing strategy for cheese in the snack food sector.

### Collaborating Institutions: UCD

**Teagasc project team:** Dr. Linda Giblin (PI)  
Dr. Tom Beresford  
Dr. Alina Kondrashina  
Dr. Sanja Seratlic

**External collaborators:** Dr. Aifric O'Sullivan (UCD)

### 1. Project background:

Evidence from epidemiological and intervention studies indicate that consumption of dairy foods can increase feelings of fullness. Feelings of fullness are complex and are governed by a range of signals including stomach expansion and satiety hormone production from specialized cells located in the gut (enteroendocrine). Dairy proteins can interact with these enteroendocrine cells to influence satiety hormone levels. Certainly cleavage of milk proteins in the course of cheese manufacture and ripening will result in the generation of peptides, many of which undoubtedly exhibit satiating effects. In this study, we screened commercial Irish cheddar cheese at 2, 4, 6, 8 and 10 months ripening for their ability to increase secretion of the satiety hormone GLP-1 from the enteroendocrine cell line, STC-1.

### 2. Questions addressed by the project:

Can Irish cheddar cheese increase satiety hormone production (GLP-1, PYY, CCK) from enteroendocrine cells?

Can ripening time influence it's satiating effect?

What components in Irish cheese have a satiating effect?

Can Irish cheese have a satiety effect, if consumed as a snack?

### 3. The experimental studies:

Ten commercial Irish cheddar cheese at 5 different ripening times (n=50 test samples) were sourced from FHI industry partners. Macronutrient composition analysis was performed and water soluble extracts (protein component) prepared. STC-1 cells were exposed for 4 hours to test samples (10mg/ml) and levels of secreted active GLP-1, PYY mRNA transcript and CCK mRNA transcript measured. Total protein content, amino acid composition and volatile compound analysis were performed. A cumulative food intake study was performed in mice (n=10) who were fed 750mg/kg body weight of the most potent test sample. A simulated gastrointestinal digestion was performed to track the fate of bioactivity, as the test sample transited the upper gut. In a double blinded, cross over study, 32 healthy male volunteers consumed this cheese or alternatively egg or scone (isocaloric and macronutrient controlled) as a snack. Blood samples were taken at various times over a 6 hour period to measure post-prandial glucose, insulin and GLP-1 levels. Appetite ratings and amount of food consumed at the next meal were also recorded.

### 4. Main results:

Significant increases in GLP-1 were observed at 2 months ripening for 4 cheese samples, at 6 months ripening for 7 samples and at 10 months ripening for 9 samples compared to control ( $p < 0.05$ ). The largest increase in mean GLP-1 secretion was observed for water soluble extracts between 4 to 8 months ripening. The most potent sample, C2-WSE-8M, dose dependently (1-25mg/ml) increased GLP-1 (4.73ng/ml to 35ng/ml) from STC-1 cells. PYY and CCK levels in STC-1 cells were not altered by incubation with C2-WSE-8M. Amino acid composition nor volatile compounds were correlated with GLP-1 bioactivity. C57BL/6 mice (n=10 male mice, 12-13 weeks old) that received 750mg C2-WSE-8M per kg body weight by oral gavage ate less at 6 hours compared to those who received a control cheese (C6-WSE-8M). However there was no effect on cumulative food intake. Simulated gastrointestinal digestion revealed bioactivity was significantly reduced in the gastric phase over 90 mins and complete lost within 15 mins of C2-WSE-8M entering the duodenal phase. In parallel, post-prandial levels of GLP-1 were significantly higher with 50g of this cheese, 4 hours post-consumption compared to egg or scone. However, the participants did not report differences in appetite ratings nor did they eat less at the next meal. Taking this data together with food intake data from the mouse trial allowed us to conclude that enteric protection is needed to maximize the satiating effect of water soluble extracts of cheese.

### 5. Opportunity/Benefit:

There are considerable commercial opportunities for scientifically-substantiated satiety-enhancing foods. 8-24% of European men and 10-35% of European women are obese. With obesity figures soaring worldwide, including in Ireland, its cost to health, the health services and the economy is incalculable. Identifying bioactives that alter the satiety hormonal milieu, with associated changes in several of the signals known to affect appetite, may aid in the reduction of food intake. This study revealed that the majority of Irish cheddar cheese increased satiety hormone production in vitro. In particular one cheese, at 8 months ripening, increased GLP-1 production by a remarkable 50 fold. However, to protect this bioactivity from the hydrolytic conditions of the gut, some degree of enteric protection will be required.

## 6. Dissemination:

A final summary of these results have been shared with FHI Industry partners on 24 Jan 2019, Portlaoise, Ireland.

### Main publications:

Kondrashina, A., Seratlic, S., Kahil, D., Cryan, J.F., Schellekens, H., Beresford, T. and Giblin L. (2018) 'Irish Cheddar cheese increases GLP1 secretion in vitro but bioactivity is lost during gut transit'. *Food Chemistry* 265: 9-17.

Chen, Z., Kondrashina, A., Greco, I., Gamon, L.F., Lund, M.N., Giblin, L. and Davies, M.J. (2019) 'Effects of Protein-Derived Amino Acid Modification Products Present in Infant Formula on Metabolic Function, Oxidative Stress and Intestinal Permeability Using Cell Models.' *Journal of Agriculture and Food Chemistry* in press.

Kondrashina, A., Papkovsky, D. and Giblin, L. (2018) 'Physiological Gut Oxygenation Alters GLP-1 Secretion From the Enteroendocrine Cell Line STC-1'. *Molecular Nutrition and Food Research* 62 (3): 1-8.

Kondrashina, A., Bruen, C., McGrath, B., Murray, B., McCarthy, T., Schellekens, H., Buzoianu, S., Cryan, J.F., Kelly, A.L., McSweeney, P.L.H., Lawlor, P. and Giblin, L. (2018). 'Satiating effect of a sodium caseinate hydrolysate and its fate in the upper gastrointestinal tract'. *Journal Functional Foods* 49: 306-313.

O'Halloran, F., Bruen, C., McGrath, B., Schellekens, H., Murray, B., Cryan, J.F., Kelly, A.L., McSweeney, P.L.H. and Giblin L. (2018) A casein hydrolysate increases GLP-1 secretion and reduces food intake. *Food Chemistry* 252: 300-310.

McCarthy, T., Bruen, C., O'Halloran, F., Schellekens, H., Kilcawley, K., Cryan, J.F. and Giblin, L. (2017): 'Aroma compound diacetyl suppresses glucagon-like peptide-1 production and secretion in STC-1 cells'. *Food Chemistry* 228: 35-42.

Giblin, L., McGrath, B.A., Murray, B.A., le Roux, C.W., Docherty, N.G., McSweeney, P.L., Kelly, A.L. (2017): 'Letter to the Editor Regarding Equivalent Increases in Circulating GLP-1 Following Jejunal Delivery of Intact and Hydrolysed Casein: Relevance to Satiety Induction following Bariatric Surgery'. *Obesity surgery* 27(3): 816.

### Conferences:

Kondrashina, A., (2018) 'Satiety and Cheese'. 21st March, Padjadjaran University, Bandung, Indonesia.

Kondrashina, A., Seratlic, S., Kandil, D., Cryan, J.F., Schellekens, H., Beresford, T. and Giblin, L. (2017) 'Appetite's secret ingredient'. *Advances in Nutritional Dairy Products & Ingredients Conference*, 10-12 April, Cork, Ireland.

Kondrashina, A., Seratlic, S., Kandil, D., Cryan, J.F., Schellekens, H., Beresford, T. and Giblin, L. (2017). 'Irish cheddar cheese increases GLP-1 secretion in vitro and reduces food intake in vivo'. *European Congress on Obesity*, 17-20 May, Porto, Portugal.

Kondrashina, A., Seratlic, S., Kandil, D., Treguier, N., Cryan, J.F., Schellekens, H., Beresford, T. and Giblin, L. (2018): 'Irish Cheddar cheese: satiety bioactivity and survival during gut transit'. *Cheese symposium*, 3-6 April, Rennes, France.

Giblin, L., Kondrashina, A. and Brodtkorb, A. (2019) 'Full for longer: can dairy peptides play a role in satiety?' 2nd international symposium on bioactive peptides, Invited speaker. 22-24 May, Valencia, Spain.

### Popular publications:

Giblin, L., Kondrashina, A., O'Sullivan, A. (2018) 'Satiety – Can dairy play a role?' *Dairy Nutrition Forum* 10 (2): 1-4.

## 7. Compiled by: Linda Giblin