

## Evaluating the effects of various food ingredients on gallbladder contraction

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**Background:** Gallbladder contraction is coordinated with gastric emptying and the delivery of nutrients to the duodenum [1], which initiate the powerful gut hormone signalling response. The release of bile into the gut plays an important role in digestion of fat and therefore of cholesterol regulation. Different food ingredients can trigger gallbladder contraction but which food ingredients are most effective in contracting the gallbladder and at which dose level is not well understood.

**Aim:** To identify the food ingredient that causes maximum gallbladder contraction and subsequently to carry out a dose-response study of the effect of the chosen food ingredient on gallbladder contraction using MRI.

**Methods:** The study was approved by the local Ethics Committee and all subjects gave informed written consent. At T = 0 min, subjects consumed the test product. Coronal RARE images (30 Slices, in-plane resolution 1.5 x 2.5 mm<sup>2</sup>, slice thickness 6 mm) were acquired on a 1.5 T Philips Achieva whole body scanner using a whole body T/R coil. Data acquired prior to consumption of a test product (T = -5 min) and again at T = 5, 15, 25, 35, 45, 55, 65 minutes post ingestion in order to measure the change in gallbladder volume.

**Phase A:** 8 healthy subjects (5M/3F, mean age 26.5 ± 0.8 yrs, BMI 22.5 ± 0.6 kg/m<sup>2</sup>) consumed 1 of 10 test products, randomly assigned and blinded, during each of 10 separate visits. Test Products: **A:** 25ml dairy emulsion (1.38g fat), **B:** 25ml dairy emulsion + 300mg potato protease inhibitor (1.38g fat), **C:** 67.5g yogurt drink (1.48g fat), **D:** 67.5g yogurt drink + 3g protein (1.5g fat), **E:** 67.5g yogurt drink + 80mg curcumin (1.48g fat), **F:** 250ml coffee (0g fat), **G:** 250ml tea (0g fat), **H:** 250ml semi-skimmed milk (4.5g fat), **I:** 20ml high fat emulsion (10g fat), **J:** 4ml high fat emulsion (2g fat).

**Phase B:** 22 healthy subjects (11M/11F, mean age 22 ± 1 yrs, BMI 22.5 ± 0.4 kg/m<sup>2</sup>) consumed 1 of 4 test products, randomly assigned and blinded, during each of 4 separate visits. Test Products: 150ml milk based drink containing 9g protein, and either 1.5, 3.5, 6.5 or 10 g fat. Blood samples were also collected immediately after each scan to measure plasma cholecystokinin (CCK) levels.

**Results:** **Phase A:** Fig. 1 shows the maximum % gallbladder contraction between T = 5 and 65 min for meals A-J. Meal I (20ml high fat emulsion) yielded the largest gallbladder contraction (42%) and this was significantly larger than all other test products (RM-ANOVA with Dunnett's multiple comparison, p<0.05) apart from Meal H (250ml milk, 41% contraction, p>0.05) and Meal J (4ml high fat emulsion, 27% contraction, p>0.05). Comparing drinks with equal volumes, showed milk (H) achieved a significantly higher maximum gallbladder contraction than coffee (F, 22%) and tea (G, 18%) (RM-ANOVA with Bonferroni, p<0.05 for both).

**Phase B:** Fig. 2 shows the maximum % gallbladder contraction and the maximum plasma CCK levels between T = 5 and 65 min for each level of fat. The milk drinks containing 6.5 and 10 g fat achieved significantly higher maximum % gallbladder contraction (RM-ANOVA with Dunnett's multiple comparison, p<0.01 for both) and higher maximum plasma CCK levels (Friedman's paired test with Dunnett's multiple comparison, p<0.05 for both) than the 1.5g fat milk drink. The maximum % gallbladder contraction and the maximum plasma CCK levels were highly correlated (Spearman's rank, p<0.0001).

**Discussion:** Serial MRI was an effective, non-invasive and accurate way of monitoring the effects of various food products on gallbladder contraction. In phase A, the high fat emulsion and semi-skimmed milk stimulated the highest gallbladder contraction. This can be explained with current knowledge on fat digestion and duodenal feedback. The amount of gallbladder contraction appeared to be fat-dose dependent: a small amount of fat (2g in the 4 ml high fat emulsion, J) achieved a 27% gallbladder contraction. Semi-skimmed milk performed very well but it was difficult to discriminate whether its composition in fat (4.5g) and protein (9g) had an additive effect in contracting the gallbladder. Due to the different volume, taste/aroma, colour and texture of the samples in phase A, a cephalic component of gallbladder contraction could not be excluded and therefore the milk-based products in phase B were as equal in volume/texture/flavour/colour as possible, whilst only varying the amount of fat. As predicted, increasing the fat content resulted in an increased maximum % gallbladder contraction, which was reflected in the increased plasma CCK levels seen in phase B.

**Conclusion:** Phase A showed that the high fat emulsion and semi-skimmed milk, which had the highest fat content, were the best food ingredients for stimulating gallbladder contraction, indicative of a dose response, which was subsequently probed in phase B using a milk based drink. The 1.5g fat milk drink achieved a maximum percentage gallbladder contraction of 33%, which was significantly different to the 6.5g and 10g fat meals (45% and 47% respectively) showing a dose response of fat content on the maximum % gallbladder contraction and correlating with elevated plasma CCK levels, which mediate gall bladder emptying.

**References:** [1] Marciani et al JMRI 2005; 21:82-85 **Acknowledgements:** We thank McNeil Nutritionals, LLC for their funding.

