

## DO ARTIFICIAL SWEETENERS AFFECT BLADDER CONTRACTION?

### Hypothesis / aims of study

An epidemiological study by the Leicestershire MRC Incontinence Programme (1) found daily consumption of carbonated soft drinks to be independently associated with the onset of OAB symptoms in the next twelve months (OR 1.62, 95% CI 1.18, 2.22). We therefore investigated the hypothesis that artificial sweeteners, which are important constituents of carbonated soft drinks, modulate detrusor muscle function.

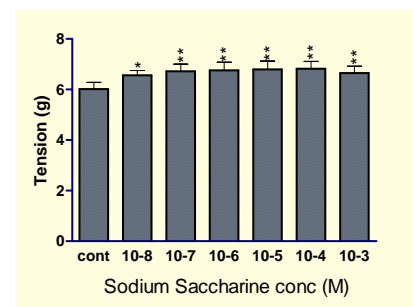
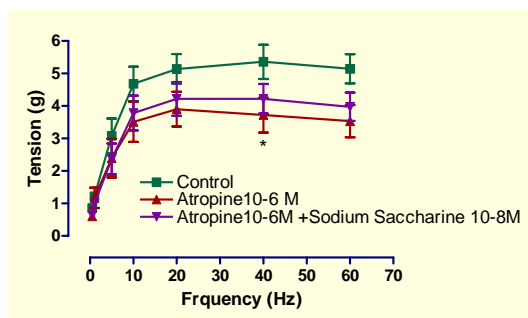
### Study design, materials and methods

Bladders were removed from male and female Wistar rats (150g-300g) which have been culled in accordance with schedule 1 procedure of the Animal (Scientific Procedures) Act 1986. Bladder muscle strips were suspended in an organ bath perfused with Krebs's solution at 37°C aerated with 95% oxygen and 5% carbon dioxide. The apex of the muscle strip was attached to an isometric transducer connected to a four-channel oscillograph. Electrical field stimulation (EFS) was delivered by platinum electrodes recessed within the organ bath chamber and connected to a Harvard Dual Impedance Research Stimulator. The effect of increasing concentrations ( $10^{-8}$  M –  $10^{-2}$  M) of aspartame, sodium saccharine and acesulfame K on the contractile response to a single frequency (10 Hz) of electrical field stimulation was determined. Those concentrations of sweetener found to significantly affect the contraction of rat bladder muscle to 10 Hz were further investigated for their effect on the frequency response curves to electrical field stimulation (0.5 Hz to 60 Hz), in the presence and absence of atropine  $10^{-6}$  M. The effects of these sweeteners on responses to carbachol ( $10^{-8}$  M –  $10^{-4}$  M) were also determined.

Statistical analysis was determined by using ANOVA repeated measures; Wilcoxon matched pairs and Students t test where appropriate. A value of  $p < 0.05$  was considered significant.

### Results

Sodium saccharine and acesulfame k ( $10^{-8}$  M -  $10^{-3}$  M) both significantly enhanced the contractile response of rat detrusor muscle to 10 Hz EFS by 9%, 11.6%, 12.4%, 13%, 13.4%, 10.5% ( $p < 0.01$ ) and 7%, 8.6%, 8.1%, 8.83%, 10%, 10.4%, 11.4% ( $p < 0.01$ ) respectively, compared to control (Fig.1). Sodium saccharine  $10^{-8}$  M increased the maximum response of rat bladder muscle to 40Hz EFS by 10% compared to control and also the atropine resistance response to EFS was increased by 14% (Fig. 2). Sodium saccharine  $10^{-7}$  M had little effect on the carbachol dose response curve although the maximum response was enhanced by 5%. Acesulfame K  $10^{-8}$  M enhanced the maximum contractile response to EFS by 9% and also the atropine resistant response to EFS by 7.5%. The carbachol evoked response was also enhanced by 7.3% in the presence of acesulfame K  $10^{-7}$  M. Aspartame  $10^{-7}$  M had little effect on the atropine resistant response to EFS although the maximum response to EFS in the presence of atropine was enhanced by 5.6%. Aspartame  $10^{-7}$  M also slightly enhanced the maximum response to the frequency response curve by 4.5%. The maximum contractile response to carbachol was however significantly increased by 11% ( $p < 0.05$ ) in the presence of aspartame  $10^{-8}$  M.



### **Interpretation of results**

Sodium saccharine, acesulfame K, and to a lesser degree aspartame, significantly enhanced the amplitude of the contractile response of rat bladder muscle.

The mechanism for this appears to be via an effect on the atropine resistant response to EFS, now known as the purinergic component, which is activated by ATP released from the nerves. Aspartame appears to have more of an enhancing effect on the contractile response to carbachol indicating either a receptor effect or an effect on intracellular calcium movement.

### **Concluding message**

These sweeteners are found in abundance in many foods and soft drinks. It is therefore possible that sweeteners, and other components of soft drinks, may have direct effects on bladder function as demonstrated so far in our study. The likely concentration of these substances in the human bladder and their effect in vivo remains to be determined.

### **References**

1. The association of diet and other lifestyle factors with overactive bladder and stress incontinence: a longitudinal study in women. [Journal Article] BJU International. 92(1): 69-77, 2003 Jul.