

Transient Receptor Potential Channel M8 (TRPM8) Antagonist Inhibits Cold-stress and Menthol Induced Detrusor Overactivity in Conscious Rats

Introduction and Objective: We showed that low temperature exposure or menthol spray induced detrusor overactivity in conscious rats. This study determined if transient receptor potential channel M8 (TRPM8) antagonist (BCTC) could inhibit the cold-stress and menthol induced detrusor overactivity.

Materials and Methods: Thirty female 10-weeks Sprague-Dawley (SD) rats were cannulated. At 2 days after, cystometric investigation for cold-stress responses of the unanesthetized rats were performed at room temperature (RT, $27\pm 2^{\circ}\text{C}$) for 20 min, and at low temperature (LT, $4\pm 2^{\circ}\text{C}$) for 20 min. Ten minutes before transferring to LT, the rats were intravenously administrated with 0 (control), 2, 20, or 200 μM /200g-body weight BCTC ($n=6$ in each dose). Cystometric investigations for menthol responses of other 6 rats were performed at only RT. Legs of the rats administrated with saline were sprayed with 90% menthol. Thirty minutes after first menthol spraying, the rats were administrated with 200 μM -BCTC, and then secondly sprayed. During these cystometric investigations, the micturition parameters were recorded.

Results: After transferring to LT, the voiding interval and bladder capacity of control and 2 μM -BCTC administrated rats were significantly decreased (Table 1). However, 20 or 200 μM -BCTC administrated rats did not show decreases of the voiding interval and bladder capacity induced by cold-stress (Table 1). The voiding interval and bladder capacity of the saline-administrated rats were decreased with spraying menthol (from 4.76 ± 0.42 to 2.19 ± 0.22 min, from 0.88 ± 0.09 to 0.44 ± 0.03 ml, respectively). However, the voiding interval and bladder capacity of the 200 μM -BCTC administrated rats were not decreased with spraying menthol (5.68 ± 0.57 min and 1.01 ± 0.10 ml, respectively).

Conclusions: Voiding interval and bladder capacity of high dose BCTC-administrated rats were not decreased by cold-stress and menthol spraying. Therefore, TRPM8 antagonist, BCTC partially inhibited cold-stress and menthol spraying induced detrusor overactivity.

Table 1. Voiding interval and bladder capacity of BCTC-administrated rats at RT and LT

	0 μM BCTC (Control)		2 μM BCTC		20 μM BCTC		200 μM BCTC	
	RT	LT	RT	LT	RT	LT	RT	LT
Voiding interval (min)	4.57 ± 0.21	$2.20\pm 0.16^*$	4.56 ± 0.49	$1.59\pm 0.17^*$	3.21 ± 0.27	3.52 ± 0.55	3.49 ± 0.66	4.26 ± 0.35
Bladder capacity (ml)	0.84 ± 0.04	$0.42\pm 0.02^*$	0.77 ± 0.08	$0.28\pm 0.03^*$	0.57 ± 0.06	0.65 ± 0.10	0.61 ± 0.10	0.74 ± 0.06

* $P<0.01$, compared to RT in each dose.