

## THE EFFECT OF CAPSAICIN ON FLUID AND ELECTROLYTE TRANSPORT IN RAT ILEUM

WATCHARAT LIMRATANA,<sup>a</sup> BOONTIUM KONGSAKTRAKOON<sup>a</sup> and KAJIT RUNGSRIAWAD<sup>b</sup>

- a. *Department of Physiology, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand.*
- b. *Department of Clinical Chemistry, Faculty of Associated Medical Sciences, Khon Kaen University, Khon Kaen 40002, Thailand.*

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### Abstract

*The effect of capsaicin on intestinal net fluid and electrolyte transport was studied in the ileum of anaesthetized rats. The loop of the mid ileum was instilled with fluid in two consecutive 30-min periods. The control group was instilled with saline-bicarbonate solution in both periods. The three test groups were instilled with saline-bicarbonate solution containing capsaicin at concentrations of 0.14 or 0.21 or 0.28 mg/ml in the first period and instilled with saline-bicarbonate solution in the second period. The net transport of fluid, Na<sup>+</sup>, Cl<sup>-</sup> and HCO<sub>3</sub><sup>-</sup> of each tested group was compared with that of the control. The results of this study indicate that capsaicin can cause an augmentation in net fluid, Na<sup>+</sup> and HCO<sub>3</sub><sup>-</sup> absorption while it has no effect on net Cl<sup>-</sup> transport.*

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Capsaicin is the active principle responsible for the pungent and irritating effect of hot paprika or chilli peppers. Actions of capsaicin on cardiovascular, respiratory and neurophysiological functions have been communicated<sup>1</sup>. The effects of capsaicin on the gastrointestinal system have also been studied. It has been reported that capsaicin contracts isolated guinea-pig ileum<sup>2</sup>. Augmentation in gastric acid secretion and mucosal blood flow in the rat by capsaicin has been reported<sup>3</sup>. It has been shown that capsaicin produces exfoliation of the gastric and duodenal epithelial cells<sup>4-6</sup>. There are studies demonstrating that capsaicin inhibits the absorption of glucose, sodium and water of the everted jejunal sac of hamster and rat when capsaicin is added in the mucosal solution<sup>7,8</sup>. It has been suggested that capsaicin reduces the ATP content and Na<sup>+</sup>-K<sup>+</sup>-ATPase activities of the intestinal mucosal cells<sup>7,9</sup>. Our previous study by instillation of 0.10 mg/ml capsaicin in normal saline solution in the ileum of anaesthetized rats found that absorption of water was slightly increased (unpublished observations). The purpose of this study was to test

whether capsaicin could stimulate water and ion absorption in the ileum of anaesthetized rats when capsaicin was placed in the ileum.

Male white rats weighing 220-270 g were fasted 18-24 hrs before the experiment with free access to water. Anaesthesia was induced with 20% urethane i.p. (0.2 g/100 g body weight). The trachea was cannulated and the abdominal cavity was opened by midline incision. The ileum was flushed with warm isotonic saline then a loop of mid ileum about 15 cm in length was tied at both ends. A polyethylene catheter with a stopcock was intubated at the oral end and the abdominal contents replaced. The abdominal wall was closed with the stopcock outside and the rat allowed to lie on its side.

Rats were divided into one control and three tested groups; 6 animals in each group. The experiment was designed to use two 30-min periods. The control group was instilled in both periods with saline-bicarbonate solution (pH 7.6) which contained  $\text{Na}^+$  150 mM,  $\text{Cl}^-$  125 mM,  $\text{HCO}_3^-$  25 mM and 10 mg/ml polyethylene glycol (PEG, mol.wt. 4000) as a non-absorbable marker. The test groups were instilled in the first period with a test solution which had the same composition as the control solution but contained capsaicin at a concentration of 0.14 or 0.21 or 0.28 mg/ml. (Capsaicin was purified capsaicin grade I purchased from Sigma Chemical Co. St. Louis, MO, USA) In the second period, every tested group was instilled with saline-bicarbonate solution.

The solution, warmed to 38°C, was measured to 4 ml in a 5-ml syringe. Three ml were infused into the loop via the catheter and then withdrawn back. This maneuver was performed twice and 3 ml were instilled while one ml was kept for analysis. Thirty minutes after the instillation, all of the luminal fluid was removed and kept. The loop was washed twice with warm isotonic saline and the solution of the second period was instilled by the same procedure as in the first period. At the end of the second period the fluid was removed and the loop was stripped free from the mesentery and its length measured to the nearest centimeter. Fluids collected were analysed for  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Cl}^-$  and  $\text{HCO}_3^-$  (Electrolyte Analyser Model E4A, Beckman Instruments), and PEG<sup>10</sup>. The luminal fluid volume was estimated<sup>10</sup>, and net transport rates of water,  $\text{Na}^+$ ,  $\text{Cl}^-$  and  $\text{HCO}_3^-$  were measured. Two-factor analysis of variance was used to determine the difference in net water and net ion transport between the four groups. Rates of transport in periods 1 and 2 of each tested group were compared with the rate in the corresponding period of the control group. The difference in transport rates between periods 1 and 2 was tested by Student's t-test for paired data (Table 1).

There were significant differences in water absorption rates in the four groups (F ratio = 4.419,  $P < 0.01$ ). Absorption in period 1 of the group tested with 0.14 mg/ml capsaicin was significantly higher than that of the control (Table 1). Water absorption in period 2 (without capsaicin) was not significantly different from the rate in period 2 of the control group, and the rate in period 2 of this group was significantly lower than the rate in period 1. Water absorption in period 1 of the group with 0.21 mg/ml capsaicin was

**TABLE 1** NET ABSORPTION OF WATER ( $\mu\text{l}/\text{cm}/\text{hr}$ ), AND OF IONS ( $\mu\text{mol}/\text{cm}/\text{hr}$ ) OF THE CONTROL GROUP (INSTILLED WITH SALINE-BICARBONATE SOLUTION IN BOTH PERIODS) AND CAPSAICIN TESTED GROUPS (INSTILLED WITH SALINE-BICARBONATE SOLUTION CONTAINING CAPSAICIN IN PERIOD 1, SALINE-BICARBONATE SOLUTION IN PERIOD 2). VALUES ARE MEAN  $\pm$  SE OF 6 ANIMALS IN EACH GROUP.

Group	Period 1	Period 2
<b>WATER</b>		
Control	62.84 $\pm$ 8.08	59.46 $\pm$ 7.65
0.14 mg/ml	96.10 $\pm$ 9.92 <sup>a</sup>	67.59 $\pm$ 9.69 <sup>b</sup>
0.21 mg/ml	80.92 $\pm$ 9.00	103.49 $\pm$ 8.18 <sup>a,b</sup>
0.28 mg/ml	94.54 $\pm$ 11.49 <sup>a</sup>	77.50 $\pm$ 7.73 <sup>b</sup>
<b>SODIUM</b>		
Control	9.64 $\pm$ 1.31	8.42 $\pm$ 1.17
0.14 mg/ml	16.08 $\pm$ 1.33 <sup>a</sup>	10.65 $\pm$ 1.38 <sup>b</sup>
0.21 mg/ml	12.52 $\pm$ 1.30 <sup>a</sup>	14.88 $\pm$ 1.16 <sup>a</sup>
0.28 mg/ml	15.63 $\pm$ 1.86 <sup>a</sup>	12.08 $\pm$ 1.87 <sup>a,b</sup>
<b>CHLORIDE</b>		
control	6.57 $\pm$ 1.77	5.51 $\pm$ 1.44
0.14 mg/ml	9.17 $\pm$ 2.15	5.54 $\pm$ 1.83
0.21 mg/ml	6.71 $\pm$ 1.33	8.34 $\pm$ 0.86
0.28 mg/ml	9.46 $\pm$ 2.53	7.68 $\pm$ 2.16
<b>BICARBONATE</b>		
Control	2.20 $\pm$ 0.78	1.85 $\pm$ 0.69
0.14 mg/ml	5.70 $\pm$ 1.06 <sup>a</sup>	4.62 $\pm$ 0.88 <sup>a,b</sup>
0.21 mg/ml	5.33 $\pm$ 0.31 <sup>a</sup>	5.08 $\pm$ 0.31 <sup>a</sup>
0.28 mg/ml	5.74 $\pm$ 1.23 <sup>a</sup>	4.43 $\pm$ 1.21 <sup>a,b</sup>

<sup>a</sup> P < 0.05 capsaicin vs. control in the corresponding period;

<sup>b</sup> P < 0.05 period 1 vs. period 2

found to be higher than that of the control but not statistically significant. Absorption in period 2 was significantly higher than that of the control group. The absorption rate in period 2 was significantly higher than the rate in period 1. The group instilled with 0.28 mg/ml capsaicin had significantly higher rate of water absorption than the control group in period 1, while the rate in period 2 was not significantly different from that of the control. The absorption rate in period 2 of this group was significantly lower than the rate in period 1.

Sodium absorption rates of the four groups were significantly different (F ratio = 5.325,  $P < 0.01$ ). The rates of sodium absorption in period 1 of every capsaicin group were significantly higher than the rate in this period of the control (Table 1). In period 2, the 0.14 mg/ml capsaicin group absorbed sodium as equal as the control, whereas the 0.21 and 0.28 mg/ml capsaicin groups absorbed sodium at the rates higher than the control. When comparing the absorption rate in period 1 with period 2, there was a significant difference in the groups tested with 0.14 and 0.28 mg/ml capsaicin.

There was no statistically significant difference in the absorption rates of chloride of the four groups. Thus it was concluded that capsaicin at concentrations from 0.14 to 0.28 mg/ml, when instilled in the ileum of anaesthetized rats, had no any effect on net chloride transport.

Rates of bicarbonate absorption of the four groups were significantly different (F ratio = 6.370,  $P < 0.01$ ). Bicarbonate absorption in both period 1 and period 2 in all of the capsaicin groups was significantly higher than that of the control in the corresponding period. The 0.14 and 0.28 mg/ml capsaicin groups showed less bicarbonate absorption in period 2 than in period 1.

The results indicated that in the presence of 0.14 mg/ml and 0.28 mg/ml capsaicin in the ileum of anaesthetized rats, water absorption was stimulated. Stimulation of  $\text{Na}^+$  and  $\text{HCO}_3^-$  absorption was found when 0.14, 0.21 and 0.28 mg/ml capsaicin were instilled in the loop. Interestingly, in the post capsaicin period, augmentation of net water absorption was found in the 0.21 mg/ml capsaicin group, of  $\text{Na}^+$  absorption in the 0.21 and 0.28 mg/ml capsaicin groups and of  $\text{HCO}_3^-$  absorption in every group. These results may reflect the sustained effect of capsaicin.

The present finding is different from that of Monsereenusorn who experimented in everted jejunal sac and found that 0.14 mg/ml capsaicin inhibited fluid and sodium absorption of the rat and hamster<sup>8</sup>. Differences in the region or/and in the method of investigation may account for the discrepancy.

Limlomwongse et al. found that synthetic capsaicin caused a significant increase in gastric acid secretion in the rat and suggested that capsaicin might exert its effect by causing the release of some neurohumoral substances<sup>3</sup>. Although it has not been proved that capsaicin induces activation of the enteric neurons participating in fluid and ion transport, it has been demonstrated that capsaicin either administered into the circulation

or applied locally can stimulate nerve endings of various abdominal visceral organs<sup>2,11-14</sup>. It has been established that stimulation of net fluid and ion transport of the small intestine is capable of being induced by both stimulation of the nerve supplying the small intestinal mucosa and by humoral factors<sup>15-20</sup>. Since capsaicin is moderately absorbed from mucosal fluid into the intestinal wall and to the serosal fluid of rats and hamsters<sup>21</sup>, it may be possible that capsaicin when instilled in the ileal lumen initiates activation of the enteric neurons or release of neurohumoral substances so that augmentation in net fluid and NaHCO<sub>3</sub> absorption is produced. This presumption, however, needs further studies to confirm.

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### บทคัดย่อ

การศึกษารั้วนี้เพื่อทดสอบว่าแคปซูลอินซึ่งเป็นสารที่ทำให้มีรสเผ็ดมีอยู่ในพืชตระกูลพริกและพริกไทย จะมีผลอย่างไรต่อการดูดซึมน้ำ และอิเล็กโตรไลต์ของลำไส้เล็กส่วนปลาย (อิลีียม) หนูขาว การศึกษาทำโดยใส่สารละลายไว้ในถุงอิลีียมหนูขาวที่วางยาสลบไว้เป็น 2 คาบเวลา คาบละ 30 นาที หนูกลุ่มควบคุมใส่สารละลายโซเดียม-คลอไรด์-ไบคาร์บอเนตไว้ทั้ง 2 คาบเวลา หนูกลุ่มทดลอง, มี 3 กลุ่ม ในคาบที่ 1 ใส่สารละลายโซเดียมคลอไรด์-ไบคาร์บอเนตที่มีแคปซูลอินเข้มข้น 0.14 ม.ก./ม.ล. กลุ่มหนึ่ง, 0.21 ม.ก./ม.ล. กลุ่มหนึ่ง และ 0.28 ม.ก./ม.ล. กลุ่มหนึ่ง, ในคาบที่ 2 ใส่สารละลายโซเดียมคลอไรด์-ไบคาร์บอเนตทุกกลุ่ม กลุ่มที่ทดลองด้วย 0.14 ม.ก./ม.ล.แคปซูลอิน ในคาบที่ 1 ดูดซึมน้ำ, โซเดียมและไบคาร์บอเนตมากกว่ากลุ่มควบคุม ในคาบที่ 2 ดูดซึมน้ำ, โซเดียมและไบคาร์บอเนตมากกว่ากลุ่มควบคุม ส่วนในคาบที่ 2 ดูดซึมน้ำ, โซเดียมและไบคาร์บอเนตมากกว่ากลุ่มควบคุม กลุ่มที่ทดลองด้วย 0.28 ม.ก./ม.ล.แคปซูลอิน ดูดซึมน้ำ, โซเดียมและไบคาร์บอเนตมากกว่ากลุ่มควบคุมในคาบที่ 1 และในคาบที่ 2 ดูดซึมน้ำ, โซเดียมและไบคาร์บอเนตมากกว่ากลุ่มควบคุม การดูดซึมน้ำของลำไส้เล็กของหนูทดลองทั้ง 3 กลุ่มไม่มีคาบใดแตกต่างจากกลุ่มควบคุม ผลการทดลองนี้แสดงให้เห็นว่าแคปซูลอินสามารถกระตุ้นให้อิลีียมหนูขาวดูดซึมน้ำ, โซเดียมและไบคาร์บอเนตมากขึ้น แต่ไม่มีผลต่ออัตราการดูดซึมน้ำ