

**目的:** 研究粉防己碱对心肌的作用。 **方法:** 采用 Fura-2 和 AR-CM-MIC 阳离子测定系统测定培养大鼠单个心肌细胞胞内游离钙。 **结果:** 外钙  $1.3 \text{ mmol} \cdot \text{L}^{-1}$  时, 细胞静息钙为  $90 \pm 12 \text{ nmol} \cdot \text{L}^{-1}$ 。粉防己碱不影响静息钙, 但可明显抑制

$\text{CaCl}_2$ , KCl, 哇巴因引起的胞内钙增高; 对于去甲肾上腺素引起的胞内钙增高, 粉防己碱只有在在外钙存在时, 方对其有抑制作用。 **结论:** 粉防己碱抑制钙离子的跨膜运动, 但在心肌细胞, 它并非选择性的钙通道阻滞剂。

BIBLID: ISSN 0253-9756

Acta Pharmacologica Sinica 中国药理学报

1996 Jan; 17 (1); 58-60

## Suberogorgin vs *N*-cyclohexyl suberogorgamide effects on urine, respiration, and blood pressure in rat and cat

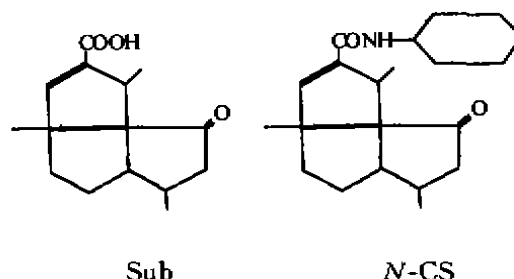
PENG Wen-Duo, XU Shi-Bo (*Pharmacology Laboratory, Department of Biology, Sun Yat-Sen University, Guangzhou 510275, China*)

**KEY WORDS** suberogorgin; *N*-cyclohexyl suberogorgamide; urine; respiration; blood pressure

**AIM:** To compare the pharmacological actions of suberogorgin (Sub) and *N*-cyclohexyl suberogorgamide (*N*-CS). **METHODS:** Urine was collected from rats and anesthetized cats which had been loaded with water. The concentrations of  $\text{Na}^+$  and  $\text{K}^+$  in urine were determined in ICAP-9000 atomic emission spectrometry. An equitoxic ( $1/50 \text{ LD}_{50}$ ) dose of Sub and *N*-CS was used in cats. **RESULTS:** The cat urine was decreased by 63 % after iv Sub  $0.4 \text{ mg} \cdot \text{kg}^{-1}$ , but increased by 25 % after iv *N*-CS  $1.5 \text{ mg} \cdot \text{kg}^{-1}$ , lasting at least 9 h. Sub and *N*-CS increased the respiratory rate and tidal volume, but did not change the blood pressure. The rat urine was decreased by 48 % after ip Sub  $1.3 \text{ mg} \cdot \text{kg}^{-1}$ , but increased by 14 % after ip *N*-CS  $3.2 \text{ mg} \cdot \text{kg}^{-1}$ . Sub and *N*-CS increased the concentrations of  $\text{Na}^+$  and  $\text{K}^+$  in rat urine. These effects lasted at least 24 h. **CONCLUSION:** Sub is an anti-diuretic, while *N*-CS is a diuretic drug.

Suberogorgin (Sub) was isolated from *Gorgonia suberogorgia* sp from South China Sea, with iv  $\text{LD}_{50}$  of  $22.8 \pm 1.8 \text{ mg} \cdot \text{kg}^{-1}$  in mice<sup>[1]</sup>. It inhibited acetylcholinesterase (AChE)<sup>[2]</sup>. *N*-Cyclohexyl suberogorgamide (*N*-CS) showed a very weak inhibition on AChE, but a diuretic action was accidentally observed. In this study, the ef-

fects of Sub and *N*-CS on urine, respiration and blood pressure in rats and anesthetized cats were compared.



### MATERIALS AND METHODS

Sub was isolated by Department of Chemistry, Sun Yat-Sen University; *N*-CS was synthesized in our laboratory. Both were spectrum pure.

Sprague Dawley rats ( $n=15$ ) weighing  $280 \pm 15 \text{ g}$ , bred in our laboratory, were fasted in metabolic cages for 18 h. Then, they were given ig with water  $30 \text{ mL} \cdot \text{kg}^{-1}$ , and the urine recorded in 2 h was  $11.4-13.5 \text{ mL} \cdot \text{kg}^{-1}$ . The rats were normally raised for 1 d and then fasted for 18 h. After that, they were injected ip with Sub or *N*-CS  $5 \text{ mL} \cdot \text{kg}^{-1}$ , and given ig with water  $25 \text{ mL} \cdot \text{kg}^{-1}$ . Their urine volume in 24 h was recorded. The concentrations of  $\text{Na}^+$  and  $\text{K}^+$  in urine were determined in ICAP-9000 atomic emission spectrometry after the urine was digested with nitric acid<sup>[3]</sup>.

Cats ( $n=3$ ), ♂, weighing  $3.5 \pm 0.4 \text{ kg}$ , were anesthetized with sodium pentobarbital  $30 \text{ mg} \cdot \text{kg}^{-1}$ .  $\text{NaCl}$   $0.15 \text{ mol} \cdot \text{L}^{-1}$  solution was injected gtt into saphenous vein at  $0.34 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ . Urine was collected by bladder intubations. The urine in 10 min was recorded for 9 h. Respiration was recorded with respiratory belts. Tidal volume ( $V_t$ ), calculated with square-method, time

respiratory rate (FR) resulted in minute ventilation<sup>14</sup>. Blood pressure was recorded from the common carotid artery.

Cats were injected iv with an equi-toxic (1/50 LD<sub>50</sub>) dose of Sub or *N*-CS.

## RESULTS

The urine of rats and cats was decreased by Sub, increased by *N*-CS, lasting more than 9 and 24 h in cats and rats, respectively (Fig 1).

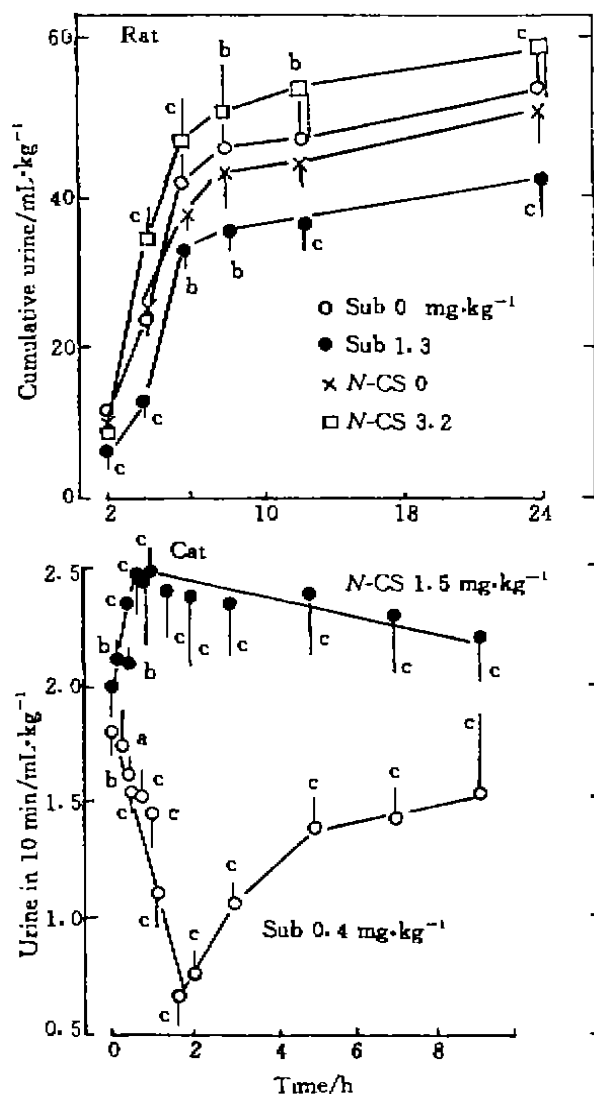


Fig 1. Effects of Sub and *N*-CS on urine volume of rats and anesthetized cats.  $n=15$  rats or 3 cats.  $\bar{x}\pm s$ . \* $P>0.05$ , \* $P<0.05$ , \* $P<0.01$  vs control.

Sub and *N*-CS increased the concentrations of Na<sup>+</sup> and K<sup>+</sup> in rat urine, highest at 2 and 6 h after Sub and *N*-CS, respectively. These effects were still noted at 24 h (Tab 1).

Tab 1. Effects of Sub and *N*-CS on the concentrations of Na<sup>+</sup> and K<sup>+</sup> in rat urine.  $n=5$  rats,  $\bar{x}\pm s$ . \* $P>0.05$ , \* $P<0.05$ , \* $P<0.01$  vs 0 mg·kg<sup>-1</sup>.

Time/h	Sub/mg·kg <sup>-1</sup>		<i>N</i> -CS/mg·kg <sup>-1</sup>	
	0	1.3	0	3.2
	Na <sup>+</sup> /mg·L <sup>-1</sup>			
2	110±19	758±98 <sup>c</sup>	136±29	470±67 <sup>c</sup>
4	160±75	907±156 <sup>c</sup>	165±27	580±45 <sup>c</sup>
6	180±88		271±44	3 130±143 <sup>c</sup>
8		1 050±159		4 020±381
12	1 020±123	1 910±248 <sup>c</sup>	1 084±20	4 800±500 <sup>c</sup>
24	1 690±192	3 162±428 <sup>c</sup>	1 596±203	2 160±118 <sup>c</sup>
	K <sup>+</sup> /mg·L <sup>-1</sup>			
2	942±154	2 515±242 <sup>c</sup>	953±87	1 624±123 <sup>c</sup>
4	1 630±143	2 838±397 <sup>c</sup>	1 608±45	2 293±199 <sup>c</sup>
6	2 486±196	3 097±505 <sup>b</sup>	2 511±53	11 000±2 050 <sup>c</sup>
8		3 296±283	1 587±316	3 164±316 <sup>c</sup>
12	4 021±541	4 391±594 <sup>c</sup>	3 805±695	4 100±789 <sup>c</sup>
24	5 681±1 158	6 532±1 154 <sup>b</sup>	5 440±588	6 263±827 <sup>b</sup>

In cats, Sub 0.4 mg·kg<sup>-1</sup> increased the FR, V<sub>i</sub> and minute ventilation by 19 % ( $P<0.05$ ), 26 % ( $P<0.01$ ), and 40 % ( $P<0.01$ ) respectively; *N*-CS 1.5 mg·kg<sup>-1</sup> increased the above parameters by 50 % ( $P<0.01$ ), 21 % ( $P<0.01$ ), and 70 % ( $P<0.01$ ), respectively (Tab 2).

The blood pressure of cats tended to decrease or increase within 3 h after iv Sub 0.4 mg·kg<sup>-1</sup> or *N*-CS 1.5 mg·kg<sup>-1</sup> ( $P>0.05$ ) (Tab 3).

## DISCUSSION

The different effects between Sub and *N*-CS on urine showed that the mechanism of pharmacological actions between Sub and *N*-CS might be different, and offered a possibility to transform the structure of Sub to invent some new compounds with obvious activities.

Intracerebroventricular administration of hypertonic saline induces the diuresis and hypertention<sup>15</sup>. The diuresis and the slight hypertention of *N*-CS indicated that *N*-CS might cause an increase in GFR, and a decrease in reabsorption of water and sodium in the proximal tubule. But this question is remaining to be clarified in future studies.

**Tab 2. Excitant effects of Sub 0.4 and N-CS 1.5 mg·kg<sup>-1</sup> on respirations in anesthetized cats. n=3 cats,  $\bar{x} \pm s$ . \*P>0.05. <sup>b</sup>P<0.05. <sup>c</sup>P<0.01 vs 0 min.**

Time/ min	Respiratory frequency/ times·min <sup>-1</sup>		Tidal volume/mL		Minute ventilation/mL·min <sup>-1</sup>	
	Sub	N-CS	Sub	N-CS	Sub	N-CS
0	26±4	14±2	16.7±1.8	19.8±2.0	434±72	277±30
1	31±6 <sup>b</sup>	18±3 <sup>c</sup>	18.0±2.5 <sup>a</sup>	24.0±2.8 <sup>c</sup>	558±81 <sup>c</sup>	432±57 <sup>c</sup>
2	30±6 <sup>a</sup>	17±3 <sup>c</sup>	18.0±2.5 <sup>a</sup>	24.0±2.4 <sup>c</sup>	540±81 <sup>b</sup>	408±51 <sup>c</sup>
5	31±6 <sup>b</sup>	19±4 <sup>c</sup>	17.5±2.8 <sup>a</sup>	22.0±2.1 <sup>b</sup>	542±88 <sup>b</sup>	418±61 <sup>c</sup>
10	29±7 <sup>a</sup>	21±6 <sup>c</sup>	19.5±1.5 <sup>c</sup>	22.4±2.0 <sup>b</sup>	566±100 <sup>c</sup>	470±65 <sup>c</sup>
30	29±5 <sup>a</sup>	21±6 <sup>c</sup>	21.0±3.4 <sup>c</sup>	19.9±2.6 <sup>a</sup>	609±99 <sup>c</sup>	418±74 <sup>c</sup>
60	27±5 <sup>a</sup>	20±5 <sup>c</sup>		19.5±3.4 <sup>a</sup>		390±76 <sup>b</sup>
120	27±6 <sup>a</sup>	18±4 <sup>c</sup>	17.6±1.9 <sup>a</sup>	21.0±1.8 <sup>a</sup>	475±80 <sup>a</sup>	378±51 <sup>b</sup>

**Tab 3. Effects of single iv Sub or N-CS on blood pressure in anesthetized cats. n=3 cats,  $\bar{x} \pm s$ . \*P>0.05 vs 0 min.**

Time/ min	Blood pressure / kPa			
	Sub/mg·kg <sup>-1</sup>		N-CS/mg·kg <sup>-1</sup>	
	0	0.4	0	1.5
0	14.9±1.0	14.2±1.3	15.3±0.8	14.6±1.0
1	14.4±1.0 <sup>a</sup>	14.2±1.3 <sup>a</sup>	15.3±0.8 <sup>a</sup>	15.2±1.5 <sup>a</sup>
2	14.9±1.0 <sup>a</sup>	14.2±1.3 <sup>a</sup>	15.3±0.8 <sup>a</sup>	15.5±1.2 <sup>a</sup>
5	15.0±0.8 <sup>a</sup>	14.0±1.3 <sup>a</sup>	15.3±0.8 <sup>a</sup>	15.5±1.2 <sup>a</sup>
10	15.1±1.2 <sup>a</sup>	13.8±0.9 <sup>a</sup>	15.3±0.8 <sup>a</sup>	14.9±2.1 <sup>a</sup>
30	14.9±1.2 <sup>a</sup>	13.6±1.1 <sup>a</sup>	15.5±1.2 <sup>a</sup>	14.5±1.9 <sup>a</sup>
60	15.2±1.6 <sup>a</sup>	13.2±1.4 <sup>a</sup>	15.6±0.8 <sup>a</sup>	15.4±0.7 <sup>a</sup>
120	15.2±1.6 <sup>a</sup>	13.2±1.4 <sup>a</sup>	15.6±0.8 <sup>a</sup>	15.0±1.7 <sup>a</sup>
180	14.9±1.2 <sup>a</sup>	13.5±0.5 <sup>a</sup>	15.1±2.4 <sup>a</sup>	14.8±2.0 <sup>a</sup>

**REFERENCES**

- Niu LW, Dai JB, Wan ZL, Liang DC, Wu ZD, Yao ZN, et al. Molecular structure and absolute configuration of suberogorgin. *Sci Sin [B]* 1986; 29: 40-9.
- Xu SB, Peng WD, Hu YT, Wang YF. Excitant effect of sodium suberogorgin on isolated rabbit ileum. *Acta Pharmacol Sin* 1992; 13: 459-63.
- Zheng GJ, Ding YY, Xu Y, Qian SZ. K, Na, Ca and Mg contents in the diet of Nanjing workers. *Acta Pharmacol Sin* 1982; 3: 142-4.
- Ge XQ, Xu PC, Bian CF. Relationship between morphine-induced respiratory depression and the cholinergic system of respiratory center.

*Acta Pharmacol Sin* 1990; 25: 566-72.

5 He XR, Zhang JF, Yao T. Intracerebroventricular administration of hypertonic saline inhibits the reabsorption of water and sodium in the proximal tubule.

*Acta Physiol Sin* 1989; 41: 421-7.

**柳珊瑚酸与 N-环己基柳珊瑚酰胺对大鼠和猫尿量、呼吸和血压的影响**

彭汶铎, 许实波

(中山大学生物系药理室, 广州510275, 中国)

**关键词** 柳珊瑚酸; N-环己基柳珊瑚酰胺; 尿; 呼吸; 血压

目的: 比较柳珊瑚酸(suberogorgin, Sub)与 N-环己基柳珊瑚酰胺(N-cyclohexyl suberogorgamide, N-CS)的药理作用。方法: 大鼠和麻醉猫给予水负荷和 Sub 或 N-CS 后记录其尿量, 并测定尿 Na<sup>+</sup>, K<sup>+</sup>浓度; 猫实验中 Sub 和 N-CS 采用等毒性剂量(1/50 LD<sub>50</sub>)。结果: Sub 0.4 mg·kg<sup>-1</sup>和 N-CS 1.5 mg·kg<sup>-1</sup> iv 分别使猫尿量减少63 %和增加25 %, 这种作用维持9 h 以上。Sub 和 N-CS 均明显提高猫呼吸频率和潮气量, 但对血压无明显影响。Sub 1.3 mg·kg<sup>-1</sup>和 N-CS 3.2 mg·kg<sup>-1</sup> ip 分别使大鼠尿量减少48 %和增加14 %, 并有明显的排 Na<sup>+</sup>, K<sup>+</sup>作用。结论: Sub 具抗利尿作用而 N-CS 却具利尿利用。