1-(2,6-二甲基苯氧基)-2-(3,4-二甲氧基苯乙基氨基) 丙烷酸盐酸的降压作用

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摘要：1-(2,6-二甲基苯氧基)-2-(3,4-二甲氧基苯乙基氨基) 丙烷酸盐酸的降压作用研究

一、材料和方法

二、结果

三、讨论

四、结论
表 1. Effects of iv 3-(2,6-dimethylphenoxy)-2-(3,4-dimethoxyphenoxy)trimino propan hydrochloride on mean arterial pressure (MAP, kPa) and heart rate (HR, beats/min) of unsedated normotensive rats (ANR, n = 7) and conscious normotensive rats (CNR, n = 5-6) and conscious renal hypertensive rats (CHR, n = 5).

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<th>1 min</th>
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<td>ANR MAP</td>
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<td>11.2±2.3</td>
<td>11.2±2.3</td>
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<tr>
<td>CNR MAP</td>
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<td>15.2±2.9</td>
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<tr>
<td>HR</td>
<td>3</td>
<td>392±23</td>
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<tr>
<td>CHR MAP</td>
<td>3</td>
<td>23.2±2.1</td>
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<tr>
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<td>3</td>
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以上实验，每个标本只用作一组对照。

结果

对正常和高血压大鼠血压的影响：实验表明，采用iv D2, mg/kg, 给MAP可立即下降，1-2 min后MAP降至最低点，之后回升，但1 h MAP未能恢复到正常水平。HR则MAP下降而减慢，恢复慢比MAP快，结果见表 1。
Fig. 1. Effects of iv 1-(2,5-dimethylphenox)-2-(3,4-dimethoxyphenylethylamino)propane hydrochloride (D) on methoxamine and B-HT 920 induced increase in diastolic pressure of pithed rats, n = 5-7, X ± SD.

D 0.1 0.3 1 µmol/L and methoxamine 3, 10, 30 nmol/L/pt did not change the activity. Methoxamine 1 mg/kg significantly increased the activity of pithed rats.

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Fig. 2. Effects of methoxamine in the absence (○) or presence of D or prazosin in rabbit aorta, portal veins and rat transmural muscles, n = 5-7, X ± SD.

Fig. 5. Effects of D and verapamil on KCl-induced (40 mmol/L) contraction of rabbit aorta, n = 5, X ± SD.

In the aortic segment, D 100 100 µmol/L and KCl 100 nmol/L did not alter the contractile response in macrovascular preparations. D 100 µmol/L and KCl 100 nmol/L decreased the contractile response in microvascular preparations. D 100 100 µmol/L and KCl 100 nmol/L did not alter the contractile response in macrovascular preparations. D 100 µmol/L and KCl 100 nmol/L decreased the contractile response in microvascular preparations.
图4. Effects of D and prazosin on the contractile force to methoxamine (100 μM/L) in epidermal portion of rat vas deferens, n = 5, X ± SD, P < 0.05, **P < 0.01 vs control.

图5. Effects of D and yohimbine (Yoh) on the dose-response curves for clonidine to inhibit electrical stimulation-evoked (3 ms, 1 Hz, 20–60 V) Vasoconstriction of the prostatic portion of the rat vas deferens, n = 5, X ± SD

选用阻断节前交感神经的药物D和α2阻断剂yohimbine (Yoh)抑制电刺激诱发的血管收缩。

D对兔主动脉和门静脉、大鼠肛尾肌和精管无效。

讨论

实验结果表明D对麻醉、清醒正常血压大鼠和清醒清醒血压大鼠均有效抑制持续的刺激所引起的血管收缩，降低血管的收缩，提示D的降压作用机制与直接扩张血管及扩张不同，即不是通过直接扩张血管平滑肌而降低MAP，与HR不呈平行关系，说明HR减慢在降压过程中不起主要作用。

参考资料

Hypotensive effect of 1-(2,6-dimethylphenoxyl)-2-(3,4-dimethoxy-phenethylamino) propane hydrochloride

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ABSTRACT 1-(2,6-dimethylphenoxyl)-2-(3,4-dimethoxyphenethylamino) propane hydrochloride (D) was synthesized by Nanjing College of Pharmacy according to the structural characteristic of maxilamine.

The influence of D on blood pressure of rats and possible mechanism were studied. D 3. 10 mg/kg iv lowered mean arterial pressure in pentobarbitone-anesthetized normotensive rats. Conscious normotensive rats and conscious renal hypertensive rats. In pithed rats pretreated with D 3. 10 mg/kg shifted log dose-response curve of methoxamine to the right in parallel manner but D 10 mg/kg reduced the maximal response of B-HT 920. In rabbit aorta, portal vein and rat anococcygeus muscle D 0.1, 0.3, 1 µmol/L shifted methoxamine cumulative dose-response curves rightward parallelly with pA2 values of 7.15, 6.92 and 7.33 respectively. D inhibited the contraction evoked by KCl 40 mmol/L in rabbit aorta with a IC50 value of 93 µmol/L. The dose-response curve for clonidine to inhibit electrical stimulation-evoked contraction of the prostatic portion of rat vas deferens was shifted rightward parallelly by D 30. 100 µmol/L with a pA2 value of 5.1.

These results suggest that D can block a1 and a2-adrenoceptors. The selective ratio for D to block a1-adrenoceptors in anococcygeus muscle and a2-adrenoceptors in vas deferens from the same rat (a1/a2) was 162. Possibly, D also possesses a calcium antagonistic effect.

KEY WORDS 1-(2,6-dimethylphenoxyl)-2-(3,4-dimethoxyphenethylamino) propane, methoxamine, prazosin, clonidine, yohimbine, thoracic aorta, portal vein, anococcygeus muscles, vas deferens