Title	Structure and hypotensive activity relationships of tetrandrine derivatives in stroke-prone spontaneously hypertensive rats
Sub Title	
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Publisher	共立薬科大学
Publication year	1990
Jtitle	共立薬科大学研究年報 (The annual report of the Kyoritsu College of Pharmacy). No.35 (1990.),p.64- 64
JaLC DOI	
Abstract	
Notes	抄録
Genre	Technical Report
URL	https://koara.lib.keio.ac.jp/xoonips/modules/xoonips/detail.php?koara_id=AN00062898-00000035-0064

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Structure and Hypotensive Activity Relationships of Tetrandrine Derivatives in Stroke-Prone Spontaneously Hypertensive Rats*

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1. Structure and hypotensive activity relationships of tetrandrine (TD), an alkaloid isolated from the Chinese herb *Redix stephaniae tetrandrae* and its derivatives were investigated in conscious stroke-prone spontaneously hypertensive rats (SHRSP).

2. Derivatives substituted at the 7-O position with various types of alkyl group produced varying degrees of hypotensive effect.

3 While the demethylated derivative, fangchinoline (FC), and its acetylated compound had no effect on blood pressure, 7-O-methyl FC (TD), and 7-O-ethyl and 7-O-isopropyl FC at oral doses of 25 and 50 mg/kg produced a gradual and sustained hypotensive effect without any significant effects on heart rate and plasma renin concentration.

4. Substitution at the 7-O position with longer side chains such as n-propyl, n-butyl and n-pentyl groups reduced both the degree and duration of hypotensive activity.

5. Substitution of N-methyl groups at the 2 and 2' positions with quaternary ammonium or N-oxide attenuated the hypotensive activity.

6. The results of this study suggest a possibility that 7-O-ethyl and 7-O-isopropyl derivatives as well as TD can be considered as potential antihypertensive drugs because of the gradual onset and long duration of their hypotensive action in SHRSP.

* 本報告は *Gen. Pharmac.* Vol. 21, No. 3, pp. 343—347, 1990 に発表.

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