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Author	川島, 紘一郎(Kawashima, Koichiro) 早川, 晃正(Hayakawa, Terumasa) 三輪, 裕子(Miwa, Yuko) 大畑, 尚代(Ohata, Hisayo) 鈴木, 岳之(Suzuki, Takeshi) 藤本, 和子(Fujimoto, Kazuko) 荻野, 達則(Ogino, Tatsunori) 陳, 政雄(Chen, Zhengxiong)
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Structure and Hypotensive Activity Relationships of Tetrandrine Derivatives in Stroke-Prone Spontaneously Hypertensive Rats*

Koichiro KAWASHIMA, Terumasa HAYAKAWA, Yuko MIWA, Hisayo OOHATA, Takeshi SUZUKI, Kazuko FUJIMOTO, Tatsunori OGINO** and Zhengxiong CHEN (Masao CHIN)**

川島紘一郎，早川晃正，三輪裕子，大畑尚代，鈴木岳之，藤本和子，荻野達則**，陳　政雄**

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.

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** 津村研究所