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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.

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