SOME 8-O-SUBSTITUTED DERIVATIVES OF PSORALEN AND THEIR SPASMOLYTIC ACTIVITY

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UDC 547.985

The spasmolytic action is one of the main properties determining the clinical use or trial of certain coumarins – of pastinacin [1], athamantin [2], suksdorfin [3], pteryxin [4], and visnadin [5]. Investigations on isolated animal organs to determine the dependence of the spasmolytic action on the structure of substances of a coumarin nature are known [6, 7].

We have studied the influence of the structure of certain radicals at C_8 of psoralen on spasmolytic activity. Psoralen, xanthotoxol, xanthotoxin, and imperatorin were isolated from various plants, and by the acylation of xanthotoxol in pyridine with nicotinoyl chloride and acetic anhydride we synthesized psoralen 8-O-nicotinate [mp 193-195°C, UV spectrum: $\lambda_{max}^{C_2H_5OH}$ 244, 290, and 325 nm (log ε 4.79, 4.09, 3.77) shoulder], which is a new compound, and psoralen 8-O-acetate (Table 1).

The spasmolytic activity was determined on white mice by a published method [8].

The comparative evaluation of the results obtained shows that the introduction of a hydroxy group into the C_8 position of psoralen (xanthotoxol) increases its activity by only 10%. A methoxy group in this position of psoralen (xanthotoxin) raises the activity by 30%. The strongest spasmolytics proved to be imperatorin, which has a γ,γ-dimethylallyloxy group at C_8, and xanthotoxol acetate. They are 3.4 and 2.9 times, respectively, stronger than psoralen. Of the two acyl derivatives of psoralen studied, the acetyl derivative has the greater activity; the nicotinic acid residue increased the activity by only 50%.

TABLE 1

Substance	Radical at C_8	Spasmolytic activity
Psoralen $C_{11}H_6O_3$	—H	1
Xanthotoxol $C_{11}H_6O_4$	—OH	1,1
Xanthotoxin $C_{12}H_8O_4$	$-OCH_3$	1,3
Imperatorin $C_{16}H_{14}O_4$	$-O-CH_2-CH=C(CH_3)_2$	3,4
Xanthotoxol acetate $C_{13}H_8O_5$	$-O-CO-CH_3$	2.9
Xanthotoxol nicotinate $C_{17}H_9O_5$	$-O-CO-C_5H_4N$	1,5

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Khar'kov Scientific-Research Institute of Pharmaceutical Chemicals. Translated from Khimiya Prirodnykh Soedinenii, No. 1, pp. 110-111, January-February, 1973. Original article submitted April 14, 1972.