A NOTE ON THE TUBERCULOSTATIC ACTIVITY OF BENZOYLHYDRAZIDES

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The discovery of the powerful tuberculostatic activity of isoniazid (*iso*nicotinyl hydrazide)[1,2,3], led us to examine the activity of the hydrazides of several substituted benzoic acids which were at our disposal. The results are shown in Table I.

TABLE I

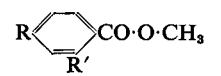
In vitro activities against H37 Rv strain of *Mycobacterium tuberculosis* in Dubos medium.

	R	R′	*In vitro* activity inhibitory concentration in μg./ml.
I	NH_2	H	20
II	NH_2	OH	12·5
III	NO_2	H	100
IV	Cl	H	20
V	OH	H	5
VI	CH_3O	H	20
VII	C_2H_5O	H	20
VIII	*n*-C_3H_7O	H	20
IX	*n*-C_4H_9O	H	20
X	*n*-$C_5H_{11}O$	H	20
XI	Isoniazid		0·05–0·1

Several of these compounds (I, III, IV, V, VI) have already been tested against the BCG strain of *Myco. tuberculosis*[1,4], or against the H37 Rv strain (II)[5]. Our results confirm that the activity of the benzoylhydrazides is small compared with that of isoniazid. The greatest activity is shown by

TABLE II

Properties of methyl esters

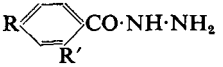


R	R′	M.pt. ° C.	B.pt. 20 mm. Hg. ° C.
NH_2	H	112	
NH_2	OH	121 to 222	
NO_2	H	95 to 96	
Cl	H	43 to 44	113 to 115
OH	H	131	
CH_3O	H	45 to 46	160
C_2H_5O	H	37 to 99	160
n-C_3H_7O	H		155 to 160
n-C_4H_9O	H		190 to 195
n-$C_5H_{11}O$	H		180 to 185

the hydrazide of *p*-hydroxybenzoic acid; but replacing the hydroxy- by an alkoxy- group decreases the tuberculostatic power, and this is not influenced by the size of the alkoxy-group.

TABLE III

PROPERTIES OF HYDRAZIDES



R	R′	M.pt. °C.	Calculated per cent.	Nitrogen found per cent.
NH_2[6]	H	220		
NH_2[7]	OH	198 200		
NO_2[8]	H	210		
Cl	H	163		
OH[10]	H	260		
CH_3O[11]	H	136		
C_2H_5O	H	123 to 125	15·55	15·51, 15·56
n-C_3H_7O	H	104 to 106	14·43	14·43, 14·40
n-C_4H_9O	H	108 to 110	13·48	13·47, 13·49
n-$C_5H_{11}O$	H	82 to 84	12·60	12·63, 12·60

EXPERIMENTAL

The methyl esters containing chlorine were prepared by refluxing the acids in methanol containing hydrogen chloride; for *p*-aminosalicylic acid the boron trifluoride catalyst was used[12]. After isolation, the esters were purified by crystallisation or distillation *in vacuo*.

The hydrazides were prepared by heating 2·0 g. of the methyl ester for 4 hours in 5 ml. of methanol containing 1 ml. of hydrazine hydrate. After cooling, the crystals were filtered off and recrystallised from ethanol; in preparing certain compounds ether must be added.

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