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NOTE

Hydrazino Di-methyl Substituted Quinolines as Antitubercular/Antibacterial Agents

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Alkyl-substituted 4-chloroquinolines have been condensed with hydrazine compounds and antitubercular/antibacterial activity of such substituted hydrazino compounds has been examimed.

At this research centre some quinoline derivatives of acetyl dapsone, sulphaphenazole and sulfathiazole have proved effective against *Mycobacterium tuberculosis* $H_{37}R_v$ at 5 μg/mL.[1]

Some new sulfonamides have recently been reported as antibacterial or antimicrobial agents.[2–4] Drug resistance of two strains, isolated from TB patients, has been tested against hydrazinamide, isoniazid and rifampicin which proved ineffective.[5] However, modified quinoline substituted thiosemicarbazones and isonicotinoyl hydrazines have proved effective against the two strains.[6]

2,8(A); 2,5(B) or 2,6(C) Dimethyl-2-methyl-8-methoxy(D); 2-methyl-6-methoxy(E); 2-methyl-6-chloro(F)-4-chloro quinolines (0.01 M) were in turn condensed with (0.01 M) (I) 0-2-6-dichlorophenyl iminoacetyl hydrazine, or (II) 2-(3′-trifluoromethyl phenyl-imino)-3-pyridoyl hydrazine, or (III) 2,3 : 6,7 dibenzoazocin-1-yl-carbonyl hydrazine by refluxing in butanol (25 mL) for 3 h.[7] Respective products thus obtained were crystallised from aq. ethanol. These are:

(A) Corresponding alkyl substituted (A, B, C, D, E or F)-4-(0-2′,6′-dichlorophenyl iminophenyl acetyl hydrazino) quinolines; m.p.s (dec) above 240°C.

(B) Corresponding alkyl substituted (A,B,C,D,E, or F)-4-2′-(3″-trifluoromethyl imino)-3′-pyridoyl-hydrazino-quinolines, mps (dec) above 260°C.

(C) Corresponding alkyl-substituted-(A, B, C, D, E or F)-4-(2′,'3 : 6′,7-dibenzoazocin-1-yl-carbonyl hydrazino)-quinolines, m.p.s (dec) respectively 228, 216, 230, 205, 218, 235°C.

The products were characterized and their structures were confirmed by nitrogen determination, molecular weight determination by non-aqueous titration method, IR and NMR in some cases, as well as by TLC. Antibacterial and antitubercular activities were determined by known method.[1].

4-Cl-band disappears after condensation, substituted quinoline 1610–1330 cm^{-1}, (3)C—H (CH_3) 3080 cm^{-1}, C—F (CF_3) 1120 cm^{-1}, —CO—NH 1670 cm^{-1}, NH 3500–3300 cm^{-1}, (Cl chloro compounds) 745 cm^{-1}, —OCH_3 2840 cm^{-1}

NMR δ: —CH_3— 2.66, —OCH_3 3.96, —Ar—H 6.9–8.0, —NH—NH doublet 8.49–8.6, —NH singlet 8.3.

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From Table-1, it appears that products A, C, E, F (I), A, D, F (II) and B, D (III) are effective against *Mycobacterium tuberculosis* $H_{37}R_v$ at 5 μg mL^{-1} inhibiting its growth. It has already been observed previously that 2—CH_3 does not contribute to activity; hence 6—CH_3, 8—CH_3, 6—OCH_3, 8—OCH_3, CONH, CF_3 and pyridoyl groups contribute to antitubercular activity at 5 μg/mL. Thus nine products have anti-TB activity out of eighteen. These results confirm earlier observations regarding group effects.[1] Further, the alkyl-substituted derivatives of parent compounds A, B, C are effective at 5 μg mL and enhanced anti-TB activity.

TABLE-1
ANTITUBERCULAR/ANTIBACTERIAL ACTIVITY OF HYDRAZINO QUINOLINE COMPOUNDS

Compound		Anti-TB activity	Average inhibition zone (in mm)		
		Myco. tuberculosis $H_{37}Rv$	*S. aureus*	*E. coli*	*Sal. paratyphi B*
Parental					
a.	0-2,6-Dichlorophenyl imino acetyl hydrazine	+	16	10	10
b.	2-3′-Triphenyl methyl phenyl imino-3-pyridoyl hydrazine	++	12	17	10
c.	2,3 : 6,7-Dibenzoazocin-1-yl-carbonyl hydrazine	+	9	10	15
Derivatives					
I.	A	—	8	6	9
	B	++	9	6	8
	C	—	8	6	6
	D	++	8	6	6
	E	—	8	6	6
	F	—	8	6	9
II.	A	—	9	6	8
	B	++	8	6	6
	C	+++	8	6	7
	D	—	8	7	6
	E	++	8	6	6
	F	—	8	6	6
III.	A	+++	6	6	6
	B	—	8	6	6
	C	++	7	7	6
	D	—	8	6	6
	E	++	7	6	6
	F	+++	11	6	6

+ = Growth; − = No growth.

It is observed that parent (a, b, c) compounds have higher antibacterial activity which gets reduced in derivatives confirming also earlier results.

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