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NOTE

Quinolinyl Substituted Sulfa Drugs as Antitubercular Agents, Part I

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Dimethyl quinolinyl substituted sulfa drugs, such as sulfadiazine, sulfaphenazole and sulfisomidine have been prepared and tested against *Mycobacterium tuberculosis* $H_{37}Rv$ for antitubercular activity.

It was reported that many quinolinyl substituted drugs are more inhibitory than the parent agents against *Mycobacterium. tuberculosis* $H_{37}Rv$ (a reference strain) at MIC 5 μg/mL. The most effective substituents in the quinolinyl nucleus have been 6-methyl, 6-chloro, 6-ethoxy or 8-methoxy.[1]

In the present investigation many such quinolinyl substituted sulfa drugs, *viz.*, sulfadiazine, sulfaphenazole and sulfisomidine have been reported and tested for antitubercular activity against *Mycobaterium. tuberculosis* $H_{37}Rv$. 2-Methyl-4-chloro-quinoline synthesised by the known method, has been condensed with the amine group of the sulfa drug. The purity and identity of the products were confirmed by melting point, elemental analysis, TLC, IR and NMR spectra and molecular weight determination by non-aqueous titration method. Two aldehyde condensed sulfadiazine products have also been included. The details are given in Table-1.

The parent sulfa drugs are not effective against $H_{37}Rv$ at 5 μg/mL 6-Methy, 8-methoxy, 5-methyl and 6-methoxy substituents in quinolinyl substituted sulfadiazine impart activity to the parent at 5 μg/mL, while the same substituents except 6-methoxy, are not effective in sulfaphenazole and sulfisomidine at 5 μg/mL. Sulfadiazine is inhibitory at 10 μg/mL, while sulfaphenazole is inactive. Out of 14 products only five are effective at 5 μg/mL.

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TABLE-1
ANTITUBERCULAR ACTIVITY OF THE COMPLEXES

Sr. No.	Complex	m.p (°C)	Yield (%)	Activity against $H_{37}Rv$	*M. tuberculosis* (μg/mL)
1.	2,8-Dimethyl-4-quinolinyl-sulfadiazine	271	45	+	–
2.	2-5-Dimethyl-4-quinolinyl-sulfadiazine	275	52	–	–
3.	2,6-Dimethyl-4-quinolinyl-sulfadiazine	287	42	–	–
4.	2-Methyl-8-methoxy-4-quinolinyl-sulfadiazine	283	49	–	–
5.	2-Methyl-6-methoxy-4-quinolinyl-sulfadiazine	301	36	–	–
6.	2,8-Dimethyl-4-quinolinyl-sulfaphenazole	277	60	++	++
7.	2,5-Dimethyl-4-quinolinyl-sulfaphenazole	270	52	++	+
8.	2,6-Dimethyl-4-quinolinyl-sulfaphenazole	315	56	++	–
9.	2-Methyl-8-methoxy-4-quinolinyl-sulfaphenazole	253	84	+	–
10.	2-Methyl-6-ethoxy-4-quinolinyl-sulfaphenazole	303	43	–	–
11.	4-Methoxybenzylidene-sulfadiazine	252	65	+	+
12.	2-Chlorobenzylidene-sulfadiazine	234	85	+	+
13.	2-Methyl-6-methoxy-4-quinolinyl-sulfisomidine	270	36	+	+
14.	2-Methyl-8-methoxy-4-quinolinyl-sulfisomidine	295	42	+	+

Symbols "-" = No growth., "+" = Scanty growth., "++" = Moderate growth.

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