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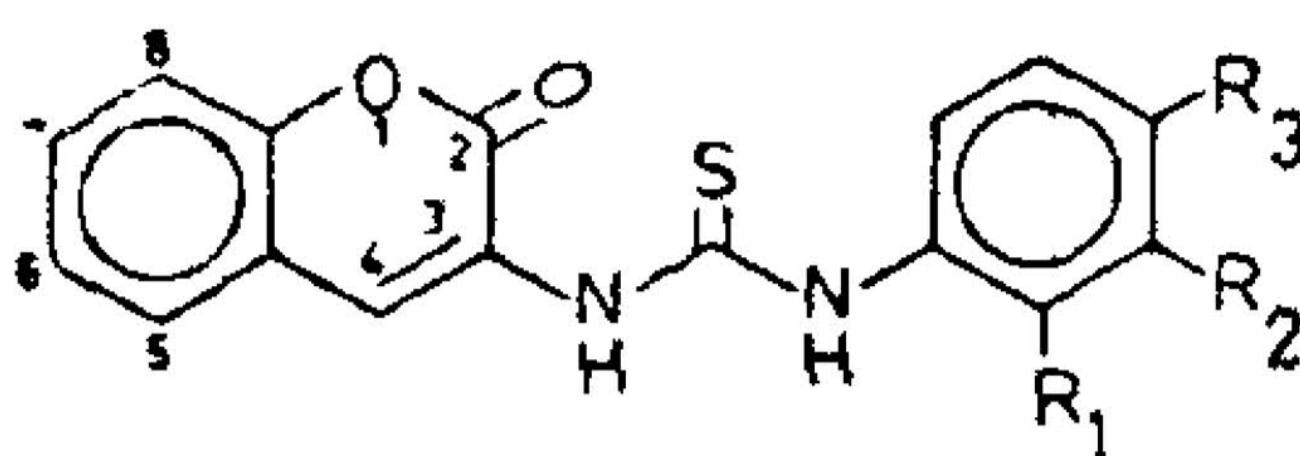
**SYNTHESIS OF NEW COUMARYLTHIOUREAS  
WITH ANTITUBERCULOUS ACTIVITY**

COUMARINS and substituted coumarins are known to be physiologically active and several of them possess antibacterial and antifungal properties<sup>1</sup>. Both 3- and 4-pyridylcoumarins are reported to be potential central nervous system depressants<sup>2</sup>. Also 3-aminocoumarins are found to have antibacterial properties<sup>3</sup>. Further, the usefulness of thioureas as antituberculous agents is well known<sup>4</sup>. It was, therefore, thought of interest to combine both the 3-aminocoumarin and the thiourea moieties into one structure and synthesise 3-coumarylthioureas having the general formula shown and test them for their antituberculous activity.

The synthesis of these compounds was carried out by condensation of 3-aminocoumarin<sup>5</sup> with different phenyl-isothiocyanates (prepared as described in literature) in boiling alcohol solution when the resulting thioureas were obtained as crystalline solids from alcohol or acetone in about 75-80% yields.

The I.R. spectrum of a typical coumarylthiourea showed the following bands: 3300 (-NH stretching), 1690 (-C=O of lactone), 1640, 1550, 1510 (aromatic), 1240 (C=S)  $\text{cm}^{-1}$ . The N.M.R. spectrum of the compound was also fully consistent with the structure.

Screening for antituberculous property of the compounds was done *in vitro*. Youman's liquid medium<sup>6</sup> was used for growing the organism, H<sub>37</sub>Rv strain of



No.	Colour	M.P.	Anti-T.B. activity $\mu\text{g/ml}$
1. $R_1 = R_2 = R_3 = \text{H}$	Colourless	197°	10
2. $R_1 = \text{CH}_3, R_2 = R_3 = \text{H}$	Pale yellow	168-9°	5
3. $R_1 = \text{H}, R_2 = \text{CH}_3, R_3 = \text{H}$	Cream	205°	5
4. $R_1 = R_2 = \text{H}, R_3 = \text{CH}_3$	Colourless	211°	10
5. $R_1 = \text{H}, R_2 = \text{Cl}, R_3 = \text{H}$	Pale yellow	217-8°	100
6. $R_1 = R_2 = \text{H}, R_3 = \text{Cl}$	Light brown	227-8°	1
7. $R_1 = R_2 = \text{H}, R_3 = \text{OCH}_3$	Yellow	172°	1
8. $R_1 = R_2 = \text{H}, R_3 = \text{OC}_2\text{H}_5$	Yellow	197°	1
9. $R_1 = R_2 = \text{H}, R_3 = \text{OC}_3\text{H}_7 (n)$	Yellow	286-8°	100
10. $R_1 = R_2 = \text{H}, R_3 = \text{OC}_4\text{H}_9 (n)$	Yellow	302-3°	100
11. $R_1 = R_2 = \text{H}, R_3 = \text{OC}_5\text{H}_{11} (n)$	Yellow	131-2°	10
12. $R_1 = R_2 = \text{H}, R_3 = \text{OC}_5\text{H}_{11} (\text{iso})$	Pale yellow	196°	10

*Mycobacterium tuberculosis* var. *hominis*. Eight days old culture of the test organism in Youman's liquid medium was used for inoculation. Thereafter, the incubation was carried out at 37° for 28 days. The results were noted by observation of pellicular growth at surface.

The minimum concentration of the compounds (mentioned in  $\mu\text{g/ml}$ ) which completely inhibited the growth of the test organism are presented in last column of the table.

For comparison the activity under similar conditions for streptomycin is 1  $\mu\text{g/ml}$  and that of I.N.H. is 0.04  $\mu\text{g/ml}$ .

All the compounds gave satisfactory elemental analysis. The screening tests were carried out at Haffkine Institute, Bombay.

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