PART-I

SYNTHESIS AND ANTIHISTAMINIC ACTIVITY OF 2-(3-SUBSTITUTEDPROPYLTHIO)-3-(SUBSTITUTEDPHENYL) QUINAZOLIN-4(3*H*)-ONES

ABSTRACT

A series of novel 2-(3-substitutedpropylthio)-3-(substitutedphenyl) quinazolin-4(3*H*)-ones were synthesized by the reaction of 2-(3-bromopropylthio)-3-(substitutedphenyl) quinazolin-4(3*H*)-one with a variety of amines. The starting material, 2-(3-bromopropylthio)-3-(substitutedphenyl) quinazolin-4(3*H*)-one was synthesized from substituted aniline. The title compounds containing substituted propylthio group at C-2 and substituted phenyl group at N-3 of quinazolines were evaluated for their *in vivo* antihistaminic activity adopting the protection against histamine induced bronchospasm on conscious guinea pigs method. While the test compounds exhibited good antihistaminic activity, percentage protection data showed that all compounds of the series found to possess significant protection in the range of 64-77%. Structure activity relationship (SAR) studies indicated that the electronic nature of the substituent group of N-3 aromatic ring led to a significant variation in antihistaminic activity. For example electron withdrawing group (chloro substituent) enhanced the biological

activity, whereas electron releasing groups (methyl) made the compounds less active. From the SAR studies it is also revealed that different substituent over the C-2 position of quinazoline ring exerted varied biological activity. The presence of *N*-methyl piperazinyl group showed most significant activity, among the test compounds, 2-(3-(4-methyl piperazin-1-yl)propylthio)-3-(4-chloro phenyl) quinazolin-4(3*H*)-one **(PC5)** exhibited the most potent activity of the series with the percentage protection of 77.53 % which is more potent than that of standard chlorpheniramine maleate (percentage protection 70.09 %). As sedation is one of the major side effects associated with antihistamines, the test compounds were also evaluated for their sedative potentials, by measuring the reduction in locomotor activity using actophotometer on Albino Swiss mice. The results of sedative-hypnotic activity indicate that the test compounds were found to exhibit only negligible sedation (6-12%), whereas the reference standard chlorpheniramine maleate showed 33% sedation. Hence the compound **PC5** series as a lead molecule of the present study which is more potent 77.53% then the standard chlorpheniramine maleate 70.09%. Interestingly this lead compound exhibited lesser sedation (7%) than the standard chlorpheniramine maleate (33%).

PART-II

SYNTHESIS AND ANTIBACTERIAL ACTIVITY OF SOME NOVEL 1-(4-OXO-3-BUTYL-3*H*-QUINAZOLIN-2-YL)-4-(SUBSTITUTED) THIOSEMICARBAZIDES

Abstract

A new series of 1-(4-oxo-3-butyl-3*H*-quinazolin-2-yl)-4-(substituted) thiosemicarbazides were synthesized by the reaction of 3-butyl-2-hydrazino-quinazolin-4(3*H*)-one with various methyl esters of dithiocarbamic acid. The starting material 3-butyl-2-hydrazino-quinazolin-4(3*H*)-one was synthesized from butyl amine. When tested for their *in vitro* antitubercular activity using H_{37}RV strain on Middle brook 7H11 agar slants with OADC Growth Supplement, all the test compounds inhibited the growth of *Mycobacterium tuberculosis* at micro gram concentration. Among the test compounds, 1-(4-oxo-3-butyl quinazolin-2-yl)-4-(2-nitro phenyl) thiosemicarbazide **(AS6)**, 1-(4-oxo-3-butyl quinazolin-2-yl)-4-(4-chloro phenyl) thiosemicarbazide **(AS7)** and 1-(4-oxo-3-butyl quinazolin-2-yl)-4-(2-pyridyl) thiosemicarbazide **(AS8)** were found to be the most active compounds against *M. tuberculosis* with the MIC of 6µg/ml. The title compounds are also screened for the antimicrobial activity against some other gram positive and gram negative bacteria by agar dilution method, Compound **AS6** shown

most potent activity against *E. Coli* and *K. pneumoniae* while the compound **AS7** showed most potent activity against *S. typhi, E. Coli, K. pneumoniae, S. enteritidis and B. subtilis.*