LETTER TO THE EDITOR

MONOAMINE OXIDASE INHIBITORY ACTIVITY OF 2-ARYL-3-(5'-CHLOROBENZOPHENON-2'-YL)-QUINAZOLIN-4-(3H)-ONES

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Sir,

MAO activity produces the biggest hindrance in the way of action of many CNS active drugs by metabolizing them. They affect many adrenergic transmitters and their synthetic derivatives, depleting their level in the brain and producing CNS disorders. Therefore, use of many MAO inhibitors has been recommended in the CNS diseases (1,2). The quinazolinones have been described to be MAO inhibitors (3,4). An interesting observation of Joshi *et al.* (5) is that the substitution with halogen group at 6, and 8 position of quinazolinone results in an increase in the MAO inhibitory activity. In a previous communication (6), the title compounds have been reported to be non-toxic, hypnotics and anticonvulsants. Therefore, it was thought worthwhile to investigate the effect of substitution of different halogens (Cl, Br. and I) at 6, and 8 positions of quinazolinone moiety. This paper describes the results.

The spectrophotometric method was used for the determination of MAO activity of rat brain homogenate using benzylamine as the substrate (7). The amount of benzaldehyde formed during the oxidative deamination of benzylamine was estimated using a Hitachi-Perkin-Elmer Spectrophotometer at 250 nm.

The compounds were dissolved in propylene glycol and added to the reaction mixture in a final concentration of 1×10^{-3}M. Two experiments were done for each compound and the mean value of the MAO inhibitory effect of the title compounds is presented in Table I.

For comparison, 'o-phenanthroline' was used as a reference standard. In one set of experiments, 'o-phenanthroline' was used in a final concentration of 1×10^{-3}M instead of synthetic compounds and the test was repeated.

Visualizing Table I, the following chemical leads are evident.

1. The substitution of halogen group at 6,8 position of quinazolinone moiety increases the MAO inhibition. The MAO inhibitory activity seems to be related to the

electro-negativity of the halogen group. The more the electro-negativity, the more was the MAO inhibition (comparison among compound 1,2,3,4 and 5). Compound 1 had the least activity in the series. Substitution with 'iodo' group (E.N.=2.4) at 6 position increased inhibition. Substitution with bromo group (E.N.=2.8) further increased the inhibition. Then the inhibition was increased further by the 6,8-dibromo substitution. Dichloro substitution (E.N.=3.0) increased the inhibition to the highest level among the series (75.47%).

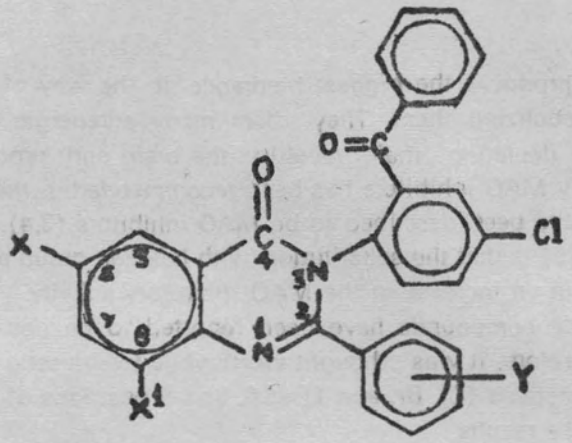

TABLE I : MAO inhibitory activity of 2-aryl-3-(5'-chlorobenzophenon-2'-yl)-quinazolin-4(3H)-ones.

Compound No.	*X*	*X*^{1}	*Y*	*MAO inhibitory activity* (%)
1	H	H	H	40.35
2	Br	H	H	56.78
3	I	H	H	43.46
4	Cl	Cl	H	75.47
5	Br	Br	H	65.39
6	I	I	o-Cl	40.74
7	Cl	Cl	o-Cl	55.58
8	Cl	Cl	p.NO_2	60.36
9	Br	H	p.NO_2	35.47
10	Br	Br	p.NO_2	47.37
Standard o-phenanthroline ($1x10^{-3}$M)				38.32

A similar trend was noticed in the case of compounds substituted with o-Cl or p.NO_2 in 'Y' position. Comparing the activity of compound 6 and 7, it can be seen that dichloro substituted quinazolone is more active than di-iodo quinazolone. Further, comparing the compounds 8,9 and 10 (Y=p.NO_2-) with one another, it is evident that dichloro quinazolone has maximum activity followed by dibromo and mono bromo quinazolones. These results correspond well with the findings of Parmar *et al.* (8) and Rastogi *et al.* (9), that an increase in MAO inhibition by the quinazolones results when they are substituted with halogens at 6 and 8 positions.

2. One more noticeable feature is that the dibromo quinazolinones are more inhibitory to MAO than their respective monobromo quinazolinones (comparing compound 10 with 9 and compound 5 with 2). Therefore, it appears that second halogen substitution at 8 position of quinazolinones, increases the inhibitory effects.

3. The standard MAO inhibitory agent, o-phenanthroline, was found to be only 38.32% inhibitory at the concentration of $1x10^{-3}$ using the same method. All compounds, except compound 9, of the present series were found to be better MAO inhibitors than o-phenanthroline.

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