INSECTICIDAL PROPERTIES AND CHEMICAL CONSTITUTION

Part I. Some Simple Flavone Derivatives

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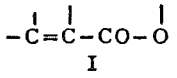
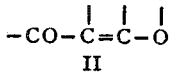
It is very difficult to give an explanation of the remarkable insecticidal properties of the pyrethrins and of rotenone and its allies in precise terms based on their chemical constitution. Their molecular structures are quite complex and further many factors of chemical and physical nature seem to contribute to their success. However, Läuger *et al.*[1] have in their important theoretical paper on natural and synthetic insecticides, suggested that in the pyrethrins the atom grouping (I) and in rotenone the grouping (II) form the toxophores. There is experimental support for grouping (I) from the study of simple coumarin derivatives and of the derivatives of pulvinic acid, a lichen product. No data appear to be available from the study of simple structures in support of grouping (II) as toxophore. The simple chromones and flavones would suggest themselves as suitable compounds for this purpose. The experiments of Mahal[2] however seem to indicate that these substances have no such action. He used chrysin, genkwanin, 7-hydroxy flavone, 6-hexyl-7-hydroxyflavone and calycopterin and found that they had no effect on round and tape worms and leeches. But calycopterin was claimed to have anthelmintic action by earlier workers[3] and karanjin, a flavonofuran, also reported to be toxic to fish.[4] There was therefore need for a careful investigation of the subject.



I



II

Using fresh-water fish (*Haplochilus panchax*) as experimental animals and adopting the criterion of toxicity already described in a previous publication[4] from these laboratories, the following series of hydroxy-flavones have now been tested for their toxic properties: 7-hydroxy flavone, 3:7 dihydroxy flavone, galangin, kæmpferol, quercetin and myricetin. In general these hydroxy compounds are found to be feebly toxic. The maximum effect is found in galangin, 3:7-dihydroxy flavone coming next. These two are fairly toxic. But there is considerable fall in 7-hydroxy flavone

on the one hand and kæmpferol and the higher members on the other. The former is found to take over 12 hours to produce the toxic effect in a concentration of 20 mg. per litre. The latter are without any appreciable toxicity. There is difficulty in experimenting with highly hydroxylated compounds owing to their sparing solubility in water.

The methyl ethers of the above compounds as also of some others (methyl ethers of herbacetin, gossypetin and quercetagetin) have been studied. They are more convenient to deal with in virtue of their greater solubility in water. But the remarkable point is that they are considerably more toxic. Obviously the factor of lipoid solubility has been provided in these ethers and these simple flavone derivatives are markedly toxic thus proving beyond doubt that the γ-pyrone ring is a toxophore. From the results given below it is clear that the simplest compound, 7-methoxy-flavone is the most toxic, and the toxicity decreases as the number of methoxy groups in the flavone molecule increases. This ether series therefore differs from the hydroxy compounds which exhibit a maximum of potency in galangin. With these strong fish poisons the curves relating to the concentration and time of toxicity indication (turning time) have the characteristic hyperbolic portions as found in similar cases.[4]

The following table gives the data obtained in one series of experiments. Though variations may arise in the exact turning times due to seasonal and individual variations in the susceptibilities of the fish which are obtained from a big tank, the compounds fall in the same order in different experiments. For the purpose of roughly indicating the degree of toxicity the reading obtained for rotenone under the same conditions is also included.

Name of the compound	Concentration per litre	Turning time
	mg.	minutes
3:7-Dihydroxyflavone ..	20	35·0
Galangin ..	20	15·0
7-methoxy flavone ..	20	2·7
	10	5·0
3:7-dimethoxy flavone ..	20	7·0
	10	19·5
Galangin trimethyl ether ..	20	7·5
Kæmpferol tetramethyl ether ..	20	9·5
Quercetin pentamethyl ether ..	30	35·0
Herbacetin pentamethyl ether ..	30	25·0
Myricetin hexamethyl ether ..	30	37·0
Quercetagetin hexamethyl ether ..	30	33·5
Rotenone ..	1·0	6·5

Though the toxicity decreases with increasing number of methoxyl groups there are a few noteworthy features. There is marked drop from

kæmpferol tetramethyl ether to quercetin pentamethyl ether, but there is not much difference between this pentamethyl ether and the next higher member, myricetin hexamethyl ether. These involve changes in the side phenyl nucleus. A rise from one to two methoxyl groups in this part is accompanied by considerable loss in toxicity, but an increase to three does not mean any further difference. Probably for this reason herbacetin pentamethyl ether is definitely more toxic than its isomer quercetin pentamethyl ether. This point could not be checked further using gossypetin hexamethyl ether due to its sparing solubility in water; comparable and effective concentrations could not be reached. But quercetagetin hexamethyl ether has more or less the same toxicity as its isomer myricetin hexamethyl ether which again, as pointed out earlier, is equal to quercetin methyl ether in this respect.

SUMMARY

The simpler methoxy flavones and some of the corresponding hydroxy compounds are markedly toxic to fish. This definitely establishes that the pyrone ring containing the atom grouping II is a toxophore.

REFERENCES

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4. Krishnaswami and Seshadri .. *Proc. Ind. Acad. Sci.*, (A), 1942, **16**, 231.