

BRIEF NOTE

PLANT FLAVONOIDS AND NUCLEIC ACID SYNTHESIS IN HUMAN LEUKOCYTES¹MICHAEL A. FARROW,² DAVID F. BLAYDES and KNOX VAN DYKE, West Virginia University, Morgantown, WV 26506

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Flavonoids and related compounds are inhibitors and stimulators of plant growth, involved in host resistance and susceptibility, and are insect attractants. These roles and the possible modes of action of the substance are discussed in J. B. Pridham (1965) and J. Harbourn (1964).

As an extension of work aimed at finding whether plant hormones affect RNA and DNA synthesis in leukocytes (as they may do in intact plants) we tested certain flavonoids on the synthesis of

flavonoids in this system and report the results here.

The microscreening system developed by Farrow and Van Dyke (1971) is based upon the uptake, phosphorylation and incorporation of uridine-5-³H into RNA of the phytohemagglutinin stimulated leukocytes of human whole blood or the uptake, phosphorylation and incorporation of thymidine-methyl-³H into DNA of the phytohemagglutinin stimulated leukocytes from human whole blood. After incubation, trichloroacetic acid was

TABLE 1
Percent Inhibition or Stimulation of Thymidine and Uridine Incorporation.**

| Thymidine* | Trihydroxy Flavone | Flavone | Fisetin | Uridine* | Fisetin |
|------------------|--------------------|---------|---------|------------------|---------|
| 10 ⁻⁴ | — | — | — | 10 ⁻⁴ | 9.8%+ |
| 10 ⁻⁵ | — | — | — | 10 ⁻⁵ | — |
| 10 ⁻⁶ | — | 66.3% | — | 10 ⁻⁶ | 28.2%+ |
| 10 ⁻⁷ | 24.9%— | 76.6%— | 80.7%— | 10 ⁻⁷ | 28.0%+ |

*Molar concentrations.

**The plus (+) indicates percent stimulation of incorporation of tritiated precursor when compared to control without the test substance. The Minus (-) indicates percent inhibition of incorporation of tritiated precursor when compared to control without the substance. The incorporation values (percentages indicated above) are based on cpm corrected for efficiency and background. The data are averages of 2 duplicates of 2 sets run twice. All data presented were significantly different from the control using the Fisher Exact probability Test, Huntsberger and Leaverton (1970). The dash - indicates no significant difference in incorporation of precursor between test substance and control sample.

RNA and DNA in our human leukocyte system. In an earlier paper, we reported the inhibitory activity of naringenin and ferulic acid (Farrow *et al* 1976). We subsequently tested a number of other

used to extract the nucleic acids. This system was originally developed to screen anti-leukemic drugs; however, it can also be used to test any type of substance that acts at any step in the synthetic pathway of RNA or DNA.

The flavonoids utilized in this study included 4, 5, 7 trihydroxyflavone, flavone and fisetin and were tested at four con-

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centrations as shown in table 1. Morin dehydrate was also tested but had no effect at concentrations up to 10^{-4} M.

Low concentration of Flavone and Fisetin inhibit thymidine incorporation. Trihydroxy flavone had no effect, with the exception of one concentration. Interestingly, this inhibitory effect at a lower concentration and not at a higher concentration was observed also by Farrow *et al* (1976). At present we have no explanation for this paradox.

Fisetin stimulated uridine incorporation whereas Morin dihydrate, 4,5,7 trihydroxy flavone and Flavone were without effect on uridine incorporation. The possibility exists that the flavonoids might bring about their effects or certain of their effects in plant systems by affecting nucleic acid metabolism. Both the stimulatory and inhibitory effects ob-

observed on nucleic acid synthesis in the human leukocyte system could be accounted for by the flavonoid interacting at a step in the synthetic pathway of nucleic acid.

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