LIGNANS IN *FORSYTHIA* LEAVES AND CELL CULTURES

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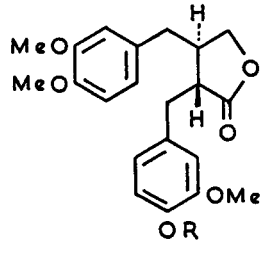
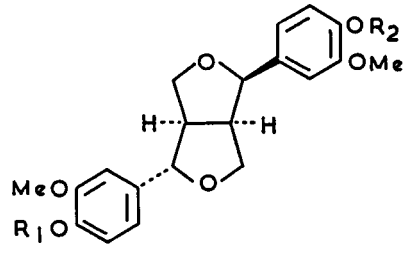
A wide variety of plant lignans has been reported to have physiological activity, and in connection with our studies on tumour-inhibitory lignans, we have investigated the lignan constituents of *Forsythia*, used in the treatment of cancer and as an antibiotic in China. A range of garden varieties of *Forsythia* were screened for lignan content, and one unidentified cultivar of *F. intermedia* was selected for further study.

In common with other species of *Forsythia* investigated (Thieme and Winkler, 1968; Kitagawa et al., 1984), leaf material from this plant contained representatives of two major classes of lignans, namely dibenzylbutyrolactones and 2,6-diaryl-3,7-dioxabicyclo[3,3,0]octanes. The known lignans, (-)-arctigenin (1),(-)-arctiin (2), (+)-phillygenin (3), (+)-phillyrin (4),(+)-epipinoresinol (5) and (+)-epipinoresinol glucoside (6) were isolated by HPLC (Partisil 10 ODS2, MeOH-H_2O) and characterised by high resolution ^1H and ^{13}C NMR spectroscopy. Typical yields from leaf material (mg/g dry wt) were: (1) 0.75, (2) 20, (3) 0.75, (4) 12, (5) 2.4, (6) 16.



(1) R=H

(2) R=Glc



(3) R_1=H, R_2=Me

(4) R_1=Glc, R_2=Me

(5) R_1=R_2=H

(6) R_1=H, R_2=Glc

When cell cultures derived from the leaf tissue were established, the pattern of lignans accumulated varied substantially. In both callus and suspension cultures, (+)-epipinoresinol glucoside (6) was the major lignan isolated, together with smaller amounts of phillyrin (4) and traces of (+)-epipinoresinol (5). For example, in cell suspension cultures (MS salts medium + 30 g/l sucrose, 0.5 g/l casein hydrolysate, 0.2 mg/l kinetin and 1 mg/l 2,4-D), yields were: (4) 2.5, (5) 0.075, (6) 7.5 mg/g dry wt after 4 weeks.

The six lignans isolated from *Forsythia* are almost certainly all derived biosynthetically from the same phenylpropane precursor coniferyl alcohol (Stöckigt and Klischies, 1977). However, it is clear that in cell cultures, biosynthetic precursors are no longer channelled into synthesis of dibenzylbutyrolactone lignans, but wholly into epipinoresinol derivatives. In addition, methylation of epipinoresinol to phillygenin seems to be inhibited.

Kitagawa, S., Hisada, S. and Nishibe, S. (1984) Phytochemistry, 23, 1635.
Stöckigt, J. and Klischies, M. (1977) Holzforschug, 31, 41.
Thieme, H. and Winkler, H.J. (1968) Pharmazie, 23, 402; 23, 519.