STRUCTURE OF MUKAADIAL, A MOLLUSCICIDE FROM THE WARBURGIA PLANTS

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The structure of a new sesquiterpene dialdehyde, mukaadial, isolated from <u>Warburgia stuhlmannii</u> and <u>W</u>. <u>ugandensis</u> and possessing molluscicidal property, has been established by means of spectroscopic and chemical data.

The barks of the East African medicinal trees, <u>Warburgia stuhlmannii</u> and <u>W. ugandensis</u> (Canellaceae) have recently yielded a series of sesquiterpene dialdehyde as insect antifeedant against the African armyworm <u>Spodoptera exempta</u>^{1,2)} with a leaf disk assay.³⁾ These insect antifeedants have been shown to possess a wide spectrum of biological activity including molluscicidal property.⁴⁾ Hence, these sesquiterpene dialdehydes are currently receiving considerable attention as potential molluscicides for the control of schistosomiasis.⁵⁾ However, the isolation of the <u>Warburgia</u> extracts was not guided by a molluscicide assay. For this reason further purification of the hexane extract of <u>W. stuhlmannii</u> (Mukaa in Swahili) has been carried out. Molluscicidal activity was monitored as described previously.⁴⁾ This has now led to the isolation of an additional new molluscicidal sesquiterpene dialdehyde, mukaadial (1),⁶⁾ which is closely related to warburganal (2).¹⁾ The molluscicidal activity of mukaadial (LD₅₀=20 ppm within 24 h against the South American snail <u>Biompholaria glabratus</u>) is about one tenth of warburganal (LD₅₀=2 ppm within 24 h).

The structure of mukaadial, mp 173°C (sublime) is based on the following evidence: $C_{15}H_{22}O_4$, (CI-MS with <u>iso</u>-butane and elemental analysis): λ_{max} (EtOH) 210 and 235(sh) nm (ε 4300 and 2000); ν_{max} (CHCl₃) 3550(OH), 3450(intramol. H-bonded OH), 2850(CHO), 1720(CHO), 1685 and 1650 cm⁻¹(enal). The ¹³C NMR(CDCl₃) spectrum showed the presence of 3 CH₃, 3 CH₂, 3 quaternary C, 2 olefinic C, and 2 carbonyl C atoms.⁷Pertinent 400 MHz ¹H NMR(CDCl₃) data are; δ 9.70(1H, s, 9-CHO), 9.47 (1H, s, 8-CHO), 7.04(1H, d, J=2 Hz, 7-H), 4.57(1H, dd, J=10, 2 Hz, 6-H), 4.1(OH), 1.90(1H, d, J=10 Hz, 5-H), 1.13(s, CH₃), 1.16(s, CH₃), 1.20 ppm(s, CH₃). The ¹H NMR spectrum is closely similar to that of warburganal, except for the additional low field signal at δ 4.57 ppm due to a new hydroxy group at C-6. The stereochemistry of this new hydroxy group was established as equatrial because the large coupling (J=10 Hz) was observed between the 6-H and 5-H.

The stereochemistry at C-9 was confirmed by conversion of mukaadial into

6-oxo-lactone (4). Mukaadial was treated with 1 mol dm^{-3} NaOH aq soln. at room temp to yield the lactone (3) $C_{15}H_{22}O_4$, M 266 through intramolecular Cannizzaro reaction. The ¹H NMR(CDCl₃) of this lactone (3) shows the AB q at δ 4.38 ppm (J=11 Hz, 11-H) instead of dialdehyde groups. Jones' oxidation of 3 gave the 6-oxo-lactone (4). The treatment of ugandensidial (cinnamodial) (5) by the similar manner gave 6-oxo-lactone (4) which was identical in all respects with the aforementioned 6-oxo-lactone (4).

The absolute configuration of mukaadial was established by the CD(EtOH), $\Delta_{e}(335)$ -0.4 and $\Delta_{e}(291)$ -0.7 which was almost identical with those of warburganal. Since the absolute configuration of warburganal was confirmed by the synthesis of the optically active warburganal from 1-abietic acid,⁸⁾ the absolute configuration of mukaadial is that shown in 1. This also established the absolute configuration of ugandensidial.

The structure-activity relationships among the sesquiterpene dialdehydes seem to be of interest since polygodial,¹⁾ warburganal and muzigadial²⁾ exhibit potent antimicrobial^{9,10)} and anticomplemental¹¹⁾ activity -- mukaadial dose not show these properties.

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 The same molluscicide was also isolated from W. <u>ugandensis</u> later.
 ¹H and ¹3C NMR spectra were recorded in CDCl₃ solution at 400 MHz and 50 MHz, respectively. 5) 6) 7) respectively.
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