Sporidesmolide I, a metabolic product of *Sporidesmium bakeri* Syd.

Current interest in the pasture fungus *Sporidesmium bakeri* Syd. (= *Pithomyces chartarum* (Berk. & Curt.) Ellis) results from its association with a disease of ruminants known as facial eczema[1-4]. One important metabolic product of this fungus[5,6] is probably identical with the "beaker test" substance[7,8] isolated from toxic pastures. This note reports the isolation and probable structure of a major component of the fungal "beaker test" substance. The name "sporidesmolide I" is proposed for this compound.

The chloroform-soluble portion of the crude isolate[6] was recrystallized to constant melting point and specific rotation from chloroform–methanol mixtures. Sporidesmolide I so obtained crystallized from 70 % (v/v) acetic acid in fine needles, m.p. 261–263° (corr.), $[\alpha]_D^{17°}$ −217° in chloroform (*c*, 1.5). (Found: C, 62.11, 61.78; H, 9.04, 9.12; O, (detd.), 20.14, 20.01; N, 8.61, 8.96. Calc. for $C_{33}H_{58}O_8N_4$: C, 62.04; H, 9.15; O, 20.04; N, 8.77.). Tests for free amino, hydroxyl and carboxyl groups were negative. Total acid hydrolysis gave α-hydroxy-isovaleric acid, together with valine, leucine and N-methylleucine. Quantitative paper chromatography of the hydrolysate[9] showed that the amino acids were present in the ratio 2:1:1, and permitted the calculation of a minimal molecular weight of 640 ± 10 %. Isopiestic measurements in chloroform gave a value of 580, but there was some indication of decomposition[10]. More satisfactory evidence for the molecular weight is being sought.

Sporidesmolide I consumed 2.0 equivalents of alkali for the formula weight of 639. From the resulting solution a mixture of two acids was isolated. One of these was sporidesmolic acid B, $C_{17}H_{32}O_5N_2$, for which the structure L-α-hydroxyisovaleryl-L-valyl-N-methyl-L-leucine has already been proposed[6]. The second, sporidesmolic acid A, was readily separated because of its insolubility in chloroform. It crystallized from aqueous acetic acid as colourless prisms, m.p. 197–199° (corr.), $[\alpha]_D^{17°}$ + 61° in glacial acetic acid (*c*, 4). (Found: C, 58.50, 58.43; H, 8.91, 9.08; O, (detd.), 24.23, 24.27; N, 8.67, 8.63. Calc. for $C_{16}H_{30}O_5N_2$: C, 58.16; H, 9.15; O, 24.21; N, 8.48. Eq. wt. (by titration) 332,328; calc.: 330). Sporidesmolic acid A possessed no free amino group. On total acid hydrolysis it yielded L-α-hydroxyisovaleric acid, D-valine and D-leucine, the amino acids being in 1:1 ratio. Partial hydrolysis (conc. HCl, 37°) for 72 h liberated leucine and no other ninhydrin-positive substance. Sporidesmolic acid A is thus L-α-hydroxy-isovaleryl-D-valyl-D-leucine.

The two sporidesmolic acids were isolated in approximately equal amount and in almost theoretical yield; no other product was detected. The evidence is consistent

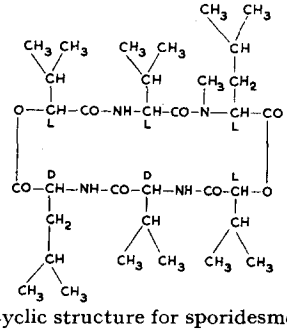

Fig. 1 Cyclic structure for sporidesmolide I.

with a cyclic structure for sporidesmolide I, in which equal numbers of residues of sporidesmolic acids A and B are combined. An 18-membered ring (Fig. 1) is considered most likely, but the question of ring size cannot be settled until unequivocal evidence for the molecular weight is available.

"Strain C" of *S. bakeri* produces in culture some 1–2 % of crude "beaker test" substance[11], of which about two-thirds is sporidesmolide I. Most of the remainder appears to be a homologue, sporidesmolide II, in which the D-valine residue is replaced by one of D-isoleucine. "Strain C" is not a single-spore isolant[12], and its production of two such substances may reflect metabolic differences between constituent true strains.

While the occurrence of D-amino acids in microbial metabolites is to-day almost commonplace, the L-configuration of the α-hydroxy-isovaleric acid residues in sporidesmolide I is noteworthy. The L-isomer does not appear to have been previously reported from natural sources. Since tests have failed to show antibiotic activity in the "beaker test" substance, it seems possible that the antibiotic action of similar compounds[13–16] may be mediated, at least in part, by the D-configuration of certain of their hydroxy acids. The configuration of the β-hydroxytridecanoic acid residue in the related antibiotic esperin[17] is unfortunately at present unknown.

Sporidesmolide I is the most recently investigated member of the class of cyclic hydroxyacyl-aminoacyl compounds for which the generic name "peptolide" was recently proposed[6]. The author's attention has since been drawn to an earlier suggestion[18] that such compounds and their straight-chain analogues be termed "depsipeptides", a name emphasising their analogy to both depsides and peptides. In these circumstances we wish to withdraw the name "peptolide". The chemistry of these compounds has recently been reviewed[19].

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