

DIUMYCIN A' AND DIUMYCIN B',
NEW MEMBERS OF THE DIUMYCIN
FAMILY OF ANTIBIOTICS

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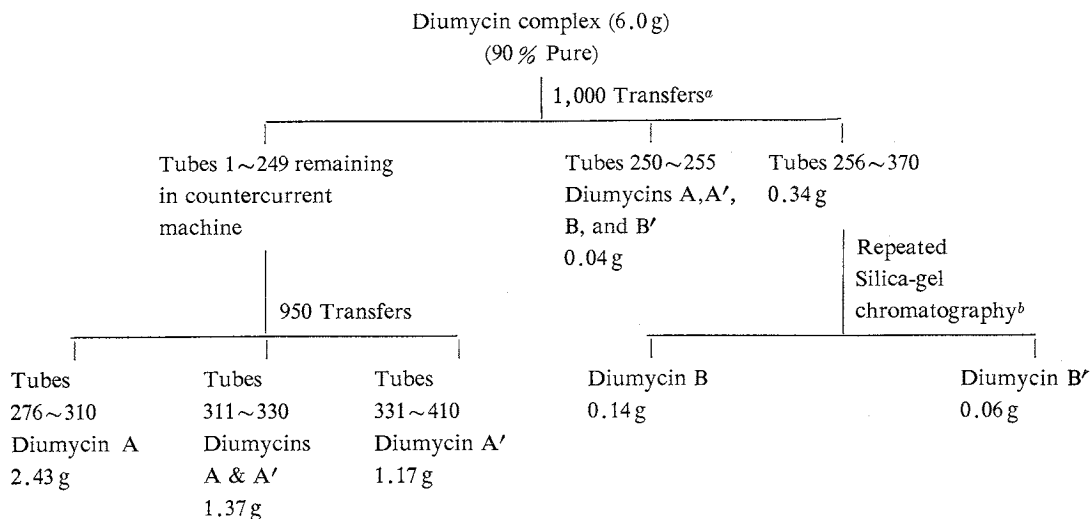
Studies of the isolation and chemical and biological characterization of the phosphorus-containing antibiotics, diumycin A and diumycin B, have been reported^{1,2,3,4,5,6}. Similar phosphorus-containing antibiotics that are described in the literature⁷ include macarbo-mycin⁸, moenomycin^{9,10}, prasinomycin¹¹, 8036 RP¹², 11,837 RP¹³ and 19,402 RP¹⁴. We now wish to report the preliminary characterization of diumycin A' and diumycin B', isolated from the diumycin complex of antibiotics produced by *Streptomyces umbrinus* ATCC 15972.

Examination of fermentation broths of *S. umbrinus* by means of paper chromatography in the system *n*-propanol-*n*-butanol-0.5 N ammonia (1:3:4) and bioautography against *Staphylococcus aureus* indicated the presence of two active components, in addition to diumycin

A and diumycin B. By use of the isolation procedure described previously¹³, followed by fractionation through an ion-exchange column [Dowex 1-2 X (OH⁻), gradient elution, 0.5~1.0% NaCl in methanol-water (8:2)], a 90% pure antibiotic preparation containing the four components detected in the initial fermentation broth was obtained. Countercurrent distribution of this complex under nitrogen in the system *n*-propanol-*n*-butanol-0.5 N ammonia (2:3:4), combined with chromatography over silica gel using *n*-propanol-2 N ammonia (8:2), gave pure samples of diumycins A, A', B and B' (Chart 1).

A comparison of the elemental analyses and neutralization equivalents of diumycins A, A', B and B' is shown in Table 1. A comparison of the physical and chemical properties of the diumycins is shown in Table 2. Diumycin A', like diumycin A, shows a strong absorption at 257 nm in water or in 0.1 N NaOH, whereas diumycin B' and diumycin B show no absorption at wavelengths greater than 220 nm. Acid hydrolysis (2 N HCl, 100°C, sealed tube, 2.5 hours) of each antibiotic, followed by paper chromatography in the systems pyridine-*n*-butanol-water (4:6:3) and *n*-butanol-acetic acid-water (12:3:5), indicated the presence of glucose in diumycins A and B, but not in diumycins A' or B'. STEIN-MOORE

Chart 1



^a *n*-Propanol-*n*-butanol-0.5 N ammonia (2:3:4)

^b *n*-Propanol-2 N ammonia on acid-washed silica gel

Table 1. Analyses*

Compound	Found (per cent)					Neutralization equivalent**
	C	H	N	P	H ₂ O of hydration	
Diumycin A	42.70	5.98	3.87	2.05	7.7	537
Diumycin A'	43.38	6.25	3.99	1.69	7.3	512
Diumycin B	42.88	6.37	3.88	1.79	10.3	678
Diumycin B'	43.06	6.17	4.23	1.62	10.1	612

* Analyses are of hydrated sodium salts.

** Potentiometric titrations of anhydrous free acids with aqueous NaOH.

Table 2 Physical and chemical properties of the diumycins

	Diumycin A	Diumycin A'	Diumycin B	Diumycin B'
Melting point of free acid	~170° (dec.)	165~170°(dec.)	~170° (dec.)	~170° (dec.)
$[\alpha]_D^{H_2O}$	+8.0°	+13°	+9.6°	+13°
$\lambda_{max}^{H_2O} (E^1\%)$	257 nm (122)	257 nm (129)		
$\lambda_{max}^{0.1N HCl} (E^1\%)$	246 nm (78)	246 nm (81)		
$\lambda_{max}^{0.1N NaOH} (E^1\%)$	257 nm (120)	257 nm (126)		
Distribution coefficient*	0.18	0.21	0.30	0.40
Rf**	0.32	0.35	0.45	0.52
Glucose	+	-	+	-
Glucosamine	+	+	+	+
Diumycinol lipid	+	+	+	+

(+) = present (-) = absent

* *n*-Propanol-*n*-butanol-0.5 N ammonia (2 : 3 : 4)** *n*-Propanol-*n*-butanol-0.5 N ammonia (1 : 3 : 4) on paper chromatography

analysis of hydrolysates (6 N HCl, 100°C, sealed tube, 16 hours) of the diumycins indicated two equivalents of glucosamine and three equivalents of ammonia for each sample, and no other amino sugars or amino acids. Acid hydrolysis (1 N HCl, 105°C, 30 min.) of diumycin A' and diumycin B' gave the same mixture of lipids, diumycinol, isodiumycinol, and diumycene, as obtained from diumycin A and diumycin B under identical conditions^{3,4}.

It appears that the only gross structural differences among these antibiotics are the presence or absence of a 257-nm chromophore and glucose. Diumycins A and A' are chromophore-containing entities, whereas diumycins B and B' are not; diumycins A and B are glucose-containing compounds, and diumycins A' and B' are not. No significant differences in antimicrobial activities have been found among the diumycins.

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