Communications to the editor

CHEMISTRY OF LEUCOMYCIN. IX

IDENTIFICATION OF LEUCOMYCIN A_3 WITH JOSAMYCIN

Sir:

Leucomycin (Kitasamycin) is a basic macrolide antibiotic discovered by HATA *et al.* in 1953. *Streptomyces kitasatoensis* HATA was reported to produce many active components, namely leucomycins A_1, A_2, B_1~B_4.[2,3] However, further studies conducted in recent years resulted in the isolation of leucomycins A_3~A_9. Furthermore, chemical structures of eight components of them[4,5] were determined. Josamycin is a macrolide antibiotic produced by *Streptomyces narbonensis* var. *josamyceticus* which was discovered by UMEZAWA *et al.*[6], and has quite similar biological properties to those of leucomycin; namely both of them show similar antibacterial spectrum and resistance pattern of macrolides which was reported by MITSUHASHI[7]. Furthermore, leucomycin A_3[8] and josamycin show similar values in their physico-chemical properties (Table 1), and those two compounds are considered to be the same from the results of their structural studies[9] that josamycin contains each one molecule of iso-valerianic acid, mycarose, and mycaminose and also, its lactone ring has aldehyde group (-CHO), methoxyl group (-OMe) and diene group (-C=C-C=C-C-). Comparison of their TLC and IR-spectra proved that leucomycin A_3 and josamycin

Fig. 1. TLC of leucomycin A_3 (A_3) and josamycin (J)

Note: Kieselguhr G 0.5 mm (benzene : acetone 2 : 1) coloration: 20 % H_2SO_4

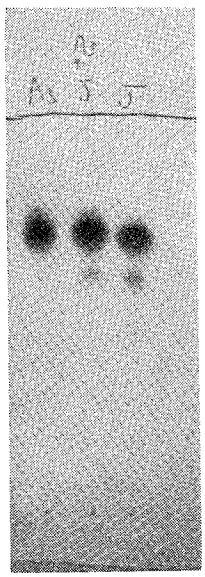
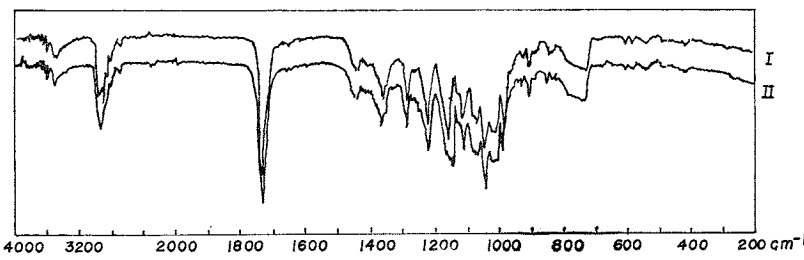


Table 1. Physico-chemical properties of leucomycin A_3 and josamycin[6,8]

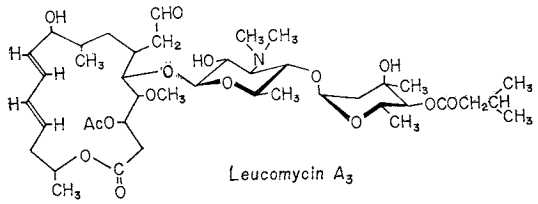
	Leucomycin A_3[8]		Josamycin[6]
Melting point	120~121°C		130~133°C
Optical rotation	$[\alpha]_D^{25}$ −55.4° (*c* 1, $CHCl_3$)		$[\alpha]_D^{25}$ −70° (*c* 1, EtOH)
Value of pKa	6.70 (50 % EtOH)		7.1 (40 % EtOH)
Analysis	(Calcd)	(Found)	
C (%)	60.93	60.57	60.63
H (%)	8.40	8.17	8.49
O (%)	1.69	1.75	1.77
Formula	$C_{42}H_{69}NO_{15}$		$C_{40}H_{69}NO_{14}$
UV spectrum	λ_{max}^{MeOH} 231~232 ($E_{1cm}^{1\%}$ 351)		λ_{max}^{HCl} 232 ($E_{1cm}^{1\%}$ 325)
Solubility			
soluble	MeOH, EtOH, EtAc, BtAc, acetone, benzene, $CHCl_3$		Same
insoluble	H_2O, petroleum ether		Same

Fig. 2. Infrared spectra of leucomycin A_3 (II) and josamycin (I) (CCl_4 method)



are completely the same, as explained in this report.

TLC of leucomycin A_3 and josamycin, recrystallized from benzene solution after extraction from commercial tablets, was conducted using a mixture of benzene and acetone (2 : 1) as developing solvent. Josamycin and leucomycin A_3, as shown in Fig. 1, gave the same Rf value (0.69). The josamycin mentioned above contained several



Leucomycin A_3

Fig. 3. UV-spectra of leucomycin A_3 and josamycin.
(95 % EtOH, 3.1×10^{-2} mg/ml)

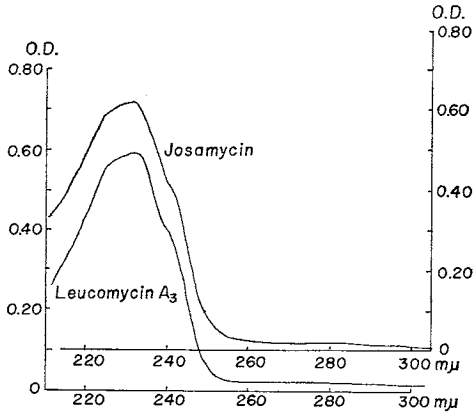
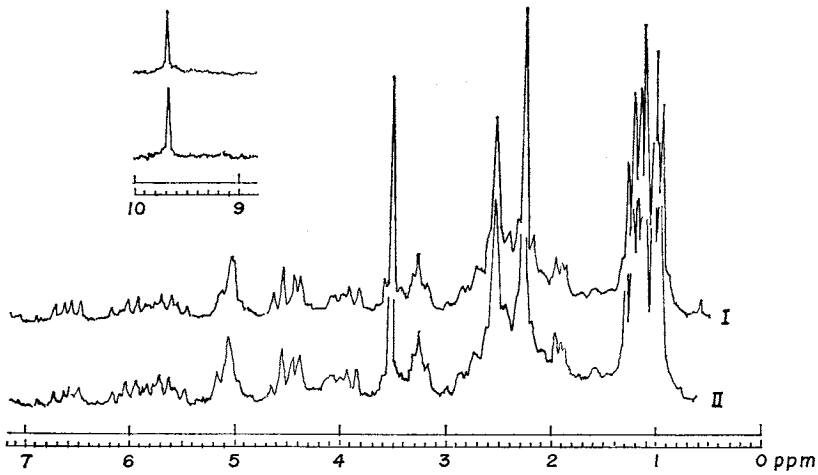


Fig. 4. NMR-spectra of leucomycin A_3(II) and josamycin (I)
(100 MHz $CDCl_3$).



other minor active components visible on TLC. Further, purification of josamycin was accomplished by silica-gel chromatography with benzene and acetone, recrystallization from its benzene solution and finally drying at 60°C for a day. Its IR-spectrum is shown in Fig. 2, along with that of leucomycin A_3. No definite conclusion could be made from mixture melting point determination as these two substances do not show a sharp melting point. However, identity of the two compounds was confirmed by complete coincidence of their IR-spectra, as well as UV- and NMR- analyses (Figs. 3 and 4).

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