IDENTITY OF MULTHIOMYCIN WITH NOSIHEPTIDE

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Multhiomycin¹⁾ was isolated as a strong anti-bacterial metabolite of *Streptomyces antibioticus* 8446 CC₁ and is a member of sulfur-containing antibiotics, such as thiostrepton, siomycins, micrococins, and thiopeptins.²⁾ The mode of action was shown to be inhibition of bacterial protein synthesis.³⁾

Degradation studies of this antibiotic showed that it contains threonine, dehydroalanine and cysteine type moieties (1 mole each), a weak acidic function and several thiazole structures.

Carbon-13 NMR spectra of multhiomycin (JNM FX-100 25.05 MHz in DMF) revealed the presence of three quartets at 12.7, 14.3 and 18.4, four triplets at 30.0, 39.1, 66.9 and 103.4, fourteen doublets at 46.2, 50.4, 57.5, 66.9, 67.5, 115.4, 120.8, 123.9, 125.1, 125.6, 126.0, 126.8, 127.7 (broad) and 129.2, and twenty eight singlets at 119.4, 125.8, 129.8, 130.3, 130.9, 131.1, 134.8, 135.0, 138.6, 144.1, 148.5, 149.9, 150.3, 151.0, 151.7, 154.8, 158.7, 160.4 (high), 160.6, 164.7, 165.9, 167.2, 168.2, 169.2, 170.4, 171.2, 173.4 and 182.1 ppm.

These figures were found to parallel those reported for nosiheptide, C₅₁H₄₃N₁₃O₁₂S₆, whose structure was determined by X-ray crystallography⁴⁾ and chemical procedures⁵⁾ as shown in Fig. 1.

The direct comparison of multhiomycin with authentic nosiheptide by thin-layer chromatography (AcOEt - MeOH = 10:1, CHCl₃ - MeOH = 10:1 on silica gel plates buffered with NaH₂PO₄) afforded the identical R_f values (0.69 and 0.42 respectively) for both antibiotics, and their IR spectra were superimposable to each other. (Fig. 2)

Consequently, multhiomycin is identical with nosiheptide and the molecular structure of multhiomycin could be depicted as shown in Fig. 1.

Fig. 1. Structure of nosiheptide and multhiomycin

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Fig. 2. IR Spectra of multhiomycin and nosiheptide

Table 1. ^{13}C -NMR chemical shifts for nosiheptide^{5b)} and multithiomycin

Fragment	Nosiheptide	Multithiomycin
$\text{C}=\text{O}$	182.3, 171.5, 170.7, 169.5, 168.4, 167.5, 166.2, 164.9	182.1, 171.2, 170.4, 169.2, 168.2, 167.2, 165.9, 164.7
$\text{=}\overset{ }{\text{C}}\text{-OH}$ A	173.6	173.4
$\text{N}=\text{C-S}$ A C	160.8, 160.7, 158.9 (br), 155.1	160.6, 160.4 (high), 158.7, 154.8
$\text{C}=\text{C-N}$ A C	152.0, 151.2, 150.6, 150.2, 148.8	151.7, 151.0, 150.3, 149.9, 148.5
pyridine <i>o</i> -	144.4, 135.2	144.1, 135.0
$\text{C}=\text{C C-9}$ E	138.9	138.6
$\text{C}=\text{C}$ A E	135.1, 131.4, 131.2, 130.5	134.8, 131.1, 130.9, 130.3
$\text{C}=\text{C C-8}$ E	130.0	129.8
$\text{C}=\text{CH-S}$ A C	129.5, 127.9, 127.7, 126.2, 125.8	129.2, 127.7 (br), 126.0, 125.6
pyridine <i>p</i> -	126.9	126.8
$\text{C}=\text{C C-4}$ E	126.0	125.8
$\text{CH}=\text{C C-6}$ E	125.3	125.1
$\text{CH}=\text{C C-5}$ E	124.1	123.9
$\text{CH}=\text{C}$?	121.0	120.8
$\text{C}=\text{C C-3}$ E	119.6	119.4
$\text{CH}=\text{C C-7}$ E	115.6	115.4
$\text{CH}_2=\text{C}$	103.6	103.4
$\text{CH}_2\text{-O, CH-O}$ B D E	67.7, 67.1, 67.1	67.5, 66.9, 66.9
CH-N B	57.7	57.5
CH-N D	50.6	50.4
CH ?	46.4	46.2
$\text{CH}_2\text{-C}$ D	39.5	39.1
CH_2 ?	30.2	30.0
CH_3 B	18.6	18.4
CH_3 ?	14.4	14.3
CH_3 E	12.7	12.5

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