

NOTE

MATCHAMYCIN: A NEW
ANTIBIOTIC PRODUCED BY
STREPTOMYCES E-753

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In the course of our search for new antibiotics, a new antibacterial substance was found in fermented broth of a *Streptomyces* species indexed E-753 in our culture collection. *Streptomyces* E-753 was isolated from a soil sample of Sonoda, Osaka Prefecture, in 1963. Some properties of this organism on various agar media are summarized in Table 1. Detailed morphological studies on the organism which will be published elsewhere established that it was a new strain designated *Streptomyces amagasakiensis* nov. sp.¹⁾

In V-medium (corn starch 10 g, glycerol

5 g, soybean meal 10 g, corn steep liquor 5 g, NaCl 3 g, CaCO₃ 3.5 g in one liter of water), the strain produced a green antibacterial substance. After purification, this was characterized as a new antibiotic, and named "Matchamycin" (matcha means green tea in Japanese). When the crude antibiotic was chromatographed on silicic acid, inactive substances were eluted by various organic solvents such as petroleum ether, benzol, acetone, chloroform, and ethyl acetate, whereas matchamycin remained on the column, and was finally eluted with methanol.

The physicochemical properties of matchamycin are summarized in Table 2. It has green color and copper was detected in its emission spectrum with a quartz spectrometer (9F-60, Shimadzu). The presence of copper in its molecule was further confirmed by elemental analysis. Matchamycin shows an absorption maximum at 320 m μ (Fig. 1), and its infrared spectrum is shown in Fig. 2. Color and biological activity of matchamycin change with pH as shown in Table 2 and Fig. 3. It has rather stronger antibacterial

Table 1. Identification of *Streptomyces* E-753

Medium*	Vegetative mycelium		Aerial mycelium (spiral)			Soluble pigment
	Growth	Color	Growth	Color of spore	Form of sporulation	
1	moderate	liquefaction in 30 days				
2	moderate	pale yellow	moderate	yellowish white (white)	—	—
3	abundant	pale yellow	good	pinkish gray (white)	lichenous	—
4	abundant	pale yellow (brown)	poor (moderate)	pinkish gray (white)	—	—
5	abundant	grayish yellow green	abundant	purplish gray	velvety	—
6	abundant	dull yellow orange	abundant	brownish white in circumference	velvety	—
7	abundant	dull yellow	abundant	white	velvety	—
8	good	gray (yellowish greenish gray)	abundant	purplish gray	powdery	—
9	good	grayish white	poor	—	—	—

Observations were carried out after 7 days and 14 days.

* Media; (1) gelatin medium: meat extract 0.3, peptone 0.3, NaCl 0.1, gelatin 30%.

(2) glucose-asparagine agar: glucose 1.0, K₂HPO₄·12H₂O 0.05, asparagine 0.05, agar 2.0%.

(3) nutrient agar: peptone 0.5, meat extract 0.5, NaCl 0.2, agar 2.0%.

(4) nutrient-glucose agar: (3) +glucose 1.0%.

(5) starch agar: potato-soluble-starch 1.0, K₂HPO₄ 0.03, MgSO₄ 0.1, NaCl 0.05, NaNO₃ 0.1, agar 2.0%.

(6) yeast-extract agar: yeast extract 1.0, glucose 1.0, agar 2.0%.

(7) milk medium: skim milk powder 10.0, B.T.B. solution 0.2%.

(8) Czapek agar: NaNO₃ 0.2, K₂HPO₄ 0.05, MgSO₄ 0.05, KCl 0.05, FeSO₄ 0.001, sucrose 3.0, agar 2.0%.

(9) tyrosine agar: glucose 1.0, tyrosine 0.1, (NH₄)₂SO₄ 0.05, K₂HPO₄ 0.05, agar 2.0%.

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activity on *Bacillus subtilis* PCI-219 at pH 6.0 than at 7.0 or 8.0 when tested by a pulp-disc method using 10 mm discs (Fig. 3). The antibacterial spectrum of matchamycin tested by an agar-streak-dilution method is shown in Table 3.

In order to confirm that matchamycin is a new substance, it was compared with phleomycins^{2,3,4}) and bleomycin^{5,6}), the only other examples of copper-containing antibiotics. Both of these are ninhydrin-positive, whereas matchamycin is ninhydrin-negative. Since even the hydrolysate of matchamycin is ninhydrin-negative, the antibiotic seems not to contain any amino acids. In addition the infrared and ultraviolet absorption spectra of matchamycin show that it is different from phleomycins and bleomycin.

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Table 2. Physicochemical properties of matchamycin

(1) Color	green
(2) m. p.	150~156°C (green to brown)
(3) Elemental analysis	<i>Anal.</i> found: C 52.82, H 2.75, O 21.72, N 9.12, Cu 13.59% <i>Calcd.</i> for $C_{20}H_{13}O_6N_3Cu$: C 52.80, H 2.86, O 21.12, N 9.24, Cu 13.86%
(4) Optical rotation	$[\alpha]_D^{25} +33^\circ \pm 12^\circ$ (c 0.1, dimethylsulfoxide)
(5) Ninhydrin reaction	negative
(6) Color change	<pre> acid alkali / / green (matchamycin) --> faint green --> no change \ \ alkali acid \ \ dark brown --> faint green </pre>

Fig. 1. Ultraviolet absorption spectrum of matchamycin.

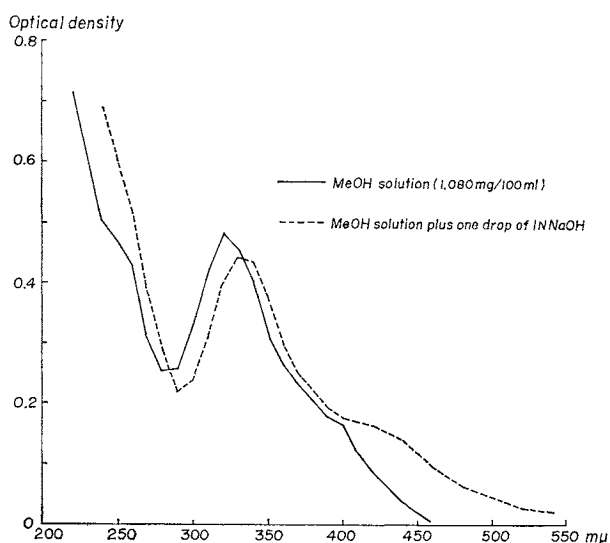


Fig. 2. Infrared spectrum of matchamycin (KBr).

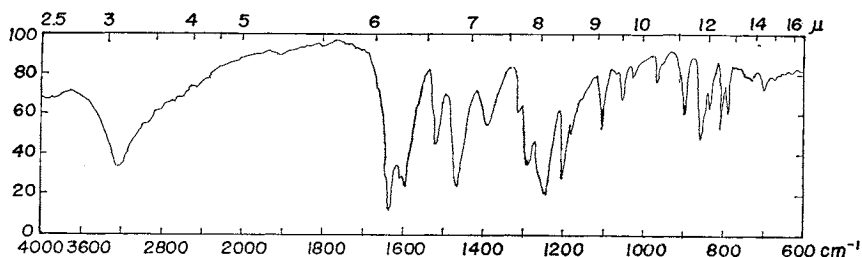


Table 3. Minimal inhibitory concentration of matchamycin

Test organisms	Concentration (mcg/ml)	Test organisms	Concentration (mcg/ml)
<i>Shigella dysenteriae</i>	50	<i>Sarcina lutea</i>	50
<i>Shigella paradysenteriae</i> , Ohara	50	<i>Diplococcus pneumoniae</i> I	20
<i>Salmonella paratyphi</i> A	50	" " I-V	20
<i>Escherichia coli</i> , Umezawa	50	" " II	20
<i>Pseudomonas aeruginosa</i>	50	" " III	20
<i>Klebsiella pneumoniae</i>	50	<i>Streptococcus hemolyticus</i> , DE.	50
<i>Bacillus subtilis</i> , PCI-219	50	" " , HA.	50
<i>Bacillus anthracis</i>	10	<i>Corynebacterium diphtheriae</i> , S.	20
<i>Staphylococcus aureus</i> , 209P	50	" " , T.	50

References

- 1) NISHIMURA, H.: The production of a new antibiotic, matchamycin. Japanese Patent 45-14,879, May 26, 1970
- 2) MAEDA, K.; H. KOSAKA, K. YAGISHITA & H. UMEZAWA: A new antibiotic, phleomycin. J. Antibiotics, Ser. A 9: 82~85, 1956
- 3) TAKITA, T.; K. MAEDA & H. UMEZAWA: Studies on phleomycin. J. Antibiotics, Ser. A 12: 111, 1959
- 4) IKEKAWA, T.; F. IWAMI, H. HIRANAKA & H. UMEZAWA: Separation of phleomycin components and their properties. J. Antibiotics, Ser. A 17: 194~199, 1964
- 5) UMEZAWA, H.; K. MAEDA, T. TAKEUCHI & Y. OKAMI: New antibiotics, bleomycins A and B. J. Antibiotics, Ser. A 19: 200~209, 1966
- 6) UMEZAWA, H.; Y. SUHARA, T. TAKITA & K. MAEDA: Purification of bleomycins. J. Antibiotics, Ser. A 19: 210~215, 1966

Fig. 3. Dose response curve of matchamycin (pulp disc method).

