

ANTIMICROBIAL ACTIVITIES OF
INDOLE

MASAMI OIMOMI

Dr. Oimomi's Office, 1131 Mega, Shikama-ku,
Himeji-shi, Hyogo-ken, Japan

MASA HAMADA and TAKESHI HARA

Institute of Microbial Chemistry, Kamiosaki,
Shinagawa-ku, Tokyo, Japan

(Received for publication October 11, 1974)

OIMOMI found that *Escherichia coli* 443, *E. coli* 5 and *Enterococcus* 1294 produced an ether-extractable compound active against *Candida*¹⁾, and applied this ether extract locally for treatment of nasal complications of the common cold and trichophytiasis of the feet.^{2,3)} The results suggested some effect of this crude extract, which was found also to inhibit growth of staphylococci and streptococci.^{2,8)} The purification of the active agent was attempted, and as described in this paper the main antimicrobial agent in the extract was found to be indole.

E. coli 5 was grown in stationary culture in ether-washed 2.0 % peptone water (20 g of peptone was washed with 1.0 liter ether and used for preparation of the medium) for 5 days at 37°C. The cultured broth was centrifuged at 10,000 rpm for 30 minutes, and the clear supernatant (pH 8.0, 5 liters) was extracted with the same volume of ether. The ether extract was chilled to -30°C and filtered. The filtered ether solution was concentrated under reduced pressure, 10 mm Hg, and dried in a dessicator over P₂O₅. The faintly yellowish-colored solid (578 mg) thus obtained was subjected to sublimation at 55°C under reduced pressure at 0.15 mm Hg for 30 minutes, yielding colorless crystals (184 mg) which were trapped in a tube in dry ice. Further sublimation of the extract gave similar crystals (362 mg), mp 53°C, m/e 117 (M⁺). Thus, more than 93 % of the solid in the extract was obtained as crystals. The crystals had an indole-like odor and identity with indole was confirmed by comparison of the infrared spectrum, the ultraviolet spectrum and the melting point with those of an authentic sample.

ZSOLNAI⁴⁾ and KOIVISTOINEN⁵⁾ have described

Table 1. Antibacterial spectrum of indole. The figures mean the minimal concentrations ($\mu\text{g/ml}$) in inhibiting the growth completely.

Microorganism	$\mu\text{g/ml}$
1 <i>Staphylococcus aureus</i>	> 400
2 <i>Staphylococcus aureus</i> FDA 209P	> 400
3 <i>Micrococcus flavus</i> FDA 16	> 400
4 <i>Sarcina lutea</i> PCI 1001	> 400
5 <i>Corynebacterium bovis</i> 1810	> 400
6 <i>Bacillus subtilis</i> NRRL B-558	> 400
7 <i>Bacillus subtilis</i> PCI 219	> 400
8 <i>Bacillus anthracis</i>	400
9 <i>Bacillus cereus</i> ATCC 10702	> 400
10 <i>Escherichia coli</i> NIHJ	> 400
11 <i>Escherichia coli</i> K-12	> 400
12 <i>Escherichia coli</i> K-12 ML 1629	> 400
13 <i>Escherichia coli</i> W 677	> 400
14 <i>Escherichia coli</i> JR 66/W 677	> 400
15 <i>Escherichia freundii</i> GN 346	> 400
16 <i>Klebsiella pneumoniae</i>	400
17 <i>Shigella flexneri</i> 4b JS 11811	400
18 <i>Salmonella typhi</i> T-63	> 400
19 <i>Proteus vulgaris</i> OX 19	400
20 <i>Proteus mirabilis</i> IFM OM-9	> 400
21 <i>Proteus rettgeri</i> GN 311	> 400
22 <i>Pseudomonas aeruginosa</i> NO 12	> 400
23 <i>Pseudomonas fluorescens</i>	400
24 <i>Aeromonas salmonicida</i> ATCC 14174	400
25 <i>Aeromonas punctata</i> IAM 1646	400
26 <i>Aeromonas</i> sp. (KT-444)	400
27 <i>Serratia marcescens</i>	400
28 <i>Vibrio anguillarum</i> NCBM 6	400
29 <i>Mycobacterium smegmatis</i> ATCC 607	> 400
30 <i>Mycobacterium phlei</i>	> 400
31 <i>Candida albicans</i> 3147	400
32 <i>Candida tropicalis</i> NI 7495	200
33 <i>Candida pseudotropicalis</i> NI 7494	400
34 <i>Candida krusei</i> NI 7492	400
35 <i>Candida</i> Yu-1200	400
36 <i>Saccharomyces cerevisiae</i>	400
37 <i>Cryptococcus neoformans</i> NI 7496	200
38 <i>Ophiobolus miyabeanus</i>	200
39 <i>Pyricularia oryzae</i>	100
40 <i>Pellicularia filamentosa</i> (sasakii)	200
41 <i>Aspergillus niger</i>	200
42 <i>Trichophyton asteroides</i> 429	100
43 <i>Trichophyton mentagrophytes</i>	100
44 <i>Xanthomonas citri</i>	200
45 <i>Xanthomonas oryzae</i>	200

the effect of indole on several fungi, however there is no report which described the antimicrobial spectrum of indole in detail. Therefore, we examined the activity of this compound against various microorganisms growing on agar media with the results shown in Table 1.

Though the antimicrobial activity in inhibiting the growth is not so strong, indole was found to have a wide antifungal spectrum and to inhibit a few species of bacteria. OIMOMI observed that the crude extract prevents nasal secretion and is effective in removing nasal obstruction. It is not known if this pharmacological effect is due only to indole.

Acknowledgement

The authors express their hearty thanks to Prof. Dr. H. UMEZAWA for his kindly guidance throughout the studies.

References

- 1) OIMOMI, M.: Method of extracting a fungicidal substance which inhibits candida and yeast. U.S. Patent 3,753,862, 1973
- 2) OIMOMI, M.: A candidicidal substance produced by *Enterobacter* 444. Japan J. Med. Mycol. 14: 163, 1973 (in Japanese)
- 3) OIMOMI, M.: Candidicidal substances from the cultures of intestinal flora. 1st Intersectional Congress of the International Association of Microbiological Societies, Tokyo, September 1974 (Abstracts p. 75)
- 4) ZSOLNAI, T.: Versuche zur Entdeckung neuer Fungistakita. VI. Hydrazin-Derivate und organische Basen bzw. ihre Salze. Biochem. Pharm. 11: 995~1016, 1962
- 5) KOIVISTOINEN, P.; E. RISSER & O. POHJAKALLIO: The inhibitory effect of certain indole compounds upon the growth of *Sclerotinia trifoliorum* ERIKSS. Acta Agr. Scand. 9: 403~411, 1959