MAGNESIDIN, A NOVEL MAGNESIUM-CONTAINING ANTIBIOTIC

Sir:

In the course of our search for new antibiotics, a novel magnesium-containing antibiotic named magnesidin has been obtained from the cell mass of a pinkcoloured bacterium. The antibiotic-producing culture was isolated from the washings of the marine alga, *Caulerpa peltata*, collected from the rocky shores near Bombay, India.

Magnesidin is a unique magnesium-containing naturally occurring compound and to the best of our knowledge, is the first antibiotic having this cation. Taxonomically, the bacterium has been identified as a new species of the genus *Pseudomonas* and has been named *Pseudomonas magnesiorubra* nov. sp. (ATCC No. 21856), as its morphological and biochemical characteristics (Table 1) differ from all the known species of *Pseudomonas* described in BERGEY's Manual[1]. The bacterium produces a pinkcolouration when grown on various nutrient media and the pigments have been isolated and identified as a mixture of prodigiosin and its higher homologues. Fermentations were carried out under submerged culture conditions for 24~30 hours at 28°C in a medium containing 2% glucose, 1.5% peptone, 0.5% yeast extract, 0.5% soluble starch, 3% NaCl and 0.1% $MgSO_4 \cdot 7H_2O$ (pH of the medium 7.4). At the end of the fermentation, the cells containing the antibiotic were harvested by centrifugation and the cell mass was repeatedly extracted with hot acetone until the extract was colourless. The orange red extract was decolourised by activated charcoal and the colourless filtrate was concentrated *in vacuo* to a small volume and chilled. The amorphous crude magnesidin which precipitated out was collected and purified by extraction with ether in a Soxhlet apparatus. The active ether extract was dried and crystallised twice from methanol to give pure magnesidin (yield: 250 mg from cell mass obtained from a liter of culture fluid). Magnesidin forms colourless plates, melting point undefined with shrinking and softening from 123~150°C, λ max (methanol) 257 nm ($E^{1\%}_{1cm}$ 747.3). It is soluble in ether, ethyl acetate, chloroform, acetic acid, methanol, ethanol, butanol, acetone and pyridine, but insoluble in water. It is very stable even up to 121°C and over a pH range of 2~8. The antibiotic spectrum determined by the serial dilution method is shown in Table 2.

The antibiotic magnesidin is effective only against gram-positive bacteria, particularly the spore bearers. It has been found to be toxic (LD_{50} for mice, 50 mg/kg i.p.) and is not absorbed orally. *In vivo* tests indicate that the

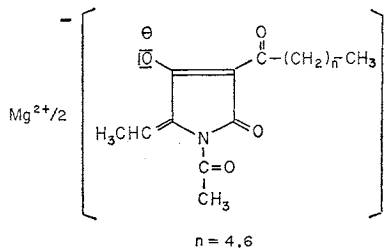
Table 1. Morphological and biochemical characteristics of *Pseudomonas magnesiorubra* nov. sp. (ATCC No. 21856)

Characteristics	Observation/ Results
Morphological	
Size (μ)	0.8~1.0×1.6~2.6
Flagellar arrangement	Polar
Biochemical and physiological	
Growth in	
Distilled water media	Poor
Sea-water media	+
Milk broth	+
12~30% salt solutions	−
Hydrolysis of	
Casein	+
Gelatin	+
Starch	+
Nitrate reduction	+
Acetoin production	−
Indole production	−
H_2S production	−
Cellulose attacked	−
Acid produced from	
Arabinose	−
Glucose	+
Galactose	+
Lactose	−
Maltose	+
Sucrose	+
Raffinose	−
Trehalose	−
Mannitol	+
Sorbitol	−
Dulcitol	−
Salicin	+
KOVAC's oxidase test	+
Pigment production	Produces prodigiosin and its higher homologues

Table 2. Antibacterial spectrum of magnesidin

Test organisms	Minimal inhibitory concentration (mcg/ml)
Bacillus subtilis ATCC 6633	3
Bacillus megatherium	2
Bacillus anthracis	2
Staphylococcus aureus FDA 209 P	3
Staphylococcus albus	4
Sarcina lutea	2
Gaffkya tetragena	5
Streptococcus faecalis	7
Escherichia coli	>100
Salmonella typhimurium	>100
Proteus vulgaris	>100

Fig. 1. Magnesidin



antibiotic does not protect mice challenged with *Streptococcus pyogenes*.

Magnesidin is represented by the structure (1)*. It has also been synthesised. It is a mixture of the magnesium salts of two new tetramic acids, 1-acetyl-3-n-hexanoyl-5-ethylidenetetramic acid (n=4) and 1-acetyl-3-n-octanoyl-5-ethylidenetetramic acid (n=6) which are present in *ca.* 1:1 ratio.

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References

1) BREED, S.; E. G. D. MURRAY & N. R. SMITH: BERGEY's Manual of Determinative Bacteriology. 7th Edition, p. 93. The Williams and Wilkins Co., Baltimore, 1957.

* Evidence for the structure of magnesidin and its synthesis were presented at the 14th IUPAC meeting at Hamburg, West Germany, September 1973.