peptides to liberate dipeptide from the N-terminal.

From these results the original enzyme from which nylon oligomer hydrolase was derived was estimated.

## 특 별 강 연 초 록 (Ⅱ)

### Some Problems in New Antibiotic Research

酒井平一(Hirosuke Sakai)
Department of Agricultural Chemistry,
Osaka Prefectural Uiversity, Japan

It is certainly a difficult work to find out novel-type "practical" antibiotic from natural sources. In fact, chemically modified antibiotics, such as synthetic penicillins, cephalosporins, derivatives of tetracycline, lincomycin, rifamycin and kanamycin are most widely used in medical practice at present. However, as the possibility of success gained by chemical modification is limited, it would be the buty of our applied microbiologists to offer novel antibiotics to chemist and physician without interruption. In this lecture, some practical problems in new antibiotic reserch will be discussed.

**1, Object of Screening**

At the beginning of screening for new antibiotic, it is important to determine the main purpose of the programme. As the majority of the workers in this field is occupied by employees of pharmaceutical companies, estimation of screening object shown in Table is made on the view point of industrial researchers. If the screening is planned in public or academic institute, some different estimation would be made in the Table.

**2. Screening Process**

The ordinary process used for screening new microbial product from natural sources is schematically shown in Figure. The organism which plays most important role in antibiotic producer is actinomycetes. Soil samples are usually used for isolation of microorganisms. It can be said that new product is generally obtained from cultures of freshly isolated organisms. However, as the new isolate apt to diminsh its special activity rapidly, it is important to keep the novel ability by successive selection for superior strain. A key to success in new antibiotic screening would be to abandon known or uninteresting candidate as early as possible. For doing this selection satisfactorily, accumulation of wide experience and ceaseless documentation of new microbial substance are primarily necessary.

**3. Recent Trends in Screening for New Microbial Products.**

(1) Search for now microbial origin: Most of the antibiotic producer belongs to *Streptomyces* species. However, other genus of *Actinomycetes* namely, *Micromonospora*, *Nocardia* or *Actinoplanes* have become the objects of new antibiotic screening. *Basidiomycetes*, *Pseudomonas* related bacteria and marine microorganisms also attract interests of many workers. Studies on nutritional mutants bring artificial new antibiotic such as hybrimycin from neomycin producing strain.

2) Control of cultural conditions: New antibiotics can often be found out by modifying customary cultural conditions. The most succssful example was achieved by Imanaka. He added unordinary much phosphate to medium and kept the pH value slightly acidic throughout the fermentation. Using this process, he could discover many novel type antibiotic such as pyrrolnitrin, thiopeptin and bicyclomycin. Some examples can also be mentioned cryomycin was discovered by Ogata under low temperature cultivation; mimosamycin and chlorocarcias were isolated by Arai from vigorously aerated culture of streptothricin producing *St. lavendulae*.

3) Trials of new screening methods: Varieties of new or reformed screening methods were tried to obtain novel products from microbial sources. They would be divided into the four categories; 1) using modified microbe as test organism, 2) using intact animal or plant bodies as physiological test organism, 3) screening for specific enzyme inhibitor, 4) usinh specific chemical reaction (e. g. color test). The striking success in recent antibiotic research would be the discovery of nocardicins by Fujisawa group using $\beta$-lactam sensitive mutant as the assay organism. Moreover, some new micrrobial products such as pepstatins, derivatives of fusaric acid screened out as specific enzyme inhibitors became

the center of attention in medical societies.

**Table.** Estimation of screening object.

| Object of screening | | Social-necessity | Market-ability | Technical possibility |
|---|---|---|---|---|
| Antibacterial | Gram positive | ++ | ++ | +++ |
| | Gram negative | ++ | ++ | + |
| | Broad spectrum | + | ++ | + |
| | Tuberculosis | ++ | + | + |
| Antifungal | Dermatophile | + | + | ++ |
| | Deep saprophyte | + | + | ++ |
| Anticancer | Leucocytosis | ++ | + | ++ |
| | Other cancer | ++ | ++ | + |
| Anti plant disease | | ++ | + | + |
| Feed additive | | + | + | ++ |
| Veterinary (esp. anticoccidium) | | ++ | ++ | + |

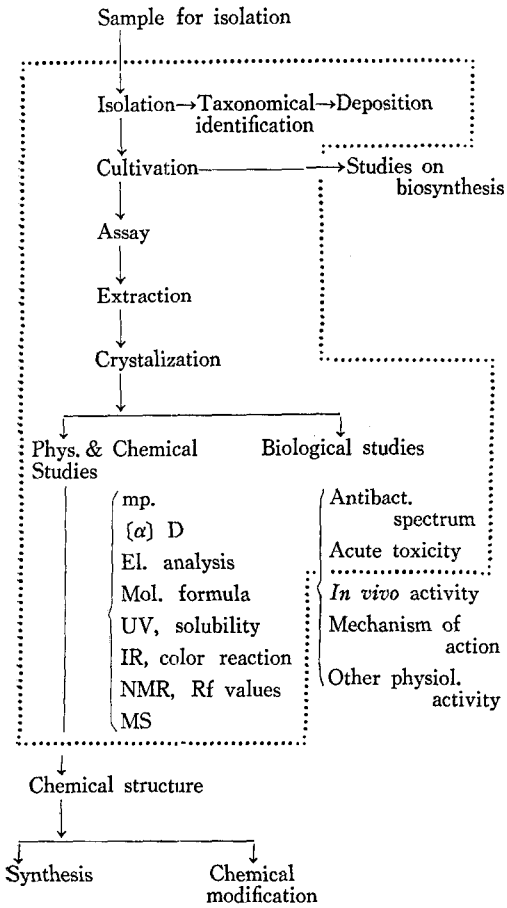


**Figure.** Scheme of screening process.
Data in broken line are necessary for patent application.

## 특 별 강 연 초 록 (Ⅲ)

### · 新代謝拮抗物質 plumbemycin A 및 B에 관한 硏究 ·


朴 富 吉
江原大學校 農化學科


代謝拮抗物質에 의한 微生物의 生育阻害는 그 試驗系에 代謝物質을 添加하므로써 回復되는 것이며 最少檢定培地에 대한 代謝阻害에 代謝物質, 例로 amino酸, 核酸등을 添加해서 阻害回復을 screening 하므로써 그들 物質(amino酸 核酸等)의 代謝에 拮抗하는 새로운 化合物을 發見할수가 있다. 이러한 見地에서 放線菌이 生産하는 새로운 amino 酸代謝拮抗物質이 探索을 目的으로하여 screening한 結果 土壤에서 새로이 分離한 *Streptomyces* 1株의 培養液中에 L-threonine에만 拮抗作用을 나타내는 물질의 存在를 確認하고 類似構造를 갖는 2種의 tripeptide型 代謝拮抗物質의 單離에 성공하였으며 이들을 plumbemycin A 및 B라고 명명하였다.

이하 plumbemycin A와 B에 관해 生産菌株의 screening 및 固定 單離精製와 化學構造決定, 그의 生物學的性質에 관해 그 要約을 기술하고져 한다.

**1. 代謝拮抗物質生産菌의 screening**

各地의 土壤에서 分離한 放線菌 約 2500株를 振盪法으로 培養한 후 그 培養液을 檢定試料로 해서 paper disc 寒天平板法에 의해 試驗菌 *Escherichia coli*, *Pseudomonas ovalis*에 對해 bioassay를 하였다. 檢定培地는 Stephenson-Whetham 最少培地(S-W培地)로 하였으며 對照培地로 S-W 培地에 polypeptone, yeast extract를 加하였다. 結果 S-W培地에만 抗菌活性을 나타내는 菌株 172株를 얻고 다시금 amino酸에 對한 拮抗作用 有無를 시험한 結果 L-threonine에만 拮抗作用을 나타내는 한 菌株를 얻었다.

**2. 生産菌의 分類同定**

生産菌株에 대해 形態學的, 生理學的 諸性質을 檢討한 結果이 菌은 *Streptomyces*屬의 Gray series에 屬하였다.

Bergey's Manual of Determinative Bacteriology 第8版, ISP 報告等에서 檢討하고, 4種의 類綠菌과 比較檢討한 結果 本菌을 新菌種으로 認定하였으며 *Streptomyces plumbeus* n. sp., SAKAI et PARK이라 命名하였다.