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THE ADVANCEMENT OF SCIENCE IN CHINA DURING THE PAST THIRTY YEARS

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I

EVER since the establishment of the Republic of China on October 10, 1911, the development of science in this country has entered a new era of activities in its own history. Unlike the early Ming and the late Ch'ing dynasties,[1] when science was superficially introduced into China, this time we have fostered modern-science from quite a different point of view and on a solid foundation. Characteristic features are easily to be noted. Firstly, scientific researches along various branches of science were duly initiated. Original work undertaken at institutes, laboratories and universities made valuable contributions to modern science either of universal nature or of local character. Secondly, since the beginning of this new period, the work of developing science has been entirely entrusted to the Chinese themselves, although a few foreign institutions inherited from the last century were still to be seen in the country, but were not very active. Thirdly, a large number of Chinese scientists, both trained abroad and at home, have served the country in various capacities—in government departments and private institutions. Fourthly, scientific education has received ever so much attention and considerable progress has been observed. Scientific courses were not only taught in schools, colleges and universities, but also gained an important position in their respective curricula. Fifthly, the application of science in various walks of life shows another phase of scientific activities from daily life to national de-

[1] Chungshee H. Liu, *The China Journal*, 34: 3, 120–125; 5, 210–219, 1941.

inoculated with a spore suspension of *P. notatum*.[2] Czapek-Dox medium (Florey et al.[3]) containing 4 per cent. glucose and 0.1 per cent. Difco yeast extract was employed. A continuous flow of the medium is started 24 hours after the inoculation and growth of the fungus usually becomes well established by the 5th day. In one of the columns the medium was allowed to collect and was drained off daily instead of continuously. In this case there was a marked inhibition of growth, even with vigorous aeration. This column was, therefore, converted after several days to continuous flow arrangement. Ordinary surface cultures of *P. notatum* in the same medium served as controls for comparative purposes on the amount of penicillin produced.

The rate of flow of medium has been varied from 400 to 1,000 ml daily and the sugar content from 1 to 4 per cent. with little influence on penicillin titer. After growth is well established, yeast extract does not appear to be essential for penicillin production, but a 4 per cent. concentration of sugar may be of some value inasmuch as all but a fraction of a mgm of sugar per ml is utilized during the flow of the medium through the growth column.

One column has been in satisfactory operation and free from bacterial contamination for 15 days. The rate of flow of the medium through this column has varied from 600 to 800 ml daily and the effluent has had a pH of 7.0–7.3. Serial dilutions in broth of the penicillin-containing effluent were inoculated with *Staphylococcus aureus*. Growth in the various dilutions following 20 hours incubation at 37° C. was compared with that of a control culture of *S. aureus* and with serial dilutions tests on ordinary surface cultures of *P. notatum*. Typical results are presented in Table 1.

TABLE 1

PENICILLIN TITER IN CONSTANT FLOW AND ORDINARY CULTURES OF PENICILLIUM NOTATUM

Fluid from	Age of culture in days	Dilutions				
		1–10	1–20	1–40	1–80	1–160
Constant flow apparatus	5	–	–	–	‡	+
	10	–	–	–	–	+
	15	–	–	–	‡	+
Ordinary culture, maximum titer	6	–	–	–	–	+

– no growth, ‡ slight growth, + full growth of *S. aureus*.

It is apparent that the penicillin titer of the effluent from the constant flow apparatus approaches that observed with the fluid from ordinary surface cultures of *P. notatum*. Only one strain of *P. notatum* and one medium has been thoroughly tested thus far. Higher titers might well be obtained with other strains of the fungus or in other media. In incomplete studies the substitution of corn steep liquor in place of yeast extract more than doubled the amounts of penicillin produced. The constant flow method appears to have the advantage that once growth of the organism is well established, penicillin is produced continuously and a large volume of penicillin-containing liquid can be obtained with a minimum of equipment in a short period of time.

Doubling the length of column by connecting two tubes in series appears to increase the penicillin concentration in the effluent to a slight extent. Some difficulty was experienced in obtaining satisfactory growth in the second column due to the rapid depletion of the culture medium. Therefore, the influence of an increased rate of flow of a more concentrated medium was tested, but bacterial contamination was encountered before entirely conclusive results could be obtained.

Further studies on factors influencing the production of penicillin in a flow of medium continuously trickling in a thin stream over the fungus growing on a column of shavings are in progress. The prevention of bacterial contamination appears to be the most difficult, but not insurmountable, obstacle to the production of penicillin on a large scale. The apparatus employed in this study may also prove satisfactory for the growth of other aerobic organisms producing antibiotic agents. The results of these preliminary studies suggest that a fairly high penicillin titer can be obtained under the conditions described and that penicillin may be produced rapidly and in large quantities in acetic acid generators.

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[2] The culture of *P. notatum*, from the original Fleming strain, was provided through the courtesy of the Cutter Laboratories, Berkeley, Calif.

[3] E. P. Abraham, E. Chain, C. M. Fletcher, H. D. Gardner, N. G. Wheatley, M. A. Jennings and H. W. Florey, *Lancet*, 241: 177–88, 1941.

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