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Memorandum

Re:

Use of Penicillin - B in combination with certain other compounds

The effect of Penicillin B is that of a three benzene ring chemical compound probably based on the oxygen carrying ability, and its ability to surround bacilli with hydrogen peroxide. This results in speeding up their metabolism and burning the bacilli.

This is a process which simulates, more or less, the fight of the human organism, whereas sulfa drugs and Penicillin A represent more of a slowing-down process to the point of starvation and suffocation of the bacilli.

My clinical research work has shown evidence beyond any doubt that in the simultaneous application of sulfa drugs and vitamin B complex, especially in the new form of a composition containing amino acids and vitamin B compounds, as described in my pending U.S. patent application, the B-complex not only interferes with the effect of the sulfa drug, but influences the metabolism of the bacilli to such an extent that they are resistant to the sulfa drug treatment.

Penicillin B acts, as mentioned above, in an opposite manner, and is, therefore, benefited by the concurrent applic-

ation of a suitable amino acid and vitamin B complex.

In order to prove this assumption, laboratory tests will be conducted, in which animal tests will be supplemented by the direct mixture of the above mentioned agents and cultures. Should the assumption prove correct, a further extension of the inventive idea is intended. It will ultimately result in the creation of a new chemical compound, either consisting of a direct union between riboflavin, chosen from its origin from the original yellow enzyme, or the more complicated compound of vitamin B-complex-amino acid and Penicillin B to be tried in various positions of the three benzene rings. The expectation is a reduction in the therapeutic doses of Penicillin B or the creation of a new compound of improved therapeutic properties.

It is intended to make tests with mixtures and compounds of

- a) Penicillin B and amino acids;
- b) Penicillin B and amino acids and vitamin B-complex;
- c) Penicillin B and B-complex.

any amino acid having a detoxifying effect may be used.

The above facts were given to Dr. J. Martin of the Warner Research Institute and a first conference with him was held at Warner Research Institute on September 16, 1943. The subject of this conference was the development of the ideas described in my note of September 14, 1943.

The conversation was based on a discussion of the research idea and a basic agreement was reached on the first test to be undertaken.

The first part of this test will be an attempt to confirm the invention idea on cultures. As Penicillin B is available as a colloidal solution, the use of bouillon as culture medium is indicated. In order to determine what part amino acids and vitamin B-complex play on the action of Penicillin B, two principal courses will be considered. The influence of amino acids will be investigated by the addition of detoxifying amino acids and also by variation of the dilution of the bouillon medium. The second series of tests will consist of tests made with Penicillin B in the presence of various amounts of vitamin B₁, B₂ and nicotinic acid^{amide} with identical and varying concentrations of bouillon, for the purpose of obtaining the most favorable results. All tests will be carried out with *Staphylococcus aureus*, and, of course, in the presence of Penicillin B.

The object of the tests is to investigate whether under any of the conditions used the quantity of Penicillin B may be efficiently reduced.

There are, among others, the following four principal possibilities of applying the results of the aforementioned tests.

- (1) to increase the yield of Penicillin B;
- (2) to create a special amine acid to improve the action of Penicillin B or to make possible the application of Penicillin B compounded or in conjunction with amine acids;
- (3) to improve Penicillin action through the addition of B complex or compounded with B complex;
- (4) to add amine acid-B complex to Penicillin B or compounded with Penicillin B.