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MEMORANDUM

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TO : Chief, PLANS
ATTN. :
FROM :

10 January 1962

Memo No. 1381

SUBJECT : ALCOHOL ANTAGONISTS

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1. Recently I requested _____, OSI, to provide the available information on alcohol antagonists and the effect of Benzedrine, in particular. The initial studies indicate four possible approaches to the problem which have not been exhaustively studied.

- a. Use of alcohol antagonists before drinking.
 - 1. Benzedrine
 - 2. Forvitin

- b. Adsorption of alcohol in the digestive tract.
 - 1. Charcoal
 - 2. Aluminum gel preparations

- c. Heavy Sating of starches and sugars before and while drinking.

- d. Accelerated alcohol oxidation (elimination).
 - 1. Enzyme adjuvants, such as nicotinic acid.

G+R
B

2. If it is anticipated that a preparation in liquid pill or capsule form should be provided for use, _____ has suggested that further research could be instigated at _____ and culminated quite rapidly to determine the most effective medium. This work might be conducted as part of the "ARTICHOKE" program.

3. A summary of the initial technical findings are attached for information purposes. It does not represent an extensive coverage of the subject.

Attachment: Intoxication and Alcohol Absorption and Antagonists

Intoxication and Alcohol Absorption and Antagonists

1. The degree of intoxication is a function of the blood-alcohol level. This relationship was determined during the increasing and decreasing phases of the symptoms, and it was shown to be approximately linear.

2. The appearance of symptoms occurred when the "appearance threshold" was attained (0.31 to 0.65% alcohol/blood). The disappearance when the "disappearance threshold" (0.36 to 0.75%) was reached.

3. Attempts to minimize the intoxicative effects following the ingestion of alcohol have been concentrated upon the following mechanisms.

- a. Absorption at the gastric mucosa
- b. Acceleration of the oxidation of alcohol by the liver.
- c. Retardation of assimilation by the cells of the body (particularly cortical brain cells).
- d. Increased rapidity of excretion.

Of these, only researches involving the first two have proven at all fruitful and studies of adsorption have been most thoroughly considered.

4. Some of the earliest work on the absorption of alcohol (1916) shows that absorption is prolonged and appears later when the alcohol is taken after food. The same workers found that the intake of food with alcohol not only delayed absorption but that the absorption never reached values found when alcohol was given on an empty stomach. It is claimed that this disappearance of alcohol is due in part to the alcohol never being absorbed as such. The claimants ascribe this to the alcohol being bound to some constituent parts of the food such as proteins and amino-acids. This theory of dilution seems to be confirmed since the blood-alcohol level varies with the quantity of food ingested.

5. More germane to the problem at hand than the physiological mechanism of absorption is the search for a specific substance to lessen the absorption rate and hence lower the blood-alcohol level. Of the limited number of foods tested, milk had the greatest effect.

6. Attempts to reduce intoxication with drugs usually aim at an increase in the rate of oxidation of the alcohol in the liver. This rate is established by an enzyme process in the liver which can be influenced by drugs. The enzyme process is a nicotinic acid-riboflavin system that is responsible for the oxidation of alcohol to acetaldehyde and aldehyde-mutase in the oxidation of acetaldehyde to acetic acid.

7. Drugs which accelerate alcohol metabolism include alanine and insulin-glucose. It is claimed that insulin and insulin-free pancreatic extract are capable of increasing the rate of alcohol metabolism approximately 50% in therapeutic doses in man.

8. Autonomic drugs such as adrenergic substances like amphetamine sulfate (benzedrine) are found to be most effective. It has been given in amounts ranging from 0.5 to 0.7 grams/kilo-body weight to 17 subjects and found to show a definite inhibiting effect which was greatest after 30 minutes but then diminished. The drug was given both orally and intravenously with consistent results that were related directly and exclusively to the amount of amphetamine given. Paradrine, adronalin and atropine sulfate were also tested and found to be effective in the order listed.