Reports

Monoamine Oxidase, Psychoenergizers, and Tranquilizers

Abstract. 1-Benzyl-2-methyl-5-methoxytryptamine (BAS) inhibits monoamine oxidase in man. This finding confirms the findings of Woolley in mice. Since BAS, a tranquilizing agent, and Marsilid, a psychoenergizer, are both monoamine oxidase inhibitors, doubt is cast upon the hypothesis that the stimulatory effect of Marsilid is due to its ability to inhibit monoamine oxidase.

Marsilid has been shown to be an inhibitor of monoamine oxidase (*1*). The attractive hypothesis has been put forth that the antidepressant action of Marsilid is due to its ability to inhibit the enzyme (*2, 3*) and, more specifically, that the increased level of brain serotonin or norepinephrine is responsible for the central stimulatory effects of Marsilid (*4*). A parallelism between the enzymatic inhibition and clinical effectiveness of Marsilid and its analogs has been reported (*3*); Resnick (*5*), however, reported a lack of correlation between the degree of enzymatic inhibition and the clinical effectiveness of Marsilid in several patients.

Woolley *et al.* (*6*) reported that 1-benzyl-2-methyl-5-methoxytryptamine (BAS) is a monoamine oxidase inhibitor in mice. We have confirmed this finding in man. In our first study, BAS (100 mg/day) was administered orally to four schizophrenic patients for the first 2 weeks. During the third and fourth weeks, BAS and D,L-5-hydroxytryptophan (5-HTP) (30 mg/day) was administered intramuscularly. BAS alone did not affect the excretion of endogenously formed 5-hydroxyindoleacetic acid (5-HIAA), but it did prevent the expected increase of 5-HIAA due to the metabolism of 5-HTP in three of the four patients; only 40 percent of the L-5-HTP was recovered in the fourth patient. In our second study, two patients received BAS for 1 week and BAS and 5-HTP (100 mg/day), intramuscularly, for the next 3 weeks. Again the BAS prevented the expected increase in urinary 5-HIAA. This was confirmed by a two-dimensional paper chromatogram which showed the usual amount of 5-HIAA and a large increase in serotonin and 5-HTP, presumably the D-form.

Although BAS and Marsilid are both monoamine oxidase inhibitors, BAS, unlike Marsilid, has tranquilization properties. Woolley and his co-workers (*7*) first observed the tranquilizing action of BAS in mice. Wilkins *et al.* (*8*), in a study of BAS on patients with hypertension, noted a state of sedation and tranquilization. Rudy and his co-workers (*9*) administered BAS to 24 moderately disturbed, chronic psychotic female patients and reported "a strong tranquilization action not unlike that of reserpine."

Thus we have a new and very interesting situation of two monoamine oxidase inhibitors, one a psychoenergizer (Marsilid), the other a tranquilizer (BAS). This finding casts some doubt on the hypothesis that Marsilid exerts its central stimulatory action by virtue of its ability to inhibit monoamine oxidase. It should be noted, however, that although BAS does possess central activity, it does not readily pass into the brain (*7*) and, further, that we have measured the inhibition of monoamine oxidase in the whole organism and not in the brain specifically.

It is relevant that isoniazid (Rimifon) is not a monoamine oxidase inhibitor (*1*) but that it nevertheless possesses central stimulatory properties in man (*10*) and has been used successfully in the treatment of depression (*11*). Since Rimifon is closely related structurally to Marsilid, it seems likely that a common mechanism underlies the psychoenergizing properties of Marsilid, Rimifon, Marplan, and other analogs. The possibility that the central stimulatory action of these compounds is due to their ability to produce a pyridoxine deficiency (*12*), to inhibit decarboxylase activity (*13*), and to inhibit transaminase activity (*14*) should be considered (*15*).

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15. We thank D. W. Woolley for suggesting the study and for supplies of BAS and 5-hydroxytryptophan. We acknowledge completion of the work under a grant from the Ford Foundation and the Scottish Rite Committee.
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Instructions for preparing reports. Begin the report with an abstract of from 45 to 55 words. The abstract should *not* repeat phrases employed in the title. It should work with the title to give the reader a summary of the results presented in the report proper.

Type manuscripts double-spaced and submit one ribbon copy and one carbon copy.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to *one* 2-column figure (that is, a figure whose width equals two columns of text) or to *one* 2-column table or to *two* 1-column illustrations, which may consist of two figures or two tables or one of each.

For further details see "Suggestions to Contributors" [*Science* 125, 16 (1957)].

Disappearance of Guard Cell Chloroplasts in Ultraviolet-Irradiated Leaves

Abstract. Ultraviolet irradiation of kidney-bean leaves results in the disappearance of chloroplasts from guard cells. The evidence indicates that ultraviolet irradiation causes plastid breakdown indirectly through an effect on guard-cell metabolism.

In some earlier experiments (*1*) the disappearance of guard-cell chloroplasts in ultraviolet-irradiated bean leaves was observed, but not reported. Cells of irra-