CC/NUMBER 28
JULY 12, 1982

This Week's Citation Classic

Knoll J & Magyar K. Some puzzling pharmacological effects of monoamine oxidase inhibitors. *Advan. Biochem. Psychopharmacol.* 5:393-408, 1972.
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No selective inhibitor for the B type of monoamine oxidase (MAO) was known until we demonstrated that (-) Deprenil, developed by us in 1964, is a preferential inhibitor of the metabolism of benzylamine and metaiodobenzylamine. Thus it was this paper which introduced (-) Deprenil, the first highly selective inhibitor of MAO-B. [The *SCI*® indicates that this paper has been cited in over 215 publications since 1972.]

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January 15, 1982

"Monoamine oxidase (MAO) inhibitors played an unforgettable role in the development of modern biological psychiatry. They were introduced into clinical practice as antidepressant agents, but because of the blockade of intestinal and liver MAO, the inhibited metabolism of pressor amines (mainly tyramine) in foodstuffs (e.g., cheeses) led in a number of cases to serious, sometimes fatal, hypertensive crises. The 'cheese effect' discredited the MAO inhibitors, the use of which became strictly limited.

"The discovery that two kinds of mitochondrial MAO, A and B type, exist started a new chapter in the history of MAO. Two studies, Johnston's[1] and ours, played the rate limiting role in the realization of the dual nature of mitochondrial MAO. Johnston developed a new MAO inhibitor, clorgyline, in 1968, and found that this substance inhibited the oxidative deamination of serotonin in low concentration and left the metabolism of benzylamine unchanged. He introduced the name MAO-A for the 'clorgyline-sensitive' form of the enzyme and MAO-B for the 'clorgyline-insensitive' one. This terminology is still in use.

"No selective inhibitor for MAO-B was known until, in 1971, we succeeded in demonstrating that Deprenil developed by us[2] inhibits in low concentrations the metabolism of benzylamine and metaiodobenzylamine leaving the oxidative deamination of serotonin unaffected.

"Deprenil and clorgyline became and are still indispensable tools for the mapping of the two forms of MAO in the brain and other tissues and were used in hundreds of papers during the last six to eight years. Our paper is regularly quoted because it introduced (-) Deprenil as the first, and still the best, highly selective inhibitor of MAO-B.

"As (-) Deprenil is the only MAO inhibitor without the 'cheese effect,' it is successfully combined with levodopa in the long-term chemotherapy of parkinsonism.[3]

"There is an age-related increase in the activity of MAO-B which might be in causal relationship with the decreased dopaminergic tone of the aging brain.

"The possibility of improving the quality of life in senescence by counteracting the consequences of this biochemical lesion by the long-term administration of (-) Deprenil which facilitates dopaminergic tone in the brain was recently suggested and is now open for careful clinical scrutiny. A review has recently been published."[4]

1. **Johnston J P.** Some observations upon a new inhibitor of monoamine oxidase in brain tissue. *Biochem. Pharmacol.* 17:1285-97, 1968.
2. **Knoll J, Ecsery Z, Kelemen K, Nievel J & Knoll B.** Phenylisopropylmethylpropinylamine (E-250), a new spectrum energizer. *Arch. Int. Pharmacodyn. Ther.* 155:154-64, 1965.
3. **Birkmayer W & Riederer P.** *Die Parkinson Krankheit (Biochemie, Klinik, Therapie).* Vienna: Springer-Verlag, 1980.
4. **Knoll J.** The pharmacology of selective MAO inhibitors. (Youdim M B H & Paykel E S, eds.) *Monoamine oxidase inhibitors—the state of the art.* New York: Wiley, 1981. p. 45-61.

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