Effects of N-(Ethyl-2 Pyrrolidinyl-Methyl)-2-Methoxy-5-Sulfamoyl-Benzamide (Sulpyrid) on the Central Nervous System in Rats and Mice

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Abstract. Sulpyrid is a new psychoactive drug and several clinical studies indicate a series of polymorphic therapeutic indications. Experimentally, sulpyrid blocks muricide reactions by isolation in rats but it is not active on aggressiveness in mice. Sulpyrid also modifies the exploratory activity in mice in which it decreases the brain 5-hydroxytryptamine turnover, as well as in rats.

Key words: Sulpyrid — Aggressiveness by Isolation — Muricide Behavior — Exploratory Activity — Brain Amines.

Introduction

Sulpyrid (Fig. 1) is one of several compounds introduced in the last few years in the field of psychoactive drugs. This compound was first described by Justin-Besançon et al. on 1967 and further widely studied for its pharmacological properties in laboratory animals (Bel, 1969; Hukuhara et al., 1969; Laville and Margarit, 1969; Borenstein et al., 1969; Marmo et al., 1971). The classical screening tests used for this compound showed numerous interesting effects which, however, did not indicate the mode of action of sulpyrid on the Central Nervous System.

Sulpyrid has been described as very effective in different psychiatric disturbances such as depressive syndromes, delirious psychoses, schizophrenia and other mental illnesses (Morel, 1969; Benoit et al., 1969;
Borenstein et al., 1969; Borenstein and Cujo, 1969; Katz, 1970; Puyelo et al., 1970; Collard, 1970; Ciccarelli and Nosé, 1971). However, no data exist in the literature about the possible effects exerted by sulpyrid on brain neurotransmitters, nor on laboratory models concerned with normal or altered aspects of behavior, such as exploratory behavior and aggressiveness by isolation (Valzelli, 1967, 1969, 1971a; Valzelli and Bernasconi, 1971; Valzelli et al., 1967).

Materials and Methods

Male Sprague Dawley rats, weighing 180 ± 5 g and male Albino Swiss mice, weighing 20 ± 2 g, were kept in groups of six in Makrolon cages of different sizes at a constant room temperature (22 ± C ± 1) and relative humidity (60 ± \%) and fed “ad libitum”. Brain noradrenaline (NAD) and dopamine (DPA) were determined spectrofluorimetrically according to Laverty and Taylor (1968). Brain serotonin (5 HT) and 5-hydroxyindolacetic acid (5 HIAA) were simultaneously extracted from the same tissue sample and measured spectrofluorometrically as described by Giacalone and Valzelli (1969); 5 HT turnover was calculated by the method of Tozer et al. (1966).

Aggressive Albino Swiss mice and muricide rats of the Wistar strain, were obtained by isolation, as described elsewhere (Valzelli, 1969, 1971 b; Valzelli and Bernasconi, 1971) and their aggressive behavior was scored according to Valzelli et al. (1967) and Valzelli and Bernasconi (1971).

The hole-board test (Boissier et al., 1964) was performed in normal and aggressive mice (Valzelli, 1969, 1971a).

Sulpyrid, generously supplied by the Firm Ravizza S. p. A.\(^1\), was administered to the animals by the intraperitoneal route.

Results and Discussion

As reported in Tables 1 and 2, administration of 100 mg/kg of sulpyrid in mice or rats did not significantly modify the absolute levels of serotonin, noradrenaline and dopamine in the brain. However, the brain 5 HIAA levels in mice were increased in such a way to suggest the possibility of a change of brain 5 HT turnover in these animals. As brain 5 HT turnover differs between normal and aggressive mice (Garattini et al., 1967), the effect of sulpyrid on this parameter was compared in these two groups (Table 3). In fact, the results obtained show a significant decrease of 5 HT turnover in both types of animals, without any statistically significant difference between the two groups. A decrease of brain 5 HT turnover also takes place in rats following the administration

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