PHARMACOLOGICAL EFFECTS OF CEGABA,
A NEW AMINOACID OCCURRING IN MAMMALIAN BRAIN

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N-carboxyethyl γ-aminobutyric acid (CEGABA) was synthesized in our laboratories (1). Recently, CEGABA has been identified by us in bovine brain and human cerebrospinal fluid (2).

As a subject for our researches we were looking for CEGABA as an intermediate step in a postulated metabolic pathway leading to GABA from spermidine via putreanine/isoputreanine.

Putreanine was already isolated peculiarly in mammalian brain (3) and both isoputreanine and putreanine were demonstrated to originate from spermidine (4-5).

In fact, CEGABA obtained by synthesis, in preliminary tests, shows some pharmacological characters that are typical of GABA-agonists (anticonvulsivant activity) (6) and other characters approaching it to polyamines (stimulation of cell growth and proliferation) (7).

Further interest on this compound rises from its low toxicity (LD₅₀ = 783 mg/kg in mice and 877 mg/kg in rats, i.p.) (6). EEG synchronization (6) and anti-convulsivant activity upon i.v. administration, demonstrate CEGABA capability to cross the blood-brain barrier.

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It is worth noting that CEGABA behavioural (sedation) or hormonal effects (Prolactin release inhibition) are higher than those of GABA when both substances are administered intraventricularly (8).

As is known, polyamines are among the components of cellular membranes and play essential roles in cellular growth (whether normal or neoplastic) and differentiation (9).

Unfortunately, the high toxicity of these substances hinders their administration in humans. Because of the low toxicity and the reported effects of CEGABA, we decided to test it for possible protective or reparative effects in experimental allergic encephalomyelitis (EAE). This model shows significant similarities to multiple sclerosis.

Ordinary experimental allergic encephalomyelitis (EAE) was induced in 20 guinea pigs by routine methods (subcutaneous inoculation of an

![Graph showing EAE results](image)

**Fig. 1**

EAE control group (1).
EAE CEGABA treatment immediately after sensitization (2).
EAE CEGABA treatment beginning 12 days after sensitization (3).

A: EAE dead animals: black; survivors: white.
B: Histology positive: black; negative: white.
C: Clinical assessment positive: black; negative: white.

In the third group (3) three moribund animals were sacrificed before starting with CEGABA treatment.
Neuropathological studies showed that two of these animals developed EAE.
emulsion of guinea pig spinal cord and physiological saline in Freund's complete adjuvant).

The animals were divided into 3 groups: — sensitized for EAE and not treated; — sensitized and treated with CEGABA (50 mg/kg/day i.p.) on the same day as sensitization; — sensitized and treated with CEGABA at the 12th day during the post-sensitization period. The animals were checked daily for body weight losses and for neurological symptoms. Serum and cerebrospinal fluid were submitted to Isoelectric Focusing, blotting on nitrocellulose paper, immunofixation by anti-IgG antiserum and albumin/IgG determination (immuno-nephelometric method). For neuropathological studies of the brain and spinal cord, histological preparations were stained with hematoxylin/eosin, Luxol Fast Blue and Klüven-Barrera reagent.

In this preliminary study, evidence was obtained that animals treated with CEGABA showed reduced incidence of deaths and neurological signs (ataxia, tremor, paralysis of hindpaws). Reduction was also observed in weight loss and in development of the typical EAE pathological patterns (Fig. 1).

According to these significantly positive data, we are now planning further experiments in order to detect any activity of this new substances and its derivatives in induced pathological states of central and peripheral nervous system.

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