Pharmacological Reports
2011, 63, 1–11
ISSN 1734-1140

Review

Melatonin in experimental seizures and epilepsy

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Abstract:
Although melatonin is approved only for the treatment of jet-lag syndrome and some types of insomnia, clinical data suggest that it is effective in the adjunctive therapy of osteoporosis, cataract, sepsis, neurodegenerative diseases, hypertension, and even cancer. Melatonin also modulates the electrical activity of neurons by reducing glutamatergic and enhancing GABA-ergic neurotransmission. The indoleamine may also be metabolized to kynurenic acid, an endogenous anticonvulsant. Finally, the hormone and its metabolites act as free radical scavengers and antioxidants. The vast majority of experimental data indicates anticonvulsant properties of the hormone. Melatonin inhibited audiogenic and electrical seizures, as well as reduced convulsions induced by pentetrazole, pilocarpine, L-cysteine and kainate. Only a few studies have shown direct or indirect proconvulsant effects of melatonin. For instance, melatonin enhanced low Mg^{2+}-induced epileptiform activity in the hippocampus, whereas melatonin antagonists delayed the onset of pilocarpine-induced seizures. However, the relatively high doses of melatonin required to inhibit experimental seizures can induce some undesired effects (e.g., cognitive and motor impairment and decreased body temperature).
In humans, melatonin may attenuate seizures, and it is most effective in the treatment of juvenile intractable epilepsy. Its additional benefits include improved physical, emotional, cognitive, and social functions. On the other hand, melatonin has been shown to induce electroencephalographic abnormalities in patients with temporal lobe epilepsy and increase seizure activity in neurologically disabled children. The hormone showed very low toxicity in clinical practice. The reported adverse effects (nightmares, hypotension, and sleep disorders) were rare and mild. However, more placebo-controlled, double-blind randomized clinical trials are needed to establish the usefulness of melatonin in the adjunctive treatment of epilepsy.

Key words:
melatonin, epilepsy, seizures, pineal gland