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Elisabetsky E, Costa-Campos L. The alkaloid alstonine: a review of its pharmacological properties. *Evid Based Complement Alternat Med*. March 2006;3(1):39-48.

The indole alkaloid, alstonine, is the major component of a plant-based remedy traditionally used to treat mental illness in Nigeria. Alstonine may also possess anticancer and antimalarial activity. Alstonine can be found in many plants: *Alstonia boonei*, Madagascar periwinkle (*Catharanthus roseus*), *Picralima nitida*, *Rauwolfia caffra*, and *Rauwolfia vomitoria*. This paper reviews the effects of alstonine in the central nervous system.

In 1993, an ethnopharmacological expedition by the Igbo people in Nigeria led to the discovery of alstonine as an antipsychotic. A traditional psychiatrist named Dr C.O. would treat "mad" patients with a plant medicine named *uhuma obi-nwok*, which in Igbo translates to "the heart of man." He boiled the ground root and had patients drink the tea. After 1 hour, the patient would fall asleep for 2-3 days. Then he would taper off the dose until the "madness" was cured. Dr C.O. gave the researchers some dried root powder to analyze. An ethanol extract was found to contain reserpine-like alkaloids, with alstonine being the dominant component.

Antipsychotic properties of alstonine

Schizophrenia is associated with abnormalities of many neurotransmitter systems, including dopamine, serotonin, gamma-aminobutyric acid (GABA), and glutamate. Therapeutic strategies with novel drugs include normalization of dopamine and serotonin levels and modulation of cerebral protein synthesis. Mice models of schizophrenia show that alstonine has a dose-dependent and potent antipsychotic profile. Similar to the so-called newer atypical antipsychotics the data show that alstonine's mechanism of action is complex and involves more than one neurotransmitter system; nevertheless, the specific antipsychotic profile of alstonine has not been reported for any other antipsychotic drug. Among other mice models relevant to schizophrenia, alstonine prevents amphetamine lethality in grouped mice, amphetamine-induced stereotype, and haloperidol-induced catatonia (a form of

schizophrenia, or a negative symptom of schizophrenia, characterized by a tendency to remain in a fixed unresponsive state for long periods). Haloperidol-induced catatonia can also be prevented by anticholinergics, dopamine agonists, serotonin modulators, and glutamate NMDA antagonists. Alstonine has hypnotic properties (induces sleep) in mice, which is consistent with properties of other antipsychotics and with Dr C.O.'s description of clinical effects.

Anxiolytic properties of alstonine

Many people with schizophrenia also experience anxiety. In animal models, alstonine behaves as an anxiolytic (alleviates anxiety). The anxiolytic properties may involve an interaction of alstonine with 5HT₂ receptors (a type of serotonin receptor) and with NMDA receptors. It has been proposed that new compounds that modulate 5HT₂ receptors would have a significant impact on mental disease management. Also it has been proposed that NMDA antagonists have the potential to be nonclassical anxiolytics. Binding studies of alstonine are needed to determine the exact mode of the anxiolytic action.

Alstonine lacks epileptogenic properties

Many antipsychotic drugs can induce seizures. Therefore it was important to determine whether alstonine has pro-convulsant properties. Animal studies have shown that alstonine lacks pro-convulsant properties.

Alstonine and glutamate

A variety of schizophrenic symptoms can be attributed to alterations in NMDA-mediated glutaminergic neurotransmission. Mice studies show that alstonine does not directly interfere with NMDA receptors, glutamate release, and glutamate uptake. However, the interaction of alstonine with the NMDA receptor may be via an indirect modulation of glutamate transmission exerted by alstonine through the serotonin system. Some antipsychotics inhibit 5HT_{2A} receptors reducing the response to NMDA antagonists; this would enable 5HT₂ antagonists to increase NMDA glutaminergic transmission. Alstonine may function in a similar manner.

According to historical use and studies in animals, alstonine has the potential to be an efficacious and novel type of antipsychotic drug. Studies in humans should be conducted.

—Heather S. Oliff, PhD

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