

LE Magazine July 1997

## Late Breaking NEWS

### How And Why Picamilon Works

Studies from Russia demonstrate that Picamilon improves nervous control, recovery time after work, blood pressure and memory. The drug even shows benefits in treating brain trauma.

By R. P. Kruglikova

Drugs that normalize the gamma aminobutyric acid (GABA) system consist mainly of substances that activate GABA receptors, inhibit GABA utilization or increase the permeability of the blood-brain barrier to GABA. One way of creating preparations of this kind is to use substances that are carriers of the GABA molecule, including vitamins or their derivatives and, in particular, nicotinic acid (niacin).

Niacin has been chosen as the carrier because of its valuable pharmacological properties, its low toxicity, and its high biological availability. It has therefore been suggested that a combination of niacin and GABA in the same molecule would increase the potency of each component.

Picamilon (nicotinyl- $\gamma$ -aminobutyric acid) was first synthesized at the All-Union Vitamin Research Institute in 1970. It is a white crystalline powder that is odorless, highly hygroscopic (takes up moisture readily), and readily soluble in water.

In studies in animals Picamilon has been shown to have positive action on the cerebral circulation, and also exhibits the properties of a tranquilizer with a stimulating component.

**Unlike tranquilizer drugs, Picamilon does not induce muscle relaxation, drowsiness or lethargy.**

The action of the compound on cerebral circulation and on neural regulation was studied in anesthetized cats; conscious, unrestrained cats; and on unanesthetized rabbits. Picamilon stimulated cerebral circulation and lowered vascular tone in both arterial systems of the brain. The increase in the blood supply to the brain in conscious animals took place to a more marked degree than in cats under general anesthesia. The drug also lowered blood pressure. It must be emphasized that these effects manifested themselves after both intravenous and oral administration of the compound. In all the animals, Picamilon increased blood flow.

In the strength and duration of its cerebrovascular effect, Picamilon is much superior both to GABA and to niacin. Under the same experimental conditions, GABA in a dose of 10 mg/kg (intravenously) caused no change in cerebral blood flow, and only when given in a dose of 300 mg/kg did it increase blood flow, with the effect lasting three to five minutes. Niacin in large doses (50 to 100 mg/kg) increased cerebral blood flow by 5 to 10 percent.

#### BRAIN BLOOD FLOW

In its effect on cerebral circulation, Picamilon was shown to be more effective than papaverine, nialamide, complamin (xantinol nicotinate), and dihydroergotoxin (redergin).

An essential role in the mechanism of action of Picamilon is its effect on nervous control of the cerebral circulation. It weakens changes in cerebral blood flow during the vasomotor reflex, considerably inhibits constrictor responses of vessels in the carotid and vertebrobasilar basins due to stimulation of afferent fibers of somatic nerves, and causes gradually developing inhibition of tonic and reflex activity in sympathetic nerves.

Neuropharmacological screening tests on Picamilon have demonstrated its tranquilizing properties in small doses. For instance, at a dose of 1 mg/kg, Picamilon prevents the negative consequences of emotional stress (in cats it normalizes the orienting reaction when disturbed by the response to rage and fear). Like diazepam, it has an inhibitory effect on motivated aggression,

associated with fighting for territory in rats.

Investigation of Picamilon's effect on the threshold of "self-stimulation" showed that in higher doses (80 and 160 mg/kg), in contrast with small doses which have a tranquilizing effect, Picamilon lowered the "self-stimulation" threshold (like amphetamine), but at the same time reduced the number of self-stimulation. The stimulating action of the drug also has been shown in general anesthesia. For instance, at a dose of 100 mg/kg, Picamilon reduced by 1.7 times the duration of the sedative effect of hexobarbital sodium and reduced by half the duration of thiopental anesthesia.

Unlike tranquilizer drugs (chlorodiazepoxide, diazepam, relanium, phenazepam), Picamilon does not induce muscle relaxation, drowsiness or lethargy. Clinicians have stated that the drug closely resembles cavinton (the ethyl ester of apovincamic acid), but comparison of the properties of the two compounds showed that Picamilon is superior.

After the administration of Picamilon at a dose of 5 mg/kg, defense-conditioned reflexes (jumping onto a rod) were restored after their disappearance due to fatigue (by 130 percent, compared with 12 percent in the control). Given to rats at a dose of 50 mg/kg it restored physical working capacity during a rest period of one hour by 76 percent, compared with 38 percent in the controls.

In a model of shock-induced amnesia of the conditioned passive avoidance reaction, like other GABA-ergic drugs (sodium hydroxy butyrate, fenibut, pantogam), Picamilon exhibited anti-amnesiac properties. In hypoxic states, the compound was found to have antihypoxic activity. The presence of anti-amnesiac and antihypoxic properties in the spectrum of action of Picamilon places it in the group of nootropic agents.

There is evidence that activation of the GABA-ergic system in various kinds of stress can prevent damage to the body when exposed to various stimuli. In confirmation of this hypothesis, scientists who studied the effect of GABA derivatives on the development of toxic (nicotinic) cerebral edema (fluid on the brain), showed that Picamilon in a dose of 500 mg/kg, injected 30 minutes before nicotine (40 mcg/kg), prevented the development of edema. If the compound was given at a dose of 200 to 300 mg/kg, the density of the brain tissue was increased, but not up to the control level, and the total water content had no significant change. They suggested that the mechanism of the anti-edematous action of Picamilon is linked with a change in energy metabolism in neurologic tissue.

### **QUICKLY THROUGH THE BLOOD BARRIER**

Thirty minutes after injections of Picamilon into rats at a dose of 100 mg/kg (intraperitoneally) the concentration of the oxidized form of nicotinamide adenine dinucleotide (NAD) in the brain rises by 67 percent above the control level, and that serum lactate dehydrogenase activity falls by 23 percent, with glutamateoxalate transaminase activity showing no significant change. A more prolonged action of the compound led to normalization of the NAD level in the rats' brains.

The study of the effect of Picamilon on active GABA uptake by synaptosomes in the rat cerebral cortex showed that it moderately inhibits GABA uptake by synaptosomes, whereas niacin has no appreciable inhibitory action on this process.

Scientists at the Department of Biochemistry, Odessa University, found that Picamilon passes quickly through the blood-brain barrier. As early as 30 minutes after subcutaneous injection, the compound was found in the brain, penetrating it by an order of magnitude more rapidly than GABA. The time course of accumulation of Picamilon in the brain correlated with its blood level. Accumulation of the compound in muscle tissue one to two hours after injection was greater (10 times) than that of GABA. Picamilon is retained in the body longer than GABA.

A six-month toxicity study showed that Picamilon does not change the behavior or condition of rats when administered in doses of three to 75 mg/kg, and causes no significant changes in the blood, urine and internal organs of the animals. Some morphological changes were found in the kidneys of rats receiving Picamilon in a dose of 75 mg/kg (15 times higher than the therapeutic dose). A microscopic study of the kidneys indicated manifestations of glomerulonephritis and nephrosclerosis, which led to the consideration of renal pathology as a contraindication to Picamilon. However, during clinical studies with Picamilon—even when administered over a long period or in repeated courses—no disturbances were found in the kidneys or the urinary system.

### **ADVERSE EFFECTS FEW**

Picamilon produces no allergenic, teratogenic, embryotoxic or carcinogenic effects. On this basis, the pharmacological committee of the Ministry of the Health (Russia) recommended clinical trials of Picamilon for cerebrovascular disturbances, as a daytime tranquilizer, as a stimulant in depressive and asthenic (weakening) states, and to improve physical and mental working capacity. Picamilon was studied in a large number of scientific facilities within Russia. The total number of patients under observation was 984. Picamilon tablets were prescribed two to three times a day at a dose of 0.02 to 0.05 grams, and in a daily dose of 0.04 to 0.3 grams. Courses of treatment lasted from two weeks to one-and-a-half months. The effectiveness of treatment was assessed by clinical and laboratory tests. Cerebral blood movements were evaluated by objective methods, including

echopulsography, echoencephalography, rheo-encephalography, ultrasonic scanning, biomicroscopy of the conjunctiva, and electroencephalography.

In patients with acute cerebrovascular disturbances, improvement occurred on the fourth or fifth day, when the severity of neurologic symptoms was reduced. Later, headache, dizziness, noise in the head and memory disorders were reduced, motor and speech disorders began to regress rapidly, sleep improved, and irritability, emotional stress and anxiety were reduced. The velocity of cerebral blood flow was increased.

Administration of Picamilon to patients suffering from the results of cerebrovascular disturbances (more than a month later) proved effective after the second or third day of treatment. The patients' emotional background, speech and memory were improved, and levels of enzyme activity (AST, ALT, LDH) and lactate concentration were restored to normal.

Scientists who studied the effects of GABA derivatives on the development of toxic cerebral edema (fluid on the brain) showed that Picamilon in specific doses prevented the development of edema.

In chronic cerebral insufficiency, Picamilon improved the mood and memory of the patients, reduced irritability and tearfulness, abolished autonomic vascular manifestations, and reduced metabolic disturbances. In patients with memory disorders (global amnesia), considerable improvement in memorization and recall was observed on the fifth to seventh day of treatment, and the patients were able to return to work.

In patients with astheno-neurotic anxiety and depression, activation of mental functions and motor activity was observed, including improved speed and quality of operative activity, concentration of attention and mood, relief of anxiety, improved working capacity, and so on. The use of Picamilon in depression, along with moderate doses of tricyclic antidepressants, enabled the doses of the latter to be reduced. In patients with alcoholism, Picamilon abolished many withdrawal symptoms, especially apathy, weariness and lethargy. The patients later become more tranquil, less fussy and anxious, and their working capacity improved.

### **LOWERS BLOOD PRESSURE**

The effect of Picamilon on cerebral blood flow was compared with that of papaverine and complamin. The scientists found that Picamilon had a stronger blood pressure-lowering effect than papaverine; complamin mainly affects the peripheral circulation, and it exhibits neither tranquilizing nor stimulating properties.

Picamilon is an approved drug in Russia. It is intended for use in adults as a vasoactive (effecting the caliber of blood vessels) and nootropic (benefiting cognition and nerves) agent for acute cerebrovascular disturbances of mild severity, chronic cerebrovascular insufficiency, and vegetovascular dystonia (an imbalance between sympathetic and parasympathetic influences on vascular tone). The drug is indicated as a tranquilizer for states of anxiety, fear, increased irritability and emotional stress. Picamilon is recommended for depressive disorders in the elderly and for senile psychoses. In management of drug addictions, the compound can be used to abolish withdrawal symptoms in chronic alcoholics. Picamilon is supplied in 0.01, 0.02, and 0.05 gram tablets. It has a useful shelf life of three years.

[Back to the Magazine Forum](#)

All Contents Copyright © 1995-2009 Life Extension Foundation All rights reserved.

**LifeExtension®**

These statements have not been evaluated by the FDA. These products are not intended to diagnose, treat, cure or prevent any disease. The information provided on this site is for informational purposes only and is not intended as a substitute for advice from your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.