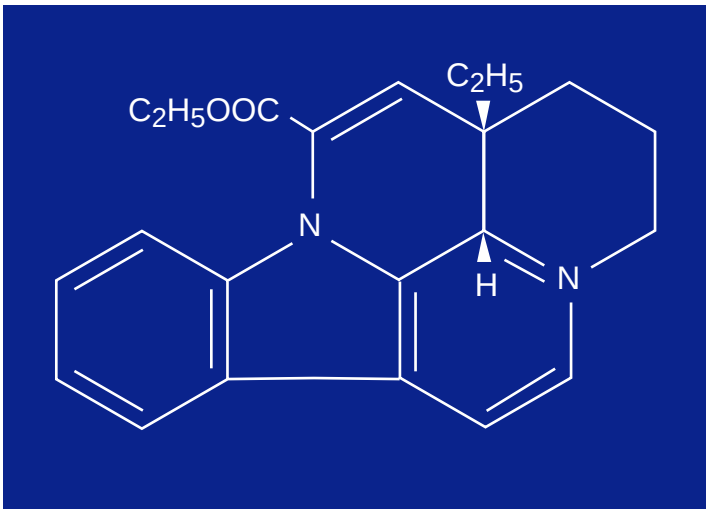
*Chemical Structure of Vinpocetine*




# Vinpocetine

## Description

Vinpocetine (vinpocetine-ethyl apovincaminate) was synthesized in the late 1960s from the alkaloid vincamine, extracted from the leaf of the lesser periwinkle plant (*Vinca minor*).[1] Vinpocetine was made available under the trade name Cavinton in 1978 and has since been used widely in Japan, Hungary, Germany, Poland, and Russia for the treatment of cerebrovascular-related pathologies.[2] Several clinical studies have confirmed the neuroprotective effects of this compound.

## Pharmacokinetics

Vinpocetine, when taken on an empty stomach, has an absorption rate of 6.7 percent.[3] When taken with food, absorption increases 60-100 percent. Vinpocetine reaches the bloodstream approximately one hour after administration, whether taken with food or on an empty stomach.[4] The elimination half-life of the oral form is one to two hours and the majority of vinpocetine is eliminated from the body within eight hours. [3]

Recent studies, either following i.v. infusion of vinpocetine in patients with cerebrovascular disorders or using positron emission tomography (PET) scans in animals, have shown that vinpocetine crosses the blood-brain barrier and is taken up by cerebral tissue.[5,6] PET studies have also clearly shown in human subjects vinpocetine is preferentially absorbed in the central nervous system at twice the level that would be expected according to total body distribution.[7] The highest uptake of vinpocetine was seen in the thalamus, putamen, and neocortical regions.

## Mechanisms of Action

Vinpocetine appears to have several different mechanisms of action that allow for its antioxidant, vasodilating, and neuroprotective activities.

### *Voltage-dependent Sodium Channel Inhibition*

It has been hypothesized that vinpocetine's application in ischemic stroke is secondary to its effect on voltage-dependant sodium channels in the brain.[8] Inhibition of sodium channels in neural tissue is the primary mechanism of several different drugs reported to have neuroprotective effects in experimental ischemia.[9] This action, effectively blocking accumulation of sodium in neurons, decreases the damage of reperfusion injury and may be beneficial in lessening the toxic effects of oxidative stress resulting from anoxia.[10]

### *Phosphodiesterase-1 Inhibition*

Vinpocetine inhibits $Ca^{+2}$/calmodulin-dependent phosphodiesterase (PDE) type 1.[11] This effect would theoretically lead to an increase of cyclic AMP over cyclic GMP and may be responsible for the benefits in cerebral circulation and decreased platelet aggregation observed after vinpocetine administration.[12]

### *Antioxidant Effects*

Like vitamin E, vinpocetine is an effective scavenger of hydroxyl radicals.[13] It has also been shown to inhibit lipid peroxidation in synaptosomes of murine brain tissue and to protect against global anoxia and hypoxia in animals. Vinpocetine has decreased areas of neuronal necrosis in animal models up to 60 percent in experimentally-induced ischemia.[10]

### *Other Neuroprotective Effects*

Vinpocetine has been shown to protect neurons from the toxicity of glutamate and N-methyl-d-aspartate (NMDA).[14] Vinpocetine lowers blood viscosity in patients with cerebrovascular disease,[15] has significant vasodilating properties,[16] decreases platelet aggregation,[17] and increases and maintains erythrocyte flexibility under oxidative stress,[18] all of which are potentially beneficial in cerebrovascular disease. Vinpocetine causes a selective increase in cerebral blood flow and increases cerebral metabolic rate.[19,20]

## Clinical Indications

### *Chronic Cerebral Vascular Ischemia*

Two PET studies in chronic stroke patients have shown that vinpocetine has a significant effect in increasing glucose uptake and metabolism in the healthy cortical and subcortical regions of the brain, particularly in the area surrounding the region of the stroke.[21] A study in 15 chronic ischemic stroke patients found that a two-week vinpocetine trial significantly increased cerebral blood flow in the non-symptomatic hemisphere.[10] Recent studies using Doppler sonography and near infrared spectroscopy have shown increased perfusion of the middle cerebral artery in patients with chronic cerebrovascular disease given a single infusion of vinpocetine.[10]

### *Acute Ischemic Stroke*

Although small studies have shown that vinpocetine has an immediate vasodilating effect in cerebrovascular circulation,[10] a meta-analysis of the existing studies examining short- and long-term fatality rates with vinpocetine was unable to assess efficacy.[2] In the analysis of eight studies in acute stroke patients (vinpocetine was administered within two weeks of event), only one study met the meta-analysis criteria. In the selected trial, three weeks after onset of i.v. vinpocetine therapy, 8 of 17 vinpocetine patients and 12 of 16 placebo patients were determined "dependant" (unable to live without assistance), and all were still alive. The meta-analysis authors were unable to determine a beneficial effect of vinpocetine, but did state that considering the *in vitro* studies and animal data, vinpocetine has potential to be effective in acute stroke. Properly designed studies have not yet been conducted.

### *Degenerative Senile Cerebral Dysfunction*

A meta-analysis of six randomized, controlled trials involving 731 patients with degenerative senile cerebral dysfunction showed that vinpocetine was highly effective in the treatment of senile cerebral dysfunction. Using several psychometric testing scales in addition to physical symptoms (speech and movement capacity, muscular coordination and strength, sensory-perceptual ability) the researchers were able to show a highly significant effect of vinpocetine on both cognitive and motor functions.[22]

### *Alzheimer's Disease*

Although evidence has been limited to one small study, the results suggest that vinpocetine supplementation may not be effective as a therapy for Alzheimer's disease. A double-blind, placebo-controlled study of vinpocetine in 15 Alzheimer patients, treated with increasing doses of vinpocetine (30, 45, and 60 mg per day) in an open-

label pilot trial during a one-year period, resulted in no improvement.[23]

### *Tinnitus/ Meniere's Disease/Visual Impairment*

Vinpocetine has been used in the treatment of acoustic trauma with subsequent hearing loss and tinnitus.[24] Disappearance of tinnitus occurred in 50 percent of those who started vinpocetine within one week of the trauma. Regardless of the time since the incident, 79 percent of patients had improved hearing and 66 percent had a significant decrease in the severity of the tinnitus.

Vinpocetine has also been found to be effective in treating Meniere's disease and in visual impairment secondary to arteriosclerosis.[25,26]

## Drug Interactions

Because vinpocetine decreases platelet aggregation it should be avoided in patients on blood thinning medications.

## Safety/Toxicity

Some studies have noted flushing, rashes, or minor gastrointestinal problems in some subjects; however, these side effects did not warrant discontinuation of the medication.[22]

In one study no significant side effects were reported, even in larger doses of 20 mg three times daily.[23]

## Dosage

All of the above studies used either 10 mg vinpocetine 3 times daily orally or i.v. vinpocetine. Patients with chronic cerebrovascular disorders that were included in the meta-analysis[22] had been on an oral dosage of 10 mg three times daily.

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