Piracetam

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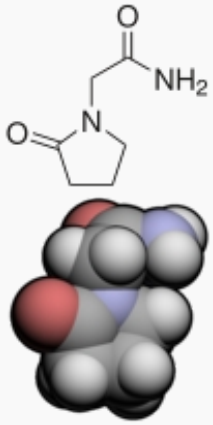

Systematic (IUPAC) name	
2-oxo-1-pyrrolidineacetamide	
Clinical data	
Trade names	Breinox, Dinagen, Lucetam, Nootropil, Nootropyl, Oikamid, and many others
AHFS/Drugs.com	International Drug Names
Pregnancy cat.	?
Legal status	POM (UK)
Routes	Oral and parenteral
Pharmacokinetic data	
Bioavailability	~100%
Half-life	4 - 5 hr
Excretion	Urinary
Identifiers	
CAS number	7491-74-9
ATC code	N06BX03
PubChem	CID 4843
ChemSpider	4677 ✓
UNII	ZH516LNZ10 ✓
KEGG	D01914 ✓
ChEMBL	CHEMBL36715 ✓
Chemical data	
Formula	C6H10N2O2
SMILES	eMolecules & PubChem
InChI	

Piracetam (sold under many brand names) is a nootropic drug. Piracetam's chemical name is 2-oxo-1-pyrrolidine acetamide; it shares the same 2-oxo-pyrrolidone base structure with 2-oxo-pyrrolidine carboxylic acid(pyroglutamate). Piracetam is a cyclic derivative of GABA. It is one of the group of racetams. Piracetam is prescribed by doctors for some conditions, mainly myoclonus,[1] but is used off-label for a much wider range of applications.

Popular trade names for Piracetam in Europe are "Nootropil" and "Lucetam", among many others. In South America, it is made by Laboratorios Farma S.A. and sold under the brand name of **Breinox** in Venezuela and Ecuador.

Contents

Effects

There is very little data on piracetam's effect on healthy people, with most studies focusing on people with seizures, dementia, concussions, or other neurological problems. However, a two week regimen of piracetam was found to enhance verbal memory in healthy college students in a double-blind, placebo-controlled study.[2]

In 2008, a committee of the British Academy of Medical Sciences noted that many of the clinical trials of piracetam for dementia were methodologically flawed.[3] However, numerous positive individual studies support the use of piracetam in people suffering from a wide range of cognitive disorders,[4] [5] and a 2002 meta-analysis concluded that piracetam had a therapeutic effect in older patients with cognitive impairment.[6]

Several meta-reviews of literature on piracetam indicate that piracetam increases performance on a variety of cognitive tasks among dyslexic children, though this may reflect its enhancement of cross-hemispheric communication and of cognitive function in general, rather than a specific improvement in whatever causes dyslexia. Piracetam also seems to inhibit brain damage caused by a variety of factors including hypoxia and excessive alcohol consumption.[7][8]

Piracetam has been studied in an extensive number of clinical experiments, and has shown positive results in the treatment of post-stroke aphasia, epilepsy, cognitive decline following heart and brain surgery, dementia,[6] and myoclonus.[9][10] Its peripheral vascular effect has indicated its use for vertigo, dyslexia, and sickle cell anemia as well.[4

Piracetam possesses pronounced antihypoxic and antiarrhythmic effect; the latter is carried out by decreasing the rhythm rate and increasing the contraction amplitude. The animals treated with piracetam in a dose when its antiarrhythmic effects (300 mg/kg) exhibited a decrease of the membrane potential of erythrocytes as compared with control. Similar effects occurred in the animals treated with lidocaine. It can be concluded that in certain types of arrhythmias the use of piracetam restores the normal rhythm of contractions that is perhaps connected with its positive influence on metabolic processes in the myocardium.[11]

Piracetam appears to increase communication between the two hemispheres of the brain, and increases activity of the corpus callosum.[12][13]

Mechanisms of action

Piracetam's mechanism of action, as with racetams in general, is not fully understood. The drug influences neuronal and vascular functions and influences cognitive function without acting as a sedative or stimulant.[4] Piracetam is a positive allosteric modulator of the AMPA receptor.[14] It is hypothesized to act on ion channels orion carriers,[*citation needed*] thus leading to non-specific increased neuron excitability, while explaining its lack of agonistic or inhibitory effect on synaptic action (quite unlike most neurotransmitters), and its low toxicity.[15] GABA brain metabolism and GABA receptors are not affected by piracetam. It has been found to increase blood flow and oxygen consumption in parts of the brain but this may be a side effect of increased brain activity rather than a primary effect or mechanism of action for the drug.[16]

Piracetam improves the function of the neurotransmitter acetylcholine via muscarinic cholinergic (ACh) receptors which are implicated in memory processes.[17]Furthermore, Piracetam may have an effect on NMDA glutamate receptors, which are involved with learning and memory processes. Piracetam is thought to increase cell membrane permeability.[17][18] Piracetam may exert its global effect on brain neurotransmission via modulation of ion channels (*i.e.*, Na+, K+).[15] It has been found to increase oxygen consumption in the brain, apparently in connection to ATP metabolism, and increases the activity of adenylate kinase in rat brains.[19][20] Piracetam appears to increase the synthesis of cytochrome b5,[21] which is a part of the electron transport mechanism in mitochondria. It also increases the permeability of the mitochondria of some intermediaries of the Krebs cycle.[19]

History

Piracetam was first synthesized in 1964 by scientists at the Belgian pharmaceutical company UCB led by Dr Corneliu E. Giurgea; struck by its apparent ability to boost mental functioning in even healthy individuals and by its safety, Giurgea coined the term nootropic to describe it and other substances. Piracetam (trade name "Nootropil") was launched clinically by UCB in the early 1970s, and later is in use in many European countries.[22]

Approval and usage

Piracetam is primarily used in Europe, Asia, South America and the US. Piracetam is legal to import into the United Kingdom for personal use with or without prescription, and was unregulated in the United States, as of 2006.[23] However, in August 2010, the FDA issued a single letter to one supplier ordering the discontinuation of the sale of Piracetam in the US as a dietary supplement owing to the relatively strict definition of what constitutes a dietary supplement. Under section 201(ff)(1) of the Act, 21 U.S.C. § 321(ff)(1): Piracetam is not a vitamin, mineral, amino acid, herb or other botanical, or dietary substance for use by man to supplement the diet by increasing the total dietary intake. Further, piracetam is not a concentrate, metabolite, constituent, extract or combination of any such dietary ingredient.[24] As of April 2011, Piracetam continues to be widely available online and in some shops in the United States, but is no longer marketed as a dietary supplement. Piracetam has no DIN in Canada, and thus cannot be sold but can be imported for personal use in Canada.[*citation needed*] It has become popular as a cognitive enhancement drug among students.[25] It is used by parents as a treatment for childhood autism,[*citation needed*] a practice at least partially supported by clinical research.[26]

Aging

Piracetam appears to reverse the effects of aging in the brains of mice.[27][28]

Piracetam appears to reduce levels of lipofuscin in the rat brain.[29] (Lipofuscin accumulation is a common symptom of aging and alcoholism.)

Alcoholism

Piracetam appears to be effective in treating cognitive impairment in alcoholism.[30][31][32][33][34][35]

Alzheimer's and senile dementia

Piracetam appears to be effective for improving cognition in Alzheimer's disease and senile dementia patients,[36][37][38][39][40] although these findings are still challenged.[41]

Clotting, coagulation, vasospastic disorders

Piracetam is useful as a long-term treatment for clotting, coagulation, and vasospastic disorders such as Raynaud's phenomenon[42] and deep-vein thrombosis.[17][43] It is an extremely safe anti-thrombotic agent that operates through the novel mechanism of inhibiting platelet aggregation and enhancing blood-cell deformability.[17]Because traditional anti-thrombotic drugs operate through the separate mechanism of inhibiting clotting factors, co-administration of piracetam has been shown to

highly complement the efficacy and safety of traditional Warfarin/Heparin anti-coagulation therapy.[44] The most effective treatment range for this use is a daily dose of 4.8 to 9.6 grams divided into three daily doses at 8 hours apart.[43] Piracetam was investigated as a complement or alternative to Warfarin as a safe and effective long-term treatment for recurring deep-vein thrombosis.[43]

Depression and anxiety

Some sources suggests that its overall effect on lowering depression and anxiety is higher than improving memory.[45]

Stroke, ischemia and symptoms

Piracetam has been found to improve cognition after stroke, and reduce symptoms, such as aphasia.[37] It also improves cognition in cases of chronic ischemia.[46][47]

Dyspraxia and dysgraphia

Due to its supposed effect on nerves and muscles it is sometimes prescribed as an aid to muscle or dexterity training, particularly in cases of dysgraphia and dyspraxia. There has not been a specific study as to whether it is beneficial in this aspect. Vinpocetine, another purported nootropic with which piracetam is indirectly synergistic, is confirmed to help with these conditions to a certain degree. [*citation needed*]

Schizophrenia

Piracetam improves cognitive performance of schizophrenics as it does with non-schizophrenics, but does not improve or worsen the chronic schizophrenia disease state.[48]

Preventive for breath-holding spells

Two articles support the use of Piracetam as a prophylactic for severe cases of breath-holding spells. A 2008 study in the International Journal of Psychiatry Medicine supported the notion that Piracetam was effective as a preventive, but did not use a control to evaluate results against normal recovery times from severe BHS.[49] A 1998 study by the Turkish ministry of health evaluated 76 children, half of them in a control group. Children in the experimental group were three times as, and almost completely likely, to exhibit "overall control" over their BHS, with BHS episodes dropping by 60% over two months.[50]

The 2008 study notes:

> Breath holding spells (BHS) are apparently frightening events occurring in otherwise healthy children. Generally, no medical treatment is recommended and parental reassurance is believed to be enough, however, severe BHS can be very stressful for the parents and a pharmacological agent may be desired in some of these children.

Closed craniocerebral trauma

Piracetam has positive therapeutic effects on adolescents with closed craniocerebral trauma (CCT). Treatment with piracetam was initiated 1.5 to 5 years after trauma. Compared to controls, after one month of daily treatment with 1600–2400 mg of piracetam there were meaningful and statistically

significant improvements in the higher mental functions (visual memory, attention and executive), motor functions (gait, balance and sequential limb movements) and in the rates of cognitive and motor operations.[51]

Dosage

For blood coagulation, clotting, and vasospastic disorders such as Raynaud's phenomenon or deep-vein thrombosis, the most effective treatment range is a daily dose of 4.8 to 9.6 grams divided into three daily doses at 8 hours apart.[17][42][43] Many people take a dosage of 800mg twice per day to improve cognition.[52] The LD-50for oral consumption in humans has not been determined.[15]

Side effects

Piracetam has been found to have very few side effects, and those it has are typically "few, mild, and transient."[53] A large-scale, 12-week trial of high-dose piracetam found no adverse effects occurred in the group taking piracetam as compared to the placebo group.[54] Many other studies have likewise found piracetam to be well-tolerated.[9][53][55]

Symptoms of general excitability,
including anxiety, insomnia, irritability, headache, agitation, nervousness, and tremor, are occasionally reported.[56][57] Headache from large doses of piracetam may be alleviated by coadministration of an acetylcholine biosynthetic precursor, or a drug with cholinergic effects, such as choline bitartrate,choline citrate, choline alfoscerate, lecithin, cyprodenate or centrophenoxine.[56][57]

Availability

Piracetam is sold under a wide variety of brand names world wide.

- **Nootropyl** - United States
- **Nootropil**, **Lucetam**, **Oikamid** - Europe
- **Breinox** - Ecuador, Venezuela
- **Dinagen** - Mexico

Notes

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See also

- Hydergine

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External links

- Erowid Piracetam Vault
- Erowid Piracetam FAQ
- Collection of Scientific Abstracts on Piracetam
- Piracetam (Nootropyl) by Ward Dean, M.D., and John Morgenthaler