4-Aminopyridine

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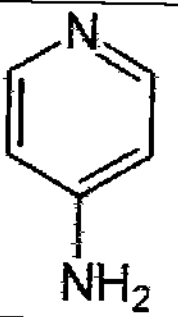
4-Aminopyridine is an organic compound with the formula $H_2NC_5H_4N$. The molecule is one of the three isomeric amines of pyridine. It is used primarily as a research tool, in characterizing subtypes of potassium channel, and has also been used to manage some of the symptoms of multiple sclerosis,[1][2] for which it has orphan drug status in the United States and is undergoing Phase III clinical trials as of 2008.

4-Aminopyridine



IUPAC name	pyridin-4-amine
Other names	4-pyridinamine, 4-Pyridylamine, Fampridine
Identifiers	
CAS number	[504-24-5]
PubChem	1727
MeSH	4-Aminopyridine
SMILES	C1=CN=CC=C1N
Properties	
Molecular formula	$C_5H_6N_2$
Molar mass	94.1146
Appearance	colourless solid
Melting point	155-158 °C
Boiling point	273 °C
Solubility in water	polar organic solvents

Except where noted otherwise, data are given for materials in their standard state (at 25 °C, 100 kPa)
Infobox references

Contents

Production

4-Aminopyridine (4-AP) is prepared by the decarbonylation of pyridine-4-carboxyamide using sodium hypochlorite via the Hofmann rearrangement. The pyridine carboxamide is generated from the corresponding nitrile, which in turn is obtained from ammoxidation of 4-methylpyridine.[3]

Applications

The largest scale industrial application of 4-aminopyridine is as a precursor to the drug pinacidil, which affects potassium ion channels.

In the laboratory, 4-AP is a useful pharmacological tool in studying various potassium conductances in physiology and biophysics. It is a relatively selective blocker of members of Kv1 (Shaker, KCNA) family of voltage-activated K+ channels. At concentration of 1 mM it selectively and reversibly inhibits Shaker channels without significant effect on other sodium, calcium, and potassium conductances. 4-Aminopyridine is also used as a bird control agent, under the trade name Avitrol; it causes convulsions and rarely death, depending on dosage. The use of 4-aminopyridine in bird control has been criticized by the Humane Society of the United States.[4]

Medical use

Fampridine has been used clinically in Lambert-Eaton myasthenic syndrome and multiple sclerosis because by blocking potassium channels it prolongs action potentials thereby increasing transmitter release at the neuromuscular junction and elsewhere.[5] The drug, known as Neurelan, has been shown to reverse tetrodotoxin toxicity in animal experiments.[6]

Multiple sclerosis

Fampridine has been shown to improve visual function and motor skills and relieve fatigue in patients with Multiple Sclerosis (MS). 4-AP is most effective in patients with the chronic progressive form of MS, in patients who are temperature sensitive, and in patients who have had MS for longer than three years. Common side effects include dizziness, nervousness and nausea, and the incidence of adverse effects was shown to be less than 5% in all studies.

4-AP works as a potassium channel blocker. Electrophysiologic studies of demyelinated axons show that augmented potassium currents increase extracellular potassium ion concentration which decreases action potential duration and amplitude which may cause conduction failure. Potassium channel blockade reverses this effect.

MS patients treated with 4-AP exhibited a response rate of 29.5% to 80%. A long-term study (32 months) indicated that 80-90% of patients who initially responded to 4-AP exhibited long-term benefits. Although improving symptoms, 4-AP does not inhibit progression of MS.

Spinal cord injury patients have also seen improvement with 4-AP therapy. These improvements include sensory, motor and pulmonary function, with a decrease in spasticity and pain.[7]

Overdose

Conditions associated with overdose have included parasthesias, seizures,[8] and atrial fibrillation.[9]

See also

- 4-Dimethylaminopyridine, a popular "super base," which is not prepared from 4-aminopyridine, but instead directly from pyridine.[3]
- pyridine

References

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