Nicorandil

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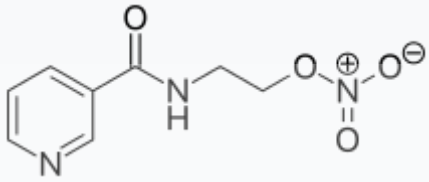

Clinical data	
AHFS/Drugs.com	International Drug Names
Pregnancy category	AU: B3
Routes of administration	Oral
ATC code	C01DX16 (WHO)
Legal status	
Legal status	UK: POM (Prescription only)
Pharmacokinetic data	
Bioavailability	75 to 80%
Protein binding	25%
Metabolism	Hepatic
Elimination half-life	1 hour
Excretion	Renal (21%)
Identifiers	
IUPAC name[show]	
CAS Number	65141-46-0 ✓
PubChem CID	47528
IUPHAR/BPS	2411

ChemSpider	43240 ✓
UNII	260456HAM0
KEGG	D01810 ✓
ChEBI	CHEBI:31905 ✗
ChEMBL	CHEMBL284906 ✓
ECHA InfoCard	100.059.541
Chemical and physical data	
Formula	$C_8H_9N_3O_4$
Molar mass	211.175 g/mol
3D model (JSmol)	Interactive image
SMILES[show]	
InChI[show]	
✗✓ (what is this?) (verify)	

Nicorandil is a vasodilatory drug used to treat angina. It is marketed under the trade names **Ikorel** (in the United Kingdom, Australia and most of Europe), **Angedil** (in Romania, Poland), **Dancor** (in Switzerland), **Nikoran**, **PCA** (in India), **Aprior** (in the Philippines), **Nitorubin** (in Japan), and **Sigmart** (in Japan, South Korea and Taiwan). Nicorandil is not available in the United States.

Angina is chest pain that results from episodes of transient myocardial ischemia. This can be caused by diseases such as atherosclerosis, coronary artery disease and aortic stenosis. Angina commonly arises from vasospasm of the coronary arteries. There are multiple mechanisms causing the increased smooth muscle contraction involved in coronary vasospasm, including increased Rho-kinase activity. Increased levels of Rho-kinase inhibit myosin phosphatase activity, leading to increased calcium sensitivity and hypercontraction.[1] Rho-kinase also decreases nitric oxide synthase activity, which reduces nitric oxide concentrations.[2] Lower levels of nitric oxide are present in spastic coronary arteries.[3] L-type calcium channel expression increases in spastic vascular smooth muscle cells, which could result in excessive calcium influx, and hypercontraction.[4]

Nicorandil is an anti-angina medication that has the dual properties of a nitrate and K+ATP channel agonist.[5] In humans, the nitrate action of nicorandil dilates the large coronary arteries at low plasma concentrations.[5] At high plasma concentrations nicorandil reduces coronary vascular resistance, which is associated with increased K+ATP channel opening.[5]

Mechanism of action

Nicorandil stimulates guanylate cyclase to increase formation of cyclic GMP (cGMP).[6] cGMP activates protein kinase G (PKG), which phosphorylates and inhibits GTPase RhoA and decreases Rho-kinase activity.[6]Reduced Rho-kinase activity permits an increase in myosin phosphatase activity, decreasing the calcium sensitivity of the smooth muscle.[6]

PKG also activates the sarcolemma calcium pump to remove activating calcium.[7] PKG acts on K+ channels to promote K+ efflux and the ensuing hyperpolarization inhibits voltage-gated calcium channels.[5] Overall, this leads to relaxation of the smooth muscle and coronary vasodilation.

The effect of nicorandil as a vasodilator is mainly attributed to its nitrate property.[5] Yet, nicorandil is effective in cases where nitrates, such as nitroglycerine, are not effective.[5] Studies show that this is due to its K+ATP channel agonist action which causes pharmacological preconditioning and provides cardioprotective effects against ischemia.[5] Nicorandil activates K+ATP channels in the mitochondria of the myocardium, which appears to relay the cardioprotective effects, although the mechanism is still unclear.[8]

Side effects

Side effects listed in the British National Formulary include flushing, palpitations, weakness and vomiting. More recently, perianal, ileal and peristomal ulceration has been reported as a side effect. Anal ulceration is now included in the British National Formulary as a reported side effect. Other side effects include severe toothache, and nasal congestion.

References

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