WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Review on the Drug Nicorandil

Abesh Das

*Department of Pharmaceutics, Guru Nanak Institute of Pharmaceutical Sciences

ABSTRACT

Nicorandil (Nicorandil) is a new vasodilator with structural similarities to nicotinamide (Nicotinamide) and nitrate (Nitrate). Mitochondrial smooth muscle cells (MSMs) appear to relax when nicorandil increases the membrane potassium conductance (K) and hyperpolarization (H), resulting in a decrease in calcium influx via voltage-gated (VGA) calcium channels. Nicorandil, or N-[2-Hydroxyethyl] nicotinamide nitrate (ester), is a newly developed chemical used for the treatment of Angina Pectoris and Hypertension. It has a short elimination half-life and is highly hydrophilic. The main adverse effects of Nicorandil are ulcers and a variety of other side effects (headache, dizziness, etc.). As a balanced vasodilator, Nicorandil opens the K+ ATP channel in the circulatory system and donates NO to the circulatory system. Mitochondrial ischemia may also be treated with nicorandil. Cardioprotective effects may be derived from nicorandil therapy.

Keywords: Nicorandil, K+ ATP, MSMs, VGA.

Introduction

Nicorandil is a vasodilator that has been sold in Japan since 1984. It is licensed in the UK and is used to prevent and long-term treat chronic angina pectoralis. Angina pectis is both a cause of disability as well as a marker of underlying coronary heart disease. It is difficult to accurately diagnose angina pectis, but it is estimated to affect between 2.3% and 5.1% of men between 40–59 years of age.

Nicoricandil is another popular vasodilator used to treat chronic stable angina, but it is currently not available in the US. Nicoricandil works by 'balancing' the dilatation of both the arteries and the veins, mediated by two different anti-angina mechanism. Nicoricinil does not cause tolerance and rebound angina. There is some (but inconclusive) evidence that prognostic benefit may be gained from nicoricinil due to reduced oxidative stress in myocardial ischemia reperfusion injury.

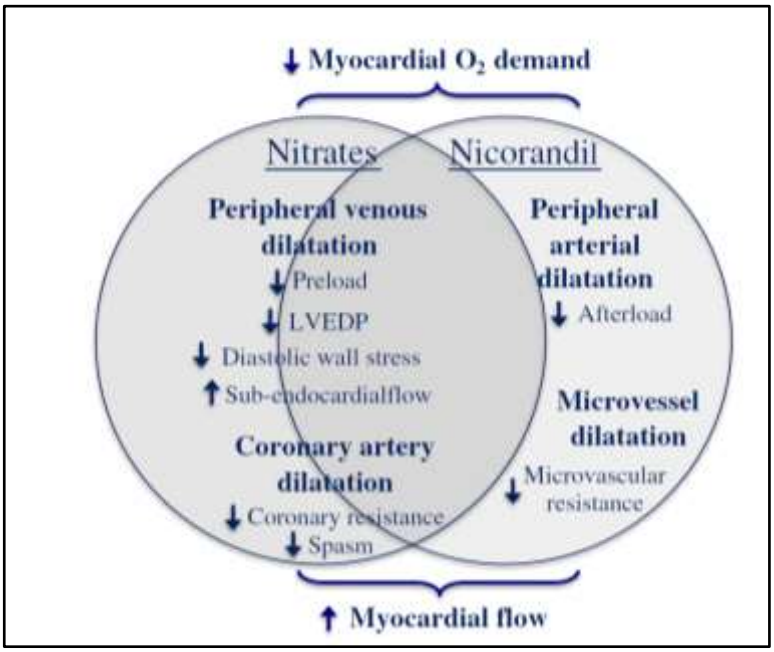


Figure: Anti-angina actions of nitrates and nicorandil

Structure of Nicorandil

One medication used to treat and lessen angina-related chest discomfort is called nerandil. It functions by enlarging and relaxing your blood vessels and supplying your heart with more blood and oxygen. Usually, nicorandil is prescribed by your doctor if other heart medications haven't worked for you or aren't appropriate.

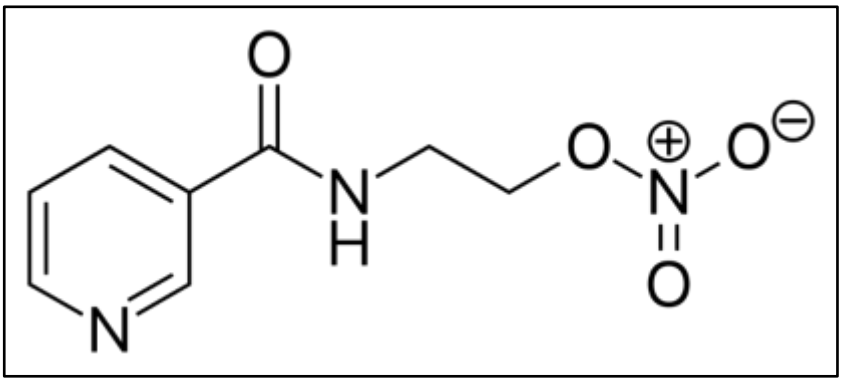
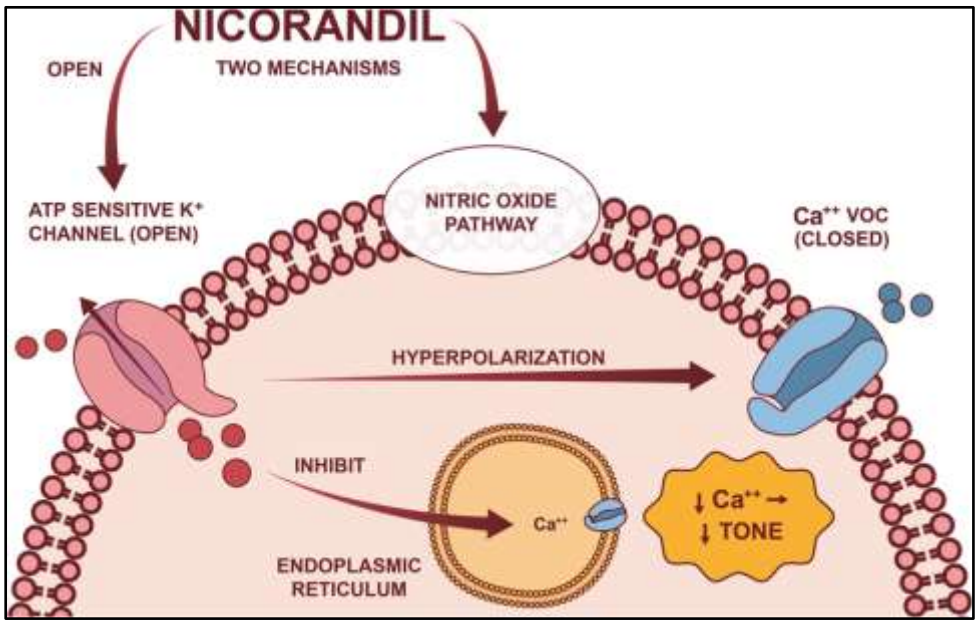


Figure: Structure of Nicorandil

Mechanical Action

Two primary processes underlie the therapeutic efficacy of neriparandil. Nicorandil functions as an ATP-sensitive (ATP-dependent) potassium channel opener and activator. KATP channels are made up of sulfonylurea receptor (SUR) subunits and Kir6.x-type subunits. Sulfonylurea receptor 2 (SUR2), regulatory subunits of the ATP-sensitive potassium channel 4 that show an ATPase activity 2, has nicotinamide binding sites. The nucleotide-binding domains (NBD) of the two subunit forms of SUR2, 2A and 2B, are identical. SUR2A is mostly expressed in skeletal and cardiac myocytes, while SUR2B is found in smooth muscle cells 2. Nicorandil induces hyperpolarization by activating SUR2B/Kir6.2 channels more strongly than SUR2A/Kir6.2 channels. Nicorandil's channel signaling is influenced by the ATP-NBD1 interaction, and ATP or ADP interaction with NBD2 enhances and facilitates the channel's response to nicorandil. The effect of ATP-sensitive channels' heightened activity in preventing intracellular calcium excess and decreasing the length of action potentials is cardioprotective. 6. By maintaining cellular energetics and eventually cell viability, this reduces cellular damage 6. By controlling intracellular Ca2+ mobilization in smooth muscle cells and reducing Ca2+ inflow through voltage-gated Ca2+ channels, KATP channel-dependent membrane hyperpolarization can also result in vasodilation. Nicorandil, like other nitroglycerin esters 5, is an effective dilator of vascular smooth muscle because it possesses a nitrate moiety in its structure. Increased intracellular cyclic GMP (cGMP) levels and NO-donor-mediated guanylyl cyclase stimulation result in direct relaxation of the venous vascular system. At greater dosages of the medication, elevated cGMP levels add to nicorandil's overall relaxing impact.



Toxicity

Lethargy, back discomfort, chest pain, infection, and a weakening sensation are typical side effects. Hypotension, elevated heart rate at larger doses, palpitations, exacerbation of angina pectoris, and vasodilation/flush may be seen in the cardiovascular system. Gastrointestinal diseases can cause dyspepsia, nausea, and vomiting. Vasodilation may result in headaches. Myalgia, bronchitis, dyspnea, and respiratory issues are other typical adverse effects. Research on the carcinogenic, mutagenic, and genotoxic effects of nicotinendil has not revealed any potential effects on the fertility of male or female rats. In mice, rats, and dogs, the oral LD50 values are 626 mg/kg, 1220 mg/kg, and 62.5 mg/kg, correspondingly.

Drug Interaction

Lethargy, back discomfort, chest pain, infection, and a weakening sensation are typical side effects. Hypotension, elevated heart rate at larger doses, palpitations, exacerbation of angina pectoris, and vasodilation/flush may be seen in the cardiovascular system. Gastrointestinal diseases can cause dyspepsia, nausea, and vomiting. Vasodilation may result in headaches. Myalgia, bronchitis, dyspnea, and respiratory issues are other typical adverse effects. Research on the carcinogenic, mutagenic, and genotoxic effects of nicotine did has not revealed any potential effects on the fertility of male or female rats. In mice, rats, and dogs, the oral LD50 values are 626 mg/kg, 1220 mg/kg, and 62.5 mg/kg, correspondingly. Nicorandil showed decreased heart rate in patients treated from the last four to fifth weeks but did not produce any change in blood pressure. Contrarily, propranolol dramatically lowered patients' blood pressure, heart rates, and some side effects like headaches and gastrointestinal problems. Gliclazide24's activity is shown to be reduced in another study due to the potential for drug interactions. An impact on atrioventricular nodal conduction and cardiac contractility was observed when diltiazem hydrochloride and nicorandil were administered, particularly during beta-blocking agent or other calcium antagonist therapy. Furthermore, even when combined with beta-blockers or calcium antagonists, nicorandil does not cause an adverse reaction.

Dose and Administration

The manufacturer suggests a starting oral dosage of 10 mg of nicorandil twice a day; in patients who experience side effects, especially headaches, this dosage may be halved.

2. Depending on the response, the dose can be gradually increased up to a maximum of 30 mg twice daily. The recommended twice-daily therapeutic dose is 10–20 mg.

Conclusion

One of the key components of cardiovascular therapy appears to be the development of novel dosage forms, such as capsules and nanoparticles, that have better patient compliance, enhance drug action, and have fewer adverse effects. Another strategy with the greatest potential for systemic therapy is the formulation of nicorandil in nanoparticle form. There are various technologies available for developing nanoparticle formulation, such as spray drying and FBD. By using nanoparticle formulation, it is possible to overcome current negative effects like ulceration. One method for developing immediate action therapy is the use of nicorandil mouth dissolve tablets, as angina pectoris sometimes requires a quick acting drug to maintain an imbalance between oxygen supply and demand.

Reference

1. Kukovetz WR, Holzmann S, Poch G: Molecular mechanism of action of nicorandil. J Cardiovasc Pharmacol. 1992;20 Suppl 3:S1-7. [Article]
2. Russ U, Lange U, Loffler-Walz C, Hambrock A, Quast U: Binding and effect of K ATP channel openers in the absence of Mg2+. Br J Pharmacol. 2003 May;139(2):368-80. [Article]
3. Yamada M, Kurachi Y: The nucleotide-binding domains of sulfonylurea receptor 2A and 2B play different functional roles in nicorandil-induced activation of ATP-sensitive K+ channels. Mol Pharmacol. 2004 May;65(5):1198-207. [Article]
4. Tamura Y, Tanabe K, Kitagawa W, Uchida S, Schreiner GF, Johnson RJ, Nakagawa T: Nicorandil, a K(atp) channel opener, alleviates chronic renal injury by targeting podocytes and macrophages. Am J Physiol Renal Physiol. 2012 Aug 1;303(3):F339-49. doi: 10.1152/ajprenal.00158.2012. Epub 2012 May 23. [Article]
5. Fujiwara T, Angus JA: Analysis of relaxation and repolarization mechanisms of nicorandil in rat mesenteric artery. Br J Pharmacol. 1996 Dec;119(8):1549-56. [Article]
6. Jahangir A, Terzic A: K(ATP) channel therapeutics at the bedside. J Mol Cell Cardiol. 2005 Jul;39(1):99-112. [Article]
7. Kane GC, Liu XK, Yamada S, Olson TM, Terzic A: Cardiac KATP channels in health and disease. J Mol Cell Cardiol. 2005 Jun;38(6):937-43. Epub 2005 Apr 25. [Article]
8. Frampton J, Buckley MM, Fitton A: Nicorandil. A review of its pharmacology and therapeutic efficacy in angina pectoris. Drugs. 1992 Oct;44(4):625-55. [Article]

9. Frydman A: Pharmacokinetic profile of nicorandil in humans: an overview. J Cardiovasc Pharmacol. 1992;20 Suppl 3:S34-44. [Article]

10. Goldschmidt M, Landzberg BR, Frishman WH: Nicorandil: a potassium channel opening drug for treatment of ischemic heart disease. J Clin Pharmacol. 1996 Jul;36(7):559-72. [Article]

11. 21. (2012). In Rang and Dale's Pharmacology (7th ed., pp. 261). Edinburgh: Elsevier/Churchill Livingstone. [ISBN:978-0-7020-3471-8]

12. IKOREL (Nicorandil) Product Information [Link]

13. UK Medicines and Healthcare products Regulatory Agency (MHRA): Nicorandil Tablets_Scientific Discussion [Link]