A Review of HNS-32:
A Novel Azulene-1-Carboxamidine Derivative
with Multiple Cardiovascular Protective Actions

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ABSTRACT

HNS-32 \([N^1,N^1\text{-dimethyl-N}^2\text{-}(2\text{-pyridylmethyl})\text{-5-isopropyl-3,8-dimethylazulene-1-carboxamidine}]\) (CAS Registry Number: 186086-10-2) is a newly synthesized azulene derivative. Computer simulation showed that its three dimensional structure is similar to that of the class Ib antiarrhythmic drugs, e.g., lidocaine or mexiletine. HNS-32 potently suppressed ventricular arrhythmias induced by ischemia due to coronary ligation and/or ischemia-reperfusion in dogs and rats. In the isolated dog and guinea pig cardiac tissues, HNS-32 had negative inotropic and chronotropic actions, prolonged atrial-His and His-ventricular conduction time and increased coronary blood flow. In the isolated guinea pig ventricular papillary muscle, HNS-32 decreased maximal rate of action potential upstroke (\(V_{\text{max}}\)) and shortened action potential duration (APD). These findings suggest that HNS-32 inhibits inward Na\(^{+}\) and Ca\(^{2+}\) channel currents. In the isolated pig coronary and rabbit conduit arteries, HNS-32 inhibited both Ca\(^{2+}\) channel-dependent and -independent contractions induced by a wide variety of chemical stimuli. HNS-32 is a potent inhibitor of protein kinase C (PKC)-mediated constriction of cerebral arteries. It is likely to block both, Na\(^{+}\) and Ca\(^{2+}\) channels expressed in cardiac and vascular smooth muscles. These multiple ion channel blocking effects are largely responsible for the antiarrhythmic and vasorelaxant actions of HNS-32. This drug may represent a novel approach to the treatment of arrhythmias.