

New Product Highlights

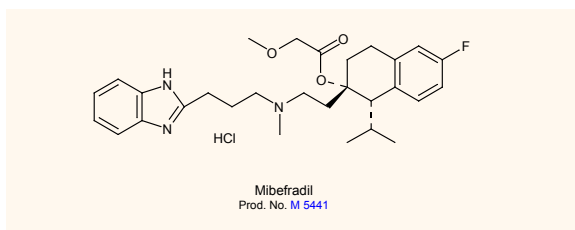
Mibefradil: The first selective T-type calcium channel antagonist

The movement of calcium ions into cells, made possible by the opening of specific, voltage-gated channels, initiates a wide range of physiological responses, including muscle contraction. Two types of calcium channels that differ considerably in their biophysical characteristics and distribution, referred to as L-type (long-lasting, high voltage-activated) and T-type (transient, low voltage-activated), are found in the cardiovascular system. The L-type channel is responsible for normal myocardial and vascular smooth muscle contractility and is blocked by a range of traditional calcium channel antagonists including Verapamil (Prod. Nos. [V 4629](#), [V-105](#) and [V-106](#)), Nifedipine (Prod. No. [N 7634](#)), Nimodipine (Prod. No. [N-149](#)) and Diltiazem (Prod. No. [D 2521](#)). In contrast, T-type calcium channels are not normally found in the adult myocardium, but are present in conducting and pacemaker cells where they help regulate vascular tone, signal conduction and cardiac pacemaking. In addition, T-type calcium channels appear to play an important role in normal growth processes and in the tissue remodeling that occurs in pathologic processes such as cardiac hypertrophy [1,2].

Unlike the large number of L-type calcium channel antagonists that are available to researchers, a selective T-type blocker has not been commercially available. Sigma-RBI is therefore pleased to offer the first selective T-type calcium channel antagonist, mibefradil (Prod. No. [M 5441](#)), a novel benzimidazolyl-substituted tetraline derivative. Also referred to as Ro 40-5967, mibefradil is approximately 30-100 times more potent at blocking T-type channels versus L-type channels in vascular smooth muscle [3-6]. It is a potent vasodilator that possesses high selectivity for the coronary vasculature over the

peripheral vasculature and the myocardium. Mibefradil can relax vascular muscle and slow the heart without reducing contractility. In addition, it does not stimulate neurohormonal reflexes and exhibits a good pharmacokinetic profile characterized by a long duration of action. In addition to its actions on coronary vasculature, mibefradil has also been found to inhibit T-type calcium channels in several neuronal preparations, including neuroblastoma cells [7], sensory neurons [8], spinal motoneurons [9] and cerebellar Purkinje neurons [10].

Mibefradil will prove to be a valuable tool for researchers investigating the role of T-type calcium channels in cardiovascular and nervous system function.



References

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