32.93 ± 3.39 μg min/mL.

Effect on Blood Pressure

A hypotensive effect and the mechanism of $[Ca^{+2}]i$ regulation, underlying rutaecarpine-induced vasodilation was reported by Wang et al.[13] An intravenous bolus injection of rutaecarpine (10, 30, or 100 μg/kg) in anesthetized S.D. rats produced a dose-dependent hypotensive effect. Mean arterial pressure (MAP) before rutaecarpine treatment was 95 ± 6 mmHg in anesthetized rats. The maximum hypotension induced by rutaecarpine (100 μg/kg) was 25 ± 7 mmHg.[13] As determined by the Fura-2/AM method, rutaecarpine (10 μM) in the presence of extracellular Ca^{+2} suppressed the KCl (30 mM)-induced increment in $[Ca^{+2}]i$ of cultured vascular smooth muscle cells (VSMC).[13] Rutaecarpine (10 μM) also attenuated the norepinephrine-induced peak rise of $[Ca^{+2}]i$ in VSMC placed in a Ca^{+2}-free solution. On the other hand, rutaecarpine (1 and 10 μM) increased the level of $[Ca^{+2}]i$ of cultured endothelial cells (EC) in the presence of extracellular Ca^{+2}.[13] Therefore, rutaecarpine acts on both VSMC and EC directly. In VSMC, it reduces $[Ca^{+2}]i$ through the inhibition of Ca^{+2} influx and Ca^{+2} release from intracellular stores. In EC, rutaecarpine augments EC $[Ca^{+2}]i$ by increasing Ca^{+2} influx, possibly leading to nitric oxide release.[13] The paradoxical regulation of Ca^{+2} in both VSMC and EC acts simultaneously to cause vasorelaxation, which could account, at least in part, for its hypotensive action.[13]

Effect on Cerebral Protection

Cerebral metabolic activator cerebrovasodilators have received attention for the improvement of disorders following cerebral injuries due to traffic accidents. Currently available cerebral metabolic activators and cerebrovasodilators, which are used for the treatment of post disorders of cerebral infarction and cerebral hemorrhage as well as cerebroarteriosclerosis, are recognized as having antianoxic action which is effective against ischemia.[14]

Brain tissue has a very high oxygen requirement as compared to other tissues and is quite sensitive to lower oxygen conditions caused by ischemia. Cyanidine compounds, such as KCN, are known to interfere with cytochrome oxidase in mitochondria, thereby inhibiting cellular respiration.[15]

In KCN-induced anoxia studies, all mice in the control group, which received a KCN (30 mg/kg, I.V.) injection through a tail vein, had respiratory arrest following about 1 min of repeated convulsive attacks, leading to death.[16] In mice treated with rutaecarpine at 50 mg/kg, I.P., there was a significant life-prolonging effect as compared to the control. The mean survival duration was 142.1 ± 15.7 s with the survival rate of 5 out of 10 (mortality: 50%) for rutaecarpine-treated rats as compared to the control groups, whose mean survival duration was 69.4 ± 13.0 s with a 1 out of 10 survival rate (mortality: 90%).[16] These results suggest that rutaecarpine has antianoxic action in the KCN-induced anoxia model.

Antithrombotic Effect

Intravascular thrombosis is one of the generators of a wide variety of cardiovascular diseases. The initiation of an intraluminal thrombosis is believed to involve platelet adherence and aggregation. In normal circulation, platelets cannot aggregate by themselves. However, when a blood vessel is damaged, platelets adhere to the disrupted surface, and the adhering platelets release some biologically active constituents and aggregate.[17] Thus, platelet aggregation may play a crucial role in the atherothrombotic process. Indeed, antiplatelet agents (i.e., aspirin and triflavin) have been shown to reduce the incidence of thrombosis in vivo.[18,19]

It has been reported that platelet thrombi were induced by irradiation of filtered light in microvasculature of mice pretreated intravenously with fluorescein sodium.[20] We used this model to evaluate the *in vivo* antithrombotic effect of rutaecarpine on platelet plug formation. Additionally, we also tested its antithrombotic activity in experimental acute pulmonary thrombosis of mice.[21]

In anesthetized mice, pretreatment with fluorescein sodium (10 and 20 μg/kg) or a combination of fluorescein sodium (20 μg/kg) with heparin (1.5 U/g), aspirin (250 μg/g), or rutaecarpine (200 μg/g) did not significantly change the base-line blood pressure within 2 h (data not shown). The latent period for inducing platelet plug formation was shortened as the administered dose of fluorescein sodium was increased.[22] When fluorescein sodium was given at 10 or 20 μg/kg, the occlusion times required were 127 ± 25 and 54 ± 9