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Editorial

Special Issue "Nature or Synthetic Compounds for Treating Arterial Thrombosis and Ischemic Stroke"

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Stroke is the second main cause of mortality and morbidity globally. It has been estimated that approximately 80% of strokes are affected by focal cerebral ischemia due to arterial occlusion, while up to 20% are caused by intracerebral hemorrhages. In roughly one-third of ischemic stroke patients, embolism to the brain is caused by the heart, particularly atrial fibrillation. The thromboembolic occlusion of major or multiple smaller intracerebral arteries results in the focal impairment of the downstream blood flow and in secondary thrombus formation within the cerebral microvasculature. Research shows that it is necessary to employ exogenous natural drugs to counter cerebral ischemia. Currently, there are few effective neuroprotective agents that can be used for treating ischemic stroke. There have been abundant efforts taken to improve stroke outcome through the use of antiplatelet and anticoagulants. This Special Issue is intended to invite research as well as review papers concerning thromboembolic stroke treatment by using natural and synthetic compounds.

This Special Issue has collected and published a total of eight papers, including seven original contributions and one review paper, on the different aspects of stroke treatment. One paper in this issue investigated the inhibitory effect of pterostilbene (PTE), a natural stilbenoid present in citrus types of fruits, and a dimethylated analog of resveratrol in NF-κB-mediated signal events, the effect of which was compared with that of standard NF-κB inhibitors [1]. The authors found that PTE inhibited platelet aggregation by diminishing NF-κB signaling molecules, including IKK, IκBα, and p65 phosphorylation, and reversed IκBα degradation. In this paper, these authors also found that PTE showed more potent activity than the NF-κB inhibitor, BAY11-7082, in an in vivo acute pulmonary thromboembolism model. They determined a distinctive activation pathway of NF-κB and Akt, which are involved in PTE-mediated antiplatelet aggregation. Overall, they demonstrated that PTE could act as a dominant prophylactic and as clinical therapy for cardiovascular diseases.

Jayakumar et al. [2] proved the potential anti-oxidative and anti-inflammatory mechanisms of the same compound PTE. They discovered that PTE reduced the pro-inflammatory activation of macrophages via the NF-κB/ERK signaling pathway-mediated attenuation of pro-inflammatory mediators (iNOS and NO) and cytokines (TNF-α and IL-1β). PTE was also found to regulate lipoteichoic acid (LTA)-induced inflammatory actions by elevating the activity of enzymatic (catalase) and non-enzymatic (reduced glutathione) antioxidants or by increasing the protein expression of heme oxygenase-1 (HO-1) [2]. This study suggested that PTE displays anti-oxidant and anti-inflammatory effects in LTA-stimulated RAW 264.7 cells via the regulation of antioxidants as well as NF-κB/ERK signaling pathways. Regarding anti-inflammatory effects, Chiu et al. [3] also reported that platonin, a cyanine photosensitizing dye, improves inflammatory responses in vascular smooth muscle cells (VSMCs) by controlling NF-κB and the AP-1 signaling pathways in LPS/IFN-induced and ox-LDL-induced vascular inflammation, respectively. Another interesting paper published by Hung et al. [4] investigated the antioxidative role of TQ-6, a ruthenium (II)-compound, [Ru(η 6-cymene)2-(1H-benzoimidazol-2-yl)-quinoline Cl]BF4 in cell-free

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and RAW 264.7 cell model systems. They demonstrated that TQ-6 scavenged DPPH, hydroxyl, galvinoxyl, and superoxide free radicals. Moreover, they found that TQ-6 showed anti-inflammatory action by inducing Nrf2/HO-1 pathway in vitro [4].

Ko et al. [5] provided an inhibitory activity of magnolol, l (a traditional Chinese medicine) on thrombin and PAR-1 (protease-activated receptor 1). These findings may provide insights into the treatment strategies of the pathogenesis of in-stent restenosis and offer a variety of medical options for patients with thrombin/PAR-1-related diseases. Finally, they identified magnolol's novel mechanism as the thrombin activity inhibitor and PAR-1 antagonist. They suggested that magnolol could decrease the thrombin-induced connective tissue growth factor (CTGF) expression in VSMCs via PAR-1/JNK-1/AP-1 signaling. Another interesting paper from Hsia et al. [6] reported the anti-platelet and anti-thrombotic effect of columbianadin (CBN), a coumarin derivative in human platelets and mice, respectively. They found that CBN potently inhibited platelet aggregation by reducing hydroxyl radical (HO•) formation and NF-κB activation in human platelets. This compound was also found to prolong closure time of the platelet plug in human whole blood and it did not significantly prolong the bleeding time in mice [6]. These authors suggested this study that CBN could be a novel candidate for clinical treatment for thromboembolic diseases.

An interesting study conducted by Thu Trang et al. [7] used a novel microchip (K-kit) as a specimen kit for the in situ imaging of human platelet granules in an aqueous solution using a transmission electron microscope (TEM). They suggested that this microchip technique might offer researchers the ability to observe the nanogranules of biological specimens in aqueous conditions in faster and better selections when applying a TEM. Finally, a major review in this Special Issue elucidated the causes of induced thrombus formation and discussed the drugs that are supposed to inhibit this thromboembolism [8]. This review has been summarized with the help of current research papers regarding the methods of how the anticoagulant heparin locally binds to biodegradable materials and also the methods to find the duration of persistent heparin release [8]. Overall, this Special Issue provides solid evidence that drug treatment for thrombotic events is effective in decreasing cardiovascular diseases. Although the treatment modality for cardiovascular risk factors using pharmacological agents and certain anti-thrombotic drugs has been enormously increased, still there is increasing awareness of the possible role of natural products in the prevention of thromboembolic diseases. Considering this, the current Special Issue may provide scientific validation for the further understanding of the pathology underlying cerebral–neurovascular diseases and strategies in order to prevent and treat these diseases.

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