Cerebral ischemia (stroke) is one of the leading cause of death and disability worldwide. Neuronal damage following cerebral ischemia develops as a result of a series of complex pathophysiological events. For instance, glutamate mediated excitotoxicity and inflammation may lead to calcium overload, peri-infarct depolarization, oxidative stress, stress signaling, neurovascular pathophysiology and neuronal cell death (apoptosis/necrosis).

Cerebral ischemia caused by the obstruction of blood vessels and hemorrhagic stroke. Even though restoration of blood flow to an ischaemic organ is essential to prevent irreversible tissue injury, reperfusion may result in a local and systemic inflammatory response that may augment tissue injury in excess of that produced by ischemia alone. Cellular damage after reperfusion of previously viable ischemic tissues is defined as I/R injury. I/R injury is characterized by oxidant production, complement activation, leucocyte–endothelial cell adhesion, platelet–leucocyte aggregation, increased microvascular permeability and decreased endothelium-dependent relaxation. I/R injury can lead to multiorgan dysfunction or death.

Therapeutic interventions such as ischemic preconditioning, controlled reperfusion and antioxidant, complement or neutrophil therapy may significantly prevent or limit I/R-induced injury in humans. In recent decades, although significant breakthroughs have occurred, particularly with respect to the development of advanced therapeutic drugs such as tissue plasminogen activator (t-PA) or edaravone (a free radical scavenger), the limited time window during which these compounds have clinical utility and their adverse side effects restrict their application in practice. Therefore, it is still important to explore new therapeutic class of compounds and post-stroke strategies.

Recent studies suggest that pyrimidine derivatives that have been shown to inhibit lipid peroxidation in biological membrane. Pyrimidine derivatives can protect the brain by their ability to modulate intracellular signals promoting
cellular survival. Pyrimidines have received much attention of researchers because of their vasodilator and antioxidant properties in the recent years. Studies on cerebroprotective mechanism of pyrimidine derivatives on cerebral I/R injury are limited. Hence it is worthwhile to study the role of pyrimidines as cerebroprotective agents and evaluated for their possible inherent underlying mechanisms.