Statins have recently been shown to act as protectants against several neuropathological conditions. They have received special attention in the field of Alzheimer’s disease (AD), where epidemiological studies indicating a lower prevalence of AD/dementia in statin-prescribed populations. Excitotoxicity, which derives from the overstimulation of glutamate receptors, is one of the major causes of neuron death in several neurological diseases, including AD. Aims We have carried out a comparative study to investigate the effects of 5 statins on AD-like neurodegeneration mouse model. The systemic administration of kainate to mice was used to induce neuron damage and death in the brain regions involved in etiology of AD, as well memory impairment. The effect of all the commercially available statins (simvastatin, lovastatin, fluvastatin, pravastatin and atorvastatin) on KA-induced neurodegeneration was analyzed by seizure score scale, integral memory test and neuropathology. Simvastatin was the most effective statin in reducing the deleterious effects caused by kainate, including the severity of seizures, excitotoxicity, oxidative damage, neuritic dystrophy and apoptosis in the hippocampus and limbic structures of the cortex. Lovastatin was the second most efficient statin in preventing seizures and histopathological signs of excitotoxicity, whilst fluvastatin, pravastatin and atorvastatin showed neither antiepileptic nor neuroprotective effects. Furthermore, only simvastatin protects against KA-induced cognitive impairment. To the best of our knowledge this is the first in vivo study to analyze the neuroprotective effect of all the commercially available statins. Our results suggest that especially simvastatin may well have therapeutic potential in the treatment of neurodegenerative diseases involving excitotoxicity and memory impairment, including AD.