Neuropathy is defined as a collection of disorders that occurs due to the damage to the nerves. Although more commonly referred to the damage to the peripheral nervous tissue, neuropathy can be damage and associated dysfunction in either the central or peripheral nervous system. Current understanding of the pathology encompasses oxidative stress, inflammatory reactions, mitochondrial dysfunction and apoptosis in the nervous tissue. Over production of reactive oxygen species (ROS) and reactive nitrogen species (RNS), a decreased antioxidant defense system or both results in oxidative stress and have been implicated in neuropathy.

Effective management of neuropathic symptoms by the various drugs available is limited due to their side effects. Hence, in general there is a need for alternative medicine for management of neuropathy especially in diabetes, chemotherapy induced or toxin induced neuropathy. In the recent past, various herbal actives including spices and phytoconstituents are being extensively employed as complementary therapeutic agents in the management of neuropathy. Humans have been consuming various spices since time immemorial either as a component of various food preparations or medicinal formulations. Hence, in this proposal, the neuroprotective efficacy of selected spice actives were investigated employing Drosophila system, cell model (human neuroblastoma cell line) and the efficacy were further validated in two models of neuropathy (neurotoxin and diabetic model). To induce neurotoxicity and neuropathy, a well-known neurotoxin, acrylamide (ACR) was employed in fly/ rat model, while streptozotocin (STZ) was used to induce diabetic neuropathy (DN) among rats.

Evidence obtained in the Drosophila model for the first time demonstrated the utility value of the system in understanding the neurotoxicity of ACR. Development of locomotor phenotype and induction of oxidative stress in this system was consistent with those reported in higher animals with ACR intoxication. Mitochondrial oxidative stress coupled with altered cholinergic function (acetyl cholinesterase (AChE) activity) and depleted dopamine (DA) levels among flies with ACR exposure corroborate with biochemical
perturbations demonstrated in the brain/ peripheral nerves of rodent models. Spice active (eugenol, EU; isoeugenol, IE; curcumin, CU; geraniol, GE) enrichment markedly abrogated the ACR induced lethality, locomotor dysfunction, oxidative stress (head and body) with concomitant increase in GSH levels. EU enhanced the depleted DA levels in head region, and IE and EU restored the cholinergic function (AChE activity in head/ body regions). Flies maintained on medium enriched with GE and CU exhibited robust decrease in the levels of ROS and hydroperoxides, suggesting their propensity to attenuate oxidative damage which in part may be related to enhanced levels of GSH and activities of antioxidant enzymes. Further, similar protective effect was also discernible in the mitochondrial enzymatic and neurotoxicity markers (restoration of AChE activity and DA levels).

In view of the increased exposure of humans to ACR through consumption of various thermally processed foods, it is highly imperative to explore newer therapeutic strategies to abrogate ACR-induced neurotoxicity/ neuropathy. Accordingly, the neuroprotective efficacy of spice actives was validated in vivo. Data obtained in the ACR- rat model clearly demonstrates the beneficial effects of spice actives/ phytoconstituents in alleviating neuropathy-associated locomotor dysfunctions and oxidative stress -mediated impairments in sciatic nerve (SN) and brain regions.

Having demonstrated the efficacy of selected spice actives in the ACR-model, their potential to modulate various biochemical/neurochemical markers was investigated in cell models and experimentally induced DN model. Data obtained in the DN rat model demonstrated that GE (a monoterpane) markedly attenuates behavioral responses, oxidative stress and mitochondrial dysfunctions. The protective effect of GE was highly comparable to that of CU. Interestingly, EU supplements exhibited significant curative potential in an intervention model of DN. Collectively these findings suggest the possible therapeutic usage of these actives as adjuvants in the management of diabetic and other forms of neuropathy in humans.