Abstract

Deterioration of cholesterol metabolism has recently been a frontier subject of investigation in the research field of Alzheimer’s disease (AD). While, amyloid-β precursor protein (APP) primes the pathological cascade, changes in the cholesterol levels and its intermediates Geranyl Geranyl pyrophosphate (GGPP), and Farnesyl pyrophosphate (FPP) could have a different consequences on the APP processing and amyloid-β (Aβ) generation. Though, the use of statins, (HMG-CoA reductase inhibitor) has been widely implicated in slowing down the pathogenic progression of AD, epidemiological reports on its biological effect remains controversial. Considering the fact, the choice of drug that could maintain the cholesterol homeostasis without altering its biosynthesis could yield a better therapeutic efficacy on AD. Thus, present study focus on to determine the influence of cholesterol and isoprenoids on amyloidogenic-cleavage of APP, besides Resveratrol (RSV) as potent therapeutic drug in CHO-APPswe cell lines. Immunoblotting findings revealed that high levels of cholesterol enhance the maturation of APP whereas high isoprenoids increased both maturation as well as amyloidogenic-cleavage of AβPP which was evident in β-CTF production. On other hand, confocal results demonstrated the altered expression and subcellular localization of ADAM10, BACE1 and PS1 thereby promoting Aβ generation in the presence of high cholesterol. Interestingly, the therapeutic efficacy of RSV maintained cholesterol homeostasis and reduced the amyloidogenic burden through its ability to enhance SIRT1 expression and thereby regulating differential expression of AD determinants.