Development of senomorphics for aging and age-related diseases

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Cellular senescence, an irreversible state of growth arrest, underlies organismal aging and age-related diseases. Recent evidence suggests that aging intervention based on inhibition of cellular senescence might be a promising strategy for treatment of aging and age-related diseases. We tried to explore single compounds with anti-senescence activity using human fibroblasts and endothelial cells under stress-induced premature senescence and replicative senescence. We found that a variety of single compounds isolated from plant extracts, such as epifriedelanol, (-)-loliolide, juglanin, britanin, rutaecarpine, ursolic acid, quercetin 3-glucuronide, and quercetagetin 3,4’-dimethyl ether revealed inhibitory activity against cellular senescence, which was confirmed by observing senescence-associated -galactosidase (SA--gal) activity, the levels of p53 and p21 proteins, and intracellular ROS levels. In addition, we demonstrated that platelet-derived growth factor-BB and miRNAs in mouse embryonic stem cell-conditioned media (mESC-CM) plays a critical role in anti-senescence effect of mESC-CM. Taken together, our results suggest that single compounds and ESC-CM with anti-senescence activity might emerge as a novel therapeutic strategy for aging and age-related diseases.