Dual Antioxidant and Anti-Tyrosinase Effects of Cannabidiol-Thiosemicarbazone

Sanaa Musa
Department of Biotechnology, Tel-Hai Academic College, Kiryat Shmona, Israel
Natural Compounds and Organic Synthesis Laboratory, Migal-Galilee Research Institute, Kiryat Shmona, Israel

Abstract:
Cannabidiol (CBD), a non-psychoactive cannabinoid, serves as a valuable scaffold for designing multifunctional bioactive molecules. In this study, we synthesized a series of CBD-based thiosemicarbazones and identified CBD-TSC as the most potent derivative. We extended our evaluation beyond biochemical assays to cell-based studies in human melanocytes. Human tyrosinase (hTYR), purified from G361 melanoma cells, exhibited strong susceptibility to CBD-TSC, which inhibited its diphenolase activity with an IC_{50} of 34.47 ± 2.46 µM, outperforming kojic acid (IC_{50} > 100 µM). In human melanocytes, CBD-TSC further demonstrated robust intracellular antioxidant activity, significantly reducing oxidative stress. Complementary in vivo evaluation in zebrafish revealed a marked reduction in melanin levels following CBD-TSC treatment, confirming its anti-melanogenic efficacy. These findings highlight CBD-TSC as a promising dual-acting candidate with both antioxidant and tyrosinase-inhibitory properties, supporting its potential application in managing hyperpigmentation and other melanogenesis-related disorders.