As part of continued efforts for the development of new tyrosinase inhibitors, (*Z*)-5-(substituted benzylidene)-2-iminothiazolidin-4-one derivatives (1a – 1l) were rationally synthesized and evaluated for their inhibitory potential *in vitro*. These compounds were designed and synthesized based on the structural attributes of a β-phenyl-α,β-unsaturated carbonyl scaffold template. Among these compounds, (*Z*)-5-(3-hydroxy-4-methoxybenzylidene)-2-iminothiazolidin-4-one (1e, MHY773) exhibited the greatest tyrosinase inhibition (IC_{50} = 2.87 μM and 8.06 μM for monophenolase and diphenolase), and outperformed the positive control, kojic acid (IC_{50} = 15.59 and 31.61 μM). The kinetic and docking studies demonstrated that MHY773 interacted with active site of tyrosinase. Moreover, a melanin quantification assay demonstrated that MHY773 attenuates α-melanocyte-stimulating hormone (α-MSH) and 3-isobutyl-1-methylxanthine (IBMX)-induced melanin contents in B16F10 melanoma cells. Taken together, these data suggest that MHY773 suppressed the melanin production via the inhibition of tyrosinase activity. MHY773 is a promising for the development of effective pharmacological and cosmetic agents for skin-whitening.

Binding mode and affinity of MHY773 with tyrosinase was investigated by enzyme kinetics and docking simulations. MHY773 showed potent tyrosinase inhibitory activity.