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Synthesis and anti-tyrosinase evaluation of some novel derivatives of kojic acid

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Background and Aims: Melanin is a dark pigment produced by skin cells in the innermost layer of epidermis. Melanogenesis is initiated with the first step of tyrosine oxidation by tyrosinase. Tyrosinase is an enzyme that catalyzes the hydroxylation of L-tyrosine and the subsequent oxidation of L-DOPA to dopaquinone in biosynthesis pathway of melanin. Therefore, the discovery of new tyrosinase inhibitors are useful for their potential applications in preventing pigmentation disorders and other melanin-related health problems in human beings. Among the many kinds of tyrosinase inhibitors, kojic acid has been a good inhibitory effect on tyrosinase. In the present study, some novel derivatives of kojic acid were synthetized and theire inhibitory effect was evaluated by dooachrome method with ELISA reader.
Methods: For preparation of the desired derivatives, at first the C-3 phenolic OH of 3-hydroxypyran-4-one ring (kojic acid) was protected by benzyl chloride to prevent polymerization reactions. Protected kojic acid was then reacted with ammonia or methyl amine to produce 3-benzyloxypyridine-4-one and 3-benzyloxy-1-methylpyridine-4-one ring. C-6 hydroxymethyl moiety was thereafter oxidized to aldehyde by MnO2. This aldehyde was reacted with proper amines or hydrazine to give imines which were debenzylated by hydrogenation with Pd/C to produce final compounds. The tyrosinase inhibition ability of compounds was determined by using dophacrome method by ELISA readr with slight modifications.
Results: Identification and structural elucidation of compounds were achieved by Mass, IR, 1H-NMR spectra. The inhibitory effect of synthesized compounds was not very effectivnes than kojic acid.
Conclusion: Tautomerism occuring in 3-benzyloxypyridine-4-one compounds caused complications in their 1H-NMR spectra. In fact, tautomerism caused each hydrogen to appear twice in their 1H-NMR spectra. Olso, our results showed that compounds with lower polarity than the origin compound had poor inhibitory effect on tyrosinase and hydroxyl groups play an important role in the expression of tyrosinase inhibitory.

Keywords: Tyrosinase inhibition; Kojic acid; Hyperpigmentation