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Synthesis and antioxidant evaluation of novel schiff base derivatives of 3-hydroxy-pyridine-4-one containing hydrazone and oxime moiety at C-6 position of the pyridinone ring

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Background and Aims: Free radicals are produced naturally in biological processes and their production is unavoidable in body. Antioxidants are compounds which can destroy oxidants or disrupt their effects. In this study we aimed to design antioxidants iron chelators which inhibite Fentone and Haber-weiss reactions by chelation of Fe2+ and Fe3+ while presented free radical scavenging activity.
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. Antioxidant evaluation was done by: Determination of DPPH radical scavenging effect and Fe2+ chelating ability evaluation.
Results: Identification and structural elucidation of compounds were achieved by Mass, IR, 1H-NMR spectra. Compounds presented good DPPH radical scavenging effect and Fe2+ chelation ability although their Fe2+ chelation abilities were not more significant in comparison with standard compounds.
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. Also free radical scavenging activity of 3-hydroxypyridine-4-one was better than 3-hydrox-1-methylypyridine-4-one derivatives, compared with standards. It confirmed tautomerism phenomenon occurred in these structures. Tautomerism caused the conversion of 4-keto to 4-phenolic moiety and formation of catecolic situation on the pyridinone ring of 3-hydroxypyridine-4-ones. Imine moiety in these derivatives caused to stabilization of catecolic tautomer and more antioxidant activity. Fe2+ chelation ability of synthesized compounds was not more significant in comparison with standard compounds because they are specific Fe3+ chelator.

Keywords: Oxime; Hydrazone; Hydroxypyridinone; Antioxidant evaluation