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Research Article

Synthesis of Kojic Ester Derivatives as Potential Antibacterial Agent

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The search for lead product with beneficial pharmacological properties has become a great challenge and costly. Extraction and synthetic modification of bioactive compounds from natural resources has gained great attention and is cost effective. In this study, kojic acid was produced from fungal fermentation, using sago waste as substrate, and chemically incorporated with chalcones and azobenzene to form a series of kojic ester derivatives and evaluated for antibacterial activities. Kojic ester bearing halogenated chalcone demonstrated active inhibition against *Staphylococcus aureus* compared to that of standard ampicillin. The inhibition increased as the electronegativity of halogens decreased, while incorporation of azobenzene derivatives on kojic acid backbone demonstrated fair antibacterial activity against *Escherichia coli* with minimum inhibitory concentration (MIC) of 190–330 ppm. The presence of C=C and N=N reactive moieties in both chalcone and azo molecules contributed to the potential biological activities of the kojic acid ester.

1. Introduction

Kojic acid is a natural pyrone produced from fungal fermentation from various types of carbon substrates in the presence of fungi [1, 2]. Kojic acid and its derivatives have drawn attention and were studied intensively due to its significant biological activities in medicine and pharmacological field such as antifungal, antibiotic [3, 4], anti-inflammatory and analgesic [5], and antibacterial [6] properties.

Many recent studies reported on chemical modification of kojic acid for various applications such as antibacterial activity [7] and dye sensitized solar cell (DSSC) [8]. Synthesis of bioactive molecules employing kojic acid as a precursor via esterification of available hydroxyl groups has been widely reported to overcome the drawbacks of its hydrophilic properties in various applications [9–12]. Esterification of kojic acid, for instance, is able to enhance the hydrophobic properties which in turn improved its performance as tyrosinase inhibitor and antioxidant [13, 14].

Incorporation of kojic acid into other biological active compounds has also been reported with enhanced biological activities [15, 16]. Chalcones are an example of biological active compound which is derived from natural sources such as fruits, vegetables, spices, tea, and soy-based foodstuff [17, 18] and used as an intermediate precursor of flavonoids and isoflavonoids [19]. Chalcone is also commonly prepared via Claisen Schmidt condensation. The synthesis of chalcone has drawn much attentions due to the presence of its α,β-unsaturated ketone moieties which contributes to various biological activities such as antimalaria [20], anticancer [21], antiprotozoal, anti-inflammatory, antibacterial, antifilarial, anticonvulsant [22], antifungal, insect antifeedant, antimutagenic [23], and antioxidant [24, 25]. The presence of halogen substituents particularly at the *para* position of chalcone backbone has been reported with excellent biological activities such as antibacterial [26] and anti-inflammatory [27], while azobenzene bearing aryl/alkyl and N=N reactive moieties have been extensively reported due to its excellent antibacterial [28, 29], antioxidant [30], anti-inflammatory [31], antifungal [32], and antitumor [33] properties. Azobenzene is also recognized for its medicinal properties such as antineoplastic [34], antidiabetic [35], and antiseptic [36].

Herein, we report on the isolation of kojic acid from sago waste and utilized it as a precursor for the synthesis