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IN SILICO AND IN VIVO ANTIOXIDANT ACTIVITY OF CAFESTOL AND ITS p-METHOXYBENZOATE DERIVATIVE

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Cafestol is an *ent*-kaurane diterpene alcohol found in coffee beans (*Coffea arabica* L. and *C. canephora* P., Rubiaceae) that exhibits antioxidant activity through modulation of the Nrf2/Keap1 pathway, which protects against oxidative stress, a process implicated in diseases such as cancer, atherosclerosis, and Alzheimer.[1] This study aimed to evaluate the antioxidant activity of cafestol and a novel 4-methoxybenzoate derivative (**1**) using *in silico* and *in vivo* approaches, with *Saccharomyces cerevisiae* as a model organism. Molecular docking was conducted in AutoDock 1.5.7 using Keap1 (PDB ID: 1U6D), cafestol (PubChem CID: 108052) and **1**, designed in Spartan. Derivative **1** was synthesized by esterification of cafestol with 4-methoxybenzoic acid, DMAP, and EDC·HCl (24 h, 40 °C), characterized by 1D and 2D ^{1}H and ^{13}C NMR, as also its melting point. For viability assays, *S. cerevisiae* strain BY4741 was treated with cafestol or compound **1** (20 µM), incubated at 28 °C for 1 h with shaking at 180 rpm, and subsequently exposed to 1 mM H_2O_2. Colonies were counted after 5 days. Data were analyzed by one-way ANOVA followed by Tukey's test. Docking analyses revealed binding energies of –14.04 kcal/mol for the compound **1** and –11.02 kcal/mol for cafestol, suggesting a stronger interaction between **1** with Keap1, which can be correlated with its higher antioxidant potential. In cell viability assays, neither cafestol nor **1** showed cytotoxicity, with survival rates above 90% in non-stressed cells. Under oxidative stress conditions, cell viability was 48% for cafestol and 61% for compound **1**.

In conclusion, the structural modification of cafestol as 4-methoxybenzoate derivative (**1**) gave a good reaction yield 60% which led to an increase in antioxidant activity, as demonstrated by both computational and biological assays.

Keywords: *Coffee, Saccharomyces cerevisiae, Oxidative stress, Antioxidant activity, Molecular docking*