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(1E)-1-(2-pyrazinyl)ethanone thiosemicarbazone (PT) as a tyrosinase inhibitor with anti-browning activity: Spectroscopy, DFT and molecular docking studies

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ABSTRACT

In this study, (1E)-1-(2-Pyrazinyl)ethanone thiosemicarbazone (PT) was synthesized and characterized using Fourier-transform infrared (FTIR), ultraviolet-visible (UV–Vis), proton nuclear magnetic resonance (^{1}HNMR) and carbon-13 nuclear magnetic resonance (^{13}CNMR) spectroscopy. The vibrational frequencies were analysed using the Vibrational Energy Distribution Analysis (VEDA) program. The chemical properties of PT, including electron density distribution and intramolecular interactions, were characterized using in-silico methods based on Mulliken atomic charges, molecular electrostatic potential (MEP), quantum theory of atoms in molecules and reduced density gradient noncovalent interaction approaches. PT exhibits a significant inhibitory effect on enzymatic browning (6 and 24 h) and tyrosinase enzymes (IC50 = 7.75 μM). Kinetic analysis shows that PT is a mixed-type inhibitor, with respective Km and Vmax values of 0.632 mM and 0.0044 μM/s, and that it forms a reversible enzyme-inhibitor interaction. The PT-tyrosinase interaction was experimentally evaluated based on 1D, second derivatives of 1D, 2D and 3D IR spectroscopy. Furthermore, analysis of absorption, distribution, metabolism, excretions and toxicity properties revealed good physicochemical properties of PT according to the drug scores and Lipinski's Rule of Five. Lastly, the mechanisms of PT against tyrosinase were visualized and supported by means of a molecular docking approach.

1. Introduction

Food browning is one of the major current problems faced by the food industries, which is also closely related to consumer safety [1]. Preventing enzymatic browning is an effective way to improve food quality and safety. Browning of food is primarily induced by copper-containing tyrosinase enzymes containing polyphenol oxidases that are involved in the hydroxylation of monophenols to o-diphenols and the oxidation of diphenols to quinones, both of which undergo further processes that result in the formation of brown pigments [2]. However, some foods, like bread, soy sauce, black tea, cocoa and raisins, need browning to have a unique colour and taste [3].

Tyrosinase (EC 1.14.18.1) is a metalloenzyme that regulates the formation of melanin, a group of natural pigments found in humans, animals and plants [4]. Tyrosinase causes undesired browning in fruits, vegetables and beverages. Currently, scientists and fruit processing industries are exploring an innovative, efficient and safe tyrosinase inhibitor to avoid market loss during post-harvest and subsequently improve food quality [5]. According to Zolghadari et al. [6], tyrosinase inhibitors could be useful as skin whitening compounds in addition to antibrowning agents in the food and beverage industry.

Thiosemicarbazide, also known as hydrazine carbodithioamide, is a

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