INTEGRATED THERMAL KINETICS AND MOLECULAR DOCKING ANALYSIS OF *ARBUTUS UNEDO* POLYPHENOLS FOR ANTIDIABETIC APPLICATIONS

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ABSTRACT

Arbutus unedo L. is a Mediterranean species rich in bioactive polyphenols, including gallic acid, catechin, quercetin, and arbutin, which exhibit pronounced inhibitory activity toward α-glucosidase and α-amylase, often exceeding that of the standard antidiabetic drug Acarbose. However, the practical valorization of phytotherapeutic formulations based on *A. unedo* is limited by the thermal lability of its polyphenolic constituents, affecting stability during drying, extraction, formulation, and storage.

In this work, the thermal behavior of *A. unedo* fruit was investigated by thermogravimetric analysis (TGA) under inert and oxidative atmospheres at multiple heating rates. The kinetics of thermal and thermo-oxidative degradation were evaluated using four complementary isoconversion methods: Kissinger–Akahira–Sunose (KAS), Ozawa–Flynn–Wall (OFW), Starink, and Kissinger, through activation energies as a function of conversion. The variation of activation energy revealed distinct degradation phases, attributed to moisture and volatile loss, degradation of phenolic and sugar constituents, and carbonization reactions. The agreement among the four methods confirms the reliability of the obtained kinetic parameters, while comparison between inert and oxidative regimes highlights the role of oxygen in accelerating polyphenol degradation.

In parallel, molecular docking of the major polyphenols of *A. unedo*, previously characterized by UPLC–MS, was performed with the crystal structures of α-glucosidase and α-amylase, and binding affinities were compared with that of Acarbose. The integration of experimentally determined thermal stability with computationally predicted enzyme affinity enables ranking of polyphenols according to both criteria, providing a rational basis for selecting candidates for stable phytotherapeutic formulations based on *A. unedo.*

Keywords: Thermal kinetics, molecular docking, antidiabetic, thermogravimetry.