The Antihypertensive Effect of L-Ergothioneine (ET) on Angiotensin I-Converting Enzyme (ACE) Inhibitory Activity and Nitric Oxide (NO) Production to Effectively Prevent and Treat Cardiovascular Diseases

Agarwal, Aryaa (School: Academies of Loudoun)

Hypertension is a significant risk factor for cardiovascular diseases, affecting 1.3 billion people and attributing to 17.9 million deaths worldwide per year, making it the leading preventable risk factor for premature death. However, existing commercially-available drugs harbor strong side effects, heightened dosage frequency, and only target a single biomarker of hypertension. This novel research studies a promising and more comfortable solution: L-Ergothioneine (ET), a naturally-occurring, biodegradable derivative of histidine (amino acid) that is absorbed via a specific high-affinity transporter, OTCN1. OTCN1 has increased expression in tissues predisposed to higher oxidative stress and inflammation (e.g. hypertensive oxidized-LDLs) as a cytoprotective mechanism. It is proposed that ET will target two critical biomarkers for hypertension, the overexpression of angiotensin I-converting enzyme (ACE) and reduced nitric oxide (NO) activity. Through cellular viability, ACE inhibition, and NO production assays in an endothelial cell line (HUVEC) closely mimicking the human blood vessels, this research found that ET can inhibit ACE activity up to 6.077 nmol/min (20.85% greater than the control) and upregulate NO up to 0.041 nmol/uL (49.88% greater than the control) at a concentration of 10 umol. ET even had 3.900 nmol/min (14.04%) stronger ACE inhibitory activity compared to the ACE Positive Control (current hypertension drug). Hence, this study proposes ET as a groundbreaking, low-cost, and multifunctional bioactive peptide with antihypertensive effects to simultaneously target vasoconstriction and vasodilation at a greater rate than commercial drugs to effectively prevent and treat cardiovascular diseases.