鏈黴菌代謝物 Homogentisic Acid 及 β-Phenylpyruvic Acid

之抗氧化壓力效果評估

Effects of the Streptomyces Metabolites, Homogentisic Acid and β-Phenylpyruvic Acid Against Oxidative Stress

中文摘要

生物體內因代謝反應、紫外線或放射線照射等現象所產生的自由基 (free radicals) 或
活性氧屬 (reactive oxygen species, ROS)，是造成細胞損傷、組織老化、腦部疾病，
甚至生物體內各種病變的主因之一；這樣的過氧化傷害機制，在生物體內雖可藉由外來或
內在的各種抗氧化防禦機制予以減輕或防止，但有時並不能完全有效對抗多種氧化自由基
及活性氧屬所造成的傷害，因此對人體而言在日常生活中適時地補充抗氧化劑 (antioxid
ants) 是有其必要性的。在此之前，我們實驗室曾針對微生物代謝物進行了抗氧化活性的
篩選，並由其中一株本土性土壤分離菌株 Streptomyces lavandulae SY-815 的發酵液中，
成功地分離出兩個主要的抗氧化活性代謝物。分子結構鑑定的結果證實兩者分別爲 homoge
ntisic acid (HA) 及 β-phenylpyruvic acid (β-PPA)。接著在抑制脂質過氧化 (lipi
d peroxidation) 的初步評估實驗，我們亦確認了這兩個物質的抗氧化活性。本研究爲
了接續此一發現，擬進一步探討這兩種微生物代謝物，在接近生物體實際狀態之自由基清
除及抗氧化能力，乃針對人體氧化傷害較重要的紅血球、肝臟及腦部等三個部位，建立相
關的抗氧化壓力效果評估系統以進行更深度的體外抗氧化活性評估實驗。在清除自由基及
抑制脂質過氧化的評估實驗方面，我們選定了下列五種體外實驗模式系統進行受測物的抗
氧化活性探討，包括（一）人類紅血球空細胞膜系統 (human erythrocyte ghost membra

ne system)；（二）大白鼠肝微粒體系統 (rat liver microsome system)；（三）大白
鼠腦均質液系統 (rat brain homogenate system)；（四）利用流式細胞儀 (flow cytom
eter) 來偵測完整紅血球脂質過氧化作用的評估系統；以及（五）利用大白鼠初代肝細胞
(rat primary hepatocyte) 培養模式，來觀測物質對肝細胞的細胞毒性及其協助肝細胞
對抗氧化壓力能力的評估系統。由實驗結果得知，在人類紅血球空細胞膜系統、大白鼠肝
微粒體系統及大白鼠腦均質液系統等三種實驗模式中，兩種鏈黴菌代謝物都表現出顯著抑
制脂質過氧化的能力；在利用流式細胞儀偵測脂質過氧化程度的實驗中，我們也發現此兩
種物質都較 α-tocopherol (α-TOH) 具有更強抑制脂質過氧化的能力。在利用大白鼠初
代肝細胞培養觀測抗氧化活性的實驗模式中，得知此兩種物質對大白鼠初代肝細胞不呈任
何細胞毒性，然而兩者對抗氧化壓力的效果亦不如 α-TOH 明顯。

英文摘要

Free radicals and reactive oxygen species (ROS), generated in most biologicals ystems by metabolic reactions, ultraviolet rays or radioirradiation, have been implicated as the causative factors in cell injury, aging processes and the p athogenesis of numerous diseases. Althought such kinds of oxidative damages ca n be prevented or reduced by the endogenous or exogenous antioxidant defending mechanisms of oxidation, it still have a need to obtain sufficient quantity o f antioxidants through daily diet to prevent the deleterious effects exerted b y free radicals and ROS. To meet this requirements, it is important to search for more potent and reliable antioxidants from environmental sources.In the pr evious study, we have isolated two Streptomyces metabolities, homogentisic aci d (HA) and β-phenylpyruvic acid (β-PPA), which have been proved to posscess inhibitory activity against lipid peroxidation. In contiuning our work to furt her understand the detailed mechanism and the antioxidant performance of these two microbial metabolites, we have established several in vitro evaluation sy stems for the investigation of antioxidant activities of the two compounds. Th ey include: (1) human erythrocyte ghost membrane system, (2) rat liver microso me system, (3) rat brain homogenate system, (4) use of intact erythrocyte as t

he model for detecting antioxidant activity against lipid peroxidation by the method of flowcytometry, (5) use of rat primary hepatocyte as the model for detecting antioxidant activity against oxidative stress.In the results, HA and β-PPA showed antioxidant effects against (1) peroxyl radical-induced lipid peroxidation both in erythrocyte ghost membrane and rat liver microsome; (2) iron-induced lipid peroxidation in rat brain homogenate, (3) lipid peroxidation in intact human erythrocyte measured by flow cytometry. Nevertheless, HA and β-PPA did not show any effects in rat primary hepatocyte against oxidant-induced oxidative stress.