雌激素與活性氧作用的氧化還原角色

The Redox Role of Estrogen reacting with reactive oxygen species

中文摘要

酚類(phenolic structure)化合物具有清除自由基而達到抗氧化及保護細胞的能力，在流行病學上 Estrogen 可以降低停經後婦女心血管疾病，其中的機轉都被認爲與酚類結構的氧化還原角色有關。

已知利用 ESR 可以直接測定自由基的產生。利用 Fenton reaction 反應所產生氫氧自由基與捕捉劑 DMPO 在 ESR 上可以得到電磁波譜，在甲醇的存在下，會產生氧甲基自由基並有新的電磁波譜的產生，而且造成 DMPO-OH 的電磁波譜裂解，而 Estrone、 Salicylic acid 與 Phenylanaline 皆可使 DMPO-OH 與 DMPO-OCH3 的電磁波譜明顯減小，但相同濃度的 Estrone 比 Salicylic acid 或 Phenylanaline 能更顯著的減少 DMPO-OH 電磁波譜。

以超螺旋型質體 pBR322 DNA 進行 DNA relaxation 實驗，在 Fenton reaction 反應下，所產生的 hydroxyl radical (OH．)在隨著不同濃度的 Estrogen 下，使超螺旋型質體被攻擊而轉型的情形減少。

利用毛細管電泳進一步分析 Estrone、β-Estadiol 在 Fenton Reaction 反應下，觀察有新生成物的產生。出現的滯留時間可能是 catechol- estrogens 或其他新產物，但需要進一步去分離分析。

利用 GC/MS 偵測 Estrone、β-Estadiol 與氫氧自由基反應的結構上變化，由 Estrone 與β-Estradiol 其分子量爲 270 與 272，而我們測得的新生成物分子量爲 284 與 286，故分子量多了 14。我們根據 ESR 圖譜的結果可以知道在 Methanol 存在下的 Fenton reaction 會產生 Methoxyl radicals，故我們推測 Estrone 與β-Estradiol 在處於 Fenton reaction 氧化環境下，可能形成的結構爲 Methoxyestrogen，分子量應分別爲 302 與 304，但 adduct ion [M-H2O2]合理，故所測得分子量少 18 而爲 284 與 286。

英文摘要

Estrogens had been shown to lower the levels of LDL and rise the concentration of HDL, and strong epidemiologic evidence has correlated the reduction of cardiovascular mortality rate with administration of the estrogen in postmenopausal women, but studies had also shown that those women were more like to develop breast and endometrial cancer. Estrogens usually metabolized in vivo through P450 oxidation into a hydroxylated product like catechol- or quinol-containing compound that could caused tumorigenesis. The chemical structure of estrogens (phenolic structure) allows for a metal- chelating ability or for donating of an H+ atom to a

peroxy radicals. Here we investigated the redoxy role of estrogen reacting with reactive oxygen species. The spin trapping technique, which employed DMPO spin adducts with oxygen-centered radicals give characteristic EPR spectra, is a powerful tool to monitor the presence of radicals in the reaction system that employed this technique to observe the individual reactions of estrogens with the radicals involved in the process. In this study, the antioxidant, radical scavenging activity of estrone, salicylic acid and phenylanaline were examined. Estrone was the best radicals scavenger among tested compounds. From DNA relaxation analysis, it shown that Estrone and β-Estadiol protected DNA from radical's attack. Estrone and β-Estadiol with Fenton reaction in Methanol produced new derivatives that showed the migration time in capillary electrophoresis. We characterized the new derivatives by GC/MS with molecular weight was shown were 284 and 286 in MS spectrum, and we proposed to be the products should be Methoxyestrogen