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• 研究人員	何元順；林仁混 Ho, Yuan-Soon；Lin, Jen-Kun
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• 英文關鍵字	Genotoxicity；Nitric oxide (NO)；Apoptosis；Antioxidant；Environmental health
• 中文摘要	NO 在以前一直被認爲僅從燃燒的廢氣產生,是一種體外的汙染物,並不受研究者的重視。最近生物醫學的進步,藥理與生化學家研究出 NO 是一種重要的內生性傳遞物質,它可在自體細胞合成,具有很強的生物功能,諸如血管的擴張鬆弛,血壓的調控,神經訊息的傳遞,基因的表現等等。其重要性很受注目, 1992 年 Science 雜誌就把 NO 選爲年度風雲分子(The Molecular of the Year)。自此這個不起眼的簡單分子,就搖身一變爲大名鼎鼎,如雷貫耳的奇異分子。GSNO(S-nitrosoglutathione)爲細胞內抗氧化物 GSH 攜帶一氧化氮之化合物,當它釋出一氧化氮時,可對細胞造成 DNA 傷害。已有許多報告指出一氧化氮自由基可造成細胞凋亡,但 GSNO 引起細胞凋亡之詳細機制尚未被研究清楚。在本實驗中,我們使用人類腸癌細胞株,來探討 GSNO 對細胞之毒性及細胞凋亡之機制。我們發現,細胞給予 GSNO 處理之同時,若一起加入銅離子(Cu/sup ++/),則細胞死亡率較單獨處理 GSNO 明顯減少。據此我們亦證實了 Cu/sup ++/在細胞外可促使 GSNO 釋出 NO？,由於 NO？不穩定,在極短時間內轉變爲硝酸鹽及亞硝酸鹽,因而降低進入細胞內 NO？之量,而減少細胞的傷害。NO？調控細胞凋亡過程中之基因表現,是我們想要嘗試了解的,以西方墨點分析來偵測基因表現的變化,結果發現 Bad、Bax 及 c-Jun 等蛋白的表現皆有增加之現象,而 p27 及 Bcl-2 的表現卻有被抑制的現象。爲了解 NO？在參與細胞內訊息傳遞所扮演之角色,我們也對 PKA 及 PKC 之表現進行探討,結果發現 PKA 與 PKC.zeta.之表現會被 NO？抑制,此結果告訴我們在 GSNO 引起之細胞凋亡中,存在一種特殊的調節機制,而 PKA 及 PKC.zeta.可能扮演一重要角色。
• 英文摘要	In this study, the amount of S-nitrosoglutathione (GSNO) was measured spectrophotometrically at 334nm. Spontaneous decrease of

absorbency at 334nm was detected when GSNO was exposed to 37.degree.C and a high pH (pH 8.0). We investigated the catalytic roles of various metal ions on the decomposition of GSNO. The degradation of GSNO (0.5mM) was enhanced by the presence of Cu/sup 2+/ and Ni/sup 2+/ ions. The amount of NO release from GSNO degradation was estimated by the Griess reaction based on nitrite accumulation. The results indicate that nitrite production was elevated by at least 2-fold in the presence of Cu/sup 2+/. Our study further indicates that Cu/sup 2+/ enhance GSNO-induced apoptosis in human colon adenocarcinoma (HT 29) cells. We also found that copper ions modulate the expression of bad, bax, and bcl-2 in GSNO-treated HT 29 cells. The levels of bax and bad proteins were significantly elevated by about 4- to 6-fold when compared with mock-treated cells at 24 h after combined treatment of GSNO plus Cu/sup 2+/ or Ni/sup 2+/. On the other hand, significant inhibition of bcl-2 occurred in HT 29 cells with simultaneous treatment of GSNO with Cu/sup 2+/ (or Ni/sup 2+/). It seemed that Cu/sup 2+/ (Ni/sup 2+/) could enhance the decomposition of GSNO that liberated NO to activate the pathways. Our results demonstrated that the apoptotic effects induced by GSNO was promoted by Ni/sup 2+/ and Cu/sup 2+/ through two different mechanisms: by depletion of intracellular GSH level and by triggered of NO release from GSNO which then promoted the NO-induced apoptotic cell death in human cells.