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(apoptosis)"˝ ¤˝¡ C S › "˝¥†‹G ¥X⁄ MS fi æ˘ƒp¤ vitamin C¡AL-N-acetyl-cysteine ¥ Sflƒ†fi ˜ S¤ NO „ ⁄ H ^ † ƒM„ " ‹ ™ SC¥"æS › S o†{ peroxynitrite ¥ ¥i»⁄ o⁄ H "˝ ø ›Mƒ"⁄'¡A Mƒ ¥ƒ»P NO "˝S ¤˝¿ ´ £ƒP¥D › nO»⁄ o† ›M^af"(necrosis)ƒ «D› ⁄'¡C¥ « e › – · yz per oxynitrite ‹ NO »P O2•¯ S ¿ ƒ ¤ ⁄ $ ¡†A"«¤ ƒ s ƒ b " ¯ fi⁄⁄"˝¥b I·` "Ł¡ A ƒ w ¤'¡°¤A¿⁄ S ¥ i » ⁄ o † ›M^af"†£¥˝ S › ^h"peroxynitrite " " £¥›" P † \ ‰–'¤£ "˝' I S l „ D ‹flfƒ†‹@"˝‹ ^ '°¡Cƒ ƒ„ ƒ „ ¥ » › p „ " S ˘ – fl ´ ™M›»¥•"˝¿U¿N' NO, NOx,»P peroxynitrite ⁄S›Pflf ´ ¡A⁄¿ ¤ „ ¤ ⁄S„D¡C

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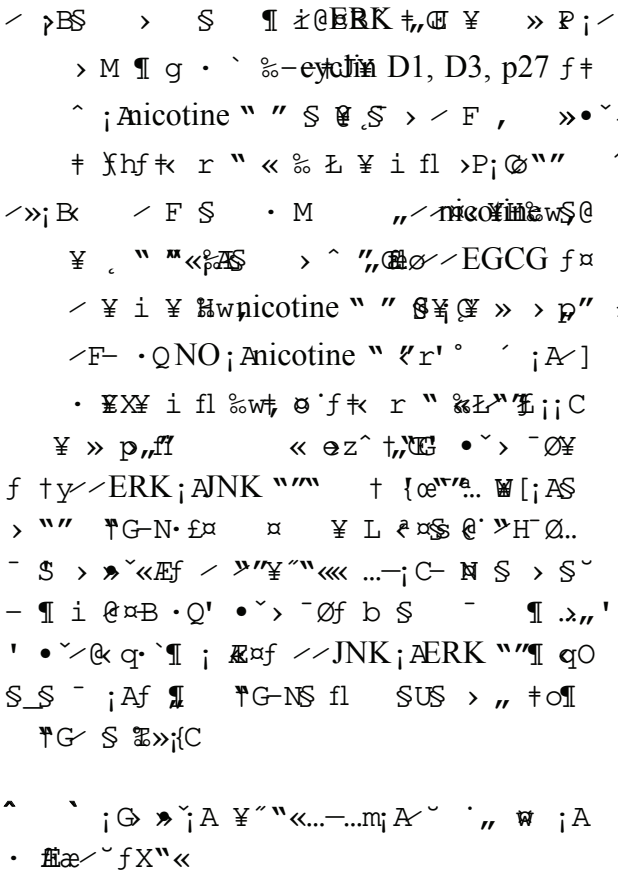

peroxynitrite formed by the interaction between cigarette tar and NO may play an important role in smoking-related diseases including lung cancer. Our previous study indicated that wild-type p53 and p21/WAF1/CIP1 expression were elevated in human cancer cells exposed to NO and these elevations eventually promote cell apoptosis. Our another study also demonstrated that NO-induced alteration in gene expression was attenuated by antioxidants such as L-N-acetyl-cysteine. In addition, by use of lung cancer cell line as a model system, we demonstrated that peroxynitrite ($ONOO^-$) in contrast to NO, induced cell death more characteristic of necrosis than apoptosis. Hence, the compositions in cigarette smoke including NO, NOx, and peroxynitrite may induce some of its damaging effects by free radical mechanisms. All these results provide us for intend research and the following specific aims will be completed:

Our study provide evidences indicate that cigarette smoking (NO, NOx) induce human cancer cells apoptosis. The mechanisms were well characterized in this study. We also demonstrated that some pollutants in enviroment such as copper ion potentiate the apoptotic effects induced by NO. Such results make us to avoid to contact the cigarette smoking and some enviromental factors. To search the naturally occurring compounds that can prevent the toxic effects of Nox. We demonstrated that the antioxidants such L-N-acetyl cysteine can prevent the apoptotic effects induced by NO. The emcahanisms were demonstrated as elevation of the intracellular glutathione. We also investigated the effects of the nicotine involved in cancer cell proliferation. We demonstrate that nicotine promote the lung cancer cells proliferation through activation of some signal transduction pathways such as activation of mitogen activation promoting kinase (MAPKs). We also demonstrate that

Abstract

Epidemiologic evidence suggests that cigarette smoking is a major factor for chronic obstructive pulmonary disease such as chronic bronchitis and emphysema, for carcinogenesis, and for cardiovascular disease. However, the precise mechanisms of these effects are incompletely understood. Cigarette smoke can be divided into two phases, gas phase and particulate matter (tar). Both phases contain high concentrations of oxidants and free radicals, especially nitric oxide (NO) and nitrogen oxides (Nox) in the gas phase and quinone/hydroquinone complex in the tar. NO is present in the gas phase of smoke, whereas O2• is generated by auto-oxidation of polyhydroxyaromatic compounds such as catechol and 1,4-hydroquinone present in the cigarette tar. Thus, potent reactive species including

nicotine activated cyclin D1, D3 and inhibit the p27 which eventually promote human cancer cells proliferation. The mechanisms was demonatrated in our study and indicate that ERK kinase significant involved in regulation of these genes. We are demonstrated that EGCG (the component of green tea extract) can attenuate the proliferation effects induced by nicotine in human lung cancer cells. The mechanisms must be still investigated in our further experiment. We also demonstrated that the ERK and JNK kinase were significantly elevated in the WBC of the somking individual. This findings provide significant results indicate that the JNK and ERK may be used as a biomarker in the individual expose to smoking.

Keywords:Cigarette smoke, biomarkers, antioxidants.

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3. S › ^ „Œ „ ⁄⁄ƒ‡¤ · Sfiæˇ"«‰Łƒp L-N-acetyl-cysteine ¥ ¥H‰ ¤ NO ' ‡ ¥ƒ¤ "˝¶ fi¸'A„ ´ »P·£ "† ›M⁄"S fiæ⁄ˇ"« ‰Ł¶qƒ‡^ ¡C
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5. S › S ¶i⁄@¤B^ „Œnicotine "˝S ¤ ¸»P‹ ¡

/ ˘ † › M ¶ g ˙ ‰ cyeli T ¥ D1, D3, p27 ƒ ‡ ¡ A " æ / @ ¤ B ¯ § ›/F, ƒ h ƒ ‡ ‹ r " « ‰ Ł ¥ fl ¡ P ø " "

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