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Involvement of estrogen receptor-alpha in lambda-cyhalothrin and cypermethrin-induced cancer growth in BG-1 ovarian cancer cells expressing estrogen receptor

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ABSTRACT

Synthetic pyrethroids (SPs) are the most common pesticides which are recently used for indoor pest control. The widespread use of SPs has resulted in the increased exposure to wild animals and humans. Recently, some SPs are suspected as endocrine disrupting chemicals (EDCs) and have been assessed for their potential estrogenicity by adopting various analyzing assays. In this study, we examined the estrogenic effects of lambda-cyhalothrin (LCT) and cypermethrin (CP), the most commonly used pesticides in Korea, in BG-1 ovarian cancer cells expressing estrogen receptors (ERs). To evaluate the estrogenic activities of two SPs, LCT and CP, we performed MTT assay and reverse-transcription polymerase chain reaction (RT-PCR) for LCT or CP treated BG-1 ovarian cancer cells. In MTT assay, LCT (10^{-6} M) and CP (10^{-5} M) significantly induced the growth of BG-1 cancer cells in a dose-dependent manner. LCT or CP-induced cell growth was reversed by addition of ICI 182,720 (10^{-8} M), an ER antagonist, suggesting that this effect appears to be mediated by an ER-dependent manner. Moreover, RT-PCR results showed that transcriptional level of ERα was significantly down-regulated by LCT and CP. Taken together, these results indicate that LCT and CP may possess estrogenic potentials to stimulate the growth of ovarian cancer cells expressing ERs via an ER-dependent manner. Based on the observations from these *in vitro* results, we will examine *in vivo* estrogenicity of LCT and CP in a xenografted mouse model transplanted with human BG-1 ovarian cancer cells.

INTRODUCTION

With increasing production and consumption of pyrethroid insecticides, more concerns on the potential effects of exposure to the pyrethroids are arising. SPs are analogues of pyrethrin, which are derived from pyrethrum plants (*Chrysanthemum cinerariaefolium*). They are high toxic to insects, and the level of toxicity greatly decreases in the order of amphibia, fish, mammals and birds. CP and LCT are synthetic pyrethroids that among the most commonly used pesticides in South Korea. SPs including CP and LCT are used to control a broad range of pests in agriculture, public health, and households, accounting for about 25% of the world wide insecticide market. Recently, several studies show that some SPs possess hormone agonist or antagonist activities. And also, chemicals classified ad SPs are suspected as being endocrine disrupting chemicals. Evidence also suggests that some SPs are capable of disrupting endocrine function through estrogenic or anti-estrogenic activities. However, little has been done to assess their potential hormonal activities using in vivo test on endocrine disruption. The purpose of the present study was to evaluate the estrogenic potential of CP and LCT by using BG-1 carcinoma cell lines as the *in vitro* model. Furthermore, Based on observations from these *in vitro* results, we will examine the estrogen activities of LCT and CP in a xenografted mouse model transplanted with human BG-1 ovarian cancer cells.

RESULTS

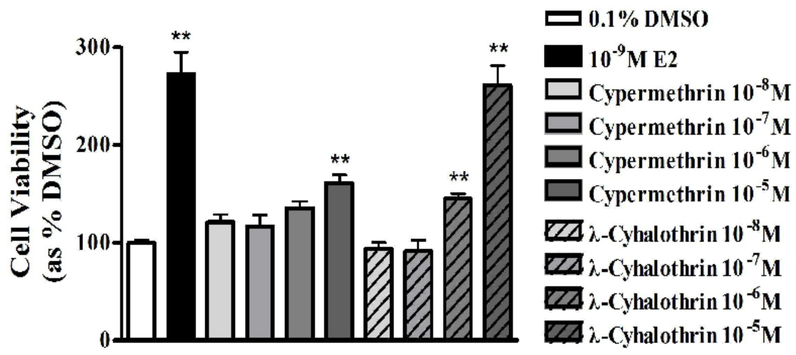

Figure 1. Cell proliferation by E2, CP or LCT-treatment in BG-1 cells for 8 days, cell growth was measured using MTT assay at 540nm. Data represent the means ± SD of triple experiment. * P<0.05, ** P<0.01 compared to a vehicle treated with DMSO.

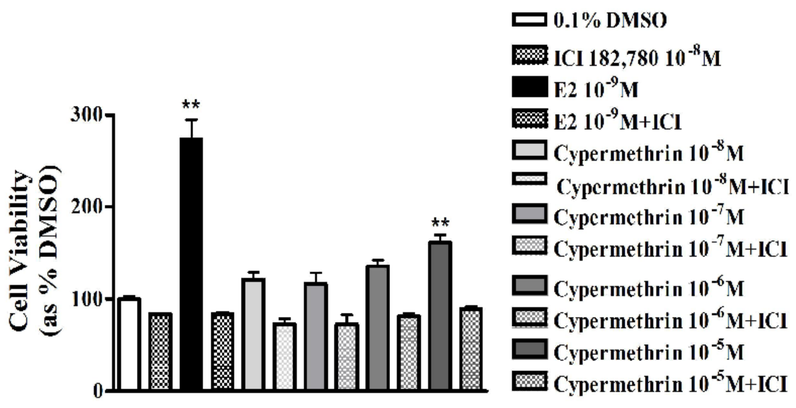

Figure 2. Cell proliferation by E2, CP-treatment with ICI 182,780 in BG-1 cells for 8 days, and the number of viable cells was measured using MTT assay at 540nm. Data represent the means ± SD of triple experiment. * P<0.05, ** P<0.01 compared to a vehicle treated with DMSO.

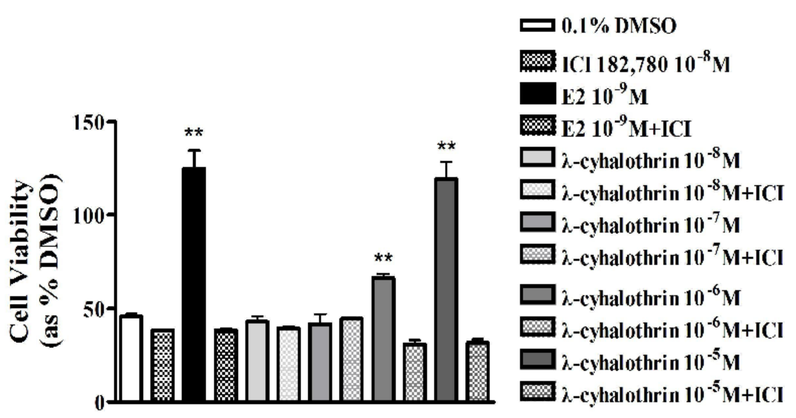

Figure 3. Cell proliferation by E2, LCT-treatment with ICI 182,780 in BG-1 cells for 8 days, and the number of viable cells was measured using MTT assay at 540nm. Data represent the means ± SD of triple experiment. * P<0.05, ** P<0.01 compared to a vehicle treated with DMSO.

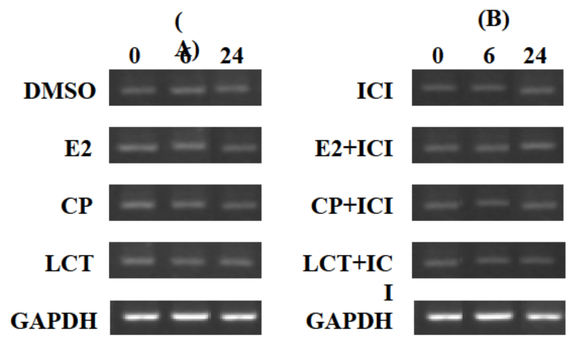

Figure 4. mRNA expression of human estrogen receptor α in BG-1 cells by exposure to CP or LCT (10^{-5} M). RNA was isolated and mRNA levels were assayed by RT-PCR. (A) mRNA levels of ERα by CP or LCT -treatment (B) mRNA levels of ERα by CP or LCT-treatment with ICI 182,780.

CONCLUSION

1. **CP or LCT induced the BG-1 cell proliferation was gradually increased in a 10^{-5} M to 10^{-6} M compared to DMSO in a dose-dependent manner as well as E2 did. However CP-treatment was weakly increased cell proliferation compared to DMSO.**

2. **Expression of human estrogen receptor α was down-regulated by treatment of CP or LCT at 10^{-5} M. Cotreatment with LCT and ICI 182,780 showed no obvious alteration of the ERα mRNA expression.**

3. **Taken together, these results indicate that LCT and CP may possess estrogenic potentials to stimulate ovarian cancer cells expressing ERs via an ER-dependent manner, and these collective results confirm the carcinogenicity of these EDCs.**

4. **Based on observations from these *in vitro* results, we will examine the estrogen activities of LCT and CP in a xenografted mouse model transplanted with human BG-1 ovarian cancer cells.**

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