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사자발쑥 EtOH 추출물이 신경모세포암 세포주 A172의 세포주기 억제에 미치는 효과

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The ethanol extract from *Artemisia princeps* Pampanini induces p53-mediated G_1 phase arrest in A172 human neuroblastoma cells

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Objectives

In the present study, we examined the ethanol extract of *Artemisia princeps* Pampanini (known locally as "Sajuarissuk") which was obtained on GangHwa Island, Korea. Many studies have reported on the isolation of eupatilin, jaceosidin, and steroids from "Sajuarissuk", and their various therapeutic effects was recently reported. To the best of our knowledge, no report has been issued concerning the anti-cancer effect of *Artemisia princeps* Pampanini and its molecular mechanism involved. Thus, we examined the cytotoxic and cell cycle regulatory effects of the ethanol extract of *Artemisia princeps* Pampanini in human neuroblastoma A172 cells.

Materials and Methods

○ Materials

Artemisia princeps Pampanini was collected from GangHwa County, Korea. The dried aerial parts (100 g) were cut and extracted three times with EtOH (3×1 L). Extract solutions were filtered and dried using a rotatory evaporator under reduced pressure to give the EtOH extract (10.6 g) defined as EAPP.

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○ Methods

1. cytotoxic effect of EAPP by MTT assay 2. proliferation of A172 cells using the trypan blue exclusion test. 3. cell cycle, using flow cytometry. 4. expressions of G_1-related proteins by Western blot analysis. 5. kinase activity of CDK-cyclin complexes by immunoprecipitation and CDKs Kinase Activity Assay. 6. p53 is involved in EAPP-induced G_1 arrest by siRNA-mediated p53 gene silencing

Results

EAPP inhibited the proliferation of A172 cells dose- and time-dependently. DNA flow cytometry analysis indicated that EAPP notably induced the G_1 phase arrest in A172 cells. Of the G_1 phase cycle-related proteins examined, the expressions of cyclin-dependent kinase 2 (CDK2), CDK4, CDK6, and of cyclin D_1, D_2, and D_3 were found to be markedly reduced by EAPP, whereas cyclin E was unaffected. Moreover the protein and mRNA levels of the CDK inhibitors $p16^{INK4a}$, $p21^{CIP1/WAF1}$ and $p27^{KIP1}$ were increased, and the activities of CDK2, CDK4 and CDK6 were reduced. Furthermore, the expressions of E2F-1 and of phosphorylated pRb were also decreased, and the protein levels of p53 and pp53 (Ser 15) were increased. $p21^{CIP1/WAF1}$ upregulation was found to be mediated by a p53-dependent pathway in EAPP-induced G_1 arrested A172 cells. Taken together with these data, the ethanol extract of *Artemisia princeps* Pampanini was found to potently inhibit the proliferation of human neuroblastoma A172 cells via G_1 phase cell cycle arrest.

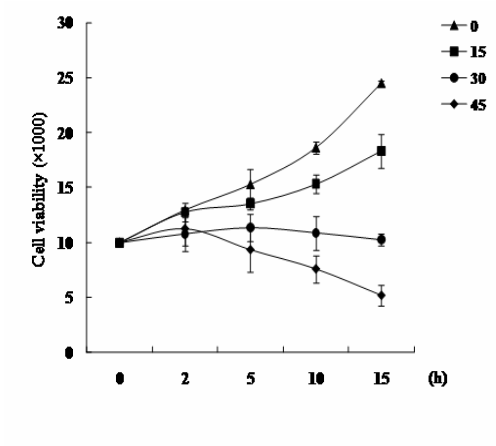

Fig. 1. Growth inhibitory effects of EAPP on A172 cells

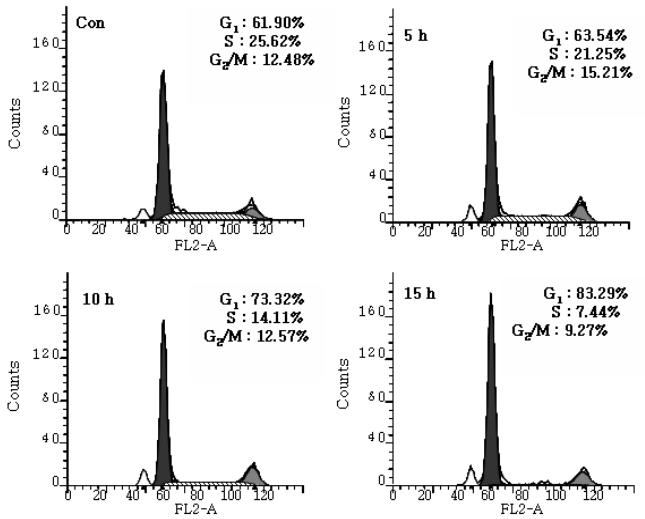

Fig. 2. DNA fluorescence flow cytometry histograms of A172 cells treated with or without EAPP