

Induction of the Poly(ADP-ribose) Polymerase Cleavage by 4 beta-acetoxyscirpene-3alpha,15-diol from *Paecilomyces tenuipes*

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Paecilomyces tenuipes is one of the famous Chinese medicinal entomopathogenic fungi that parasites in the larvae of silkworm. Three cytotoxic components were isolated from the carpophores of this fungus. The methanol extract of the fungus was subjected to chromatography over silica gel column. Elution with dichloromethane gave 5 fractions. The final purification of the fraction was made by preparative HPLC using a C18(2) reversed phase column eluted with acetonitrile: methanol: H₂O(50:40:10) and detected at 210 nm. Spectral analyses of the cytotoxic components showed that they were known acetoxyscirpendiol (ASD, 4beta-acetoxyscirpene-3alpha,15-diol), cerevisterol 6-methylester (CME, 3beta,5alpha-dihydroxy-6beta-methoxyergosta-7, 22-diene) and ergosterol peroxide (EP, 5alpha,8alpha-epidioxy-24(R)-methylcholesta -6,22-dien-3beta-ol) that were isolated from this fungus for the first time. The 50% inhibitory concentrations (IC₅₀) values of ASD, CME and EP against human gastric tumor cell line (SNU-1) were 3, 10 and 20 microgram per milliliter, respectively. The compound of ASD showed the strongest cytotoxic activity on SNU-1 cell line among the compounds. ASD induced apoptotic cell death on this cell line. It was showed that ASD and its derivatives(15-acetoxyscirpenol, diacetoxyscirpenol and 3alpha-acetyldiacetoxyscirpenol) cleaved 116 kDa poly(ADP-ribose) polymerase(PARP) into 89 kDa and 24 kDa fragments in human leukemia MOLT-4 cell line in a time-dependent manner. Among the compounds tested, diacetoxyscirpenol and 3alpha-acetyldiacetoxyscirpenol led to cleavage of PARP strongly at 48 hr. On the other hands, 15-acetoxyscirpenol and ASD showed weak cleavage activities. From these data, ASD and its derivatives seem to induce apoptosis through PARP cleavage.