

Inflammatory Environment Regulation and Anti-oxidant Induction for Endometriosis Treatment with Cymophenol

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Endometriosis, a chronic reproductive disease with pelvic pain, abdominal bloating, fatigue and infertility, affects more than 20% of women in the world. At the environment of the endometriosis lesion, hyper-inflammation and oxidative stress due to vasculogenesis for adhesion are observed. There is no specific way to prevent, and no fundamental cure for endometriosis, so long-term symptomatic treatment must be implemented. Nowadays, numerous phytochemicals have been studied for less side effects and long-term prevention. Cymophenol, a monoterpenoid phenol, is component of essential oil extracts mainly from *Origanum vulgare*. It is a well-known anti-inflammatory, anti-microbial and anti-cancer chemical. In our study, cymophenol exerted therapeutic potential on human endometriosis primary stromal cells and surgery induced mouse model. It induced autophagy and inhibited cell growth through PI3K/AKT down-regulation. This phenomena seems occur through mitochondria dysregulation and calcium homeostasis in endometriosis primary stromal cells. Similarly, Ca²⁺ selective chelator reduced cell viability by a certain level but, no synergic effects with cymophenol. Moreover, cymophenol showed anti-oxidant effects increasing the expression of antioxidant enzyme such as *HO-1*, *GCLC*, *SOD1*, *GSH-PX* and *NQO1*. This therapeutic effects were confirmed in surgery induced endometriosis mouse model. Daily intake of cymophenol for 28 days reduced lesion size and cyst. Surprisingly, cymophenol administration increased CD4 and CD8 positive T-cell population in the spleen rather there was no changes on macrophage. The immune activation related cytokines including *Ccl3*, *Il18* and *Il2* were increased in the spleen and *Il13*, *Ccr1*, *Ccl3*, *Il21r* and *Il1b* were increased in the lesion. Likewise, cymophenol induced *IL13*, *CCR1*, *CCL3*, *IL21r* and *IL1b* mRNA expression in human endometriosis primary stromal cell. Collectively, herbal component cymophenol has inflammation regulatory and antioxidant properties that could treat endometriosis.