Streszczenie w języku angielskim

Endometriosis is defined as the presence and growth of endometrial tissue in areas outside its physiological location, primarily within the ovaries and peritoneum, but also in distant organs. The disease is accompanied by chronic inflammation, numerous pain symptoms, and reproductive dysfunction resulting from the mechanisms involved in its development. The etiology of endometriosis is not fully understood, but the significant role of hormonal, inflammatory, genetic, and environmental factors is emphasized. Currently, the standard therapeutic approach is symptomatic treatment – analgesics and hormonal care – which are often associated with adverse reactions. Within endometriotic lesions, numerous cellular processes and molecular signaling pathways responsible for proliferation, apoptosis, adhesion, extracellular matrix (ECM) remodeling, and angiogenesis are dysregulated, making these processes potential targets for natural bioactive compounds.

The main aim of this study was to determine the biological potential of resveratrol and its natural derivatives (pterostilbene, piceatannol, and polydatin) in the prevention and treatment of endometriosis. *In vitro* cell models were used to assess the antiproliferative and proapoptotic effects on 12Z endometriotic cells, antioxidant, and anti-inflammatory activity in a co-culture model of 12Z cells and macrophages, and the potential of the investigated compounds to inhibit adhesion, migration, and invasion of 12Z cells. Resveratrol and its derivatives demonstrated selective antiproliferative and proapoptotic effects on 12Z cells, while exerting lower cytotoxicity towards the endometrial T HESC cell line. The strongest effects were observed with pterostilbene and resveratrol, which effectively induced apoptosis, as demonstrated by the activation of effector caspases, increased expression of proapoptotic proteins, and increased DNA fragmentation. The broad, dominant anti-inflammatory effects of resveratrol were mediated by reduced expression and secretion of key inflammatory mediators. Pterostilbene's activity, in turn, was especially associated with stimulation of antioxidant defense mechanisms, resulting in a significant reduction in the population of ROS-accumulating macrophages. All tested agents effectively inhibited 12Z cell migration and invasion, mainly by limiting ECM degradation, which was associated with modulation of MMP-2 and its tissue inhibitor TIMP-2 expression. Pterostilbene almost completely abolished 12Z cells' ability to invade the Matrigel™ model. The results indicate a series of bioactive, previously undescribed properties of stilbenes against endometriosis, which may lay the foundation for further advanced preclinical studies and the development of dietary therapeutic strategies to support its treatment.

Keywords: *in vitro* models of endometriosis, stilbenes, apoptosis, inflammation, invasion

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