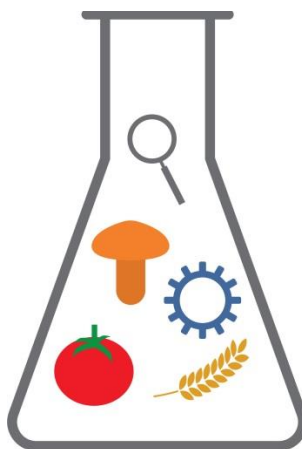




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## **TAXIFOLIN MODULATES mRNA EXPRESSION OF INVASION-ASSOCIATED MARKERS AND STIMULATES MIGRATION OF HUMAN TROPHOBLAST CELLS**

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During first trimester of pregnancy, the specific regulation of extravillous trophoblast migration and invasion into the maternal uterine wall is essential for successful placental development. Taxifolin (TAX) is a flavonoid of strong antioxidant activity that recently showed cytoprotective effects in trophoblast cells. The aim was to investigate if TAX can affect cell adhesion and migration in HTR-8/SVneo extravillous trophoblast cells as well as the expression of molecules that mediate these processes. Concentrations of TAX 10 and 100  $\mu$ M were selected according to the previously reported cytoprotective effects.

Analysis of cell adhesion by crystal violet staining on 3 different substrates (plastic, collagen, Matrigel) showed that HTR-8/SVneo cells pre-treated with 100  $\mu$ M TAX displayed increased adherence to Matrigel, substrate that imitate extracellular matrix, while adhesion to plastic and collagen was unaltered. TAX 10  $\mu$ M did not lead to a significant change in cell adhesion. Further, the influence of 24h incubation with TAX on the mRNA expression of matrix metalloproteinases 2 and 9 (*MMP2*, *MMP9*) and integrin  $\alpha$ 1,  $\alpha$ 5 and  $\beta$ 1 (*ITGA1*, *ITGA5* and *ITGB1*) was examined by qPCR. It was shown that TAX at 10  $\mu$ M can elevate the expression of all integrin subunits, as well as *MMP2* and *MMP9*, while TAX 100  $\mu$ M showed significant inhibitory effect on *MMP2* and stimulated the expression of *MMP9* and *ITGB1*, compared to the levels in untreated cells. A functional test - scratch assay, showed that TAX 10  $\mu$ M significantly promotes cell migration after the 24h incubation.

It can be concluded that TAX can influence the cell adhesion and migration and mRNA expression of proteolytic factors crucial for trophoblast invasion. These are preliminary findings of TAX effect on functional role of human trophoblast cells *in vitro* and provide rationale for further studies of its potential application in pregnancy pathologies associated with disturbed trophoblast invasion.

**Keywords:** *taxifolin, trophoblast, integrins, matrix metalloproteinases, cell migration*

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