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Polydatin (3,4',5-trihydroxystilbene-3-β-d-glucoside) is a new inhibitor of glucose-6-phosphate dehydrogenase affecting cancer metabolism and producing a strong cytotoxic and antimetastatic effect

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Polydatin (3,4',5-trihydroxystilbene-3-β-d-glucoside) is a natural precursor of resveratrol already approved for commercialization as food supplement. It is present in many types of plants, including grape, peanut, and cassia seed where it acts as antimycotic agent. Polydatin has been proposed to have effect on cancer, including HNSCC and breast cancer, with promising results, but its mechanism of action seems to be different from resveratrol and is poorly understood. Glucose-6-phosphate dehydrogenase (G6PD) is the limiting enzyme of the pentose phosphate pathway which have been widely shown to be fundamental for tumor growth and metastasis formation. In this work our results show that polydatin inhibit G6PD in a dose dependent manner affecting cancer cell viability, causing a dose-dependent apoptosis and cell cycle arrest. Moreover, treated cells showed a strong increase of the Unfolded Protein Response (UPR), activated by a stress in the endoplasmic reticulum (ER), autophagy, reduced migration and invasion ability. Moreover, we developed a metastatic orthotopic HNSCC model in immunocompromised mice and showed that treated group had reduced tumor growth and reduce lymph nodes metastases. In conclusion here we show that Polydatin exerts a significant inhibitory effect on pentose phosphate pathway inhibiting HNSCC growth and metastases, pointing out that polydatin may be a reliable anticancer drug.

References

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Keywords

G6PD; pentose phosphate pathway; ER Stress; metastasis.