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Unveiling the Impact of Natural Coumarins on Cyclin-Dependent Kinases: Insights from Computational Analysis

رونمایی از تاثیر کومارین های طبیعی بر کینازهای وابسته به سایکلین: از دیدگاه تحلیل های محاسباتی

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Abstract:

سرطان، یکی از علل اصلی مرگ و میر در جهان، با تکثیر سلولی کنترل نشده مشخص می شود. کینازهای وابسته به سایکلین (CDKs) تنظیم کننده های کلیدی چرخه سلولی و تکثیر سلولی هستند. کومارین ها دسته ای از ترکیبات طبیعی هستند که یک ویژگی ساختاری مشترک شامل حلقه های پیرون و بنزن به هم متصل شده به همراه یک گروه کربوکسیل در حلقه اول شان، است. فعالیت های متنوع بیولوژیکی برای کومارین های طبیعی، از جمله فعالیت هایی که در تنظیم رشد، اثرات ضد سرطانی و مهار متاستاز نقش دارند، شناسایی شده اند. هدف این مطالعه بررسی میانکنش بین کومارین های طبیعی اسکولتین، امپراتورین، اسکوپولتین و دافنتین باCDK4 ، CDK2، CDK1وCDK6 است. داده های این تحقیق از PubChem بدست آمده و با استفاده از ابزار تحت وب SwissTargetPrediction تجزیه و تحلیل شد. آنالیزها نشان می دهد که اسکوپولتین کمترین احتمال تعامل با CDK2 و CDK4 را داشت (۰.۰۳). امپراتورین احتمال بیشتری از تعامل با CDK2 را نشان داد (۰.۱). اسکولتین نیز احتمال میانکنش با CDK2 و CDK4 را نشان داد (۰.۰۷). دافنتین بیشترین احتمال تعامل را با CDK4 و CDK2 را نشان داد (به ترتیب ۰.۱۲ و ۰.۰۸).

Abstract:

Cancer, one of the leading causes of death worldwide, is characterized by uncontrolled cell proliferation. Cyclin-dependent kinases (CDKs) are key regulators of the cell cycle and cell proliferation. Coumarins are a class of natural compounds that share a common structural feature consisting of fused pyrone and benzene rings with a carboxyl group on the first ring. Diverse biological activities have been identified for natural coumarins, including those involved in growth regulation, anticancer effects, and inhibition of metastasis. This study aims to investigate the interaction between natural coumarins Scopoletin, Imperatorin, Esculetin, and Daphnetin, with CDK1, CDK2, CDK4, and CDK6. Data for this research was obtained from PubChem and analyzed using the SwissTargetPrediction web tool. The analysis reveals that Scopoletin had the lowest

probability of interaction with CDK2 and CDK4 (0.03). Imperatorin showed a higher probability of interaction with CDK2 (0.1). Esculetin demonstrated a probability of interaction with both CDK2 and CDK4 (0.07). Daphnetin exhibited the highest probability of interaction with CDK4 and CDK2 (0.12 and 0.08, respectively).

Method & Materials:

We utilized PubChem (https://pubchem.ncbi.nlm.nih.gov) to obtain the isomeric SMILES codes of natural coumarins Scopoletin, Imperatorin, Esculetin, and Daphnetin. Then, codes were used to estimate the probability of interaction between each agent and CDK1, CDK2, CDK4, and CDK6, which are involved in the cell cycle. To do so, the SwissTargetPrediction online tool was used, which utilizes a ligand-based method that assesses the similarity between a query molecule and known ligands of various protein targets.

Result & Conclusion:

Through the combined use of PubChem and SwissTargetPrediction, we analyzed the interaction between natural coumarins and CDKs involved in cell cycle regulation (CDK1, CDK2, CDK4, and CDK6). Results revealed that Scopoletin had the lowest probability of interaction with CDK2 and CDK4 (0.03). Imperatorin showed a higher probability of interaction with CDK2 (0.1). Esculetin demonstrated a probability of interaction with both CDK2 and CDK4 (0.07). Daphnetin exhibited the highest probability of interaction with CDK4 and CDK2 (0.12 and 0.08, respectively). These findings indicate the potential for interaction between the natural coumarins and CDKs involved in the cell cycle regulation. Designing drugs based on coumarins that interact with CDKs, which play a crucial role in cell proliferation, holds promise for the treatment of cancer characterized by abnormal cell growth.

keywords:: Scopoletin, Imperatorin, Esculetin, Daphnetin, Interaction, Cell cycle, cyclin-dependent kinase