SYNTHESIS AND ANTICANCER ACTIVITY OF NOVEL SALICYLAMIDE DERIVATIVES

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Salicylic acid amides are compounds with diverse pharmacological activities and can be classified according to the bounded amine. Salicylanilide (attached with an aromatic amine) are a group of compounds having a wide range of biological activities against microbial pathogens [1], these compounds also possess antiviral activities [2], antimycobacterial activities [3]. Latest studies described the aliphatic salicylamides as epidermal growth factor receptor tyrosine kinase inhibitors [4]. In addition, antiproliferative properties of salicylanilide were described as an important marker for protentional anticancer treatment.

Cl
\begin{align*}
\text{O} & \quad \text{N}^{\text{R}^1} \quad \text{N}^{\text{R}^2} \\
\text{R}^3 & \quad \text{O} \\
\text{R}^4 & \quad \text{H}
\end{align*}

\text{R}^1, \text{R}^2 = (S)-\text{CH}_2\text{-CH}-(\text{CH}_3)_2 \\
\text{R}^3 = \text{aromatic, alicyclic, heterocyclic} \\
\text{R}^4 = -\text{CH}_2\text{-phenyl or H}

Figure. Triamide derivatives of salicylamide

Our previous study shows interesting biological properties of salicylamides. A series of variously substituted 2-hydroxy-N-(arylalkyl)benzamides were prepared and screened for antiproliferative and cytotoxic activity in cancer cell lines [5]. Salicylamides terminated with aliphatic chain possess antiproliferative activity [6]. We introduce here the synthesis and biological characterization of 32 novel salicylamides bearing the combination of optically pure amino acids, namely aromatic phenylalanine or aliphatic leucine. All derivatives display antiproliferative activity in tested cancer cell lines and eight of them reach up single-digits micromolar GI50.

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