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Synthesis, antiproliferative activity and docking study of novel rhodanine derivatives as Bcr-Abl T1351 inhibitors

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Abstract A series of novel *N*-substituted rhodanines **6a–g** were synthesized by a microwave synthesizer, and evaluated for their anti-proliferative activity. Most of the compounds showed inhibition against K562 cells in a dose-dependent manner and in particular compounds **6a**, **6b** and **6f** exhibited most potent activity with an IC_{50} value of 19.62, 24.01 and 22.91 μg/ml by MTT assay. Further in silico docking studies of the above compounds against Bcr-Abl T1351 protein showed good binding affinity, thus indicating that the compounds behave as third generation inhibitors. A dose-dependent increase in LDH release upon treatment with **6a–g** complements the MTT assay for anti-proliferative activity. Flow cytometry of **6a** showed that it interferes with the cell division by indicating G1 phase arrest followed by apoptosis.

Keywords Rhodanine · Chalcone · Microwave-assisted synthesis · Antiproliferative activity · Molecular docking · Apoptosis

Introduction

The burden of cancer increases rapidly throughout the world and is the leading cause of death in economically developed countries and the second leading cause of death in developing countries [1]. Cancer is a dangerous disease which is very difficult to control because of the properties of cancer cells to proliferate uncontrollably, avoid apoptosis, invade and metastasize [2]. Despite many advances

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