Schiff Bases of Indoline-2,3-Dione (Isatin) with Potential Antiproliferative Activity

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Abstract:

BACKGROUND: Cancer is one of the most dreaded diseases and it is a leading cause of mankind death worldwide. Recent reports documented a remarkable antiproliferative activity of isatin nucleus against various cancer cell lines. The current work describes the antiproliferative activity of Schiff bases of combinatorial mixtures of the isatin derivatives M1-M22 as well as the individual compounds 1-11(A-K) of these combinatorial mixtures. RESULTS: The designed combinatorial library composed from eleven hydrazides A-K and eleven isatin derivatives 1-11 has been synthesized to formally generate 22 mixtures, M1-M22 of 121 Schiff bases, and their antiproliferative activity against K562 chronic myelogenous leukemia cells was evaluated. The indexed method of analysis of the prepared library was applied to elucidate the active components in the tested mixtures M1-M22. The predictions from the crossing procedure was validated through evaluation of the antiproliferative activity of individual compounds 1-11(A-K) of the library. Individual compounds 1-11(A-K) were also evaluated against the non-tumorigenic MCF-12A cell line to investigate their selectivity. A pharmacophore model was developed to further optimize the antiproliferative activity among this series of compounds. CONCLUSIONS: Variable antiproliferative activity was revealed with the investigated mixtures M1-M22 and the individual compounds 1-11(A-K). Most of the tested mixtures and several individual Schiff bases displayed high potency with IC50 values in the low micromolar range. A considerable selectivity of some individual compounds to the tumorigenic K562 cell line compared with the non-tumorigenic MCF-12A cell line was observed as indicated by their selectivity index (SI).

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