Design, drug-likeness and cytotoxicity of some bromo-salicylaldehyde aroylhydrazones

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Aroylhydrazones derived by the Schiff base condensation between salicylaldehyde and different hydrazides possess diverse pharmacological activities such as antimicrobial, antibacterial, anti-inflammatory, analgesic, antifungal, anti-tubercular, antiviral, anticancer, antioxidant etc. Various substitutions in the molecules have been made in order to improve their biological activity. Inclusion of a bromine atom in some hydrazones greatly increases the activity of the compounds.

In this work we present the comparative evaluation of *in silico* biological activity of a series of nine various bromo-derivative hydrazones. The compounds were designed by varying the position of bromo-substituent in salicylaldehyde moiety and the type of substituents at 4 position of hydrazide moiety. The drug relevant properties of the studied compounds, important for drug pharmacokinetics in the human body, were evaluated with the Lipinski's rule of five. The value of logP and the remaining parameters of drug similarity were calculated by the method based on group contributions. The approach is used only as a first step in drug discovery, to find the lead candidates with encouraging properties for further elaboration.

Some of the investigated bromo-derivative hydrazones were tested for *in vitro* cytotoxicity on a HL-60 acute myeloid leukaemia and SKW-3 T-cell leukaemia cell lines by MTT-test. The bioassay results demonstrated that the compounds exhibit concentration-dependent cytotoxic effects at low micromolar concentrations. The values of IC_{50} for 5-bromosalicylaldehyde-4-hydroxybenzoylhydrazone and 5-bromosalicylaldehyde isonicotinoyl-hydrazone are comparable to these of Cisplatin, but lower to these of Melphalan. Results confirm that the compounds are potential candidates for future drug discovery study.

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