SYNTHESIS AND CITOTOXICITY ASSAY TO COLON CANCER CELL WiDr: 3,3'-DI(5-BROMO-N-METHYL-3-YL)-5-BROMOINDOLIN-2-ONE, 3,3'-DI(5-BROMO-N-METHYL-INDOL-3-YL)-5-BROMO-N-METHYLINDOLIN-2-ONE AND 3,3'-DI(5,7-DIBROMOINDOL-3-YL)-INDOLIN-2-ONE

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ABSTRACT

Colon cancer is the third cause of cancer deaths, the incidence rate of about one million cases per year with a mortality rate of more than 500,000. The problem is not solved, because until now there has been found that specific drugs to stop cancer cell growth. Trisindoline and its derivatives are a group of compounds that have potential for cancer treatment. The presence of N-methyl and bromo group known to increase the bioactivity of trisindoline and their derivatives. This thesis reports the synthesis of three new trisindoline derivatives: 3,3'-di(5-bromo-N-methylindol-3-yl)-5-bromoindolin-2-one; 3,3'-di(5-bromo-N-methylindol-3-yl)-5-bromo-N-methylindolin-2-one; and 3,3'-di(5,7-dibromoindol-3-yl)-indolin-2-one; and their cytotoxicity against colon cancer cell WiDr lines. Methylation of 5-bromoindole with sodium hydroxide and dimethyl sulphate in anhydrous dimethyl sulphoxide afforded 5-bromo-N-methylindole in 87% yield. Electrophilic aromatic substitution of 5-bromo-N-methylindole with 5-bromoisatin under acidic conditions furnished 3,3'-di(5-bromo-N-methylindol-3-yl)-5-bromoindolin-2-one in 53% yield, which on methylation afforded 3,3'-di(5-bromo-N-methylindol-3-yl)-5-bromo-N-methyl indolin-2-one in 94% yield. 3,3'-Di(5-bromo-N-methylindol-3-yl)-5-bromoindolin-2-one; 3,3'-di(5-bromo-N-methylindol-3-yl)-5-bromo-N-methyl indolin-2-one at concentrations up to 100 μM is not cytotoxic against colon cancer cell WiDr lines. Reaction of 5,7-Dibromoindolindole with isatin under acidic conditions furnished 3,3'-di(5,7-dibromoindol-3-yl)-indolin-2-one: in 48% yield which is cytotoxic to colon cancer cells WiDr lines with IC50 6.64 μM.

Kata kunci: synthesis, indolin-2-one derivatives, citotoxic
