ABSTRACT

Liver cancer is the fifth most common cancer worldwide and the second cause of cancer death with 600,000 cases each year. Cancer therapies that exist until this day still have disadvantage, so it needs a specific drug to stop the cancer cells. Isatin and its derivatives are known to have anti-cancer activity. Isatin has cytotoxicity on leukemic cancer cells U937 with IC\textsubscript{50} 565 \(\mu\)M, substituent group at C-3 isatin affect its bioactivity, convolutamidine A and convolutamidine B can inhibit leukemic cancer cell HL-60 with IC\textsubscript{50} 0.1-25 and 12-25 \(\mu\)g/mL respectively. Substituent group at C-5 in 5-nitroisatin also affect the bioactivity to leukemic cancer cells U937 such as 5-nitroisatin with IC\textsubscript{50} 132 \(\mu\)M. It is known to have anti-cancer activity better than the isatin. Nitro groups can also decrease the cytotoxicity as the 3-hydroxy-5-nitro-3-(1\texttextit{H}-indole-3-yl)indoline-2-one that have IC\textsubscript{50} 195 \(\mu\)M to colon cancer cells WiDr, while the 3-hydroxy-3-(1\texttextit{H}-indole-3-yl)indoline-2-one have IC\textsubscript{50} 37 \(\mu\)M. 11-nitro-6-demetoksiakronisina has activity against leukemia cancer cells L1210 better than the 11-amino-6-demethoxyacronisina, whereas compounds with aromatic amine group, 1-amino-8,9-dimethoxy-5-[2-(N,N-dimethylamino)-ethyl]-5\texttextit{H}-dibenzo[c,h][1,6]napthyridin-6-one has better activity to leukemia cancer cell RPMI 8402 than aromatic nitro group, 8,9-dimethoxy-1-nitro-5-[2-(N,N-dimethylamino)-ethyl]-5\texttextit{H}-dibenzo[c,h][1,6]napthyridin-6-one. N-methyl at isatin also affect bioactivity, for example N-methylisatin (IC\textsubscript{50} 238 \(\mu\)M) is more potential than isatin (IC\textsubscript{50} 565 \(\mu\)M) as anti-cancer, but (E)-methyl 3-(N-methyl-2,3-dioxindolin-5-yl)acrylate has worse bioactivity than (E)-methyl 3-(2,3-dioxindolin-5-yl)acrylate with IC\textsubscript{50} 468 \(\mu\)M and 4636 \(\mu\)M respectively. Research has been done successfully synthesize novel isatin derivatives; 3-hydroxy-3-(1\texttextit{H}-pyrrol-2-yl)indolin-2-one, 3-hydroxy-5-nitro-3-(1\texttextit{H}-pyrrol-2-yl)indolin-2-one, 3-hydroxy-N-methyl-5-nitro -3-(1\texttextit{H}-pyrrol-2-yl)indolin-2-one, and 5-amino-3- hydroxy-3-(1\texttextit{H}-pyrrol-2-yl)indolin-2-one obtained with yield 47, 50, 63 and 47 \% respectively. Cytotoxicity test found that 3-hydroxy-5-nitro-3-(1\texttextit{H}-pyrrol-2-yl)indolin-2-one citotoxic to liver cancer cell HepG2 with IC\textsubscript{50} 468 \(\mu\)M, whereas 3-hydroxy-3-(1\texttextit{H}-pyrrol-2-yl)indolin-2-one, 3-hydroxy-N-methyl-5-nitro -3-(1\texttextit{H}-pyrrol-2-yl)indolin-2-one, and 5-amino-3- hydroxy-3-(1\texttextit{H}-pyrrol-2-yl)indolin-2-one less cytotoxic with IC\textsubscript{50} 10332, 1330 and 4636 \(\mu\)M respectively. Nitro and amino group substituken at C-5 unit isatin can enhance the cytotoxicity, whereas the presence of N-methyl group can lower cytotoxicity to liver cancer cells HepG2.
Keywords: synthesis, isatin derivatives, pyrrole, cytotoxic, liver cancer cells HepG2