Cytotoxic Activity of 1-(2,5-dihydroxyphenyl)-3-pyridine-2-yl-propenone on Colon Cancer Cell WiDr

Nur Ismiyati¹, Yuli Puspito Rini¹, Andy Eko Wibowo¹, Ratna Asmah Susidarti²

¹Diploma Program of Pharmacy, Poltekkes Bhakti Setya, Yogyakarta, Indonesia  
²Faculty of Pharmacy, Universitas Gadjah Mada, Yogyakarta, Indonesia

Abstract

Colon cancer is one of the most common death-caused cancer. The high mortality rate indicates that chemotherapy has not overcome cancer disease. Strategies and development of colon cancer treatment should be pursued. Compound 1-(2,5-dihydroxyphenyl)-3-pyridine-2-yl-propenone is the 2',5'-dihydroxycalcon derivative, of which the B ring was substituted with 2-pyridine ring. Chalcone and its derivatives have been reported to have several biological activities, such as cytotoxic, anti-inflammatory, antiHIV, and as a tyrosine kinase inhibitor. The objectives of this research was to determine the cytotoxic activity on WiDr colon cancer cells of 1-(2,5-dihydroxyphenyl)-3-pyridine-2-yl-propenone. Cytotoxic activity was measured using MTT assay. Compound 1-(2,5-dihydroxyphenyl)-3-pyridine-2-yl-propenone inhibited WiDr cell growth with the IC₅₀ of 16 µM. Morphology of WiDr cell showed that compound 1-(2,5-dihydroxyphenyl)-3-pyridine-2-yl-propenone inhibited cell growth in dose dependent.

Keywords: compound 1-(2,5-dihydroxyphenyl)-3-pyridine-2-yl-propenone, WiDr colon cancer cell line, cytotoxic activity.

INTRODUCTION

Cancer is the disease causing high number of mortality. In Indonesia, colon cancer become the most dangerous gastrointestinal disease after the hepatocellular cancer (Pusponegoro, 2004). Colon cancer could develop by the overexpression of cyclooxygenase 2 (COX-2) (Turini and Dubois, 2002). In the therapy of colon cancer, 5-fluorouracil (5-FU) is used for the main therapy, but cannot give the satisfying result and just give effectivity in the therapy for approximately 20% of colon cancer patient (Arkenau, et al., 2005; Meyerhardt and Mayer, 2005). Therefore, the research for the invention and the development for new compound for colon cancer treatment is need to be done.

One of the potential compound to develop as the cancer chemoprevention agent is the analog of calcon compound. Calcon is the compound having basic structure C₆C₃C₆, where two aromatic rings (ring A and ring B) are connected with three atomic carbon. Calcon structures are generally found in flavonoid compounds. These compounds are found in fruits, vegetables, nuts, and tea (Patil, et al., 2009). Calcon and its derivates are reported to have biological activities such as cytotoxicity, antimalaria, antileismania, antiinflammation, antiHIV, antifungi, and tyrosine kinase inhibitor (Saxena, et al., 2007).

The modification of lacton compound with the change of fenyl ring on B position of 4-cloro-2',4'-dihydroxycalcon and 2',5'-dihydroxycalcon with 2-piridyl and their activity in anticancer have not been reported. Some of the modified compounds are 1-(2,4-dihydroxyfenil)-3-piridin-2-il-propenon; 1-(2,5-dihydroxyfenil)-(3-piridin-2-il)-propenon; 4-cloro-2',4'-dihydroxycalcon; and 2',5'-dihydroxycalcon.

*Corresponding author e-mail: nur_is@yahoo.com
The aim of this research is to test the cytotoxic potency of 1-(2,5-dihydroxyfenil)-(3-piridin-2-il)-propenon in colon cancer cell WiDr. The synthesis of 1-(2,5-dihydroxyfenil)-(3-piridin-2-il)-propenon has been successfully done and showed the antiinflammation activity (Wibowo, 2013).

The result of this study hopefully could be the basic theory in the development of 1-(2,5-dihydroxyfenil)-(3-piridin-2-il)-propenon as the alternative of chemoprevention agent in colon cancer cell. Brazilein inhibits survivin protein and induces apoptosis in HepG2 hepatocellular carcinoma cells (Zhong, et al., 2009). This study was conducted to evaluate the cytotoxic effect of brazilein, both alone and in combination with doxorubicin on MCF-7/DOX cells by using MTT assay.

MATERIALS AND METHODS

Cell Culture
Colon cancer cell WiDr is the collection of CCRC Faculty of Pharmacy UGM. WiDr cells were cultured in the RPMI (Gibco). The culture media contained 10% FBS (Ginco) and 1% Penisilin Streptomycin (Gibco). Cells were cultured in the temperature of 37°C and 5% CO₂. Cells are harvested with tripsin 0.25% (Gibco).

Cytotoxic assay
Exponentially The cytotoxic assay were done by MTT Assay. WiDr cells were distributed in 96-well plate as many as 10 x 10³ cells/well. Cells were incubated for 24 hours in CO₂ incubator then were added with 100 µL of culture media containing sample in some concentration for 3 replication each concentration and then incubated again for 24 hours. As the control are the DMSO solution, WiDr cell control, and culture media control (RPMI). In the end of the incubation time, the culture media were removed and cells were washed with PBS. Then in each well were added by 100 µL MTT reagen and incubated for three hours in the temperature of 37°C and 5% CO₂. After three hours, the solution of 10 % SDS in 0.1 N HCl were added as stopper reagen. Cells were incubated for a night in the room temperature and protected from the light, and the plate were shaken horizontally (with shaker) for 10 minutes, then were read with ELISA reader (BioRad) in λ 595 nm.

RESULT AND DISCUSSION

The cytotoxic assay give the potency evaluation of 1-(2,5-dihydroxyfenil)-(3-piridin-2-il)-propenon in the inhibition of colon cancer cell WiDr growth. The parameter used in this research is the inhibition concentration 50% (IC₅₀). The lower the IC₅₀ value, the tested compound is more potent in the inhibition of cancer cell growth. The result of cytotoxic assay showed that 1-(2,5-dihydroxyfenil)-(3-piridin-2-il)-propenon in the concentration of 1-100 µM has the cytotoxic activity towards WiDr cell in dose dependent manner. The higher the concentration of 1-(2,5-dihydroxyfenil)-(3-piridin-2-il)-propenon given, the lower the percent of cell viability (Fig. 1).

Based on the calculation by the linear regression log concentration versus % cell viability showed that -(2,5-dihydroxyfenil)-(3-piridin-2-il)-propenon gives IC₅₀ values 16 µM on WiDr cell. This result showed that the tested compound has the better sensitivity and selectivity towards Colon cancer cell WiDr, than towards 5-fluorouracil (5-FU) with IC50 496 µM (Ikawati, 2008). The observation of cell morphology after the treatment with tested compound showed the number of death cells were increasing as the concentration of 1-(2,5-dhidroksifenil)-(3-piridin-2-il)-propenon were increased.
CONCLUSION

Compound 1-(2,5-dihydroxyphenyl)-3-pyridine-2-yl-propenone has the cytotoxic activity in the inhibition of colon cancer cell WiDr with IC$_{50}$ value 16 µM.

ACKNOWLEDGEMENT

We would like to say thank you for DIKTI through Hibah Penelitian Dosen Pemula for the funding given in this research, also for Poltekkes Bhakti Setya Indonesia, and fAculty of Pharmacy UGM, and Cancer Chemoprevention Research Center (CCRC) for the supports and facilities given.

REFERENCES

Arkenau, H.T., Rettig, K. and Porschen, R., 2005, Adjuvant Chemotherapy in Curative Resected Colon Carcinoma: 5-Fluorouracil/Leucovorin versus High-dose 5-Fluorouracil 24-h Infusion/Leucovorin versus High-dose 5-Fluorouracil 24-h Infusion, Int. J. Colorectal Dis., 20(3), 258-261.

Ikawati, M., 2008, Modulasi Daur Sel dan Pemacuan Apoptosis pada Sel Kanker Kolon Widr oleh Perlakuan Tunggal Pentagamavunon-0 dan Kombinasinya dengan 5-Fluorouracil, Thesis, Universitas Gadjah Mada, Yogyakarta.

Meyerhardt, J.A. and Mayer, R.J., 2005, Systemic Therapy for Colorectal
Cancer, N. Engl. J. Med., 352(5), 476-487.
Patil, B.C., Mahajan, S.K. and Katti, A.S., 2009, Chalcone: A Versatile Molecule, J. Pharm. Sci. Res., 1, 11-22.
Pusponegoro, A.D., 2004, Epidemiologi Keganasan Saluran Cerna, Proceeding Temu Ilmiah Multimodalitas Terapi Pada Keganasan Saluran Cerna, Jakarta.
Saxena, H.O., Faridi, U., Kumar, J.K., Luqman, S., Darokar, M.P., Shanker, K., et al., 2007, Synthesis of Chalcone Derivatives on Steroidal Framework and Their Anticancer Activities, Steroids, 72(13), 892-900.
Turini, M.E. and DuBois, R.N., 2002, Cyclooxygenase2: A Therapeutic Target, Annu. Rev. Med., 53(1), 35–57.