DISERTASI

PERANAN 6-IODOLAKTON (6-IL) DALAM MENURUNKAN VIABILITAS SEL MELALUI INDUKSI APOPTOSIS DAN REDIFERENSIASI PADA *CELL LINE* B-CPAP KANKER TIROID PAPILER

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ABSTRAK

PERANAN 6-IODOLAKTON (6-IL) DALAM MENURUNKAN VIABILITAS SEL MELALUI INDUKSI APOPTOSIS DAN REDIFERENSIASI PADA *CELL LINE* B-CPAP KANKER TIROID PAPILER

Yulia Kurniawati

Sel neoplasma tiroid dalam perjalanannya dapat mengalami dediferensiasi yang berkaitan dengan penurunan atau kehilangan ekspresi NIS dan/atau target ke membran plasma. Penelitian ini bertujuan untuk mengetahui efek 6-Iodolakton (6-IL) yang merupakan senyawa iodinasi dari Asam Arakhidonat dalam menginduksi rediferensiasi dan apoptosis sehingga menurunkan viabilitas sel pada sel kanker tiroid papiler.

Penelitian ini merupakan penelitian eksperimental laboratorium *in vitro* dengan *pre and post test only control group* menggunakan *cell line* B-CPAP. Uji viabilitas dilakukan untuk memperoleh nilai estimasi konsentrasi IC_{50}. Selanjutnya dilakukan uji Apoptosis dengan metode pewarnaan AO/PI, pemeriksaan gen PPARγ dan gen NIS dengan metode RT-PCR serta Imunositofloresence menggunakan metode *Corrected Total Cell Fluorescence* (CTCF) untuk mengetahui Lokasi protein NIS.

Hasil uji viabilitas menunjukkan penurunan viabilitas sel berdasarkan konsentrasi dan waktu perlakuan. Penurunan nilai viabilitas sel paling tinggi pada waktu perlakuan 72 jam (72.51%) dibandingkan 24 jam dan 48 jam (76.53% ; 84.24 %). Analisis kurva dosis-respon menggunakan regresi linear mendapatkan nilai estimasi IC_{50} yaitu 172,375 µM (24 jam);168,775 µM (48 jam) dan 122.775 µM (72 jam). 6-IL menginduksi apoptosis yang bergantung waktu (*time – dependent*) yang ditandai dengan meningkatnya jumlah sel yang mengalami apoptosis pada kelompok perlakuan 6-IL dibandingkan kelompok kontrol terutama pada 48 jam dan 72 jam dibandingkan 24 jam dengan $p<0.05$.

Analisis RT-qPCR menunjukkan bahwa perlakuan 6-IL meningkatkan ekspresi relatif gen PPARγ pada *cell line* pada waktu perlakukan 24 jam dibandingkan dengan kontrol pada seluruh waktu pengamatan ($p<0.05$), sedangkan 6-IL hanya meningkatkan ekspresi relatif gen NIS secara bermakna dibandingkan kelompok kontrol pada waktu 48 jam ($p=0,045$). Hasil analisis protein NIS menunjukkan bahwa pemberian 6-IL meningkatkan intensitas fluoresensi protein NIS secara signifikan pada *cell line* dibandingkan kelompok kontrol pada seluruh waktu inkubasi, dengan distribusi sinyal fluoresensi yang meluas dari daerah perinuclear ke perifer yaitu ke sitoplasma (*Perinuclear to cytoplasmic redistribution*).

Penelitian ini menyimpulkan terdapat penurunan viabilitas sel serta hubungan yang signifikan antara peningkatan ekspresi PPARγ, peningkatan awal ekspresi gen NIS, akumulasi dan lokasi protein NIS, dan peningkatan apoptosis

pada *cell line* B-CPAP setelah pemberian 6-iodolakton dengan konsentrasi IC_{50} dibandingkan kontrol.

Kata kunci: 6-Iodolakton, kanker tiroid papiler, *cell line* B-CPAP, viabilitas sel, PPARγ, apoptosis, ekspresi gen PPARγ, ekspresi gen NIS, Protein NIS, Translokasi NIS.

ABSTRACT

THE ROLE OF 6-IODOLACTONE (6-IL) IN REDUCING CELL VIABILITY THROUGH THE INDUCTION OF APOPTOSIS AND REDIFFERENTIATION IN THE B-CPAP PAPILLARY THYROID CANCER CELL LINE

Yulia Kurniawati

Thyroid neoplastic cells may undergo dedifferentiation during tumor progression, which is associated with decreased or loss of sodium iodide symporter (NIS) expression and/or impaired targeting to the plasma membrane. This study aimed to determine the effect of 6-Iodolactone (6-IL), an iodinated derivative of arachidonic acid, in inducing redifferentiation and apoptosis, thereby reducing cell viability in papillary thyroid cancer cells.

This study was an in vitro experimental laboratory study using a pre- and post-test only control group design which used B-CPAP cell line. Viability study performed to obtain estimated IC_{50} values and then continue with Apoptosis study which was subsequently evaluated using the acridine orange/propidium iodide (AO/PI) staining method. PPARγ and NIS gene expression were analyzed using RT-PCR, while immunocytofluorescence with *Corrected Total Cell Fluorescence* (CTCF) method was performed to determine the localization of the NIS protein.

The results showed that cell viability decreased according to consentration and time with significantly decreased at 72 hours (72.51%) compared 24 hours and 48 hours (76.53% ; 84.24 %). Estimated IC_{50} performed by regression linear curve are 172,375 µM (24 jam);168,775 µM (48 jam) dan 122.775 µM (72 jam). 6-IL induced time-dependent apoptosis, as demonstrated by an increased number of apoptotic cells in the 6-IL treatment group compared with the control group, particularly at 48 and 72 hours compared with 24 hours ($p<0.05$).

RT-qPCR analysis demonstrated that 6-IL increased the relative expression of the PPARγ gene in cell line, particularly at 24 hours of treatment compared with the control group at all observation times ($p<0.05$), whereas treatment with 6-IL significantly increased the relative expression of the NIS gene compared with the control group ($p=0.045$) only at 48 hours. Analysis of NIS protein demonstrated that treatment with 6-iodolactone (6-IL) at the IC_{50} concentration significantly increased NIS protein fluorescence intensity in the B-CPAP cell line compared with the control group at all incubation times, with fluorescence signal distribution extending from the perinuclear region toward the cell periphery, namely the cytoplasm (perinuclear-to-cytoplasmic redistribution).

This study concluded that there was a reduction in cell viability and a significant association between increased PPARγ expression, early upregulation of NIS gene expression, NIS protein accumulation and localization, and increased apoptosis in the B-CPAP cell line following treatment with 6-iodolactone at the IC_{50} concentration compared with the control group.

Keywords: 6-Iodolactone, papillary thyroid cancer, B-CPAP cell line, cell viability, PPARγ, apoptosis, PPARγ gene expression, NIS gene expression, NIS protein, NIS translocation