ID Design Press, Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2019 Nov 30; 7(22):3816-3818.
https://doi.org/10.3889/oamjms.2019.511
eISSN: 1857-9655
Herbal Medicine in Pharmaceutical and Clinical Sciences

Cytotoxic Activity of BornUSU I towards T47D Breast Cancer Cells

Nadiya Anandita Nasution[1], Urip Harahap[1*], Ginda Haro[2], Hari Purnomo[3], Denny Satria[4]

[1]Department of Pharmacology, Faculty of Pharmacy, University of Sumatera Utara, Medan; [2]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Sumatera Utara, Medan; [3]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Gadjah Mada University, Yogyakarta; [4]Department of Biology, Faculty of Pharmacy, University of Sumatera Utara, Medan

Citation: Nasution NA, Harahap U, Haro G, Purnomo H, Satria D. Cytotoxic Activity of BornUSU I towards T47D Breast Cancer Cells. Open Access Maced J Med Sci. 2019 Nov 30; 7(22):3816-3818. https://doi.org/10.3889/oamjms.2019.511

Keywords: Cytotoxicity; BornUSU I; T47D cells; Breast cancer

***Correspondence:** Urip Harahap. Department of Pharmacology, Faculty of Pharmacy, University of Sumatera Utara, Medan. E-mail: uripharahap@usu.ac.id

Received: 25-Sep-2019; **Revised:** 17-Oct-2019; **Accepted:** 18-Oct-2019; **Online first:** 14-Nov-2019

Funding: This research received financial support through "Hibah Penelitian Guru Besar 2018"

Competing Interests: The authors have declared that no competing interests exist

Abstract

AIM: The aim of this study was to determine cytotoxic activity of BornUSU I or Boronhafagama I (1,5-bis(4-hydroxyphenyl)-3-oxa-1,5-diaza-2,4-diboropentane-2,4-diol) as a boron derivate compounds which are boron neutron captured theraphy (BNCT) candidates.

METHODS: The T47D cells were treated by BornUSU I, and Tamoxifen as a positive control. The in vitro study was using MTT method with the incubation period for 24h and 48h. All data were determined using viability of cells equation for showing each IC_{50} value.

RESULTS: The IC_{50} value of BornUSU I and Tamoxifen were 72.61 ± 0.82 μM and 10.62 ± 0.06 μM for 24 h incubation period, and for the 48 h incubation period were 44.63 ± 0.23 μM and 7.79 ± 0.05 μM. The 48 h incubation period results showed the lowest IC_{50} value.

CONCLUSION: The results reveal that BornUSU I provide effective as anticancer, especially for breast cancer treatment.

Introduction

Breast cancer is the most incidence cancer and the second leading cause of cancer death among females [1]. Moreover, breast cancer ranks as the fifth cause of death from cancer overall (522,000 deaths), is the most frequent cause of cancer death in women in less developed countries (324,000 deaths, 14.3% of total), and the second cause of cancer death in developed countries (198,000 deaths, 15.4%) after lung cancer. A recent study publishedwhich breast cancer is leading in the estimated new cancer cases, and the second most common death cause among women suffering from cancer in the USA [2].

Boron Neutron Capture Therapy (BNCT) is an advanced form of radiotherapy technique which is potentially superior to all conventional techniques for cancer treatment, as it is targeted at killing individual cancerous cells with minimal damage to surrounding healthy cells [3]. Boronic compounds has been previously used in imaging and medicinal chemistry offering unique advantages associated with its low toxicity and stability [4].

BornUSU I (1,5-bis(4-hydroxyphenyl)-3-oxa-1,5-diaza-2,4-diboropentane-2,4-diol) or Boronhafagama I. The chemical structures of BornUSU I and tamoxifen are showed in Figure 1.

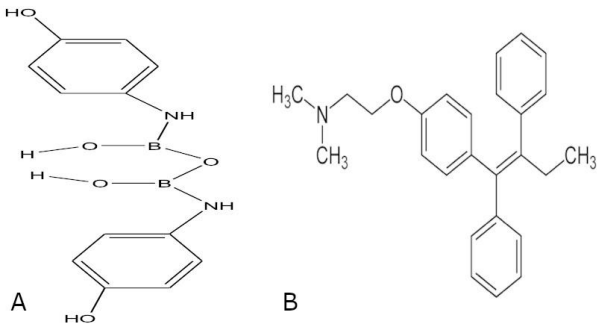

Figure 1: *Structure of A) BornUSU I and B) Tamoxifen*

Material and Methods

Chemicals Material

BornUSU I was obtained from Dr. Hari Purnomo, M.S., Apt. Chemicals used were distilled water from Water One-OneMed (Indonesia), DMSO and [3-(4,5-dimethylthiazole-2-yl)-2,5 diphenyltetrazolium bromide] (MTT) from Sigma - Aldrich (USA).

Cytotoxicity Assay

The cells were treated by BornUSU I and tamoxifen. In this test, T47D cell line was grown in RPMI-1640 medium, medium containing 10% Fetal Bovine Serum (Gibco), 1% penicillin-streptomycine (Gibco), and fungizone 0.5% (Gibco) in a petridish in a humidified atmosphere (5% CO_2) at 37°C. The inoculums seeded at 1 x 10^4 cells/mL at an optimal volume of 0.1 mL per well. After 24 h incubation, the medium was discharged and treated by BornUSU I and tamoxifen. After incubation 24 h and 48 h, the cells were incubated with 0.5 mg/mL MTT for 4 h in 37°C. Viable cells reacted with MTT to produce purple formazan crystals. After 4 h, SDS 10% as stopper (Sigma) in 0.01N HCl (Merck) was added to dissolve the formazan crystals. The cells were incubated for 24 h in room temperature and protected from light. After incubation, absorbance was measured using ELISA reader at λ 595 nm. The data which were absorbed from each well were converted to percentage of viable cells [5], [6], [7], [8], [9]. The equation to determine viability of cells:

$$Viability = \frac{Abs\ of\ treatment - Abs\ of\ medium}{Abs\ of\ control\ cells - Abs\ of\ medium}\ x\ 100\%$$

Statistic Analysis

All cytotoxic data were analyzed using SPSS 21 software by probit analysis.

Results

Inhibitory Concentration 50% (IC_{50})

MTT method was used to determine cell viability after incubation for 24h and 48h. The two different period of incubation was used to determine which one can give the lowest IC_{50} value. Cytotoxic activity of BornUSU I and tamoxifen were showed in Table 1.

Table 1: IC_{50} value of BornUSU I and tamoxifen towards T47D breast cancer cells

Treatment	IC_{50} (μM)	
	24h	48h
BornUSU I	72.61 ± 0.82	44.63 ± 0.23
Tamoxifen	10.62 ± 0.06	7.79 ± 0.05

Based on the results, it can be seen that T47D cell showed the inhibition of cell growth due to the influenced of BornUSU I and tamoxifen. The IC50 values with BornUSU I treatment for each 24 h and 48 h incubation were obtained 72.61 ± 0.82 μM and 44.63 ± 0.23 μM, also the IC50 values with tamoxifen treatment for each 24 h and 48 h incubation were obtained 10.62 ± 0.06 μM and 7.79 ± 0.05 μM. The results showed that IC50 values for 48h incubation had smaller values than 24 h incubation.

Discussion

The principle of the MTT method is cellular reduction reaction based on the breakdown of yellow MTT tetrazolium salts into purplish blue formazan crystals. This color changing is an indicator of cell proliferation. The mitochondria of proliferating cells will absorb MTT so these cells will turn purple due to the formation of tetrazolium crystals (formazan) [10].

The results showed that IC_{50} values for 48h incubation had smaller values than 24 h incubation. More decreasing of IC_{50} value means the cytotoxic activity is higher [11]. Barry et al., in 2014, reported the need for an efficient delivery of boron agents to overcome the challenge of clinical development [12]. In this study, T47D cell line was used to determine BornUSU I had the cytotoxicity activity as the clinical developing of anticancer agent. T47D breast cancer cells have positive molecular characteristics of Estrogen Receptor alpha (ER-α) overexpression [13]. Tamoxifen has become a first-line therapy for patients with breast cancer risk with ER-α for both pre and postmenopausal patients, as well as for advanced breast cancer patients [14].

In conclusion, BornUSU I is boron derivate compounds. BornUSU I has the cytotoxic activity and it is potential to develop as more effective anticancer agent.

References

1. Jemal A, Rebecca S, Xu J, Elizabeth W. Cancer statistics 2010. CA Cancer J Clin. 2010. 60:277-300. https://doi.org/10.3322/caac.20073 PMid:20610543

2. Siegel RL, Miller KD, Jemal A. Cancer statistics 2015. CA Cancer J Clin. 2015. 65(1):5-29. https://doi.org/10.3322/caac.21254 PMid:25559415

3. Payudan A, Abdullah NA, Yohannes S. Basic Principle Application and Technology of Boron Neutron Capture Cancer Therapy (BNCT) Utilizing Monte Carlo N Particle 5'S Software (MCNP 5) with Compact Neutron Generator. Ind J Phys Nuc App. 2016; 1:20-33. https://doi.org/10.24246/ijpna.v1i1.20-33

4. Trippier PC, McGuigan C. Boronic acids in medicinal chemistry: Anticancer, antibacterial and antiviral applications. Med. Chem. Commun. 2010; 1:183−198. https://doi.org/10.1039/c0md00119h

5. Dalimunthe A, Hasibuan PAZ, Satria D. Cell cycle arrest activity of Litsea cubeba Lout. heartwood and fruit extracts against T47D breast cancer cells. Asian J Pharm Clin Resc. 2017; 10(11):404-6. https://doi.org/10.22159/ajpcr.2017.v10i11.20204

6. Harahap U, Hasibuan PAZ, Sitorus P, Arfian N, Satria D. Antimigration activity of an ethylacetate fraction of Zanthoxylum acanthopodium DC. fruits in 4T1 breast cancer cells. Asian Pac J Cancer Prev. 2018; 19(2):565-9.

7. Hasibuan PAZ, Harahap U, Sitorus P, Satria D. Ethylacetate extract of Zanthoxylum acanthopodium DC. fruit against doxorubicin-resistanced T47D cells. Der Pharma Chemica. 2016; 8(20):172-174.

8. Satria D, Furqan M, Hadisahputra S, Rosidah ?. Combinational effects of ethylacetate extract of Picria fel-terrae Lour. and doxorubicin on T47D breast cancer cells. Int J Pharm Pharm Sci. 2015; 7:73-6.

9. Hasibuan PAZ, Jessy C, Denny S. Combination effect of ethylacetate extracts of Plectranthus ambonicius (Lour.) Spreng. with doxorubicin againts T47D breast cancer cells. Int J Pharm Pharm Sci. 2015; 7:155-9.

10. Radji M, Aldrat H, Harahap Y, Irawan C. Uji Sitotoksisitas Buah Merah, Mahkota Dewa dan Temu Putih terhadap Sel Kanker Serviks. Jurnal Farmasi Indonesia. 2010; 5(1):41-47.

11. Depamede SN, dan Rosyidi A. Penghambatan Proliferasi Limfosit Mencit Balb/C oleh Ekstrak Testis Sapi Bali: Peran TGF-β. Media Peternakan. 2009; 32(20):99-103.

12. Barry NPE, Barry A, Romero-Canel'on I, Tran JJ, Soldevila-Barreda J, Hands-Portman I, Smith CJ, Kirby N, Dove AP, O'Relly RK, Sadler PJ. Precious Metal Carborane Polymer Nanoparticles: Characterisation of Micellar Formulations and Anticancer Activity. Faraday Discussions. 2014; 175:229-240. https://doi.org/10.1039/C4FD00098F PMid:25270092

13. Pawlik A, Wojewodzka MS, Antosiewicz AH. Sensitization of Estrogen Receptor-Positive Breast Cancer Cell Lines to 4-Hydroxytamoxifen by Isothiocyanates Present in Cruciferous Plants. Eur J Nutr. 2016; 55:1165-1180. https://doi.org/10.1007/s00394-015-0930-1 PMid:26014809 PMCid:PMC4819954

14. Zhang MH, Man HT, Zhao DN, Ma SL. Estrogen Receptor Positive Breast Cancer Molecular Signatures and Therapeutic Potentials (Review). Biomedical Reports. 2013; 2:41-52. https://doi.org/10.3892/br.2013.187 PMid:24649067 PMCid:PMC3916982