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Original Article

Synthesis and activity evaluation of a novel lead compound 1-benzyl-3-benzoylurea as antiproliferative agent

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ABSTRACT

This research deals with designing and synthesizing a novel lead compound 1-benzyl-3-benzoylurea using the modified Schotten Baumann method and the objective is to find a more potent drug.In order to achieve the goal , the in-silico activity againts 1-UWH was calculated by Molegro Virtual Docker. Then, in-vitro antiproliferative activity against MCF-7 cell line was tested by MTT assay and compared with Hydroxyurea as a reference compound. The result showed that both in-silico and in-vitro test of 1-benzyl-3-benzoylurea were more potent than Hydroxyurea. It is highly recommended that 1-benzyl-3-benzoylurea be developed further as an antiproliferative agent.

Keywords: 1-benzyl-3-benzoylurea, designing, synthesizing, antiproliferative activity

INTRODUCTION

According to WHO data (2013), there is an increasing on cancer incidences from 12.7 millions cases to 14.1 millions between 2008 – 2012. On the other side mortality rate increase from 7.6 millions in 2008 to 8.2 millions in 2012. Cancer is a second major leading cause of death (13 %) in the world. Indonesian Fundamental Health Research (Rikesdas, 2013) reported that prevalence on cancer diseases in Indonesia is 1.4 of every 1000 citizens. Indonesian Hospital Information System statedthat breast cancer (28,7 %) has ranked at the first place. Based on Globocan estimation, International Agency for Research on Cancer (IARC) year 2012, incidents on breast cancer were 40 per 100.000 women. It was predicted at the year 2030 , 26 millions people will suffer from cancer and 17 millions will die , especially from the developing country [14]. Many efforts still constitutes a major challenge to develop in medicinal chemistry field. In this field of study, designing a novel lead compound is the first priority in order to find another alternative for theurapeutic goals. Hydroxyurea has been established and used for many decades and is still valued to cure cancer[1]. Chhttisgark (2011) reported that IC_{50}Hydroxyurea on breast cancer is 307,15 mc M. Research on urea derivative compounds has been done based on mechanism of action, kind of cell lines, receptor and activity test methods. Antiproliferative activity test using MTT assay was reported by Li et al. (2009), Lokhwani et al. (2011) and El-Shawy et al. (2012). Related to many prior research on urea derivates, urea is a pharmacophore for anticancer activity. More over, Lokhwani et al. (2011) and Lu et al. (2013) underlined that benzylurea is the key pharmacophore to inhibit tumor cells. El-Shawy et al. (2012) stated that benzyl moeity keep a role play as antiproliferative on MCF-7 cell line. In the present study , the novel lead compound was designed and synthesized as urea derivative compound. Increasing liphophilicity aspect are expected to better penetration through biological membran in order to find more potent drug candidate. 1-benzyl-3-benzoylurea was designed and synthesized using the Schotten Baumann methods[2,8]. 1-benzyl-3-benzoylurea is more liphophyl compared to hydroxyurea. In-silico activity on 1-UWH was calculated by Molegro Virtual Docker[15]. In vitro antiproliferative activity againts MCF-7 cell line was tested by MTT assay and compared with Hydroxyurea as a reference compound. The novel lead compound is expected to have more potent antiproliferative activity on MCF-7 cell line compared with Hydroxyurea as a reference compound.

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