PHARMACY: Jurnal Farmasi Indonesia p-ISSN 1693-3591
(*Pharmaceutical Journal of Indonesia*) e-ISSN 2579-910X
Vol.16 No. 02 Desember 2019:153-158

Synthesis of Curcumin Derivative Assisted by Microwave Irradiation

Sintesis Turunan Kurkumin dengan *Irradiasi Microwave*

Sabtanti Harimurti[1*], Winny Setyonugroho[2], Ardi Pramono[3], Rizky Hidayaturahmah[1]

[1]School of Pharmacy, Faculty of Medicine and Health Sciences,
Universitas Muhammadiyah Yogyakarta, Jalan Brawijaya (Lingkar Selatan), Tamantirto, Kasihan, Bantul, Yogyakarta, Indonesia, 55183
[2]Master of Hospital Management, Graduate Program,
Universitas Muhammadiyah Yogyakarta, Jalan Brawijaya (Lingkar Selatan), Tamantirto, Kasihan, Bantul, Yogyakarta, Indonesia, 55183
[3]Department of Anesthesiology, Faculty of Medicine and Health Sciences,
Universitas Muhammadiyah Yogyakarta, Jalan Brawijaya (Lingkar Selatan), Tamantirto, Kasihan, Bantul, Yogyakarta, Indonesia, 55183

*Corresponding author email: sabtanti@umy.ac.id

Received 13-11-2019 **Accepted** 26-12-2019 **Available online** 30-12-2019

ABSTRACT

Synthesis of curcumin derivate is commonly conducted using conventional heating like heating mantel. The synthesis was usually done in the very long time. An experiment on finding an efficient synthesis method may be necessary to conduct, such as using microwave to replace the energy source. The synthesis of curcumin derivate 1,5-bis(4'-hydroxy-3'-metoxyphenyl)-1,4-pentadiene-3-one or gamavuton-0 assisted by microwave irradiation has been carried out. This synthesis was done on propose of cancer drug discovery to answer the search of new cancer drug on the increase of cancer incidence recently. The synthesis was done under microwave irradiation using vanillin and acetone as the starting material, and hydrochloric acid as the catalyst. Based on the experimental data, the microwave irradiation significantly reduces the reaction time. By using microwave irradiation, the synthesis can be done in a short time.

Key words: cancer, drug, microwave, synthesis.

Introduction

One of the methods of developing a new compound is by synthesis. In chemistry, synthesis is one of the methods for finding a new compound or a method for developing an establish compound to better biological activity (Hughes et al., 2011). Synthesis is commonly conducted by combining two or more compound into more complex compound (Wanninger et al., 2015). During the synthesis, energy is

commonly required. Currently, microwave is utilized for synthesis to replace the energy source. This method has an advantage of being more environmentally process, economical and new ways of improving green chemistry (Ravichandran and Karthikeyan, 2011). Many researchers have been conducted many syntheses using microwave irradiation as the energy source. The synthesis of dibenzylidenecyclohexanone derivatives via crossed aldol condensation was successfully conducted using microwave for more environmentally production (Handayani et al., 2017). Energy efficiency in the microwave-assisted solid-state synthesis of cobalt aluminate pigment was also calculated. It is reported that the energy consumption was lower when the synthesis was conducted using microwave irradiation compared to conventional heating (Veronesi et al., 2017).

Based on the effectiveness of microwave irradiation as the energy source, in this study will be explained the effect of microwave on the synthesis of gamavuton-0. It is reported in the previous study, the gamavuton-0 was synthesized in the round bottle flask using conventional heating (heating mantel). The method commonly takes a long time and consume a lot of energy to obtain the high yield (Harimurti et al., 2017). This paper deals with a new method of gamavuton-0 synthesis using microwave irradiation to replace heating mantel as the energy source.

Materials and Methods

Materials

Starting material of vanillin was obtained from Brataco® and starting material of acetone was obtained from Sigma Aldrick®. Hydrochloric acid as the catalyst was obtained from Merck® Germany and the eluent for the qualitative analysis i.e. chloroform and ethyl acetate were obtained from the Merck® Germany.

Methods

Synthesis of gamavuton-0 using microwave irradiation was carried out in the porcelain evaporating disc under kitchen microwave irradiation. Vanillin and acetone were used as the raw materials and hydrochloric acid was used as the catalyst. The first step of the synthesis was preparing of the raw material by weighing of 8.2 grams of vanillin and pipetting 2 ml of acidified acetone to meet the mole ratio of vanillin and acetone at 2:1. The concentration of catalyst that was used is 20 µl for 10 ml of acetone. The synthesis time was conducted for 1, 2, 3, and 4 minutes with the power of the microwave used at 400 watts. At the end of the synthesis, the gamavuton-0 inside the mixture was isolated using hot water maceration. The crude gamavuton-0 is then dried and weighed to obtain the amount of gamavuton-0 produced.

Analysis

Identification of gamavuton-0 formation was conducted using TLC analysis. Silica GF254 was used as the stationary phase and chloroform-ethyl

acetate at ratio 5:1 was used as the mobile phase (Fahrurozi, 2008).

Results and Discussions

Gamavuton-0 include in the phenolic group and reported has many activities such as anticancer, anti-inflammatory, and anti-oxidants (Agrawal and Mishra, 2010; Nugroho et al., 2009; Yuniarti, 2000). Gamavuton-0 more stable compared to curcumin since this compound has a different middle chain, i.e. gamavuton-0 loss of methylene group and carbonyl group (Sardjiman, 2000). The chemical structure of curcumin and gamavuton-0 is depicted in Figure 1.

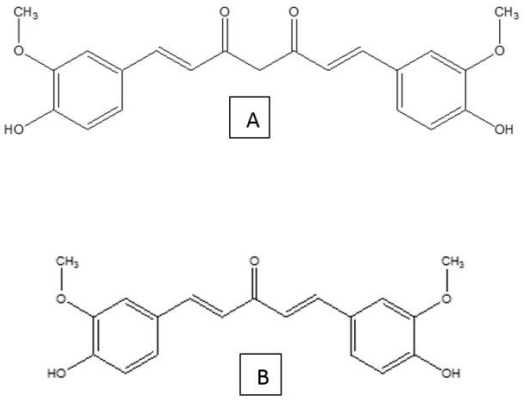

Figure 1. Chemical structure of curcumin (A) and gamavuton-0 (B).

Based on the excellence activities of gamavuton-0, production of this compound may be necessary to develop. In general, the synthesis of the curcumin derivatives is carried out by the Claisen-Schmidt condensation reaction or the Aldol Condensation of an aromatic ketone and aldehyde. The ketone, in this case, acts as a nucleophile, and the aromatic aldehyde acts as an electrophile. The aldol-condensation reaction is very popular and widely used in the formation of carbon-carbon bonds since this reaction is simple and the raw materials are easily obtained also known as environmentally friendly (Fessenden and Fessenden, 1999).

The synthesis was started by analyzing of the appropriate raw material for synthesis. Based on the disconnection analysis, vanillin and acetone can be used as the starting material of gamavuton-0. Theoretically, gamavuton-0 can be synthesized from 2 moles of vanillin and 1 mole of acetone. The detail result of disconnection analysis as explained in Figure 2.

p-ISSN 1693-3591
e-ISSN 2579-910X

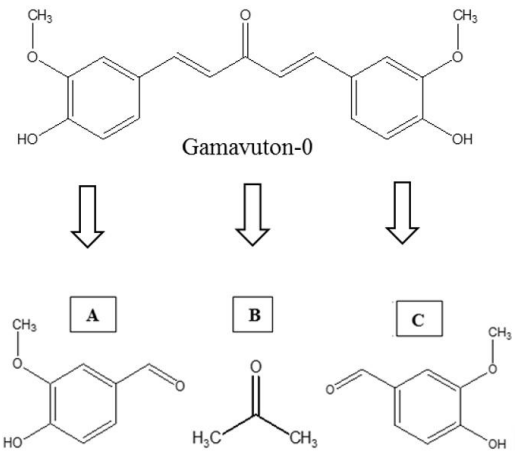

Figure 2. Appropriate raw material for synthesis of gamavuton-0 (A = vanillin; B = acetone; C = vanillin).

During the synthesis, the formation of gamavuton-0 was followed using TLC analysis, which carried out on the silica GF254 as the TLC-plat and chloroform-ethyl acetate at ratio 5:1 as the eluent (Fahrurozi, 2008). The yellow spot of gamavuton-0 appears at Rf = 0.5 and the starting material vanillin at Rf = 0.7. The yellow spot of gamavuton-0 can be observed in the visible light but for the vanillin spot only can be seen under UV light identification.

The TLC analysis of this experiment can be seen in Figure 3. It shows the crude product of the synthesis still containing raw material. Future study on purification process may be necessary to conduct to find the best quality of gamavuton-0.

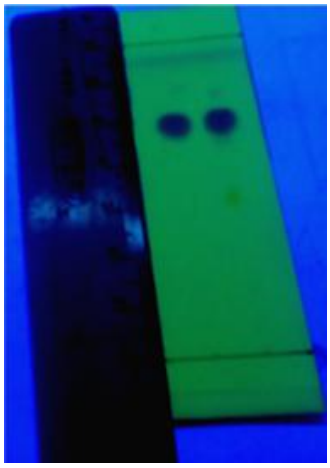

Figure 3. TLC analysis under UV light for gamavuton-0.

Table 1 shows 72.72% (7.12 grams) of crude gamavuton-0 can be produced within 2 minutes. In comparison with the previous study of synthesis gamavuton-0 using conventional heating (heating mantel), the synthesis was conducted at the longer time. It was reported, the synthesis was done for 3 hours to obtain 5,795 grams of crude gamavuton-0. (Harimurti et al., 2017).

Table 1. The yield of gamavuton-0 crude product at the different time of synthesis period under microwave irradiation

No	Irradiation Time (min)	Starting Material (g)	Crude of Gamavuton-0 (g)	Yield (%)
1	1	9.78	4.84	49.49
2	2	9.79	7.12	72.72
3	3	9.79	6.76	69.05
4	4	9.77	6.69	68.47

The faster synthesis using microwave irradiation may occur due to the thermal effect and non-thermal effects that are overheating, hot spots and selective heating, and non-thermal effects of the highly polarizing field. This may add the effects on the mobility and diffusion that may increase the probabilities of effective contacts of the starting material of synthesis (De la Hoz et al., 2005).

Conclusion

The microwave irradiation was proof to be a more promising energy source for the synthesis of curcumin derivate.

Acknowledgements

The financial support from Minister of Research, Technology, and Higher Education and facilities support from Universitas Muhammadiyah Yogyakarta to the authors are highly acknowledged.

References

Agrawal, D.K., Mishra, P.K. 2010, Curcumin and its analogues: potential anticancer agents. *Medicinal research reviews*, 30(5):818-860.

De la Hoz, A., Dı ´az-Ortiz, A., and Moreno, A. 2005. Microwaves in organic synthesis. Thermal and non-thermal microwave effects. *Chemical Social Review*, 34:164–178.

Fahrurozi. 2008. Pengaruh jumlah mol pereaksi pada sintesis senyawa GVT-0 dengan pelarut etanol dan uji sitotoksiknya terhadap sel Hela). *Skripsi*. Faculty of Phamacy, Universitas Gadjah Mada, Yogyakarta.

Fessenden, R.J. and Fessenden, J.S. 1999. *Organic Chemistry*. Part 2. Edited

by A.H. Pudjaatmaka. Jakarta: Erlangga Press.

Handayani, S., Budimarwanti, C., and Haryadi, W. 2017. Microwave-assisted organic reactions: eco-friendly synthesis of dibenzylidenecyclohexanone derivatives via crossed aldol condensation. *Indonesian Journal of Chemistry.* 17(2):336–341.

Harimurti, S., Widada, H., Kadarinah, S., Hadi, I., Wijaya, D.P., Komarudin, and Rifai, M.A. 2017. Optimization of anti-cancer gamavuton-0 synthesis using box behnken experimental design. *Advanced Science Letters*, 23:12498–12501.

Hughes, J.P., Rees, S., Kalindjian, S.B., and Philpott, K.L. 2011. Review: principles of early drug discovery. *British Journal of Pharmacology*, 162:1239–1249.

Nugroho, A. 2009. Sintesa 2-5-bis(4'-hidroksi-3'-metoksibenzilidin) siklopentanon dengan variasi suhu 28 ^{o}C, 38 ^{o}C, 48 ^{o}C pada fase pengadukan. *Skripsi.* Faculty of Pharmacy, Gadjah Mada University, Yogyakarta.

Ravichandran, S. and Karthikeyan, E. 2011. Microwave synthesis - a potential tool for green chemistry. *International Journal of ChemTech Research*, 3(1):466-470.

Sardjiman. 2000. Synthesis of some new series of curcumin analogues, antioxidative, antiinflammatory, antibacterial activities and quantitative structure activity relationship. *Dissertation*, Gadjah Mada University, Yogyakarta.

Veronesi, P., Leonelli, C., and Bondioli, F. 2017. Energy efficiency in the microwave-assisted solid-state synthesis of cobalt aluminate pigment. *Technologies,* 5(42):1-13.

Wanninger, S., Lorenz, V., Subhan, A., and Edelmann, F.T. 2015. Metal complexes of curcumin–synthetic strategies, structures and medicinal applications. *Chemical Social Review*, 44:4986–5002.

Yuniarti, N. 2006. Aktivitas antiinflamasi invivo dan invitro 1,5-bis(4'-hidroksi-3'-etoksifenil)-1,4-pentadien-3-on indometasin dan turunannya. *Thesis*. Universitas Gadjah Mada, Yogyakarta.