

Potential Combination of Nigella sativa and Allium sativum as a Modality of Herbal Therapy in Dyslipidemia Cases: A Literature Review

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Abstract. Dyslipidemia is a condition of the lipid profile in the blood at an abnormal level. Based on the 2013 Riskesdas, about 35.9% of the Indonesian population aged >14 years experienced dyslipidemia. Black cumin is an herbal plant that through its antioxidant activity can cure diseases such as dyslipidemia. Meanwhile, garlic is known to contain active substances that can play a role in helping the process of increasing lipid profile levels in the body. Some studies have examined the potential combination of these two compounds' usage in pathological conditions and yielded significant results. Therefore, this literature study was compiled to expand and summarize the analysis of the combination of black cumin and garlic potential as an alternative therapeutic modality in dyslipidemia. The writing of this paper uses a literature review study method. References are obtained from globally published journals that can be accessed through the International Library of Medicine (Pubmed), Clinical key, and PlosOne with a search time range from September 26–October 26, 2020. Based on the analysis process in this literature review, we conclude that the combination of the two compounds has also been shown to strengthen the antioxidant activity that can be given. So that the combination of Nigella sativa and Allium sativum can be used as a modality of herbal therapy in cases of dyslipidemia.

Keywords: Nigella sativa · Allium sativum · Dyslipidemia

1 Introduction

Globalization is a process of changing the economy and civilization into a more integrated system [1]. The phenomenon of globalization has an impact on technological developments, socioeconomics, and changes in the world food system in terms of high availability as well as increasing variety of food. The development of economic and social status in the world has had a significant impact on the increasing incidence of dyslipidemia in the last 10 years [1]. Dyslipidemia is a condition of the lipid profile in the blood circulation at abnormal levels. This is due to changes in the interaction of genetic factors and environmental factors that regulate endocrine function and also metabolic processes in the body. These conditions can lead to changes in the physiological function of the cardiovascular system and can usually lead to metabolic syndrome [3]. WHO data in 2008 showed that 30.3% of the total population in the Southeast Asian region had dyslipidemia. Based on RISKESDAS data in 2013, about 35.9% of the total population of Indonesia aged >14 years experienced dyslipidemia where the prevalence in women was higher than men and urban was more than rural [4].

Indonesia is a large country and is known as a mega-biodiversity country because of its high biodiversity. Indonesia's biodiversity occupies the second position after Brazil, wherefrom a total of 40,000 species of flora in the world as many as 30,000 species of flora can be found in Indonesia. Of the 30,000 species of flora, 940 species have been declared efficacious as a medium for traditional medicinal herbs that are efficacious and quite often used in Indonesia, including black cumin and garlic. Black cumin has been known as a plant that has the potential to reduce various diseases such as hypertension, diabetes mellitus, etc. [5]. Similarly, garlic does not only act as a seasoning in cooking. Garlic contains active substances that can play a role in helping the process of improving cholesterol levels in the body [6].

Nawal Al-Rasheed's research in 2014 proved that the combination of black cumin and garlic can be used as a therapeutic regimen for metabolic syndrome in rats. The same thing was also done in a study by Amina Hamed A in 2014 in a prospective study that has proven the potential of this combination in the treatment of dyslipidemia in humans. The protective effect of black cumin and garlic as antioxidants that reduce oxidative stress levels in nephrotoxicity rats has also been proven by Iman Abdelaziz in 2014. Therefore, we compiled this literature study as a study related to deepen the analysis of the potential combination of black cumin and garlic as a therapeutic modality herb in dyslipidemia [7].

2 Method

The writing of this paper uses a literature review study method derived from the analysis and synthesis of various references. The author entered several keywords into the search engine, namely Nigella sativa, Allium sativum, and dyslipidemia. Based on the journals obtained, the authors chose full-text journals in the English language, related to the writing topic, and were confirmed to have the year of publication in the last ten years. References are obtained from globally published journals that can be accessed through the International Library of Medicine (Pubmed), Clinical key, and PlosOne with a search time range from September 26–October 26, 2020. Then the analysis and synthesis of several journals that have been obtained according to the topic of writing are carried out, then this narrative review is compiled.

3 Result and Discussion

Black cumin (Nigella sativa) or also known as Habbatussauda is an herbal plant that comes from the Ranunculaceae family. Nigella sativa is known to have a very broad

pharmacological effect due to the active substances contained in it. Nigella sativa can grow to a height of about 20–90 cm. Nigella sativa seeds are black on the outside and white on the inside [2, 3].

Nigella sativa has several bioactive components, such as thymoquinone, thymohydroquinone, p-cymene dithymoquinone, carvacrol, 4-terpineol, t-anethol, sesquiterpene longifolene, -pinene, thymol, and others. Thymoquinone is the main active ingredient of Nigella sativa with high antioxidant activity. The seeds of Nigella sativa contain protein, fat, carbohydrates, fiber, various vitamins and minerals such as vitamin A and vitamin E, minerals such as Zn, Cu, P, and iron. Carotene can also be found in Nigella sativa seeds which can be converted to vitamin A when in the liver. Nigella sativa seeds are reported to be rich in unsaturated fatty acids, especially linoleic acid, oleic acid, eicosadienoic acid, and dihomolinoleic acid. Saturated fatty acids such as palmitic acid and stearic acid are also present in Nigella sativa seeds at about 30% or less [4, 5].

The antioxidant activity of Nigella sativa is played by its active ingredient, namely thymoquinone. Studies show that the methanol extract of Nigella sativa contains high levels of antioxidants. Due to its thymoquinone content, Nigella sativa can reduce lipid peroxidation and increase the activity of antioxidant enzymes which then suppress oxidative stress conditions. These conditions will resulting in the regeneration of pancreatic beta cells, increases beta-cell integrity, increases the number of islet cells, decreases insulin resistance and increase insulin secretion, and affects lipid metabolism [2]. Thymoquinone can also suppress the oxidative stress process induced by ferric nitrilotriacetate (Fe-NTA), hyperproliferative responses, and renal carcinogenesis in Wistar rats [6].

This antioxidant effect of thymoquinone has an impact on the state of dyslipidemia. Based on research conducted by Ismail, Al-Naqeep, and Chan in 2010 proved that Nigella sativa can increase total cholesterol, LDL, and triglyceride levels and significantly reduce HDL levels. This condition is caused by the antioxidant activity of Nigella sativa which can suppress the oxidative stress process that will affect lipid metabolism, decreases HMG-CoA reductase activity in the liver, increases arylesterase activity, and modulates the effect of gene regulators on cholesterol metabolism. Apart from its antioxidant activity, Nigella sativa also contains phytosterols such as beta-sitosterol and polyunsaturated fatty acids. Because of these ingredients, Nigella sativa can reduce cholesterol synthesis by hepatocytes and reduce its absorption from the small intestine. Nigella sativa also activates LDL receptors by reducing intracellular cholesterol leading to rapid clearance of LDL from the blood circulation [7–9].

Garlic (Allium sativum) is one of the plants used as one of the herbal therapy regimens due to the potential of the active substances it contains. Allium sativum is known to have several components of active substances such as alliin, allicin, E-Ajoene, Z-Ajoene, Diallyl sulfide, Diallyl disulfide, and other components of the active substance. In its application process, Allium sativum is known to have several pharmacological activities such as antibacterial, antifungal, antiprotozoal, anti-inflammatory, anticancer, and also antioxidant [10].

The pharmacological potential of Allium sativum has been studied in a scientific study. Based on preclinical research conducted by Amitai Elkayam et al. in 2013 stated that garlic intervention in the form of isolate allicin is effective enough to reduce systolic

blood pressure values (190 \pm 7 to 168 \pm 6 mmHg, with p < 0.001) and can reduce triglyceride levels (96 \pm 25 to 71 \pm 19 mg/dl, with p value = 0.009) post-intervention for six months compared with the control group in rats induced by hypertension [11].

Nigella sativa is known to have several significant pharmacological activities in humans including antidiabetic, anticancer, antibacterial, antihistamine, antiinflammatory, and antioxidant activities. Meanwhile, Allium sativum is known to have several pharmacological potentials that can be complementary to Nigella sativa. The therapeutic potential includes antibacterial, antiviral, anti-inflammatory, and antioxidant [12, 13].

Several studies have demonstrated the potential safety of using these two substrates. Based on clinical research conducted by Eman Mahmoud et al. in 2013 stated that the oral administration of Nigella sativa compound in a dose of 450 mg taken three times a day was well tolerated and relatively safe to use that shown by the low percentage of side effects that occurred after the intervention. As well as a decrease in the value of hepatitis C infection parameters in the research subjects [14].

Meanwhile, based on the meta-analysis literature compiled by Karin Reid et al. in 2013 it was stated that the medication process with the intervention of the Allium sativum regimen was proven to have a higher safety profile compared to medication using conventional anti-cholesterol drugs in general [15].

The potential application of the combination of these two compounds has been studied scientifically in several studies. Based on research conducted by Amina Hamed Alobaidi in 2014 in a Randomized Controlled Trial (RCT) study, it was proven that the simvastatin intervention with the administration of Nigella sativa and Allium sativum could provide a better effect on lipid profile levels compared to the intervention + placebo treatment group with p statistic value <0.01 [16].

Meanwhile, other studies formulated Nigella sativa and Allium sativum compounds as a polyherbal formulation in the intervention process. Based on research by Mahdi Zarvandi et al. in 2017 in a phase 1 clinical study, it was proven that polyherbal formulations can improve several pathological parameters of type 2 diabetes mellitus and can extend the condition up to 4 months after the study [17].

4 Conclusion

Black cumin is an herbal plant that is known to have the potential to cure various diseases such as dyslipidemia. Garlic is known to contain active substances that can play a role in helping the process of improving lipid profile levels in the body. The combination of the two compounds has also been shown to strengthen the antioxidant activity that can be given. So that the combination of Nigella sativa and Allium sativum can be used as a modality of herbal therapy in cases of dyslipidemia.

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References

- L. Qi, X. Ding, W. Tang, Q. Li, D. Mao, and Y. Wang, "Prevalence and risk factors associated with dyslipidemia in Chongqing, China," Int. J. Environ. Res. Public Health, vol. 12, no. 10, pp. 13455–13465, 2015, doi: https://doi.org/10.3390/ijerph121013455.
- M. Ş. Karaçil Ermumucu and N. Şanlıer, "BLACK CUMIN (Nigella sativa) AND ITS ACTIVE COMPONENT OF THYMOQUINONE: EFFECTS ON HEALTH," J. Food Heal. Sci., vol. 3, no. 4, pp. 170–183, 2017, doi: https://doi.org/10.3153/jfhs17020.
- A. Ahmad et al., "A review on therapeutic potential of Nigella sativa: A miracle herb," Asian Pac. J. Trop. Biomed., vol. 3, no. 5, pp. 337–352, 2013, doi: https://doi.org/10.1016/S2221-1691(13)60075-1.
- S. Ahmad and Z. H. Beg, "Elucidation of mechanisms of actions of thymoquinone-enriched methanolic and volatile oil extracts from Nigella sativa against cardiovascular risk parameters in experimental hyperlipidemia," Lipids Health Dis., vol. 12, no. 1, pp. 1–12, 2013, doi: https:// doi.org/10.1186/1476-511X-12-86.
- S. Asgary, A. Sahebkar, and N. Goli-Malekabadi, "Ameliorative effects of Nigella sativa on dyslipidemia," J. Endocrinol. Invest., vol. 38, no. 10, pp. 1039–1046, 2015, doi: https://doi. org/10.1007/s40618-015-0337-0.
- 6. Z. Khan, N. Hasan, N. Ahmad, and M. Khalid, "Pharmacological Activity of Nigella Sativa: A Review," Artic. World J. Pharm. Sci., no. April, 2016.
- M. Ismail, G. Al-Naqeep, and K. W. Chan, "Nigella sativa thymoquinone-rich fraction greatly improves plasma antioxidant capacity and expression of antioxidant genes in hypercholesterolemic rats," Free Radic. Biol. Med., vol. 48, no. 5, pp. 664–672, 2010, doi: https://doi. org/10.1016/j.freeradbiomed.2009.12.002.
- B. Amin and H. Hosseinzadeh, "Black Cumin (Nigella sativa) and Its Active Constituent, Thymoquinone: An Overview on the Analgesic and Anti-inflammatory Effects," Planta Med., vol. 82, no. 1–2, pp. 8–16, 2016, doi: https://doi.org/10.1055/s-0035-1557838.
- A. M. Sabzghabaee, M. Dianatkhah, N. Sarrafzadegan, S. Asgary, and G. Alireza, "Clinical evaluation of Nigella sativa seeds for the treatment of hyperlipidemia: a randomized, placebo controlled clinical trial.," Med. Arh., vol. 66, no. 3, pp. 198–200, 2012, doi: https://doi.org/ 10.5455/medarh.2012.66.198-200.
- 10. E.-S. Batiha et al., "Chemical Constituents and Pharmacological Activities of Garlic (Allium sativum L.): A Review," Nutrients, vol. 12, no. 3, p. 872, 2020.
- A. Elkayam, E. Peleg, E. Grossman, Z. Shabtay, and Y. Sharabi, "Effects of allicin on cardiovascular risk factors in spontaneously hypertensive rats," Isr. Med. Assoc. J., vol. 15, no. 3, pp. 170–173, 2013.
- P. Mikaili, S. Maadirad, M. Moloudizargari, and S. Aghajanshakeri, "Therapeutic Uses and Pharmacological Properties of Garlic, Shallot, and Their Biologically Active Compounds," Iran. J. Basic Med. Sci., vol. 16, pp. 1031–1048, 2013.
- 13. Z. Khan et al., "Pharmacological Activity of Nigella Sativa : A Review," World J. Pharm. Sci., vol. 4, no. 5, pp. 234–241, 2016.
- E. M. F. Barakat, L. M. El Wakeel, and R. S. Hagag, "Effects of Nigella sativa on outcome of hepatitis C in Egypt," World J. Gastroenterol., vol. 19, no. 16, pp. 2529–2536, 2013, doi: https://doi.org/10.3748/wjg.v19.i16.2529.

- K. Ried, C. Toben, and P. Fakler, "Effect of garlic on serum lipids: An updated meta-analysis," Nutr. Rev., vol. 71, no. 5, pp. 282–299, 2013, doi: https://doi.org/10.1111/nure.12012.
- A. Alobaidi, "Effect of Nigella Sativa and Allium Sativum Coadminstered with Simvastatin in Dyslipidemia Patients: A Prospective, Randomized, Double-Blind Trial," Antiinflamm. Antiallergy. Agents Med. Chem., vol. 13, no. 1, pp. 68–74, 2014, doi: https://doi.org/10. 2174/18715230113129990013.
- M. Zarvandi, H. Rakhshandeh, M. Abazari, R. Shafiee-Nick, and A. Ghorbani, "Safety and efficacy of a polyherbal formulation for the management of dyslipidemia and hyperglycemia in patients with advanced-stage of type-2 diabetes," Biomed. Pharmacother., vol. 89, pp. 69–75, 2017, doi: https://doi.org/10.1016/j.biopha.2017.02.016.

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