

# Potential and opportunities of nutmeg pericarp as functional foods

Rosniyati Suwarda<sup>1\*</sup>, Risma Fira Suneth<sup>1</sup>, Wahid<sup>1</sup>, and Dewi Sondari<sup>2</sup>

<sup>1</sup>Maluku Assessment Institute for Agricultural Technology (Maluku AIAT), Indonesia

<sup>2</sup>Research Center for Biomaterials, Indonesian Institute of Sciences, Cibinong Science Center, West Java, Indonesia

**Abstract.** Nutmeg (*Myristica fragrans* Houtt) is a native plant of Banda Island known as the Spice Islands. Nutmeg fruit consists of the pericarp or rind, the seed kernel inside (nutmeg), and the nutmeg is a red lacy (aryl) covering the kernel (mace). Nutmeg pericarp contributing 80-85% of the total weight of the nutmeg fruit but its use is still not getting enough attention and a lot of it is wasted as agricultural waste which can pollute the environment. This is because the economic value is considered to be lower than the seeds and mace of nutmeg. This article aims to review the potential and opportunity benefits of nutmeg meat waste (pericarp) for human health and its application in functional foods. The method used in this paper is a literature review. The results show that, the pericarp has been reported to contain bioactive compounds similar to those of nutmeg and mace oil which have pharmacological values. Phytochemical compounds are beneficial to human health as anti-inflammatory, anti-diabetes, anti-microbial agents, antioxidants, anti-depressants, anti-convulsants, and anti-cancer agents. Based on the composition, the pericarp is potentially used as a functional food to increase added value and reduce environmental pollution. In addition, the abundance of materials, relatively low prices, and the importance of healthy food for the health of the human provide opportunities for the development of functional foods based on bioactive compounds..

## 1 Introduction

Nutmeg (*Myristica fragrans*. Houtt) is native to Indonesian spread across several regions with production centers in the Maluku archipelago. The seeds and aril are commonly called nutmeg and mace respectively, are the primary products of *M. fragrans* known as spices [1,2,3,4]. Products from nutmeg are known nationally and internationally from colonial times as ingredients for the spice, cosmetic industry, food industry, and medical industry.

Nutmeg production areas in Indonesia consist of seven (7) provinces with an average contribution of production in 2015-2020: North Sulawesi (19.85%), North Maluku (19.12%), West Papua (17.56%), Aceh (17.44), Maluku (13.39%) and West Sumatra (3.44%) and West Java (3.13%) [5].

The largest exporting country of nutmeg and mace in the world is Indonesia, which is about 60% of the world's nutmeg needs and in 2019 Indonesia is the biggest nutmeg

---

\* Corresponding author: [ros\\_tpp@yahoo.co.id](mailto:ros_tpp@yahoo.co.id)

producer in the world. The total export volume of Indonesian nutmeg in the form of dry seeds and mace is 11,505,972 kg with a total export value of US \$ 50,138,286, - [6].

Prices for nutmeg oil and mace oil are relatively stable compared to other types of essential oil. Essential oil of nutmeg and mace from Indonesia are good quality and their exports dominate world nutmeg oil. Countries that import this product are the United States and the European Union.

Meanwhile, the utilization of nutmeg flesh (pericarp/rind) is still limited and a lot of it is wasted as agricultural waste, which is around 30-40% after the seeds and mace are taken. Nutmeg pericarp is the largest part of about 80-85% of the total weight of nutmeg fruit [6], but it still gets less attention because its economic value is considered lower than nutmeg and mace. They are generally taken by splitting the nutmeg directly in the nutmeg field and leaving the flesh strewn under the tree. The nutmeg and mace are generally taken by splitting the nutmeg fruit directly in the nutmeg field and leaving the flesh strewn under the tree. This nutmeg flesh/pericarp is very perishable so that it can pollute the environment and can even become a source of disease for nutmeg plants such as fruit rot. The economic value of nutmeg flesh/pericarp can be increased by diversifying its processing by producing derivative products that have socio-economic value and are highly competitive and reduce environmental pollution problems.

Nutmeg pericarp contains essential oils with hydrocarbon monoterpene components (61 – 88%) such as alpha pinene (8.7%), beta pinene (6.92%), D-limonene (8%), alpha terpinene (3.69%), acid monoterpenes (5 – 15%) and aromatic ethers (2 – 18%) such as myristicin (23.37%) and safrole (2.9%) [7]. In addition, nutmeg pericarp also contains pectin in the form of a brownish latex which has gel-forming properties [7,8]. Nutmeg pericarp also contains phytochemical compounds such as flavonoids, alkaloids, terpenoids and tannins [9,10].

Phytochemical compounds that are known to have physiological functions are carotenoids, phytosterols, saponins, glycosinolates, polyphenols, protease inhibitors, monoterpenes, phytoestrogens, sulfides, and phytic acid. According to Craig [11], a diet using large amounts of spices as a food flavoring can provide various active phytochemical components that are useful for maintaining health and protecting the body from chronic disease. These ingredients can be served in various forms, including health drinks, instant drinks, juices, syrups, candy, pickles, sweets, lunkhead, jams and jellies.

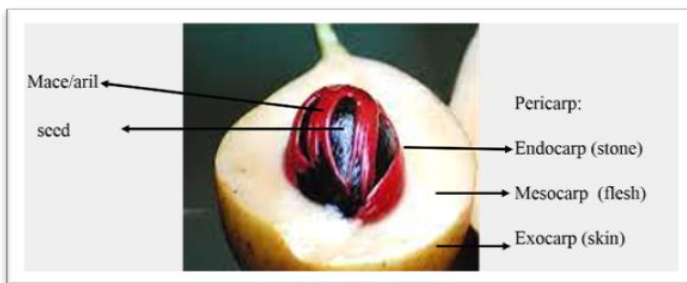
Nutmeg pericarp has great potential to be explored in functional food development because of the abundance of ingredients and relatively low prices and along with the increasing public awareness of the importance of maintaining health. In addition, nutmeg contains phytochemical compounds which refer to nutraceuticals that have a very important role for health, including their function in preventing degenerative diseases. This paper examines the potential and health benefits of nutmeg as a functional foods.

## **2 Phytochemical composition of *Myristica fragrans* fruit**

The Nutmeg fruit is commonly known as *Myristica fragrans*, consists of the pericarp, the aril and the seed. They are commonly referred to as nutmeg and mace respectively [3]. It is a type of plant with closed seeds. Seeds are covered by a fruit wall (pericarp) which consists of three (3) layers, namely exocarpium (exocarp), mesocarpium (mesocarp), and endocarpium (endocarp), but not all fruits consist of these 3 layers, some only consist of 2 layers, namely exocarp, and endocarp. Exocarpium is the outermost part of the fruit. Mesocarpium is the part of the fruit that lies beneath the Exocarpium layer. The endocarp is the part of the fruit adjacent to the seed coat. Parts of the nutmeg fruit are shown in Figure

The components contained in the pericarp are similar or not substantially different with nutmeg, and mace oil, but differ substantially in concentrations (Table 1). The chemical

composition of the pericarp, nutmeg, and mace oil from Indonesia is higher than in Malaysia and India, especially in the content of myristicin and sabine. Myristicin content in pericarp is higher than nutmeg and mace.



**Fig. 1.** Part of nutmeg fruit

**Table 1.** Phytochemical composition of volatile oil from different origin and part of *Myristica fragrans*

Part of plant/origin	Mayor component	Yield (%)	References
Pericarp /Malaysia	Terpinen-4-ol	19.1	3
	$\alpha$ -Pinene	15.2	
	Myrcene	9.1	
	Limonene	9.1	
	$\gamma$ -Terpinene	9.1	
	$\beta$ -Pinene	9.0	
	myristicine	-	
	sabine	-	
Pericarp /Indonesia	Terpinen-4-ol	14.4	12, 13
	$\alpha$ -Pinene	15.8; 39.16	
	Limonene	7.5	
	$\gamma$ -Terpinene	8.7	
	$\beta$ -Pinene	12.0	
	myristicine	15.6; 36.1	
	sabine	33.9	
	$\alpha$ -Terpineol	4.9	
Seeds (Nutmeg)/Indonesia	Sabine	21.38	14,15
	4-Terpineol	13.92, 10.77	
	Myristicin	13.57, 12.93	
	$\alpha$ -Pinene	10.23,	
	$\beta$ -Pinene	0.50	
	Limonene	5.57, 4.73	
	Safrol	4.28, 1.94	
$\alpha$ -Terpineol	3.11, 15.42		
Seeds (nutmeg)/India	Sabine	15-50	16
	4-Terpineol	0-11	
	Myristicin	0.5-13.5	
	$\alpha$ -Pinene	10-22	
	$\beta$ -Pinene	7-18	
	Myrcene	0.7-3	
	Limonene	2.7-4.1	
	Safrol	0.1-3.2	
$\alpha$ -Terpineol	-		
Mace/Indonesia	$\alpha$ -Pinene	13.08	17
	Limonene	5.60	
	$\gamma$ -Terpinene	-	
	$\beta$ -Pinene	15.14	
	myristicine	26.46	
sabine	22.93		
Mace/India	$\alpha$ -Pinene	15.24	18
	Limonene	-	
	$\gamma$ -Terpinene	1.82	
	$\beta$ -Pinene	45.52	
	myristicine	5.92	
sabine	-		

### **3 Potential benefits of *Myristica fragrans* human health**

Nutmeg has been used in culinary and medicinal. Many chemical compounds contained in nutmeg have been identified as anti-oxidant, health promoting properties and disease preventing. Nutmeg has phytochemical properties that refer to *nutraceutical* are beneficial to human health as antimicrobial agents, anti-inflammatory, anti-oxidants, anti-diabetes, antidepressants, anticonvulsants, and anticancer agents.

#### **3.1 Anti-inflammatory and antidiabetes activity**

Inflammation is a typical mechanism for protecting or infected tissue as well as to eliminating dead or damaged host cells. Phenylpropene is a natural organic compound contained in nutmeg myristicin which acts as an anti-inflammatory such as non-steroidal anti-inflammatory drugs. It has been reported that the development of new anti-inflammatory drugs have currently more focused on natural ingredients, to reduce the side effects of chemical drugs [10].

Studies of the anti-inflammatory activity in the model of nutmeg in a lipopolysaccharide-stimulated macrophage has been reported that nutmeg extract has anti-inflammatory potential, it can reduction of interleukin IL-6 or tumor necrosis factor (TNF- $\alpha$ ), increased production of IL-10, or reduction in the expression of cyclooxygenase-2 (COX-2) or inducible nitric oxide synthase (iNOS) [12].

Extracts from nutmeg can also treat diabetes and obesity. These results indicate that final body weight and weight gain rats treated with tetrahydrofuran (THF) was significantly lower than that induce obesity mice to a high-fat diet (HFD) [13]. *M. fragrans* petroleum ether extract can reduce blood glucose levels to normal in diabetic rats given glucose fed and alloxan. The hypoglycemic effect is due to the potential for insulin release from beta-cells [1,10].

The pericarp *M. fragrans* was evaluated for its bioactive components using in vitro antioxidant and anti-inflammatory assays. These results showed that the extract of hexane, ethyl acetate and methanolic inhibited lipid peroxidation (LPO) by 82.5, 70.1 and 73.2%, and cyclooxygenase enzymes COX-1 by 44, 44 and 42% and COX-2 by 47, 41 and 36%, respectively, at 100  $\mu\text{g/mL}$  [12].

#### **3.2 Antitumor and anticancer**

The benefits of nutmeg as an anti-cancer have been reported by several researchers. Myristicin compounds have cytotoxic and apoptotic effects on human neuroblastoma SK-N-SH cells with cytochrome accumulation and activation of caspase 3 in the cytosol, myristicin is an anticancer agent [14].

Cytotoxic activity test against cancer cells in mice with 4 ligands Mesodihydroguaiaretic acid (DHGA), macelignan, fragransin A2 and nectandrin B isolated from nutmeg, found that DHGA has strong cytotoxic activity against H358 with an IC50 value of 10.1  $\mu\text{M}$ . In addition, DHGA exhibited antitumor activity in a mouse model of allogeneic tumor carriers [15].

#### **3.3 Neuropharmacologic properties**

The results of a recent study reported that nutmeg is a recreational drug used by adolescents as a substitute for marijuana [10,4]. Nutmeg has long been used as a pain reliever and thus has been commonly used to replace the narcotic drug morphine [16].

Oral administration of nutmeg extract with hexane at a dose of 5 mg/kg for 3 consecutive days can improved learning and memory in young and old mice and reverse diazepam and scopolamine-induced learning and memory impairment, whereas that administration of nutmeg extract with hexane at a dose of 500 mg/kg gave a stimulant effect on the locomotor activity of rats [17,18].

### **3.4. Antimicrobial and antifungal activity**

Many studies have shown that nutmeg has good antimicrobial activity. The extract of mace with water and ethanol showed good antimicrobial property against both the Gram-positive and Gram-negative species and can inhibit the growth of *E. coli* and *Staphylococcus aureus* [18,19].

Concentration of 0.1% nutmeg essential oil can inhibit the radial growth of *Colletotrichum gloeosporoides* (98%), *Colletotrichum musae* (97%), *Fusarium oxysporum* (75%), *Fusarium semitectum* (78%), *Aspergillus niger* (71%) and *Aspergillus glaucus* (60%). Concentration of 0.3% inhibition increased, growth could be inhibited from 85% to 100% [20].

Nutmeg pericarp oil has a higher linalool content than nutmeg oil from seeds and mace (0.2%). Terpinene-4-ol is the main component of *Melaleuca alternifolia* (tea tree oil) and has strong antimicrobial, anti-inflammatory, antioxidant activity and antifungal [11].

### **3.5 Antioxidant**

Nutmeg oil extracted from nutmeg and mace has long been used clinically as an antioxidant. Nutmeg has antioxidant properties due to its ability to inhibit lipid peroxidase and inhibit superoxidation radical scavenging activity in animal experiments [16].

During the processing and storage of foods, deterioration is caused by lipid peroxidation. Polyphenolic compounds contribute multiple biological effects including antioxidant activities in both edible and inedible plants. To increase the shelf life and retard auto-oxidation in oils and fatty foods, anti-oxidants are mostly used. The study showed that anti-lipid peroxidant properties are seen in *M. fragrans* seeds [1].

The antioxidants in flesh/pericarp, seeds, and mace extracts has a rather large difference of reduction potential with radical species formed during the linoleic acid peroxidation [2].

## **4 Uses and application in functional foods**

Definition of functional foods are foods that can improve physical or mental health, reduce the risk of some illnesses, and cure some diseases. However, there are several different rules regarding the definition of functional food among regulatory bodies, namely 1) Academy of Nutrition and Dietetics, functional foods are fortified or enriched whole foods that have potential beneficial effects on health when consumed as part of a regular diet and effective, 2) the Institute of Food Technologists, functional foods as Foods and food components that give a health benefit beyond basic nutrition (for the intended population), 3) The Ministry of Health, Labour and Welfare, Japan, FOSHU (Food for Specified Health Uses), functional foods are foods containing an ingredient with functions for health and officially approved to claim its physiological effects on the human body [22,23,24].

In Indonesia, according to the POM [25], functional foods are food that naturally or have been processed contains one or more compounds that are based on scientific studies are considered to have specific physiological functions that are beneficial to health. Functional food consumed as a food or drink, have sensory characteristics, namely the

appearance, color, texture, and flavor acceptable to consumers, and not give contraindications and adverse effects on the metabolism of other nutrients when used in the recommended amounts. Although they contain compounds that are beneficial to health, functional foods are not in the form of capsules, tablets, or powders derived from natural compounds.

From this classification, functional foods are produced by enriching or strengthening food components/ingredients to increase their beneficial effects on health. Food fortification is a challenging process because it can cause several problems, such as changes in organoleptic properties, in fortified foods. While fortification materials such as encapsulations have been widely reported to address organoleptic problems, it is the best approach to incorporate health-promoting ingredients into the food system as they can mask the undesirable odors and tastes of bioactive compounds [26].

Product safety must be maintained for that a risk assessment for functional foods must be carried out. Food safety issues associated with M fragrans and its constituents are needed to determine a working strategy to obtain maximum benefits from nutmeg without being exposed to unwanted side effects.

Products from nutmeg have been used to flavor many kinds of baked goods, breads, confections, puddings, dairy products, meats, sausages, saucers, vegetables, and beverages. It is also used as a component of candies, chewing gum, syrups, curry powder, teas, and soft drinks, or is mixed in milk and alcohol [27,28,29].

Nutmeg essential oil has been used as a natural flavoring extract. It has been used as a flavoring agent, replacing ground nutmeg in order to avoid leaving particles in foods and beverages. Essential oils (EOs) and their application in food preservation has been amplified because (1) it is desired to reduce the potential health risk and increasing negative consumer perception of synthetic preservatives; and (2) foodborne diseases are a growing public health problem worldwide, calling for more effective preservation strategies [30,31]. Nutmeg essential oil and its various oleoresin extracts displayed antimicrobial and antioxidant properties that make them a promising natural food preservative to replace the synthetic ones [32,33].

Nutmeg essential oil has been used as a natural flavoring as a flavoring agent, replacing nutmeg powder to avoid leaving particles in food and drink. application of essential oils (EOs) in food preservation has been strengthened because (1) it is desirable to reduce the potential health risks and improve the negative perceptions of consumers about synthetic preservatives; and (2) foodborne disease is a growing public health problem throughout the world, demanding a more effective conservation strategy [30,31]. Nutmeg essential oil and its oleoresin extract are used as antimicrobials and antioxidants which show promising natural food preservative properties to replace synthetic preservatives [32,33].

## **5 Research gap of the nutmeg use as functional food in Indonesia**

Along with the increasing awareness of healthy living, the potential for a greater functional food market. However, in Indonesia, the circulation of functional food is still small. No data have been found on the amount of production and trade in functional food. However, there are many functional drinks on the market that have been offered. Nutmeg (seeds, mace, and pericarp) has been widely reported as efficacious for health because it contains bioactive compounds. The benefits of phytochemical components have been widely published so that knowledge and consumer interest in nutmeg-based foods (pericarp) which are rich in phytochemical components and as functional foods can be developed. Nutmeg

can be developed into health foods and drinks which are categorized as functional foods with sensory characteristics that can be accepted by the wider community.

Products based nutmeg have been circulating in the market such as juices, syrups, candies, pickles, sweets, lunkhead, jams and jellies, but these products cannot be claimed as functional foods and drinks. This can be seen from the unregistered BPOM RI as functional food. In the list of types of functional food products along with permitted claims, there are 10 categories of functional food products including spices and seasonings, beverages and jellies. However, in this category there are no products-based nutmeg. To increase these products into functional food, the thing that must be done is to make a claim. In functional food research and development, there is a gap between academics and claims compliance efforts. The existence of claims on functional food must be regulated so as not to mislead consumers. The existence of this claim also distinguishes functional food from other foods [34].

## 6 Potency and challenge

Nutmeg (seeds, mace,) is rich in bioactive components that have the potential to be developed. Nutmeg can be developed into functional food and drink (functional food) because of its bioactive components which refer to nutraceuticals.

The development of functional foods can benefit consumers, which can be beneficial for public health such as preventing disease, increasing immunity, slowing down the aging process, and improving physical appearance. Nutmeg and mace seeds can be used as psychotropic substances. This is because the levels of myristicin and elemicin contained in it can act as amphetamines when viewed from a similar biochemical structure. Because the problem of amphetamine levels is only found in supplements and cannot be used as food or drink, nutmeg and mace seeds can be functional food products that have the potential to function as supplements as well as act as food or drinks. For industry, parts of nutmeg that can be used as functional food can be formulated into product variants that have high value and have an impact on public health through technological innovation assistance.

Although functional foods provide benefits to the growth of the food industry, there are several challenges faced. Technological innovation is needed for nutmeg processing into functional food. This is a challenge in itself in diversifying processed nuts which will later become functional food that is in demand by the community organoleptically. Considering that functional food has a role as healthy food for the community, it is necessary to strive for technological innovation in answering problems and challenges in processing nutmeg as a functional food. So that it can encourage consumer interest and have implications for the growth of the industrial sector in functional food in Indonesia.

Technological innovation should be able to answer the challenges of nutmeg processing as a functional food such as providing food safety guarantees and guaranteeing health benefits. Food safety assurance needs to be a major concern when viewed from some of the phytochemical content of nutmeg which if consumed above the standard limit will become a health problem. Considering that nutmeg oil contains myristicin which is a hallucinogen. If consumed in high doses can cause poisoning while the benefit of myristicin is to prevent the formation of tumors. This of course can be handled with the establishment of innovation and technology.

The guarantee of health benefits is if in processing the quality of the phytochemical content can be maintained and reduce the loss of the quality of the phytochemical content. The challenges encountered in maintaining the quality of a phytochemical content contained in functional food products include the location of cultivation and how to obtain raw materials and processing methods used. Of course, these three things can be overcome by applying technological innovations.



In addition to the challenges of technological innovation, there are also marketing challenges. Marketing aims to facilitate the flow of agricultural products. To maintain the stability of agricultural products both in terms of quality and quantity. Limited functional food products can cause higher selling prices compared to supplements that contain the same phytochemicals. For this reason, things that need to be done are: maintaining the continuity of nutmeg production, increasing the number of markets for functional food products, shortening marketing channels, improving the quality of human resources in managing the marketing of functional food products, and maintaining production quality at the marketing stage.

## 7 Developing of nutmeg as functional foods

The development of functional food based-nutmeg can be designed with the addition of bioactive ingredients that are beneficial for health. The use of bioactive ingredients from nutmeg and functional food products is strategically and technologically possible but still requires a series of investigations; In vitro bioassays, biopharmaceuticals, animal experiments, and clinical studies also require collaboration or partnerships between multidisciplinary scientists to develop valid methodologies and avoid misjudgments.

The steps are taken in the use of nutmeg (seeds, mace, pericarp) as a functional food ingredient:

1. Selection of raw materials
2. extraction/processing techniques, proper extraction/processing techniques are developing to make sure that bioactive compounds are not lost, and must pay attention to food safety aspects
3. investigation of the biological activity of extraction/processing results, investigation results obtained from these studies are very important for formulating certain functional foods.
4. determination of the right functional food formulation
5. perform an organoleptic test
6. Labeling, labeling is important in the development of functional food, because the label contains information about the product including health claims.
7. Conduct socialization and technical guidance (BIMTEK) to farmers or business actors regarding the benefits of nutmeg for healthy food and drink or functional food

## 8 Conclusion

Nutmeg (*Myristica fragrans*) contains therapeutic value and acts as an antimicrobial, anti-inflammatory, anti-oxidant, anti-diabetic, anti-depressant, anti-convulsant and anti-cancer agent. The phytochemical components of the pericarp are similar to those of nutmeg and mace. Pericarp has the potential to be developed as a functional food with high value and as a socio-economic food because it is still an agricultural waste and the price is relatively cheap.

## References

1. Joseph J, Pushparani D, Baskar V, Sakthivel K., J. Bio. Inf.Sci. **2**, 2 (2013)
2. Assa J., Widjanarko SB, Kusnadi J, Berhimpon S., Int.J Chem. Tech. Res. **6**, 2460-8 (2014)
3. Choo LC, Wong SM, Liew KY., J. Sci. Food Agric. **79**, 13 (1999)



4. T.Ulfah, H.H. Hardjomidjodjo, E Anggraeni, *Nutmeg determination as the main commodity in South Aceh; a literature review*, in IOP Conf. Ser.: Earth Environ. 9-10 October 2019, Bogor, Indonesia, Sci. 472 012040 (2020)
5. Ministry of Agriculture, Nutmeg Production by Province (Ministry of Agriculture, 2019)
6. Directorate General of Estate Crops, Tree crop estate statistics of Indonesia, Pala Comodity 2017-2019, (Direct.General of Estate Crops, Ministry of Agriculture, 2019)
7. Raj NM, Vikram HC, Philip M, Deepa ET., *J.Plant Crop* **44**, 3 (2016)
8. Fidriany, Ruslan, Ibrahim., *J. Acta Pharm.-eutica Indonesia* **29**, 1 (2004).
9. Westerlund E, Åman P, Andersson R, Andersson RE, Rahman S.M.M., *Carbohydr. Polym.* **15**, 67-78 (1991)
10. Arrizqiyani T, Sonjaya N, Asty A., *Optimalisasi Potensi Tanaman Pala Sebagai Antibakteri Escherichia coli Menggunakan Metode Ekstraksi*, in Pros National Seminar, Hasil-hasil Penelitian dan Pengabdian Masyarakat (2017)
11. Craig, W.J., *Am. J. Clin. Nutr.* **70**, 3 (1999)
12. Gopalakrishnan M., *J. Spices Aromat. Crop* **1**, 3 (1992)
13. Mueller M, Hobiger S, Jungbauer A., *Food Chem.* **122**, 4 (2010)
14. Nguyen P.H., Le T.V.T., Kang H.W, Chae J., Kim S.K., Kwon K.I., Seo D.B., Lee S.J., Oh W.K., *Bioorg. Med Chem Lett.* **20**, 14 (2010)
15. Lee B.K., Kim J.H., Jung J.W., Choi J.W., Han E.S., Lee S.H., Ko K.H., Ryu J.H., *Toxicol Lett.* **157**, 1 (2005)
16. Thuong P.T., Hung T.M., Khoi N.M., Nhnng H.T., Chinh N.T., Quy N.T., Jang T.S., Na M., *Arch. Pharm. Res.* **37**, 3 (2014)
17. Rudgley, R., Thomas Dunne Books, St. Martin's Griffin, *The Encyclopedia of Psychoactive Substances* (Macmillan pub., 1998)
18. Parle, M.; Dhingra, D.; Kulkarni, S., *J. Med. Food* **7**, 2 (2004)
19. Ameen S.J., Antimicrobial activity of nutmeg extracts against *Staphylococcus aureus* and *Escherichia coli*, Available from: <http://www.iasj.net/ asj- func=fulltext &aId=2825> (2011)
20. El Malti J., Bourhim N., Amarouch H., *J. Food Safety* **28**, 3 (2008)
21. Sudradjat SE, Timotius KH, Mun A, Anwar E., *J. Young Pharm* **10**, 1, (2018)
22. Crowe, K.M., Francis, C., *J. Acad. Nutr. Diet.* **113**, 8 (2013)
23. Ministry of Health, Labour, and Welfare, Japan. Food for Specified Health Uses (FOSHU). <http://www.mhlw.go.jp/english/topics/foodsafety/fhc/02.html>. (2015)
24. Stein, A.J., Rodríguez-Cerezo, E., *Functional Food in the European Union, a Report Based on the ESTO Study Functional Food in European Union* (European Commission JRC IPTS: Seville, 2008)
25. Badan Pengawasan Obat dan Makanan, *Kajian proses standarisasi produk pangan fungsional di badan Pengawas Obat dan makanan, Lokakarya Kajian Penyusunan Standar Pangan Fungsional*, Badan Pengawasan Obat dan Makanan, Jakarta. (2001)
26. Mozafari, M.R., Khosravi-Darani, K., Borazan, G.G., Cui, J., Pardakhty, A., Yurdugul, S., *Int. J. Food Prop.* **11**, 4 (2008)
27. Olaleye, M.T., Akinmoladun, A.C., *Afr. J. Biotechnol.* **5**, 15 (2006)
28. Shafiei, Z., Shuhairi, N.N., Md. Fazly Shah Yap, N., Harry Sibungkil, C.A., Latip, J., *Evid. Based Complement. Altern. Med.* Article ID 825362 (2012)
29. Codex Alimentarius Commission (CAC), Joint FAO/WHO Food Standards Programme Codex Committee on Contaminants in Foods, Discussion Paper on the Establishment of a Maximum Level for Aflatoxin B1 and Total Aflatoxins in Nutmeg and Associated Sampling Plan. (2014)
30. Hyldgaard, M., Mygind, T., Meyer, R.L., *Front. Microbiol.* **3**, 12 (2012).
31. Djenane, D., Yangüela, J., Roncalés, P., Aider, M., *J. Food Res.* **2**, 3 (2013)

32. Gupta, A.D., Bansal, V.K., Babu, V., Maithil, N., J. Genet. Eng. Biotechol. **11**, 25-31 (2013)
33. Kapoor, I.P.S., Singh, B., Singh, G., De Heluani, C.S., De Lampasona, M.P., Catalan, C.A.N., Int. J. Food. Prop. **16**, 1059-1070 (2013)
34. H. Cipta, N. Harini, D. Hermawan, Pangan Fungsional Makanan untuk Kesehatan (Penerbit Univ. Muhammadiyah Malang, 2015)