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Antiaging and Skin Irritation Potential of Four Main Indonesian Essential Oils

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Abstract: Essential oils possess antiaging properties due to their antioxidant activity. This study aims to determine the antiaging activities of four main Indonesian essential oils and their irritation potential on the skin. The spot yeast and in vivo rat skin with UVB exposure methods were used to analyze the antiaging activity of essential oils on aging triggered by endogenous and exogenous factors, respectively. Meanwhile, patch tests and clinical evaluations were used for the skin irritation potential analysis. The antiaging activity results from the endogenous factor showed that the use of clove, patchouli, nutmeg, and citronella oils increased yeast viability at concentrations of 20, 40, 60, and 100 μg/mL, respectively. Furthermore, nutmeg, cloves, citronella, and patchouli oils decreased the wrinkle score on rat skin after UVB exposure (exogenous factor). The skin irritation potential results of patchouli, nutmeg, citronella, and clove oils were none (0), slightly (0.02), moderately (0.09), and very irritating (0.39), respectively.

Keywords: antiaging; Indonesian essential oils; potential skin irritation

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1. Introduction

The process of aging is a physical change and functional phenomenon that occurs with time or environmental effects, appearing at all organism levels [1]. According to Ganceviciene et al. [2], aging skin is affected by endogenous factors (intrinsic aging) and exogenous factors (extrinsic aging). Furthermore, this intrinsic aging occurs naturally from prolonged physical changes. Meanwhile, extrinsic aging is affected by external variables, such as solar exposure, smoking, and other lifestyle factors [3]. This process has been defined as a major and important aspect of skin health. Generally, these products are used to acquire smooth, soft, free, and transparent skin [2].

Antioxidants are predominantly common ingredients used in cosmetics, single substances such as idebenone, ascorbic acid (vitamin C), kinetin, tocopherol (vitamin E), ubiquinone, lipoic acid, and chemical compounds such as polyphenols, flavonoids, arbutin, and carotenoids [4,5]. Furthermore, the current trend in cosmetics has reverted to nature, where the use of natural extracts has become very popular [6,7]. Moreover, natural material so have great potential in cosmetics because they are safer [8,9] when used with in an appropriate concentration and composition [10]. Essential oils are natural ingredients that represent a functional group with antioxidant activities [11], which are effective in reducing health risks. According to Gülçin, Elmastaş, and Aboul-Enein [12], essential oils in cloves were reported to minimize or prevent fatty oxidation, retard the formation of toxic oxidation products, and maintain nutritional quality. This oil can also be used as a natural preservative to minimize or modify of the properties of food or pharmaceutical products [13]. Some antioxidants are essential antiaging substances used to protect and prevent skin damage [14]. Moreover, when combined with a cosmetic formula, antioxidants play a role in preventing skin aging primarily due to the effects of solar exposure [3]. Essential oils with aromatic components containing functional groups, such as phenols, alcohols, aldehydes, and ketones, were reported to also have an irritant effect on the skin [15].

This article discusses the antiaging activity of Indonesia's four main essential oils and their irritation potential on the skin. There have been only a few reports on the use of antioxidants from essential oils in the prevention of aging caused by endogenous or exogenous factors, especially the use of these oils. In application, safe antiaging substances are formulated into cosmetic products. Therefore, the objective of this work was to analyze the antiaging activity of Indonesia's four main essential oils using yeast viability and UVB exposure on rats' legs. In addition, irritation potential analysis was carried out in order to identify essential oils with high antiaging activity together with a low irritation potential on the skin.

2. Materials and Methods

2.1. Materials

Patchouli oil was obtained from Southeast Sulawesi, while nutmeg, clove, and citronella oils were from West Java, Indonesia, provided by PT. Sinkona Indonesia Lestari. Moreover, the yeast extract supplement (YES) and dimethyl sulfoxide (DMSO) were purchased from Merck. *Schizosaccharomyces pombe* (*S. pombe*) was cultivated at IPB University (Microbiology Laboratory, Bogor, Indonesia) while, glucose, histidine, leucine, adenine, uracil, and arginine were obtained from Sigma-Aldrich, Jakarta Indonesia. A Wilmar rat weighing 200 g was obtained from the ITB School of Pharmacy, Bandung Indonesia. Helium gas was purchased from Sangkuriang Ltd., Jakarta Indonesia. A UVB lamp (Philip) with 10 mW/cm^2 irradiation intensity, chromatography–mass spectrometry (GC–MS) equipment from Agilent, type GC 6890/MS 5975 MSD, and a HP5-MS (30 m $\times$ 0.25 mm $\times$ 0.25 m) capillary column were used to characterize the results of this study.

2.2. Methods

2.2.1. Chemical Composition Testing

The gas chromatography–mass spectrophotometry (GC–MS) was performed at an early temperature of 60 °C for 5 min. Subsequently, the temperature was increased after 10 min to 250 °C and sustained for 5 min, and then the ratio was changed to 1:20. Helium gas with constant pressure of 7.65 psi was also used as a carrier gas.

2.2.2. Antiaging Analysis in the Yeast *Saccharomyces pombe* (Spot Method)

Antiaging analysis was performed with the spot method [16]. First, the yeast cells were cultured in the YES medium solution as an inoculum culture for 24 h. This 1000 mL medium consisted of 5 g yeast extract, 30 g glucose, 0.01 g uracil, and 0.128 g of histidine, leucine, adenine, and arginine.

The culture test was inoculated with an initial 0.05 OD_{600} yeast cell and contained YES medium, *S. pombe*, and different concentrations of essential oils (20 ppm, 40 ppm, 60 ppm, 80 ppm, and 100 ppm) dissolved in DMSO. The DMSO solution was used as a negative control. Subsequently, each of these cultures was spotted on the 7th and 11th day by managing the OD_{600} values to 1 and then diluted to a series of 101, 102, 103, and 104 on a sterile microplate well (Nunc 96). Each suspension (3 µL) was then spotted on YES agar. Yeast cell viability was further checked following three days of incubation at 30 °C.

2.2.3. Antiaging Analysis in the Yeast *Saccharomyces pombe* (Chronological Age Test Method)

Chronological age testing was conducted by culturing *S. pombe* as an inoculum in 10 mL YES medium solution for 24 h within a 24 rpm shaking incubator at 30 °C. This inoculum was added to 50 mL YES media solution within a 250 mL Erlenmeyer flask with an initial 0.05 OD_{600} yeast cell. Subsequently, according to the essential oil test spot, the best concentration was added to the yeast cells as a test treatment.

In addition, negative controls were produced by culturing *S. pombe* in the YES and positive controls were produced by culturing *S. pombe* in the YES and Edinburgh Minimal Medium (EMM), respectively. The DMSO solution was also added to this culture. Cell viability amounts were measured using a total plate count (TPC) technique on the 1st, 4th, 7th, 10th, 13th, 17th, and 20th days. Moreover, the TPC was conducted by arranging OD_{600} culture to 1 per treatment on the appointed day and then attenuated to 104 dilutions. Each 100 µL dilution was distributed three times into the YES medium as a solid and the spread culture was incubated for 3 days at 30 °C for the next count of yeast colony growth [17].

2.2.4. Antiaging Analysis Using In Vivo Animal Test

The use of an in vivo method with UVB exposure in the antiaging analysis was a modification of the technique published by Tsukahara et al. [18], where the rat was immobilized with the hairless dorsal legs facing up. Dorsal legs were used in order to achieve clear observations, without fur growth interference during experiments. This test subject was exposed to radiation for two weeks, five days a week, at a minimal erythemal dose of 216 J/cm^2, which was placed 20 cm above the rat's right foot. After exposure, 10 µL of the essential oil was applied to the rat's right leg for 5 min, while the left region was treated as a control.

2.2.5. Analysis of Skin Irritation Potential

Skin irritation potential analysis was performed with in vivo semi-occlusive single patch testing and clinical evaluation, adopting the Indonesian spin control technique. The test involved 33 human test subjects, which were chosen based on the criteria of healthy Asians aged 18–65, with a variety of dry, oily, and a combination of both skin types. Initially, each subject completed a medical questionnaire describing their cosmetic use habits and then wore no cosmetics on their backs for 12 h before testing. Subsequently, an essential oil solution (10% dilution in mineral oil) was attached to the skin on their back as a sample and then removed after 48 h. Clinical evaluation of the back husk was conducted by the medical doctor where the absence of a change in the skin color indicated that the oil had no effect. In addition, pink, reddish-pink, and red coloration indicated that the skin had experienced light, moderate, and mild irritation, respectively.

3. Results and Discussion

3.1. Chemical Components

Essential oils have chemical components that represent their quality. In addition, specific gravity, refractive index, and optical rotation could indicate light or heavy components. Table 1 displays the specifications of four main Indonesian essential oils associated with their distillation conditions, which resulted in specific components. Oils with specific gravity and optical rotation above 1.02 and 1.5, respectively, have more light components than heavy components [18,19]. In this study, cloves and patchouli oil had heavy active components because their refractive index and specific gravity approached 1.5 g/mL and 1.0, respectively. However, citronella and nutmeg oil had light components with specific gravity and refractive index of less than 0.9 g/mL and 1.5, respectively.

Table 1. Essential oil specifications.

Unit	Clove Oil	Citronella Oil	Patchouli Oil	Nutmeg Oil
Specific Gravity/g/mL	1.0284	0.8857	0.9537	0.8793
Refractive Index	1.5306	1.4667	1.5138	1.4849
Optical Rotation	−0.37	−2.40	-48.85	+16.28

Figure 1 displays the chromatogram of the four main essential oil chemical components identified with GC–MS. Clove oil contained several components, such as 68.1% eugenol, 1.3% copaene, 21.2% trans-caryophyllene, 0.9% iso-eugenol, 4.0% alfa caryophyllene, and 1.3% caryophyllene oxide. According to Huang et al. [20], the main constituents of clove oil are eugenol and caryophyllene, which is similar to the Chinese variant. Moreover, citronella oil contained mainly 32.0% citronella, 9.8% citronellol, and 19.1% geraniol, as well as 3.1% limonene, 0.7% linalool, 0.9% isopulegol, 3.1% citronellyl, 4.4% geranyl acetate, 2.7% germacrene, 2.6% delta cadinene, and 10.2% cyclopentasiloxane [20]. The primary contents of Sulawesi patchouli oil included 15.2% δ guaiene, 13.1% α guaiene, 25.1% patchouli alcohol, and azulene, similar to the Aceh variant. Other constituents included 3.9% β-patchoulene, 3.8% trans-caryophyllene, 8.9% seychellene, 7.1% α-patchoulene, 6.0% beta selinene, and 3.6% globulol [21]. Meanwhile, 9.2% α pinene, 38.4% sabinene, 9.3% β-phellandrene, 5.6% terpineol, 2.0% citral, 2.5% octadienal, 2.5% safrole, 3.5% propenoic acid, 6.4% methyl eugenol, 2.6% tetradecanethyl, 6.0% myristicin, and 2.6% elemicin were observed in nutmeg oil. Although sabinene was the principal component seen in this oil [22], myristicin was the active component and is widely used as an anti-inflammatory agent [23].

3.2. Antiaging Activity of Essential Oils in Yeast Model of *Schizosaccharomyces pombe*

Spot analysis is a qualitative test used to study the potential of an active ingredient in increasing yeast viability at the final stationary phase. Conserved hallmarks of yeast are similarly regulated in human cells [24]. Since the lifespan of yeast is shorter than that of the rat, this method is suitable for intrinsic aging testing. In the yeast growth curve produced on YES medium, the organism entered a stationary phase on the 7th day and was stable until the 11th, before entering the death stage. The organism's ability to maintain its viability until the 11th incubation day indicates the effect of its survived cell longevity [16]. Moreover, endogenous factors are responsible for the antiaging activity of the yeast viability methods.

The spot in the Figure 2 indicates the density of the colony in each concentration dilution. This study shows that introducing active materials of essential oil can affect the density of yeast colonies compared with the control (+DMSO). Generally, the individual addition of the four essential oils on the 11th day maintained the yeast viability compared to the control, indicating the potential antiaging activity of essential oils. However, each of the essential oils exerted these properties at a different concentration. Citronella oils maintained yeast viability on the 11th day at a concentration of 100 µg/mL, while other essential oils, namely patchouli, clove, and nutmeg, had similar activities at lower concentrations between 20 and 60 µg/mL. Subsequently, an essential oil sample at a concentration that maintains yeast viability was examined with a chronological age test.

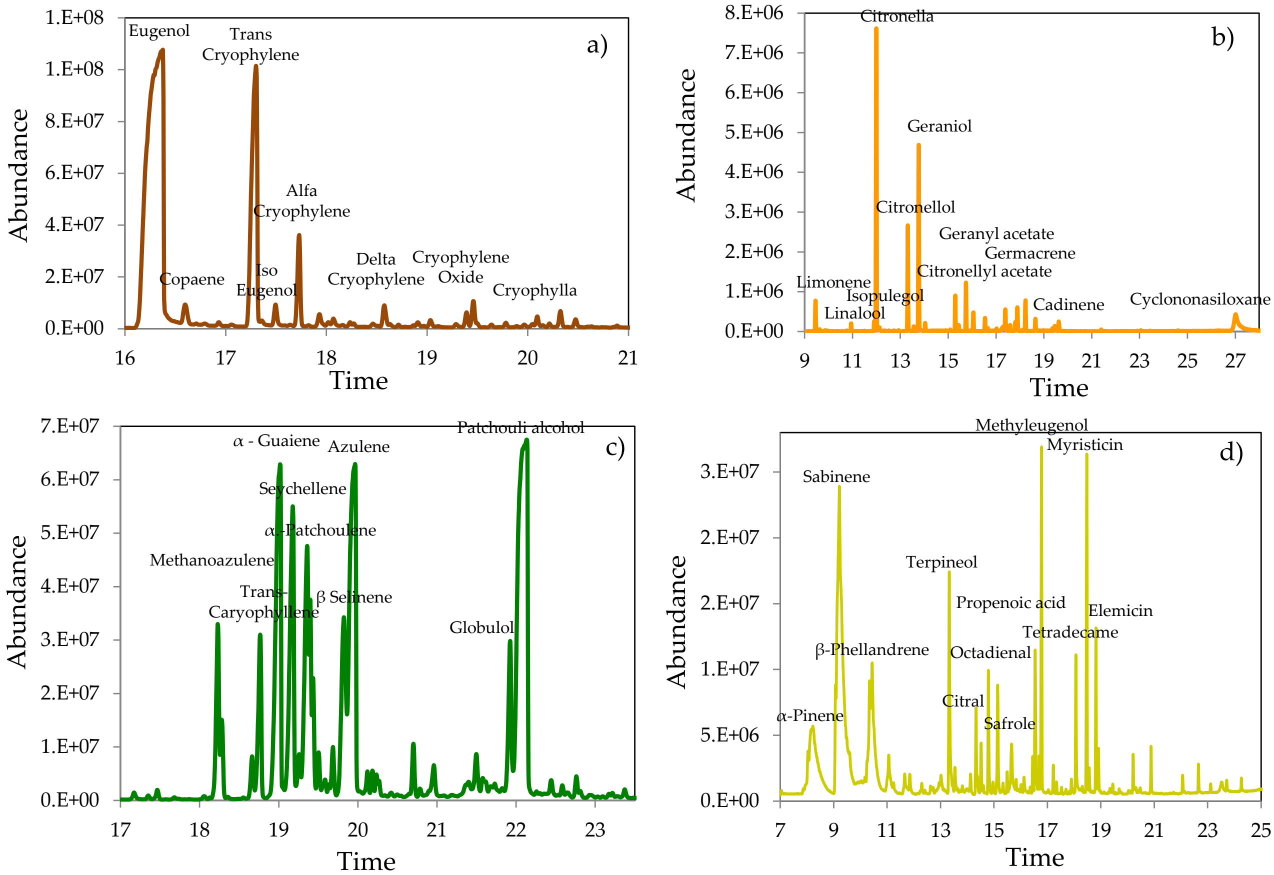

Figure 1. Chromatography spectra of (**a**) clove oil, (**b**) citronella oil, (**c**) patchouli oil, and (**d**) nutmeg oil.

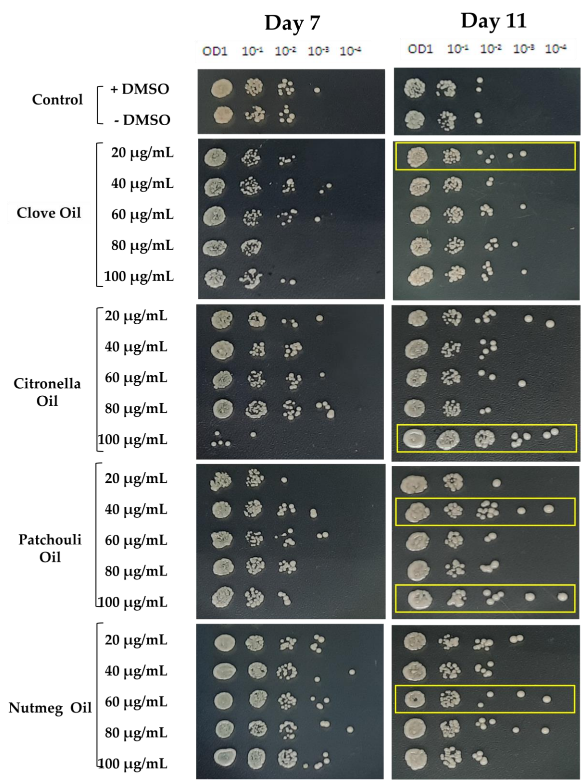

Figure 2. Effect of essential oils' antiaging properties on yeast *S. pombe*'s viability. The yeast culture in YES+DMSO and without DMSO medium was used as a control.

Furthermore, essential oils' effects were analyzed with the chronological yeast age, especially in the selected oil concentrations from the previous spot test shown in Figure 3. Generally, all the samples increased the yeast viability until the 20th day compared to their negative control with 3% glucose. Therefore, essential oils are capable of regulating yeast age in a higher percentage of cells compared to the control. The treatment with 20 μg/mL citronella and clove oil extended the organism's life in a similar approach to the positive control therapy of 0.3% glucose (caloric restrictions). Moreover, calorie treatments (CR) have reportedly extended the yeast's life through mitochondrial regulatory and autophagy cell mechanisms [25,26].

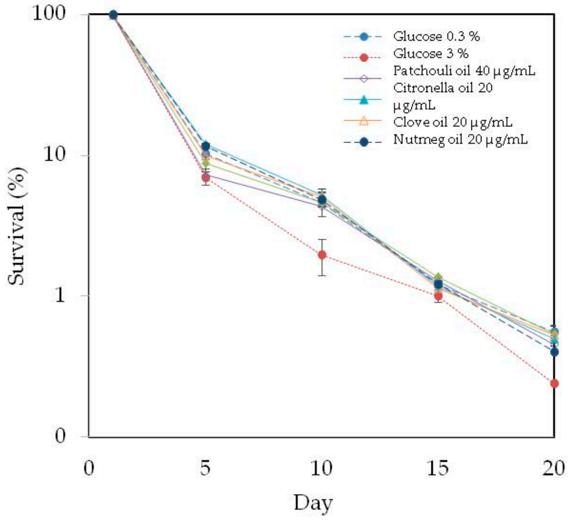

Figure 3. Effect of essential oils on yeast *S. pombe*'s aging. The yeast culture in YES + DMSO and without DMSO was used as a control. Moreover, the organism was grown on a medium of 3% and 0.3% glucose as a negative and positive control, respectively.

3.3. Antiaging with In Vivo Animal Skin

Extrinsic aging occurs due to exogenous factors [2], which was indicated in the treatment of UVB exposure on animal skin. This method was conducted on the dorsal back of a hairless rat irradiated with a dose of 216 J/cm^2, where the subject was exposed 5 days per week for 2 weeks. Moreover, 10 μL of the essential oil was applied to one foot of the rat after exposure. The results showed that the essential oils provided antiaging protection from coarse wrinkles on the foot skin. Figure 4 depicts the result of a two-week observation of wrinkle scores on the dorsal skin of the rat's back legs. The criteria for the scoring included 0 = no wrinkles, 1 = slightly coarse or shallow, 2 = some coarse, and 3 = some deep wrinkles. Subsequently, the leg wrinkles after UVB exposure in subjects with and without the essential oil treatments were compared.

The observation result (Figure 5) showed some deep and coarse wrinkles on the naive and blank samples, respectively. However, rat skin with essential oil treatment and UVB exposure had a lower level of wrinkles than the blank. The lowest score was observed in subjects with nutmeg and clove oil treatments, as well as UVB exposure. Therefore, essential oils have the potential to repair damaged aging skin caused by UVB exposure [27]. In general, natural products can be potentially antiaging active ingredients in cosmetics, such as *S. macrophylla* seed extract as an anti-UVB photoprotective ingredient [6] and sandalwood oil as an environmental stress-protective ingredient [28].

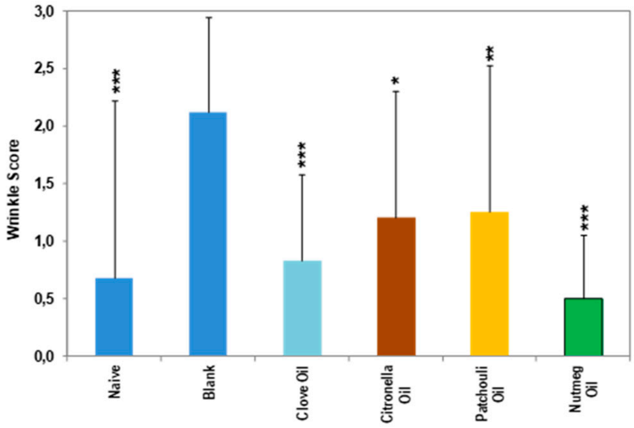

Figure 4. Wrinkle scores on rat skin after UVB exposure, where the naive was unexposed, and the blank exposed. The essential oil was a carrier subjected to UVB, with *, **, *** having values of <0.05, 0.01, and 0.001, compared to the blank.

Figure 5. Effects of UVB exposure and essential oil influence on the dorsal skin of the rat's back legs: (**a**) naive, (**b**) blank, (**c**) clove oil, (**d**) citronella oil, (**e**) patchouli oil, and (**f**) nutmeg oil. Naive is rat's back legs without being sampled and without UVB exposure. Blank is hairless rat's back legs with sampling and UVB exposure.

3.4. Effect of Essential Oil Use on Skin Irritation Potential

Essential oils as well as natural materials are considered safe and nontoxic when used at low concentrations [10]. Based on this information and the irritation test by the local cosmetic industry, in this study, a clinical evaluation on human skin was conducted. Essential oils are used in cosmetics and body care products, where a patch test on the skin is essential to determine its irritant potential (allergies) [27]. This skin irritation potential was described by the mean irritation index (MII), which was obtained from scores and subsequently divided based on the 33 subjects. Table 2 summarizes the MII values to determine the degree of irritant classification. Consequently, 0.00–0.20, 0.20–0.50, 0.50–2.00, and 2.00–3.00 were categorized as no, little, moderate, and heavy irritation, respectively. The patch of clove oil on various subjects' skin was red, while citronella was reddish-pink. Meanwhile, the patch of nutmeg oil after 48 h was pink, while patchouli did not affect the skin.

Table 2. Irritation index.

Subject Name	MII	Max	Classification
Negative Control	0.00	0.00	None
Clove Oil	0.39	2.00	Heavy
Citronella Oil	0.09	1.00	Moderate
Patchouli Oil	0.00	0.00	None
Nutmeg Oil	0.02	0.50	Little

Note: MII = Mean Irritation Index, Max = Maximum.

According to Gülçin, Elmastaş, and Aboul-Enein [12], the main component of clove oil is eugenol. Meanwhile, citronelal, citronelol, and geraniol are the primary constituents in citronella [29] and myristicin in nutmeg oil [22]. Phenol (eugenol) and alcohol (geraniol, citronelol), as well as aldehyde and ketone, caused heavy and moderate irritation, respectively, while ether caused light irritation [15]. This study result demonstrates that the irritation potential is in the order of cloves > citronella > nutmeg > patchouli oil. The high irritating potential of clove oil and citronella oil is related to their main components. Clove oil with eugenol and citronella oil with geraniol and citronellol are also on listed as allergenic ingredients [30].

4. Conclusions

Indonesia has four main essential oils with antiaging activity due to the functional groups in their chemical components, namely clove, citronella, patchouli, and nutmeg. The amount of antiaging activity depends on their chemical components. The antiaging property of these oils was observed in ascending order as follows: clove > patchouli > nutmeg > citronella oil for the endogenous factor. Meanwhile, the sequence of nutmeg > cloves > citronella > patchouli oil was seen for the exogenous factor. Given the concern about allergenic essential oils, the skin irritation potential of these oils was assessed when applied to cosmetic products and found to be in the order of clove > citronella > nutmeg > patchouli.

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