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Assessment of Cosmeceutical Potentials of Selected Mushroom Fruitbody Extracts Through Evaluation of Antioxidant, Anti-Hyaluronidase and Anti-Tyrosinase Activity

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Abstract: Cosmeceutical formulations containing naturally derived active ingredients are currently preferred by consumers worldwide. Mushrooms are one of the potential sources for cosmeceutical ingredients but relevant research is still lacking. In this study, hot- and cold-water extractions were performed on four locally-cultivated mushrooms—*Pleurotus ostreatus*, *Ganoderma lucidum*, *Auricularia polytricha* and *Schizophyllum commune*—with the aim to assess the cosmeceutical potential of these mushroom fruitbody extracts. Total phenolics, polysaccharide and glucan content were determined. Antioxidant property of the mushroom extracts was assessed by determining the DPPH radical scavenging, ferric-reducing (FRAP) and superoxide anion (SOA) scavenging activity. Anti-hyaluronidase activity was used as an indicator for the anti-aging and anti-inflammatory property, while anti-tyrosinase activity was evaluated to assess the anti-pigmentation or whitening property of these extracts. Our results showed that total polysaccharide content of *P. ostreatus* extracts was the highest (235.8–253.6 mg GE/g extract), while extracts from *G. lucidum* contained the lowest glucan (10.12–10.67%). Cold-water extract from *S. commune* exhibited substantial tyrosinase inhibition activity (98.15%) and SOA scavenging activity (94.82%). The greatest hyaluronidase activity was exhibited by *G. lucidum* hot-water extract, with the value of 72.78%. The findings from the correlation analyses suggest that the cosmeceutical properties of these mushrooms can be attributed mainly to the combination of different types of compound such as polysaccharides and phenolics. Overall, cold-water extract of *S. commune* and hot-water extract of *G. lucidum* showed the best results and may be further investigated.

Keywords: anti-tyrosinase; antioxidant; anti-hyaluronidase; mushroom; water extract

1. Introduction

Natural ingredients for healthy products, particularly cosmetics and cosmeceutical products, are now preferred by consumers compared to synthetic ingredients. The rise of natural and organic cosmetic products may be due to consumers having rising concerns about certain chemicals in skincare products, such as parabens, silicone and phthalates, and opting for natural ingredients that are deemed to be safer. Many naturally derived ingredients have been proven to be safe and widely used in cosmeceuticals and cosmetic formulations, such as *Vitis vinifera* (grape) seed oil [1] which contains polyphenols and carotenoids, *Camellia sinensis* (green tea) extracts [2], oil and other ingredients from coconut (*Cocos nucifera*) [3] and many more. Some synthetic ingredients used in cosmetics and

cosmeceutical products may cause a variety of undesirable side effects and potential allergic reactions, particularly for people with sensitive skin [4]. In order to meet the consumer demand, cosmetic brands have started offering more natural products, and pushing for extended research into more non-toxic natural-based ingredients.

There is a wide range of natural resources that can be explored and exploited to fulfil consumer demand, such as plants and herbs. Active ingredients from these natural sources have long been used traditionally in topical lotions and creams [5]. However, there are many other resources, such as algae and mushrooms, that can be further explored and exploited as new cosmetic or cosmeceutical functional ingredients. To assess the cosmeceutical potentials of new natural resources, the extracts and bioactive compounds must be investigated for their cosmeceutical-related biological properties such as antioxidant, anti-tyrosinase and anti-hyaluronidase. The antioxidant property of an extract in cosmeceutical products may protect the skin from external and internal aggressors such as ultraviolet (UV) rays, pollutants and stress, and thus may minimize the formation of dark spots and wrinkles. Extracts or compounds with an anti-hyaluronidase property may be an effective anti-aging and anti-inflammatory agent by improving skin suppleness and reducing wrinkle formation due to the inhibition of hyaluronidase enzyme that are related to the inflammation process and degradation of hyaluronic acid. Hyaluronic acid main function is to retain water to keep our skin tissues well lubricated and moist [6]. The potential of an extract or compound as anti-pigmentation or whitening ingredient can be indicated by its ability to inhibit tyrosinase enzyme. Tyrosinase is involved in the synthesis of melanin pigment in our skin, and over-exposure to UV rays may lead to hyper-pigmentation that causes skin to darken. Extracts or compounds that possess multiple cosmeceutical functionalities are highly valuable as they can address several skin issues simultaneously.

Mushrooms have been known to possess a variety of biologically active compounds such as polysaccharides, terpenoids, seleniums, vitamins and phenolic compounds. These compounds offer valuable bioactivity such as antioxidant, anti-ageing, anti-inflammatory and photo-protective effects that are useful for cosmeceutical products. According to Wu et al. [7], mushrooms make up a vast source of powerful new pharmaceutical products but are largely untapped. Several types of mushroom are now incorporated as skincare and cosmetic ingredients such as *Ganoderma lucidum* (Ling Zhi), along with *Cordyceps sinensis* and *Grifola frondosa* as well as jelly fungi (*Tremella* spp.). However, there are still plenty of other mushroom species with significant potential which might be currently undetermined or undescribed [8]. Our study attempted to evaluate the cosmeceutical properties of four mushroom species: *Pleurotus ostreatus*, *Auricularia polytricha*, *Schizophyllum commune* and *G. lucidum* (Figure 1). These mushrooms are popular for consumption in Asian countries, locally-cultivated and available all year round.

Figure 1. Mushroom species used in the study. From left: *P. ostreatus*, *A. polytricha*, *S. commune* and *G. lucidum*.

Although numerous investigations have been carried out on the biological activities of water extracts from *P. ostreatus* and *G. lucidum*, research regarding the cosmeceutical potential of these mushrooms, such as hyaluronidase and tyrosinase inhibition activity (especially on *S. commune* and *A. polytricha*) is still limited [9]. To the best of our knowledge, there is no report on anti-tyrosinase and anti-hyaluronidase activities from hot- or cold-water extract especially from *S. commune* and *A. polytricha*, but there are limited reports on their polysaccharide and beta-glucan extracts. It is widely

known that the morphological characteristics and compound compositions of mushrooms are subject to variation resulting from differences in cultivation in different geographical locations, climatic conditions and, most importantly, the substrates used [10–12]. Variation in the compositions of compounds in mushrooms fruitbodies may directly influence their biological activities. Therefore, in order to develop functional cosmeceutical products from local sources, it is important to conduct research by using locally-sourced materials to avoid inconsistencies in the quality of the final products. Water extraction is one of the most common preparation methods for mushroom supplements because most of active compounds in the vast majority of mushrooms, for example beta-glucans, are water-soluble. Water is also regarded as 'universal solvent' and one of the safest solvents to be used in the extraction process.

This preliminary study aimed to investigate and assess the cosmeceutical potentials of hot- and cold-water extracts from selected locally cultivated mushrooms by measuring the antioxidant, anti-hyaluronidase and anti-tyrosinase activity of the mushroom extracts. The biological components of these extracts such as total phenolics and polysaccharide content was also evaluated and the correlation of these components to the biological activities of the extracts was also studied.

2. Materials and Methods

2.1. Materials and Preparation of Extracts

Kukur mushrooms (*S. commune*) were purchased from Coconut Island Resources, Kedah, Malaysia. Black Jelly (*A. polytricha*), Tiram (*P. ostreatus*) and Ling Zhi (*G. lucidum*) were purchased from Vita Agrotech Sdn. Bhd., Selangor, Malaysia. All solvents and chemicals used were of analytical grade.

All mushroom fruiting bodies were cleaned, cut into smaller pieces and lyophilized in a vacuum freeze dryer (Christ Alpha 1-4 LD Plus). Five grams of dry powder of each mushroom was weighed in conical flasks using an analytical balance (Mettler Toledo, B204-S) and extracted at either 4 °C (cold water) or 100 °C (hot water) for 1 h. Water (50 mL) was used as the extracting solvent. The mixture for cold water extraction was shaken in a refrigerated incubator shaker (New Brunswick™ Innova® 42R, Eppendorf, Germany), while the mixture for hot water extraction was shaken in a water bath (Memmert). After completion of the extraction process, the extracts underwent centrifugation at 10,000 rpm for 10 min and later filtration using Whatman No. 1 filter paper to obtain a clear solution of crude extract.

The crude extract was lyophilized using a freeze dryer and stored at room temperature. All extractions were carried out in triplicate. Prior to analysis, the extract was stored at −20 °C. A total of 10 milligrams of crude extract were dissolved in 1 mL distilled water to be used for analysis.

2.2. Biological Component Assays

2.2.1. Total Polysaccharide Content

The total polysaccharide content was determined using a method described by Pawar and Mello [13]. Briefly, crude mushroom extract (0.1 g) was diluted with 1 mL distilled water, followed by 1 mL of 5% (*v*/*v*) phenol solution and 5 mL of concentrated sulfuric acid. The mixtures were incubated at room temperature for 10 min. The absorbance of each mixture at 490 nm was measured using a microplate reader (VERSAMax, Molecular Devices, San Jose, CA, USA). Glucose was used as a reference standard for the assay.

2.2.2. Total Phenolic Content

Measurement of total phenolic content was carried out according to a method by Okmen et al. [14]. An aliquot (1 mL) of each sample was added to 5 mL of Folin—Ciocalteu reagent (Merck, Kenilworth, NJ, USA). The mixture was then added to 4 mL of 7.5% sodium carbonate solution and left to react in the dark for 120 min. The absorbance at 765 nm was measured using a UV-Vis spectrophotometer

(VARIAN, Cary 50, Agilent). The calibration curve was plotted by using 0 to 200 ppm gallic acid as a standard. Results are expressed as mg/g gallic acid equivalent (GAE).

2.2.3. Total Glucan, α-Glucan and β-Glucan Content

Determination of total glucan, α-glucan and β-glucan content was performed using a Mushroom and Yeast β-Glucan Kit (Megazyme). The assay was performed according to the manufacturer's protocols. Mushroom extract (0.1 mL) was mixed with 0.1 mL exo-1,3-β-glucanase (20 U/mL) and β-glucosidase (4 U/mL) mixture and incubated at 40 °C in a water bath for 60 min. Then, 3 mL of glucose oxidase was added to each tube and incubated for 20 min. The absorbance of the aliquots was read at 510 nm for measurement of total glucan content. For α-glucan, 0.1 mL of mushroom extract was added to 0.1 mL sodium acetate buffer and mixed with 3 mL of glucose oxidase, followed by incubation at 40 °C for 20 min. The absorbance of the α-glucan aliquot was read at 510 nm. The β-glucan content was calculated by subtraction of α-glucan from total glucan. All measurements of absorbance were read using a UV-Vis spectrophotometer (VARIAN, Cary 50, Agilent).

2.3. Biological Activity Assays

2.3.1. DPPH (2,2-Diphenyl-1-Picrylhydrazyl) Radical Scavenging Activity

The assay was carried out with reference to a previously described method [15]. Mushroom extract (150 µL) was mixed with freshly prepared DPPH working solution (2850 µL) followed by incubation in the dark for 30 min. Absorbance was measured at 515 nm using a UV-Vis spectrophotometer (VARIAN, Cary 50, Agilent). Ascorbic acid was used as a positive control in this assay. The following equation was used to determine the percentage of scavenging activity:

$$\text{DPPH radical scavenging activity (\%)} = [(A - B)/A] \times 100$$

where A is the absorbance of the blank and B is the absorbance of the sample.

2.3.2. Ferric-Reducing Antioxidant Potential (FRAP)

A previously described procedure [16] was followed in carrying out the FRAP assay. An aliquot (150 µL) of the sample was reacted with a fresh FRAP working solution (2850 µL) for 30 min in the dark. The absorbance of the mixtures at 593 nm was recorded using a UV-Vis spectrophotometer. The standard curve was constructed using 0 to 2000 µM $FeSO_4$ solution. FRAP was calculated from a ferrous standard curve and the result was expressed as mM/g ferrous equivalent (FE).

2.3.3. Superoxide Anion (SOA) Scavenging Activity

The SOA scavenging assay was performed using a SOD Assay Kit-WST (Sigma) and conducted according to the manufacturer's protocols. The assay was conducted using 96-well plates. An aliquot (20 µL) of mushroom extract was added to the sample and blank 2 wells while double-distilled water (20 µL) was added to blank 1 and blank 3 wells. Water soluble tetrazolium salt (WST-1 (2-(4-Iodophenyl)-3-(4-nitrophenyl)-5-(2,4-disulfophenyl)- 2H-tetrazolium, monosodium salt)) working solution (20 µL) was added to each well followed by addition of the enzyme working solution (20 µL) to the sample and blank 1 well. The plate was then incubated for 20 min at 37 °C. The absorbance was read at 450 nm using a microplate reader. Calculation of SOA scavenging activity was done according to the following equation:

$$\text{SOA scavenging activity (\%)} = \{[A_{b1} - A_{b3}) - (A_s - A_{b2})]/(A_{b1} - A_{b3})\} \times 100$$

where A_{b1} is the absorbance of blank 1, A_{b2} is the absorbance of blank 2, A_{b3} is the absorbance of blank 3 and A_s is the absorbance of the sample.

2.3.4. Tyrosinase Inhibition Activity

Evaluation of the tyrosinase inhibition activity of mushroom extracts was performed using 3,4-dihydroxyphenylalanine (L-DOPA) as the substrate. The reference standard used in this assay was 100 µg/mL kojic acid. The assay was conducted according to a method explained by Alam et al. [17]. A mixture of 40 µL sample, 80 µL of 0.1 M phosphate buffer (pH 6.8) and 40 µL of mushroom tyrosinase (31 U/mL) was prepared. Sample and blank solutions, with and without enzyme, were also prepared. A solution of 10 millimolar L-DOPA (40 µL) was added to each sample and the blank. The final mixtures were allowed to react at 25 °C in the dark for 5 min. The absorbance of reaction mixtures was read at 475 nm using a microplate reader (VERSAMax, Molecular Devices) to determine the quantity of dopachrome produced. Tyrosinase inhibition was calculated using the following equation:

$$\% \text{ Tyrosinase inhibition} = \{[(A - B) - (C - D)]/(A - B)\} \times 100$$

where A is the absorbance of the blank solution with enzyme, B is the absorbance of the blank solution without enzyme, C is the absorbance of the sample solution with enzyme and D is the absorbance of the sample solution without enzyme.

2.3.5. Hyaluronidase Inhibition Activity

The assay was carried out according to the method previously described [18]. The reference standard used in this assay was quercetin. All solutions were freshly prepared before the assay. Hyaluronidase (4 U/mL, 100 µL) was mixed with 25 µL of sample solution and the mixture was incubated at 37 °C for 10 min. The reaction was commenced with the addition of hyaluronic acid solution (0.03% in 300 mM sodium phosphate, pH 5.4, 100 µL) and incubated at 37 °C. After 45 min, the undigested hyaluronic acid was precipitated with acid albumin solution (bovine serum albumin (0.1%) in 1 mL sodium acetate (24 mM), pH 3.8). After 10 min incubation at room temperature, absorbance was measured at 600 nm using a spectrophotometer (VARIAN, Cary 50, Agilent). The absorbance value in the absence of enzyme was used as a control. The percentage of hyaluronidase inhibition was determined using the following formula:

$$\% \text{ Inhibition} = (Ab_s/Ab_c) \times 100$$

where Ab_s is the absorbance of the sample and Ab_c is the absorbance of the control.

2.4. Statistical Analysis

Data obtained from triplicate experiments were used to calculate mean values and standard deviation. One-way analysis of variance (ANOVA) was conducted with Tukey's test at a significance level of $p < 0.05$ using Minitab Statistical Software (version 14). Correlation and regression tests were conducted using Microsoft Excel. Data are represented as a mean value ± standard deviation.

3. Results and Discussion

3.1. Extraction Yield of Extracts from Fruitbodies of Selected Mushrooms

An appropriate extraction process is crucial in order to successfully recover targeted bioactive compounds from mushroom and plant materials. Extraction efficiency can be affected by many factors, such as solvent type and concentration, temperature and time as well as the solid to solvent ratio [19]. Due to water having no toxic effect on human cells and being considered a 'green' solvent, we used water as the extraction solvent. Hot water is often involved in the extraction of mushroom fruitbodies, which essentially breaks down the chitin in the cell walls. However, hot water can destroy the bioactive compounds in the extract, and therefore cold-water extraction is also preferred. Lyophilization or freeze drying was used to dry the mushroom fruitbodies to provide constant moisture removal as

well as to ensure that the samples were consistent prior to the extraction process. The extraction yields are shown in Table 1. Large variability can be observed in the yield of each type of extract from selected mushrooms. Generally, *P. ostreatus* yielded more extract compared to other mushrooms. Extraction temperature seemed to have a substantial effect on *S. commune* extraction yield, due to larger differences in yield between cold and hot water extraction of this mushroom, compared to other mushrooms. Compared to our results, lower extraction yield was observed for water extraction of *P. ostreatus* (17.6 ± 0.26%) in a study done by Elbatrawy et al. [20]; however, it was higher than the extraction yield for other solvents such as ethanol, acetone and ethyl acetate used in that study. Similar observations were reported by a previous study [21] which indicated higher extraction yield for hot water extraction than methanol and ethanol extraction from *S. commune*. Therefore, it is presumed that a higher content of water-soluble substances may be the cause of the higher extraction yield for *S. commune* and *P. ostreatus*, compared to *A. polytricha* and *G. lucidum*. A solvent which has a polarity similar to that of the solute is able to dissolve more than one with opposing polarity [22].

Table 1. Extraction yield, total polysaccharide content and total phenolic content of extracts from multiple types of mushroom.

Mushroom	Extract	Total Extraction Yield (% *w*/*w*)	Total Polysaccharide Content (mg GE/g extract)	Total Phenolic Content (mg GAE/g extract)
S. commune	CWE	19.0 ± 1.3 ^{b}	66.7 ± 2.2 ^{e}	14.22 ± 0.02 ^{b}
	HWE	9.2 ± 0.5 ^{c}	76.3 ± 1.2 ^{e}	14.65 ± 0.01 ^{b}
A. polytricha	CWE	5.4 ± 1.1 ^{d}	168.7 ± 9.5 ^{b}	19.81 ± 0.56 ^{a}
	HWE	6.2 ± 0.2 ^{d}	140.8 ± 6.9 ^{c}	12.11 ± 0.09 ^{b}
P. ostreatus	CWE	20.3 ± 0.4 ^{b}	235.8 ± 16.5 ^{a}	13.06 ± 0.23 ^{b}
	HWE	25.1 ± 0.5 ^{a}	253.6 ± 2.2 ^{a}	12.12 ± 0.66 ^{b}
G. lucidum	CWE	3.0 ± 0.6 ^{e}	63.2 ± 0.1 ^{e}	7.15 ± 0.99 ^{c}
	HWE	4.9 ± 0.7 ^{d,e}	101.7 ± 0.1 ^{d}	20.79 ± 4.21 ^{a}

Each value is expressed as mean ± SD. Means in a column that do not share a superscript letter are significantly different at $p < 0.05$ by one-way ANOVA. CWE = cold-water extract; HWE = hot-water extract

3.2. Total Phenolic Content, Total Polysaccharide Content and Glucan Content of Mushroom Extracts

Extraction temperature can influence the chemical composition of the obtained extracts, and subsequently also affect the extracts' biological activity [23]. Polyphenols are a large group of biologically active metabolites present in mushroom species, with phenolic acids and flavonoids commonly associated with the antioxidant activity of mushrooms [24]. The phenolic content of an extract depends on the type of sample as well as the solvent and temperature used in the extraction process. In general, significant differences ($p < 0.05$) in total phenolic content were observed between cold and hot water extracts of a mushroom as well as between each mushroom type (Table 1). Our results were not in accordance with previous work [25], where it was found that aqueous extract of *P. ostreatus* contained about 4 to 5 mg GAE/g of total phenolics. Song and Van Griensven [26] reported 0.13–2.78 mg GAE/mL total phenolic content for hot-water extract from *G. lucidum*, which is consistent with our results. The value reported from a study [27] for *A. polytricha* aqueous fraction was 15.10 ± 0.13 mg GAE/g. However, it is crucial to note that the extraction methods employed by these previous works were not entirely similar—there were differences in extraction time as well as solvent and sample ratios.

Many health-promoting properties of mushrooms have also been attributed to their polysaccharide content. The majority of polysaccharides isolated from fungi are water-insoluble, and water-soluble polysaccharides are mostly heteropolysaccharides [28]. Different materials and extraction methods affect the polysaccharide concentration of mushrooms and therefore affect the overall bioactive compound content of the mushroom extracts and subsequently their biological activity [29]. As shown

in Table 1, a significantly ($p < 0.05$) higher polysaccharide content was recorded for *P. ostreatus* in both cold- and hot-water extracts, compared to other extracts from other mushrooms. Similar to the results for total phenolic content, a substantial difference in polysaccharide content was observed between cold- and hot-water extracts of *G. lucidum*. Our results show that extraction at high temperature benefited the extraction of polysaccharides from the mushrooms used in this study except for *A. polytricha*. Previous reports suggested that the optimum temperature for polysaccharide extraction from mushroom fruitbodies is in the range of 90 to 100 °C [30,31]. This is due to the fact that a high extraction temperature is required to adequately break the cell wall structure and successively release the polysaccharide compounds from the cells, as described by Yuan et al. [32].

Mushroom β-glucans are fibres that have been reported to possess various biological functions [33]. β-Glucans exhibit numerous types of biological activity such as antioxidant, anti-tumour, anti-ageing, antimicrobial, anti-inflammatory and many more [34,35], and thus can be exploited in a wide variety of industrial applications. The glucan content of hot- and cold-water extracts of the four selected edible mushrooms is reported in Table 2. Similar to the phenolic and polysaccharide content, large variability can be observed in the mushroom species. According to these preliminary data, extracts from *S. commune* seem to be the richer source of β-glucan, but more analyses are necessary to confirm these results. A previous study [36] observed a high β-glucan content from caps and stipes of *P. ostreatus* and *Auricularia* sp. Our results showed a low content of α-glucan, which is in accordance with a previous report [37] which stated that commonly cultivated mushrooms contain less than approximately 10% α-glucan.

Table 2. Total glucan, α-glucan and β-glucan content of extracts from multiple types of mushroom.

Mushroom	Extract	Total Glucan Content (%)	α-Glucan Content (%)	β-Glucan Content (%)
S. commune	CWE	34.72 ± 1.94 ^{a}	4.30 ± 0.40 ^{b}	29.97 ± 1.55 ^{a}
	HWE	34.26 ± 0.82 ^{a}	2.22 ± 1.14 ^{b}	32.05 ± 1.97 ^{a}
A. polytricha	CWE	33.42 ± 5.16 ^{a}	13.59 ± 2.63 ^{a}	19.83 ± 7.81 ^{a,b}
	HWE	31.09 ± 2.33 ^{a}	5.14 ± 0.47 ^{b}	25.96 ± 2.81 ^{a}
P. ostreatus	CWE	27.35 ± 0.28 ^{a}	1.46 ± 0.18 ^{b}	25.89 ± 0.46 ^{a}
	HWE	29.95 ± 0.98 ^{a}	2.11 ± 0.83 ^{b}	27.85 ± 1.80 ^{a}
G. lucidum	CWE	10.12 ± 0.16 ^{b}	1.69 ± 0.14 ^{b}	8.44 ± 0.29 ^{b}
	HWE	10.67 ± 1.05 ^{b}	0.96 ± 0.46 ^{b}	9.72 ± 1.51 ^{b}

Each value is expressed as mean ± SD. Means in a column that do not share a superscript letter are significantly different at $p < 0.05$ by one-way ANOVA. CWE = cold-water extract; HWE = hot-water extract

3.3. Antioxidant Activity of Mushroom Extracts

An antioxidant is 'any substance that directly scavenges reactive oxygen species (ROS) or indirectly acts to upregulate antioxidant defences or inhibit ROS production' [38]. Extracts or compounds with effective antioxidative properties are among the most important ingredients in cosmeceuticals and skincare formulations. Antioxidants protect the skin by their ability to counteract UV-induced insults to the skin. Over-exposure of skin to UV rays and air pollutants leads to the dramatic production of ROS, resulting in oxidative stress [39]. Induction of inflammation, DNA damage and alterations to lipids and proteins are some of the detrimental effects of oxidative stress in human skin cells, which consequently advance to accelerated or premature ageing as well as hyper-pigmentation. Although human skin contains a pool of protective endogenous antioxidants such as catalase and glutathione peroxidase [40], exogenous antioxidants through diet and topical applications are essential to support our body's self-protection [41]. Apart from their direct protection of human skin, antioxidants are also used to

preserve and protect skincare and cosmeceutical formulations from auto-oxidation caused by chemical degradation or exposure to air.

The antioxidant activity of hot- and cold-water extracts of selected mushrooms was analysed by means of DPPH radical scavenging, FRAP and SOA inhibition assays. These assays are based on electron transfer reactions, and measure the capacity of antioxidants to reduce an oxidant which changes colour when reduced [42]. Apak et al. [43] explained that these assays use different chromogenic redox reagents with different standard potentials. Figure 2 shows the DPPH radical scavenging activity and FRAP of cold and hot water extracts of selected mushrooms. Hot-water extract of *G. lucidum* possessed significantly ($p < 0.05$) higher DPPH scavenging activity than other mushroom extracts, with a value of 89.5 ± 0.5%. The FRAP of *G. lucidum* hot-water extract (355.9 mM FE(II)/g crude extract) was 3.5-fold higher than that of the cold-water extract and significantly ($p < 0.05$) the highest among all mushroom extracts. For both assays, extracts from *P. ostreatus* showed the lowest antioxidant activity. The current study has results consistent with those reported by Boonsong et al. [44] who observed moderate DPPH radical scavenging activity of *Auricularia* sp. water extract. Meanwhile, DPPH radical scavenging activity of 69.79 ± 0.13% and 67.17 ± 5.88% was observed for *S. commune* crude ethanol extract and its water fraction, respectively, in previous research [45].

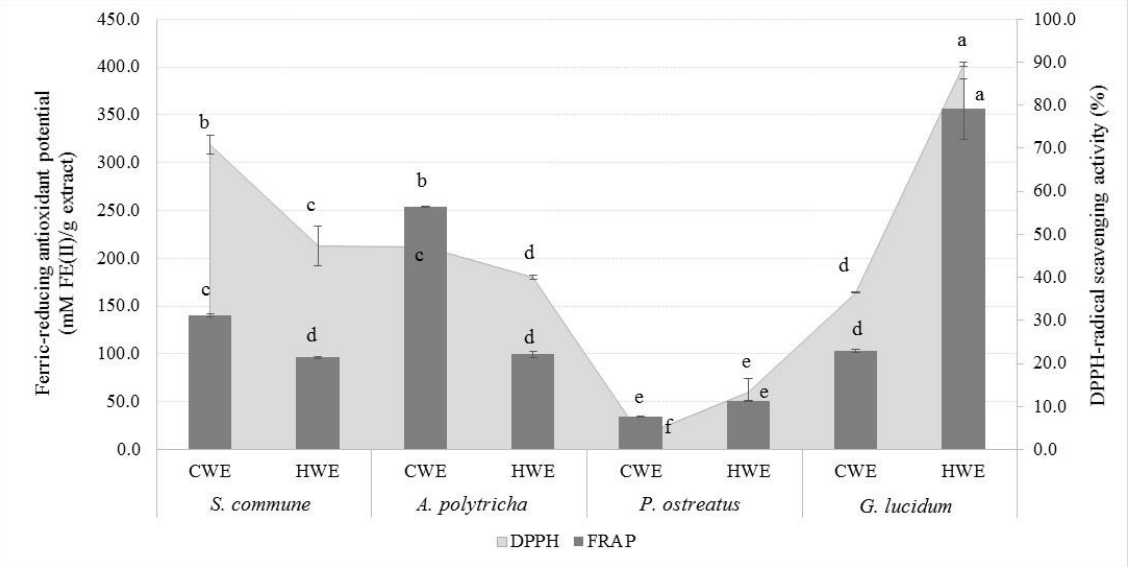

Figure 2. DPPH radical scavenging activity and ferric-reducing antioxidant potential (FRAP) of extracts from multiple types of mushroom. The values with the same letter in each category are not significantly different at $p > 0.05$ by one-way ANOVA.

SOA are the precursor of powerful free radicals such as nitric oxide [46]. Inhibition of SOA prevents the formation of ROS, and samples or extracts that are capable of SOA inhibition function as antioxidants. Our results indicate that cold-water extract of *S. commune* exhibited the highest SOA inhibition activity (94.82 ± 1.29%) and was comparable with the positive control used in this study (Figure 3). Teoh et al. [27] observed moderate SOA inhibition activity of the aqueous fraction from *A. polytricha*, while Boonsong et al. [44] reported below 40% SOA inhibition activity of *Pleurotus* water extracts. Interestingly, extraction using cold water produced substantially higher antioxidant activity for *S. commune* and *A. polytricha*, while antioxidant activity was lower in cold-water extracts compared to hot-water extracts for *P. ostreatus* and *G. lucidum*. Consistent outcomes were observed in a preceding study [25], where boiling treatment for extraction of *P. ostreatus* resulted in higher DPPH radical scavenging activity than that of the extract obtained at room temperature. This heavily implies that the effect of extraction temperature on antioxidant activity varies in different types of mushroom.

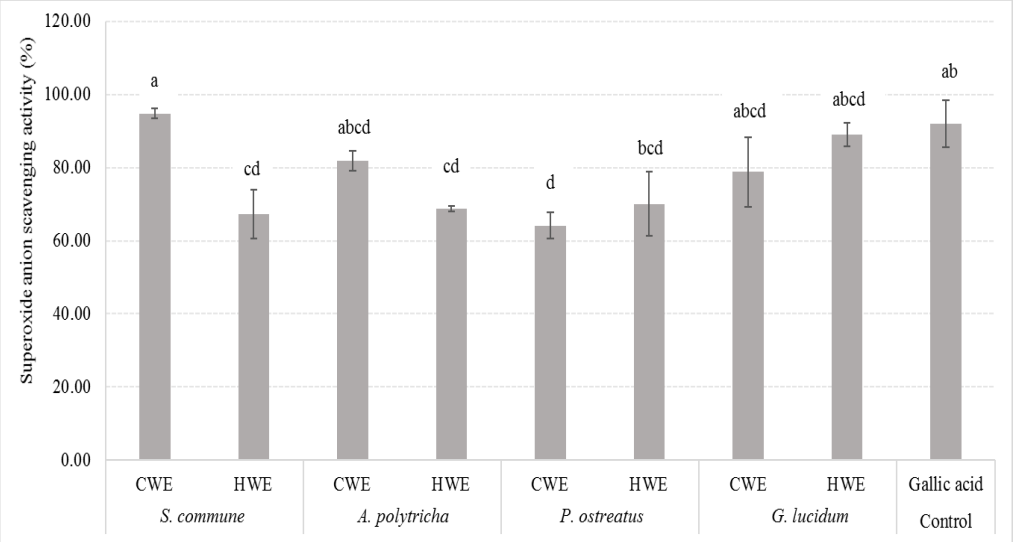

Figure 3. Superoxide anion scavenging activity of extracts from multiple types of mushroom. The values with the same letter in each category are not significantly different at $p > 0.05$ by one-way ANOVA.

The correlation coefficients of the content of different components of mushroom extracts and their respective biological activity are shown in Table 3.

Table 3. Correlation coefficients of the content of different components of mushroom extracts and their respective biological activity.

Biological Activity	Relation	Pearson *r*	R^2
Antioxidant activity (Superoxide anion scavenging activity)	SOA/TPC	0.401	0.160
	SOA/TPolC	0.541	0.293
	SOA/BG	0.373	0.139
Antioxidant activity (DPPH radical scavenging activity)	DPPH/TPC	0.572	0.327
	DPPH/TPolC	0.722	0.521
	DPPH/BG	0.323	0.104
Antioxidant activity (Ferric-reducing activity)	FRAP/TPC	0.802	0.642
	FRAP/TPolC	0.342	0.117
	FRAP/BG	0.572	0.327
Hyaluronidase inhibition activity	Anti-Hya/TPC	0.214	0.046
	Anti-Hya/TPolC	0.249	0.062
	Anti-Hya/BG	0.702	0.494
Tyrosinase inhibition activity	Anti-Tyro/TPC	0.087	0.008
	Anti-Tyro/TPolC	0.712	0.506
	Anti-Tyro/BG	0.015	0.000

TPC = total phenolic content; TPolC = total polysaccharide content; BG = β-glucan content; SOA = superoxide anion; FRAP = ferric-reducing antioxidant potential.

In general, there was insignificant ($p > 0.05$) weak correlation between antioxidant activity and the total phenolic content, total polysaccharide content and β-glucan content of mushroom extracts. However, FRAP of mushroom extracts was positively correlated ($p < 0.05$) with the total phenolic content. A similar observation was found for the correlation of DPPH radical scavenging activity with total polysaccharide content. The antioxidant activity of these mushroom extracts seems to be

determined by the concentration of the mixture of biological compounds, dependent on the mushroom species or the method of extraction. It is well known that the antioxidant activity of an extract is attributed to the interactive effects of various kinds of compound present in the extract [47,48]. The effect can be additive, synergistic or antagonistic. Polyphenols, polysaccharides, vitamins, carotenoids, ergothioneine, tocopherols and minerals are the bioactive compounds that contribute to the antioxidant activity of mushrooms [49]. Apart from antioxidative properties, some antioxidant compounds such as polyphenols also possess pro-oxidative capacity.

3.4. Hyaluronidase and Tyrosinase Inhibition Activity of Mushroom Extracts

Mushrooms are rich in anti-inflammatory components such as polysaccharides, phenolic compounds, vitamins and fatty acids [50]. In this study, the anti-inflammatory capacity of mushroom extracts was measured by determining hyaluronidase inhibition. Hyaluronidase is an enzyme related to the inflammation process, which depolymerizes hyaluronic acid present in the extracellular matrix of connective tissues [51]. The functions of hyaluronic acid, also known as hyaluronan, include lubrication of joints and hydration, and it has a key role in tissue regeneration (skin healing and wound repairing), inflammation response and angiogenesis. Therefore, hyaluronidase inhibition activity is also being used to measure the anti-ageing potential of a sample. Hyaluronidase inhibitors are effective in suppressing inflammation and also function as anti-allergenics [52].

As shown in Figure 4, cold- and hot-water extracts of *P. ostreatus* and *G. lucidum* as well as cold-water extract from *A. polytricha* reached above 50% inhibition of hyaluronidase. The results show that the hot-water extract of *G. lucidum* has significant ability to inhibit hyaluronidase compared with other extracts, with a value of 72.78%. None of the tested extracts showed hyaluronidase inhibition comparable with the positive control, 500 µg/mL quercetin, at 87.51 ± 2.31% (data not shown). Another species of *Pleurotus* has been investigated for its anti-hyaluronidase activity; the hot-water extract from *P. citrinopileatus* did not inhibit the activity of hyaluronidase enzyme [53]. To the best of our knowledge, there is no report on the hyaluronidase inhibition activity of extracts from these selected mushrooms. However, a previous study reported hyaluronidase inhibition activity of extracts from *Pleurotus tuber-regium* (Rumph. Ex Fr.) Singer and *Trametes lactinea* (Berk.) Sacc. [54,55]. There are also reports on anti-inflammatory properties evaluated using a nitric oxide inhibition assay and other in vitro and in vivo methods such as those on *G. lucidum* [56,57], *A. polytricha* [58] and *S. commune* [59]. It is interesting to note that these studies were done on different types of mushroom extract such as mycelium extract and polysaccharide extracts. So far, the bioactive compounds responsible for the hyaluronidase inhibition activity of mushrooms have not been identified and reported.

Tyrosinase is a key enzyme for melanin biosynthesis. Hyperpigmentation or overproduction of melanin may result in a darker appearance of the skin. Thus, tyrosinase inhibitors are much sought after by cosmetics companies for the purpose of lightening the skin or protecting it from hyperpigmentation. Some phenolic compounds and their derivatives such as ferulic acid, caffeic acid and *p*-coumaric acid have been described to possess anti-tyrosinase activity [9]. Antioxidant compounds may also function as tyrosinase inhibitors, as deduced by Yoon et al. [60]. Exposure of skin to UV rays causes the formation of ROS and subsequently enhances melanin production by triggering tyrosinase activity. Thus, antioxidants or ROS inhibitors may reduce pigmentation by inhibiting tyrosinase. As depicted in Figure 4, cold-water extract from *S. commune* exhibited substantially high tyrosinase inhibition activity (98.15 ± 3.21%) and was significantly ($p < 0.05$) comparable with the positive control used in the assay, kojic acid (94.4%, data not shown). Extracts from *G. lucidum* exhibited moderate tyrosinase inhibition activity (30.56–45.37%) while extracts from *A. polytricha* and *P. ostreatus* did not display any tyrosinase inhibition activity. Our results do not conform with a previous study [17] which recorded 9.60–49.60% anti-tyrosinase activity for hot-water extract of *P. ostreatus*. No inhibition of tyrosinase has been reported in extracts from *A. polytricha* and therefore no comparison can be made. Previous research [60] has described tyrosinase inhibition activity in various extracts of the basidiomycete mushroom *Lentinus lepideus*.

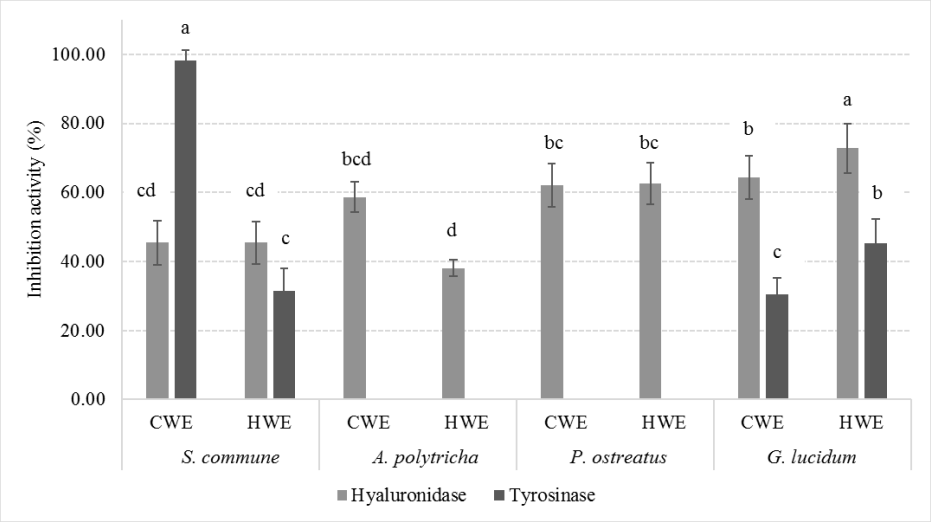

Figure 4. Hyaluronidase and tyrosinase inhibition activity of extracts from multiple types of mushroom. The values with the same letter in each category are not significantly different at $p > 0.05$ by one-way ANOVA.

There was a significant ($p < 0.05$) positive correlation between the tyrosinase inhibition activity of mushroom extracts and total polysaccharide content (Table 3). To date, there is no research regarding the relationship of mushroom polysaccharides with tyrosinase inhibition activity; however, previous studies have reported significant tyrosinase inhibition activity of polysaccharides from plant extracts [61,62]. Although phenolic compounds such as ferulic, *p*-coumaric and caffeic acids are known to be effective inhibitors of tyrosinase [63], no correlation was observed between the tyrosinase inhibition activity of the mushroom extracts studied and their corresponding phenolic content. This proves that, similar to antioxidant activity, tyrosinase inhibition activity in an extract can be attributed to the interaction between compounds present in the extract. Combinations of compounds bring about changes in the ultimate biological effects of each compound present in an extract [64].

4. Conclusions

The findings of this study demonstrate that the extraction methods used in the study resulted in varying outcomes for different types of mushroom. On the basis of the experimental evidence in this study, hot-water extract of *G. lucidum* and cold-water extract of *S. commune* possess the potential to be developed into health or cosmeceutical products. A significant strong correlation of biological activities of the mushroom extracts with its corresponding biological components was found only between DPPH radical scavenging and anti-tyrosinase activity with total polysaccharide content; and FRAP with total phenolic content. Further studies need to be conducted in order to determine the bioactive compounds responsible for the ascribed activities as well as the mechanisms of action. To fully explore the potential of these extracts, bioassay-guided fractionation and identification of compounds by chromatographic methods may be undertaken. Due to the popularity of *G. lucidum* in cosmetic preparations, future research should focus more on developing the active extracts of *S. commune*.

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