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Potentials of rose (*Rosa damascena*) petals and receptacles extract as antioxidant and antihyaluronidase

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ABSTRACT

Free radicals affect aging by unspecific lead breakdown to macromolecules, like DNA, lipids, and proteins. The degradation of the extracellular matrix affects skin aging and correlated with the hyaluronidase enzyme. Rose (*Rosa damascena*) petal extract and rose receptacle extract can scavenge free radicals, thus hindering the aging process. This study examined phenolic and flavonoid content, the antioxidant, anti-hyaluronidase potential from rose petal extract (RPE) and rose receptacle extract (RRE) inhibiting skin aging. In this study, hydrogen peroxide (H_2O_2) scavenging activity assay was done to analyze the antioxidant activity. Futhermore, the hyaluronidase inhibitory assay was done to analyse the antiaging activity. The characteristic of RPE and RRE were measured the phenolics and flavonoids content. The phenolics content of RPE and RRE were 9.66 µg GAE/mg RPE and 4.31 µg GAE/mg RRE, respectively, while the flavonoids content of RPE and RRE were 1.22 µg QE/mg RPE and 0.59 µg QE/mg RRE, respectively. The median inhibitory (IC_{50}) of H_2O_2 scavenging of RPE (207.99 µg/mL) was more active than RRE (348.24 µg/mL). RPE's anti-hyaluronidase (IC_{50}: 51.68 µg/mL) was as effective as RRE (IC_{50}: 51.98 µg/mL). Antioxidant and antiaging activities from RPE and RRE are promising natural agents for aging therapy.

Keywords: Antioxidant, antiaging, hyaluronidase, *Rosa damascena*

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INTRODUCTION

Aging is a natural process that cannot be avoided by anyone. Environmental changes that occur globally, increased air pollution, and the depletion of the ozone layer that causes direct sun radiation hit on human skin are thought to cause accelerated cell degeneration, ultimately leading to premature aging. Many factors cause premature aging, including heredity, health, endurance, mental health, free radicals, and behavior/lifestyle (Widowati et al., 2018a).

Many people use cosmetics to prevent premature aging. However, most cosmetics use synthetic ingredients so that they will have side effects and are not safe when used in the long run. Therefore, cosmetics made from natural ingredients with antioxidant and antiaging activities are needed (Pujimulyani et al., 2020).

There have been many studies that use natural ingredients to prevent aging. Benefits taken from these natural ingredients are antioxidant properties because they can bind to free radicals. There are a variety of plants that have antioxidant and antiaging effects. One of them is a rose (*Rosa damascena*).

The pharmacological effects of roses based on their chemical content include: antiviral, antibacterial, antioxidant, antitussive, relaxant, hypnotic, and antidiabetic effects. Rose vapor therapy can even cure allergies, headaches, and migraines (Boskabady et al., 2011). Ethanol extract of roses at doses of 100, 500, and 1000 mg/kg has been proven to provide analgesic effects on mice that work centrally. Analgesic effects that arise thought to be caused by quercetin and kaempferol (Rakhshandeh et al., 2008).

From the problems and research that support it and considering its utilization is still lacking in the medical field, researchers want to know whether the rose petal extract and the base of the rose (*Rosa damascena*) can function as antioxidant and antiaging (anti-hyaluronidase).

MATERIALS AND METHOD

Materials

The subjects of this study were the petal and receptacle extracts of *R. damascena*, which were obtained from Cihideung Rose Farm, West Bandung Regency, Indonesia, and were identified at Herbarium Laboratory, Department of Biology, School of Life Science and Technology, Bandung, West Java, Indonesia. The number of identification letter is 3632/11.CO2.2/PL/2019. The main ingredient used for the H_2O_2 scavenging activity assay was hydrogen peroxide (Merck 1.08597.1000), while for the anti-hyaluronidase test was hyaluronidase from bovine testes type IS (Sigma-Aldrich, H3506).

Methods

R. damascena extract preparation

The rose petals and receptacles were weighed and mashed up to get the simplicia. The wet weight of rose petals was 1400 g while the wet weight of rose receptacles was 700 g. Each petal and receptacle of *R. damascena* 250 g and 90 g, respectively, were soaked and extracted with a maceration method using distilled ethanol 70%. Every 24 h, it was filtered, and the residue was re-macerated until the filtrate was colorless. Then collected filtrate was concentrated by using an evaporator (Zhengzhou Well-known, RE-201D) at 50°C to obtain the extract. RPE and RRE yields were 88.56 g and 2.72 g, respectively. The extracts were stored at -20°C (Asan et al., 2019; Girsang et al., 2019; Liana et al., 2019; Vrianty et al., 2019; Widowati et al., 2018b).

Total phenolic content assay

Total phenolic content was measured by using the modified Folin-Ciocalteu method. In the sample well, the gallic acid, RPE, and RRE as much as 15 µL were mixed with Folin-Ciocalteu's reagent as much as 75 µL and sodium carbonate as much as 60 µL. The blank solution was introduced 135 µL of 10% DMSO and 15 µL of gallic acid, RPE, and RRE. The plate was heated for 10 mins at

50˚C. Furthermore, the absorbance was determined using a microplate reader (Multiskan Go Thermo Fisher Scientific) at 760 nm. Total phenolic content determined as gallic acid equivalence (GAE) in µg/mg sample (Widowati et al., 2016; 2017; 2018b; Prahastuti et al., 2019; 2020).

Total flavonoid content assay

Flavonoid content was conducted using the modified method (Prahastuti *et al.*, 2019; 2020). Briefly, 15 µL standard solution (quercetin) made in various concentration (100; 50; 25; 12.50; 6.25; 3.13; 1.56 µg/mL), RPE, and RRE (1000 µg/mL) were mixed with 75 µL $AlCl_3$. The absorbance read at 415 nm. The standard absorbance used to calculate the linear regression equation (y = ax + b) to analyze the sample's flavonoid content. The flavonoid content presented as quercetin equivalence (QE) in µg/mg sample (Prahastuti *et al.*, 2019; 2020).

Radical scavenging activity of H_2O_2

This assay was measured using a modified method (Utami et al., 2017). Briefly, 60 µL of the sample at various concentrations (500, 250, 125, 62.5, 31.25, and 16.625 µg/mL), 12 µL ferrous ammonium sulfate (1 mM), 3 µL of H_2O_2 5 mM were added into the sample well plate. The control well contained 12 µL ferrous ammonium sulfate and 63 µL DMSO 10%. It was incubated in a dark room at room temperature for 5 mins. After that, 75 µL 1,10-phenanthroline (1mM) was added into each sample and control well. Then it was incubated again in the same condition for 10 mins. The absorbances were determined at 510 nm (Asan et al., 2019; Jusri et al., 2019; Liana et al., 2019; Utami et al., 2017). The scavenging activities percentage of samples were calculated using this following formula :

H_2O_2 Scavenging Activity (%) = (Ac – As)/Ac × 100
Ac: control absorbance
As: sample absorbance

Hyaluronidase inhibitory activity

This activity was measured by a modified method (Widowati et al., 2016, 2017, 2018b; Asan et al., 2019; Liana et al., 2019). A mixture of RPE, RRE at various concentrations (166.67, 83.33, 41.67, 20.83, 10.42, and 5.21 µg/mL) each at 25 µL, 3 µL hyaluronidase, 12 µL phosphate buffer (300 mM, pH 5.35) was incubated at 37°C for 10 mins. Thereupon, 10 µL hyaluronic acid substrate (Sigma Aldrich, H5542) was added and incubated again at the same temperature for 45 mins. Then, 100 µL acidic albumin was added to stop the reaction. The mixed solution incubated again at room temperature for 10 minutes. The absorbance was read using a wavelength at 600 nm. The inhibition activity was calculated using the following formula:

Elastase Inhibitory Activity (%) = (Ac-As)/Ac x 100
Ac: control absorbance
As: sample absorbance

Statistical analysis

The value was presented as Mean ± Standard Deviation. Significant differences between the groups were determined using the Analysis of Variance (One Way ANOVA) followed by Tukey's HSD Post-hoc Test in SPSS software (version 20.0). The results of H_2O_2 scavenging and anti-hyaluronidase activity tests were continued by linear regression analysis to calculate the median inhibitory concentration (IC_{50}).

RESULT AND DISCUSSION

The percentage of RPE and RRE yield were 35.4% and 3.02%, respectively. These results indicated that RRE has a better yield than RPE. According to Boskabady et al. (2011), secondary metabolite compounds in *R. damascena* include flavonoids and terpenoids. According to Elfitriani et al. (2020), RPE and RRE contained flavonoids, phenolics, tannins, and alkaloids. In this study, total phenolic and flavonoid content were examined. Total phenolics were conducted by a colorimetric method (Prahastuti et al., 2019; 2020; Widowati et al., 2016; 2017; 2018b). The total polyphenols were quantified using the standard curve of gallic acid (Figure 1). The experiments declared the availability of phenolics in the RPE and RRE were 9.66 ± 1.26 µg GAE/mg RPE and 4.31±0.25 µg GAE/mg RRE, respectively. This result was higher than phenolic compounds from methanol extract of fresh flowers reported by Baydar et al. (2013), which was 0.72 mg/g dw. Rose types affected phenolic content. Yunnan rose (*R. centifolia*), China rose (*R. chinensis*), French rose (*R. gallica*), Rose (*R. rugosa*), White rose (*R. rugosa*) have phenolic content as much as 108.94; 248.8; 111.34; 312.21; 39.47 mg GAE/g, respectively (Zheng et al., 2018). Their phenolic contents were higher compared to this data result. The phenolic content in plants was correlated with total anthocyanins (Schmitzer et al., 2009). The phenol content of RPE was higher than RRE. This data was validated with previous research that petal of *R. canina* 1954 mg GAE/50 mL and fruit of *R. canina* 937 mg GAE/50 mL (Moghaddam and Shaaban, 2018).

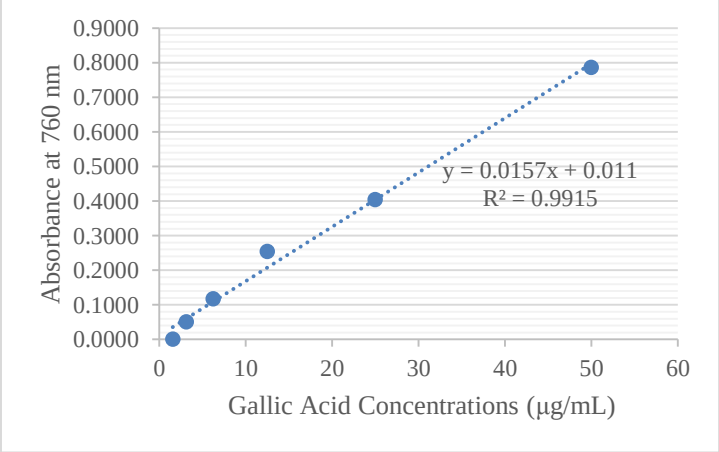

Figure 1. Standard curve of gallic acid

The standard curve of quercetin for total flavonoids determination can be seen in Figure 2. Its quantification declared that the availability of flavonoids in RPE and RRE were 1.22±0.06 µg QE/mg RPE and 0.59±0.03 µg QE/mg RRE, respectively. Shameh et al. (2019) reported that the total flavonoid of *R. canina* was 2.53 mg QE/g FW. The flavonoid content of China rose 24.13 mg Catechin equivalent/g (Zheng et al., 2018). This data was in line with previous data that the petal of *R. canina* contained 776 QE mg/ml higher than fruit of *R. canina* 450 QE mg/mL (Moghaddam and Shaaban, 2018). Different *Rosa* genotypes contain rich phytochemical compounds that have significant variations in their levels (Shameh et al., 2019).

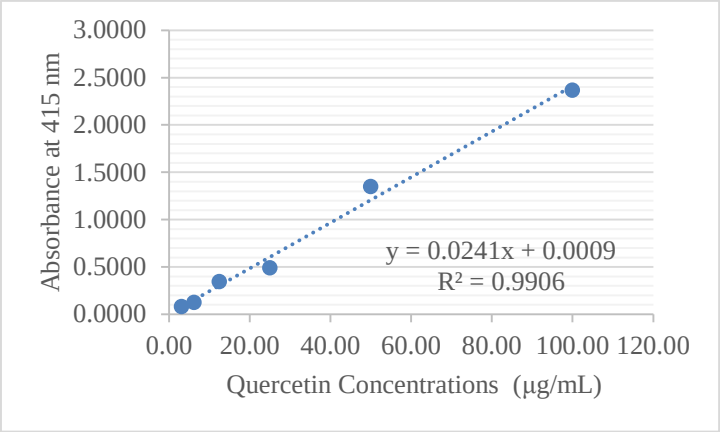

Figure 2. Standard curve of quercetin

Antioxidants are compounds that have the ability to neutralize or reduce the negative effects of free radicals, molecules that have unpaired electrons in an outer circle. From various research results, antioxidants are reported to slow the process caused by free radicals such as the presence of phenolic- and flavonoid-rich natural diets (Aryal et al., 2019).

Flavonoid compounds today are commonly studied as antioxidants because of their ability to change or reduce the risk that can be caused by free radicals (Aryal et al., 2019). Patil et al. (2015) reported that RPE showed potent antioxidant as free radical scavenging activities by DPPH, inhibiting pyrogallol red bleach by peroxynitrite, ABTS, xanthine oxidase, superoxide scavenging, and ascorbate iron-induced lipid peroxidation assay. Flavonoids and phenolics, which are polar phytoconstituents from RPE, are well-known antioxidants, free radical scavengers, and antibacterial (Tatke et al., 2015). There are still not many studies of RRE, especially of its antioxidant activity.

The results of H_2O_2 scavenging activities from RPE and RRE can be seen in Figure 3, while IC_{50} values can be seen in Table 1. RPE is more active in H_2O_2 scavenging activity than RRE. At the highest concentration (500 µg/mL), the RPE scavenging activity was at 79.26 ± 0.10%, while the RRE was at 67.29 ± 1.76%. According to Marjoni and Zulfisa (2017), RPE was categorized moderate when the IC_{50} value 101-250 µg/mL and RRE as a weak antioxidant when the IC_{50} value was above 250 µg/mL.

There are still no studies of H_2O_2 scavenging activity in *R. damascena* plants, but some studies reported its antioxidant activity. Alam *et al.* (2008) reported that *R. damascena* extract has excellent antioxidant activity against DPPH (IC_{50}=162.525 µg/mL) comparable to ascorbic acid as a standard drug (IC_{50}=64.307 µg/mL). Rose petal and rose receptacle extracts have antioxidant activity toward 2,2'-azino-bis(3-ethylbenzothiazoline-6sulfonic acid (ABTS) with IC_{50} value 4.46 µg/mL, and 15.49 µg/mL, respectively (Mawarni et al., 2020), which categorized highly active (Marjoni and Zulfisa, 2017).

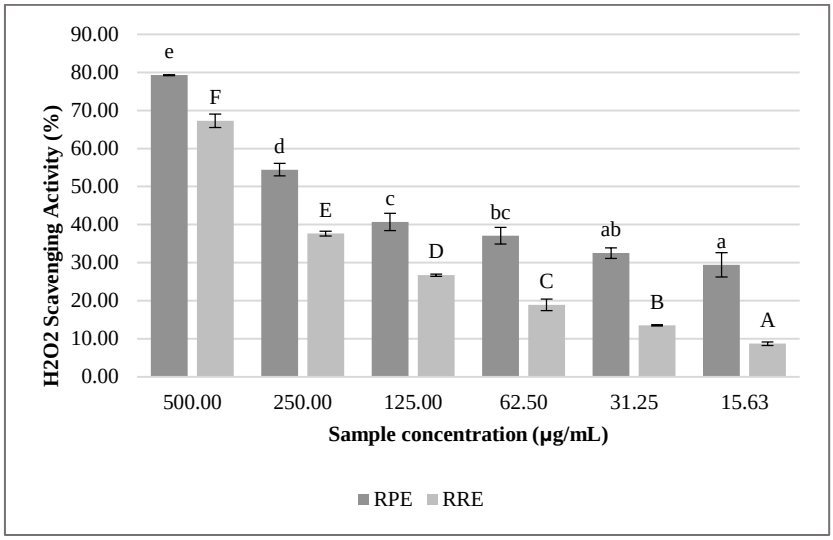

Figure 3. Histogram effects of various rose petal extract and rose receptacle extract concentrations on H_2O_2 scavenging activity

*Data are shown as means ± standard deviation. The different letters (a,ab,bc,c,d,e) among RPE concentrations and differences letters (A,B,C,D,E,F) among RRE concentrations show significant differences at P <0.05 based on Tukey HSD post hoc test.

Table 1. The IC_{50} values of rose petal extract and rose receptacle extract H_2O_2 scavenging activities

Sample	Equation	R^2	IC_{50} (µg/mL)	IC_{50} (µg/mL)
RPE (replication 1)	y = 0.1014x + 28.365	0.99	213.36	
RPE (replication 2)	y = 0.1012x + 28.952	0.98	207.98	207.99 ± 5.38
RPE (replication 3)	y = 0.0988x + 29.982	0.99	202.61	
RRE (replication 1)	y = 0.118x + 9.6511	0.99	341.94	
RRE (replication 2)	y = 0.1162x + 10.362	0.99	341.12	348.24 ± 11.63
RRE (replication 3)	y = 0.1113x + 9.7472	0.99	361.66	

The antioxidant activity test against hydrogen peroxide (H_2O_2) was determined by using the ferrous ammonium sulfate and phenanthroline reaction. When ferrous ammonium sulfate reacts with phenanthroline, an orange-colored Fe^{2+}-tri-phenanthroline complex is formed. The H_2O_2 presence in the reaction will cause the complex not to be formed. So if there is an antioxidant that traps H_2O_2, then the mixture color is orange that show the presence of Fe^{2+}-tri-phenanthroline complex (Stevenie et al., 2019; Asan et al., 2019; Jusri et al., 2019; Liana et al., 2019; Utami et al., 2017).

Hyaluronidase is a proteases group that can degrade the hyaluronic acid (HA), one of the extracellular matrix (ECM) constituents, by catalyzing hyaluronic hydrolysis reactions. It can decreases the viscosity of hyaluronan, thereby increasing ECM and tissue permeability. In this method, the enzyme activity can be detected by measuring HA levels because of its ability to react with albumin acid solution to form turbidity (turbidity). Turbidity that can be read starting from 540 nm is proportional to the concentration of HA. The enzyme inhibitory activity determined based on the HA higher concentration remaining after the reaction is stopped (Stevenie et al., 2019; Asan et al., 2019; Jusri et al., 2019; Liana et al., 2019; Utami et al., 2017).

In the anti-hyaluronidase activity test, the final concentration of the sample used was 166.67 µg/mL; 83.33 µg/mL; 41.67 µg/mL; 20.83 µg/mL; 10.42 µg/mL; and 5.22 µg/mL. The results of anti-hyaluronidase activities from RPE and RRE can be seen in Figure 4, while IC_{50} values can be seen in Table 2. The anti-hyaluronidase activity of RPE is as effective as RRE (Figure 4).

Table 2. The IC_{50} values of anti-hyaluronidase activities of rose petal extract and rose receptacle extract

Sample	Equation	R^2	IC_{50} (µg/mL)	IC_{50} (µg/mL)
RPE (replication 1)	y = 0.3277x + 32.002	0.99	54.92	
RPE (replication 2)	y = 0.3274x + 32.862	0.99	52.35	51.68 ± 3.62
RPE (replication 3)	y = 0.3447x + 33.529	0.98	47.78	
RRE (replication 1)	y = 0.4164x + 27.472	0.96	54.10	
RRE (replication 2)	y = 0.4658x + 27.165	0.99	49.02	51.98 ± 2.64
RRE (replication 3)	y = 0.4334x + 27.107	0.99	52.82	

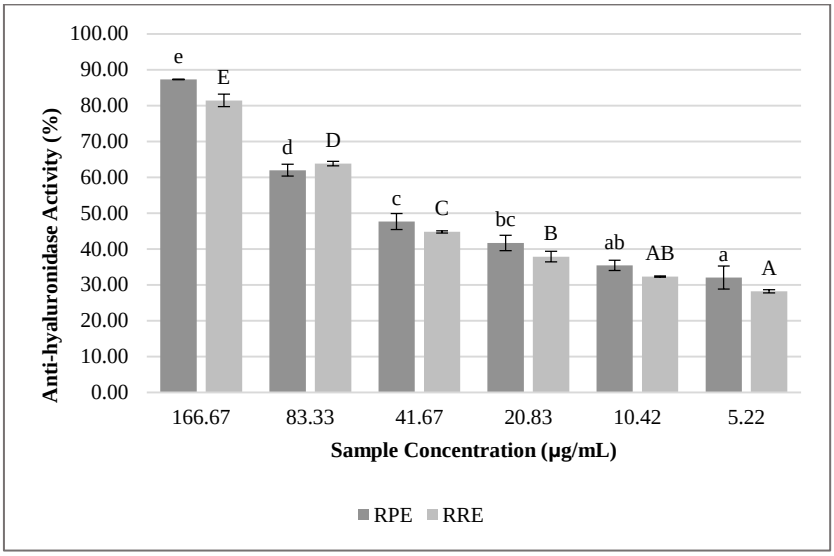

Figure 4. Effects of various rose petal extract and rose receptacle extract concentrations on the anti-hyaluronidase activity

*Data are shown as means ± standard deviation. Different letter (a,ab,bc,c,d,e) among RPE concentrations and different letter (A,AB,B,C,D,E) among RPE concentrations show significant differences at P <0.05 based on Tukey HSD post hoc test.

At the highest concentration (166.67 µg/mL), RPE had an anti-hyaluronidase activity of 87.27 ± 1.16%, followed by an RRE of 81.44 ± 3.48%. The IC_{50} value of RPE and RRE were categorized active when IC_{50} value reaches 50-100 µg/mL (Marjoni and Zulfisa, 2017).

There are still no studies of hyaluronidase activity in *R. damascena* plants, but some studies reported its antiaging activity. Rozalia et al. (2016) reported that *R. damascena* has antiaging activity inhibiting 80% of collagenase activity at 100 µg/mL. RPE and RRE had an anti-elastase activity with the IC_{50} value of 17.51 µg/mL; 58.91 µg/mL (Mawarni et al., 2020). Scotti et al. (2016) reported that polyphenolics and flavanoids act as contributing factors eliciting hyaluronidase inhibition. It also

reported that dimeric salicarinin A, B, and C had strong potential to inhibiting hyaluronidase enzyme based on IC_{50} value of 1.6 ±0.1, 1.6±0.2, and 2.5±0.2 µM, respectively.

CONCLUSION

The total phenolic content in this study were 9.66 ± 1.26 µg GAE/mg RPE and 4.31±0.25 µg α GAE/mg RRE, while the total flavonoid contents were 1.22±0.06 µg QE/mg RPE and 0.59±0.03 mg QE/g RRE. In the H_2O_2 scavenging activity, RPE was more active than RRE. In the anti-hyaluronidase activity, RPE was as effective as RRE. Overall, RPE and RRE possess antioxidant and anti-hyaluronidase activities.

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