https://scilett-fsg.uitm.edu.my/
Vol. 17(2) JUNE 2023

ISSN: 1675-7785
eISSN: 2682-8626

DOI: 10.24191/sl.v17i2.19501

Antioxidant Activities of *Ananas comosus* Peel Extracts: A Review on *In Vitro* and *In Vivo* Approaches

Erliana Safri, Norhisham Haron*, Anas Abdullah, Emida Mohamed, Siti Nazrina Camalxaman, and Azlin Sham Ramlee @ Rambely

Centre for Medical Laboratory Technology Studies, Faculty of Health Sciences, Universiti Teknologi Mara (UiTM), Selangor Branch, Puncak Alam Campus, 42300 Puncak Alam, Selangor, Malaysia.

Corresponding author: *hishamharon@uitm.edu.my*

Accepted: 1 February 2023; Published: 21 June 2023

ABSTRACT

Peel of *Ananas comosus* (pineapple) is a valuable waste as it contains antioxidant compounds that exhibit radical scavenging activity, which is capable of preventing oxidative stress, a cause of the development of chronic diseases in humans. Various *in vitro* and *in vivo* methods have been previously applied in studies investigating pineapple peel extract's antioxidant properties. However, different results were reported throughout each study, and limited papers discussed on the antioxidant properties of the peel extract. Therefore, this review summarized the antioxidant activities of *A. comosus* peel extract through different types of *in vitro* and *in vivo* models. The result showed that pineapple peel extracts were able to scavenge different types of free radicals through *in vitro* models as the antioxidant present neutralized the radicals by hydrogen electron transfer (HAT), single electron transfer (SET), or mixed of both reactions. Findings from *in vivo* models showed antioxidative effects as they regulated the level of the enzymes involved in combating free radicals and attenuated lipid peroxidation. The evidence reviewed here suggested that the peel of *A. comosus* could be a source of natural antioxidants. Thus, more studies are required in the future to evaluate its ability to scavenge free radicals effectively.

Keywords: *Ananas comosus, antioxidant, in vitro, in vivo, pineapple peel*

https://scilett-fsg.uitm.edu.my/
Vol. 17(2) JUNE 2023

ISSN: 1675-7785
eISSN: 2682-8626

DOI: 10.24191/sl.v17i2.19501

INTRODUCTION

Free radicals are compounds the human body generates through cellular and immune responses acquired through exposure to X-rays, ozone, cigarette smoke, and air pollution. These radicals include superoxide ($O_2^{\bullet-}$), hydrogen peroxide (H_2O_2), hydroxyl (OH•), nitric oxide (NO•), and singlet oxygen ($^1O_2$), which is defined as reactive oxygen species (ROS). Accumulation of these radicals in cells with the presence of low levels of antioxidants will cause oxidative stress. This condition is responsible for developing chronic diseases such as cancer, diabetes, rheumatoid arthritis, and neurological and cardiovascular diseases [1].

Antioxidants play major roles in providing cell's defense mechanisms where the molecular and enzymatic constituents of antioxidant compounds can act by scavenging chain-initiating radicals, quenching singlet oxygen, decomposing hydroperoxides, and chelating pro-oxidative metal ions [2, 3]. The actions of antioxidants in scavenging free radicals contribute to the prevention of chronic disease development caused by oxidative stress [4, 5]. Although the human body produces its antioxidants, the effectiveness of these antioxidants may not be 100 %, and it gradually decreases with age, denoting the need to gain antioxidants from other sources to maintain their optimum level in the body.

Ananas comosus, commonly known as pineapple, is a well-known plant with an edible fruit that belongs to the Bromeliaceae family. It is widely planted in tropical and subtropical countries where the fruit is fully covered with hard peel, with a crown on top. Besides being freshly consumed, the pineapple fruit is widely processed as juice and commercialized as canned food. The juice of *A. comosus* is believed to provide a source of vitamins, phenols, organic acids, and carbohydrates [6]. *Ananas comosus* also being recognized for carrying high content of bioactive phytochemicals, including phenolic, flavonoids, and other compounds, which provide radical scavenging activities and act as an effective antioxidant.

Studies conducted on different parts of *A. comosus* revealed several phytochemicals that exhibit antioxidant properties, including the peel part of *A. comosus*, which is generally considered waste [7, 8]. Various *in vitro* and *in vivo* models have been applied in studies evaluating pineapple peel extracts' antioxidant properties and scavenging abilities. Therefore, this review article emphasized the *in vitro* and *in vivo* antioxidant activities of *A. comosus* peel extracts.

Antioxidant Compounds in A. comosus Peel Extracts

Studies done on *A. comosus* (pineapple) peel extract demonstrated the presence of antioxidants such as phenolic and flavonoid compounds. The phytochemical screening conducted by Namrata *et al*. [9] revealed that ethanolic pineapple peel extract was positive for the presence of tannin, flavonoid, terpenoid, inulin, glycoside, alkaloid and phenolic compounds. A study claimed that major phenolic compounds in methanolic pineapple peel extracts were catechin (58.51 mg/100 g dry peel), epicatechin (50.00 mg/100 g), gallic acid (31.76 mg/100 g), and ferulic acid (19.50 mg/100 g) [10]. Another study done by Unanma *et al.* [11] found that there was the presence of flavonoids, tannins, reducing sugars, alkaloids, glycosides, saponins, and total phenols in the peels of *A. comosus.* Enzymatic antioxidants, known as polyphenol oxidase, catalase, ascorbate peroxidase, and guaiacol oxidase found in the pineapple peel, including non-enzymatic antioxidants such as phenol, flavonoids, carotenoids, and alkaloid [7].

https://scilett-fsg.uitm.edu.my/
Vol. 17(2) JUNE 2023

ISSN: 1675-7785
eISSN: 2682-8626

DOI: 10.24191/sl.v17i2.19501

These compounds are responsible for scavenging ROS to prevent oxidative stress. The citric and malic acid present in the methanolic extracts of pineapple peel also can chelate metal ions [12]. Table 1 summarizes the antioxidant compounds reported in the peels of *A. comosus*.

Table 1: Antioxidant compounds reported in peels of *A. comosus*

Compounds	References
Polyphenol oxidase, catalase, ascorbate peroxidase, guaiacol oxidase, phenol, flavonoids, carotenoids, and alkaloid	[7]
Tannin, flavonoid, terpenoid, inulin, glycoside, alkaloid, and phenolic compound	[9]
Catechin, epicatechin, gallic acid, and ferulic acid	[10]
Flavonoids, tannins, reducing sugars, alkaloids, glycosides, saponins, and total phenols	[11]
Citric and malic acid	[12]

In Vitro Antioxidants Activities of A comosus Peel Extracts

DPPH Scavenging Activity

Antioxidant potential of a substrate can be evaluated through its scavenging ability towards 2, 2-diphenyl-2-picrylhydrazyl (DPPH) radicals by donating a hydrogen (H^+) atom [13]. A study proved that pineapple peel extracted with absolute methanol had the highest antioxidant capacities with a 50 % inhibitory concentration (IC_{50}) of 1.74 ± 0.05 mg/mL compared to its leaves and pulp [14]. It showed that pineapple peel contains a significantly higher amount of antioxidants compared to its flesh and leaves. A methanolic extract of oven-dried peel was also found to scavenge DPPH radicals effectively with the lowest IC_{50} value (407.15 µg/mL), followed by raw and lyophilized peel [12], supported by Zaki and Ismail [15] where in their study, dried peel inhibited 74 % of DPPH radicals compared to fresh peel (58 %), showing that drying of pineapple peel by microwave at the power level of 180 W contributed to better scavenging activities.

Ferric Reducing Antioxidant Power (FRAP) Assay

The antioxidant activity in FRAP assay is measured through the ability of the antioxidant compound to reduce ferric tripyridyltriazine (Fe^{3+}-TPTZ) complex to ferrous tripyridyltriazine (Fe^{2+}-TPTZ) at low pH by donating a hydrogen atom [16]. Ethanolic extract of Bogor pineapple peel extract reported the lowest 50 % exhibitory concentration (EC_{50}) value (259.08 µg/mL) compared to the flesh (375.58 µg/mL) and bract extract (370.16 µg/mL). These findings showed a negative correlation between the reducing power and the total phenolic content (TPC) as the TPC value of peel extract (1.36 g GAE/100 g dry weight) was quite similar to the bract extract (1.46 g GAE/100 dry weight) but bract had a lower reducing power. It might be due to the high antioxidant activities possessed by phenolic compounds in peel compared to the bract, where only fewer antioxidant compounds exhibit high antioxidant activities [17]. Rathnakumar *et al.* [18] also reported that peel extracted with various concentrations (0, 20, and 40 %) of ethanol showed FRAP values

https://scilett-fsg.uitm.edu.my/
Vol. 17(2) JUNE 2023
ISSN: 1675-7785
eISSN: 2682-8626

DOI: 10.24191/sl.v17i2.19501

ranging from 704.07 to 1207.66 µmol Fe (II)/g of peel extract, which was higher than the core part. In another study conducted by Oso *et al*. [19], which evaluated the antioxidant activity of ripe and unripe peels of A. comosus, the results showed that the FRAP value were 187.33 ± 8.33 and 186.67 ± 2.517 µg/g, respectively. Thus, these results suggest that pineapple peels exhibited higher antioxidant activities than the flesh and core parts.

ABTS Radical Cation Decolorization Assay

The decolorization of the blue-green chromophore of ABTS$^{\bullet+}$, a radical cation solution, determines the ABTS [2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)] assay. Methanolic extract of pineapple peel was found to exhibit high ABTS inhibition activity with a lower IC_{50} value (46.49 µg/mL) compared to aqueous extract (55.89 µg/mL) [20]. Besides, research reported that Bali pineapple peel extracted with ethanol by ultrasonic extraction had 97 % of ABTS scavenging activity, superior to standard ascorbic acid (92.8 %) [21]. This finding is supported by Kalaiselvi *et al.* [22], where the exhaustively extracted pineapple peel from India also exhibits a high percentage of ABTS inhibition activity (62.55 %) than vitamin C (59.57 %). Antioxidants present in the peel extracts possess significant abilities in transferring hydrogen and its single electron to reduce ABTS$^{\bullet+}$ radical to a stable ABTS compound resulting in excellent antioxidant activity.

Phosphomolybdenum Method

Quantitative determination of antioxidant capacity can be provided through the formation of a phosphomolybdenum complex based on the reduction of phosphate-molybdenum, Mo (VI), to Mo (V) by antioxidant compounds [13]. The value of antioxidant activity is proportional to the extract's total antioxidant capacity (TAC). Li *et al*. [10] found that 1 g of methanolic peel extract from Bali pineapple possesses TAC equivalent to 0.037 g ascorbic acid. They reported that TAC exhibited by polyphenolic compounds found in the pineapple peel was in the order of epicatechin > catechin > gallic acid = ferulic acid. These polyphenolic compounds reduced the transition metal by hydrogen and electron transfer at different rates. The molybdenum reduction of pineapple peel extracted by water (16.0 ± 0.1 mg ascorbic acid/g) was superior to orange, banana, and honeydew peel. In this study, pineapple peel extracted with water was the most effective in reducing Mo (VI) as there was a reduction in reducing ability in methanol (8.8 ± 0.3 mg ascorbic acid/g) and ethanolic extract (5.5 ± 0.01 mg ascorbic acid/g) [23].

Nitric Oxide (NO^-) Scavenging Activity

The ability to scavenge NO^- radicals is evaluated by using sodium nitroprusside, as it generates NO^- at physiological pH, which then will interact with oxygen to produce stable nitrite and nitrate ions [13]. Azizan *et al*. [8] reported that MD 2 pineapple peel extracted with aqueous by ultrasound sonication was effective in scavenging NO^- radicals with a total of 63.60 % inhibition compared to 50 % ethanol (46.74 %) and 100 % ethanol (44.43 %). The scavenging activity of the extract was lower than the crown extracted with 50 % ethanol (65.86 %) and 100 % ethanol (70.21 %) but more effective than core extracts at all three solvents. Another study done by Oso *et al*. [19] revealed that both ripe and unripe peels of *A. comosus* had a nitric oxide scavenging potential with IC_{50} value of 339.33 ± 61.533 and 253.67 ± 8.386 mg/ml, respectively.

https://scilett-fsg.uitm.edu.my/
Vol. 17(2) JUNE 2023
ISSN: 1675-7785
eISSN: 2682-8626

DOI: 10.24191/sl.v17i2.19501

Besides, Kalaiselvi *et al*. [22] found at a concentration of 2.5 mg/mL pineapple peel from India that was exhaustively extracted with ethanol exhibited 85.21 % inhibition of NO^- radicals. The IC_{50} value of the peel extract was 1.31 mg/mL, superior against $^{the-}$ quenching activity possessed by vitamin C (1.4 mg/mL). It proved that the NO^- radicals scavenging ability of pineapple peel extract is as well as the standard vitamin C as it can compete with oxygen to scavenge NO^- radicals.

In Vivo Antioxidants Activities of A comosus Peel Extracts

Catalase (CAT) Activity

Alcohol ingestion will induce oxidative stress that leads to increased CAT activities as a counter to combat the high level of free radicals in the body. A study reported that treatment of methanolic pineapple peel extract (2.5 mL/kg and 5.0 mL/kg) overturned the effect of alcohol toxicity as a significant reduction of CAT activities detected in the plasma of alcohol-ingested rats by 87.46 % and 32.67 %, respectively [24]. Another study found that the administration of methanolic pineapple peel extract was reported to cause a reduction of CAT activities in the lung, splenic, and brain tissues of rats fed with alcohol [25 - 27]. The reduction of CAT activity reflects the antioxidant potential of the peel, which may help in degrading H_2O_2 radicals to water and oxygen (O_2).

Superoxide Dismutase (SOD) Activity

The antioxidant activity was evaluated through SOD enzyme activity in catalyzing the dismutation of superoxide anion to O_2 and H_2O_2. Treatment of peel extracts (2.5 and 5.0 mL/kg) on alcohol-fed groups of rats reduced SOD activities in brain tissues by 72.50 % and 25.03 %, respectively [25]. This finding contradicts splenic tissue, where only treatment of 5 mL/kg of methanolic peel extract caused a reduction in SOD activity (77.8 %). However, it was significantly increased with treatment of 2.5 mL/kg of the extract [26]. According to Emmanuel *et al*. [28], the rise of SOD activity in treated rats may indicate that the extract exhibits antioxidant activity against ROS in the biological system, and it was not a sign of inducing oxidative stress as he found no significant difference reported between the treated and control group.

Reduced Glutathione (GSH) Estimation

The GSH is a thiol-based non-enzymatic antioxidant, which is reduced upon alcohol ingestion as it reacts directly with ROS to protect essential thiol groups from oxidation during oxidative stress [29]. A study done by Erukainure *et al*. [25] reported that alcohol ingestion leads to a significant reduction in GSH levels. However, treatment with methanolic pineapple peel extracts (2.5 and 5.0 mL/kg) provided a reverse effect on alcohol toxicity as it caused elevation of GSH levels in brain tissue of alcohol-induced male albino rats by 58.98 % and 2.69 %, respectively. The same goes for splenic tissue, where the GSH level elevated by 49.57 % and 7.54 %, respectively [26]. These findings showed that treatment with 2.5 mL/kg of extract provided a better antioxidative effect. The ability of phenolics compounds in the extracts to act as hydrogen donors and singlet oxygen quenchers neutralized ROS, restoring the GSH level [30].

https://scilett-fsg.uitm.edu.my/
Vol. 17(2) JUNE 2023

ISSN: 1675-7785
eISSN: 2682-8626

DOI: 10.24191/sl.v17i2.19501

Lipid Peroxidation (LPO) Assay

Malondialdehyde (MDA), the end-product of ROS formed during oxidative degeneration, can be a marker of LPO [13]. Okafor *et al*. [24] found that pineapple peel extract (2.5 mL/kg) treatment in alcohol-induced rats reduced the plasma MDA level by 60.16 %, more effective than rats treated with 5.0 mL/kg of extract. Different in splenic tissue where peel extracts (2.5 and 5 mL/kg) reduced the MDA level by 61.43 % and 66.43 %, respectively, providing a protective effect in a dose-dependent manner [26]. The antioxidant potentials exhibited by the peel extract were also found to be able to reduce alcoholic lung oxidative injury, as low MDA levels were reported for rats that were treated with the peel extract (250 mg/kg) [27]. These findings indicated that the extracts are not causing toxicity by inducing oxidative stress but potentially have an antioxidant source that combats free radicals and inhibits LPO. The protective effects of the extracts were claimed to be caused by the phenols and flavonoids present, which scavenged ROS and subsequently reduced LPO. This is supported by the study done by Khan *et al.* [31] and Andrés Juan *et al.* [32], which explained the mechanism of phenols and flavonoids in scavenging ROS by direct scavenging, induction of antioxidant enzymes, as well as prevention of ROS formation. By inhibiting ROS production, MDA will be reduced and subsequently reduce LPO. Figure 1 summarizes and depicts the protective mechanisms of phenols and flavonoids against LPO.

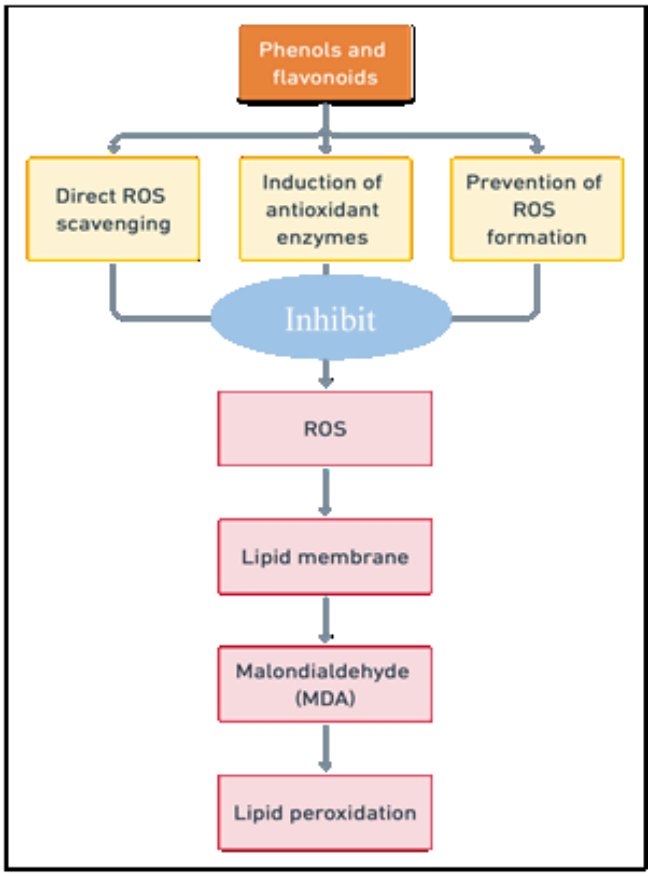

Figure 1: Mechanism of protective effects of phenols and flavonoids on lipid peroxidation induced by ROS.

https://scilett-fsg.uitm.edu.my/
Vol. 17(2) JUNE 2023

ISSN: 1675-7785
eISSN: 2682-8626

DOI: 10.24191/sl.v17i2.19501

CONCLUSION

This review summarized the antioxidant activities of *A. comosus* peel extracts through various *in vitro* and *in vivo* models, which mainly demonstrated the radical scavenging abilities of *A. comosus* peel extracts. The antioxidant compounds present in the peel extracts can scavenge different types of radicals through various mechanisms. However, each method has its strengths and limitations in evaluating the antioxidant activities of the peel extracts. Other factors, such as types of extraction solvents and methods, drying temperatures, and concentrations of the extracts, may affect its antioxidant activities. More studies are required to provide an effective antioxidant activity exhibited by *A. comosus* peel extracts.

ACKNOWLEDGMENTS

The authors fully acknowledge the Faculty of Health Sciences, Universiti Teknologi MARA, Puncak Alam Campus, for supporting and approving this project.

AUTHOR'S CONTRIBUTION

All the authors have contributed in conceptualized the central research idea, providing the theoretical framework, and writing the manuscript.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

REFERENCES

[1] Pizzino, G., Irrera, N., Cucinotta, M., Pallio, G., Mannino, F., Arcoraci, V., Squadrito, F., Altavilla, D., & Bitto, A. (2017). Oxidative stress: harms and benefits for human health. *Oxidative Medicine and Cellular Longevity*, *2017*.

[2] Martysiak-Zurowska, D., & Wenta, W. (2012). A comparison of ABTS and DPPH methods for assessing the total antioxidant capacity of human milk. *Acta Scientiarum Polonorum, Technologia Alimentaria*, *11*(1), 83–89.

[3] Carocho, M., & Ferreira, I. C. F. R. (2013). A review on antioxidants, prooxidants and related controversy: Natural and synthetic compounds, screening and analysis methodologies and future perspectives. *Food and Chemical Toxicology*, *51*(1), 15–25.

[4] Yu, J., Wang, L., Walzem, R. L., Miller, E. G., Pike, L. M., & Patil, B. S. (2005). Antioxidant activity of citrus limonoids, flavonoids, and coumarins. *Journal of Agricultural and Food Chemistry*, *53*(6), 2009–2014.

https://scilett-fsg.uitm.edu.my/
Vol. 17(2) JUNE 2023

ISSN: 1675-7785
eISSN: 2682-8626

DOI: 10.24191/sl.v17i2.19501

[5] Rajendran, P., Nandakumar, N., Rengarajan, T., Palaniswami, R., Gnanadhas, E. N., Lakshminarasaiah, U., Gopas, J., & Nishigaki, I. (2014). Antioxidants and human diseases. *Clinica Chimica Acta*, *436*, 332–347.

[6] Bamidele, O. P., & Fasogbon, M. B. (2017). Chemical and antioxidant properties of snake tomato (*Trichosanthes cucumerina*) juice and Pineapple (*Ananas comosus*) juice blends and their changes during storage. *Food Chemistry*, *220*, 184–189.

[7] Sahu, P., Sushma, D., Srivasatava, D., & Lal, N. (2017). Nutraceuticals profiling of queen and king varieties of pineapple (*Ananas comosus*) (Pineapple). *International Journal of Chemical Studies*, *5*(3), 25–31.

[8] Azizan, A., Lee, A. X., Hamid, N. A. A., Maulidiani, M., Mediani, A., Abdul Ghafar, S. Z., Zolkeflee, N. K. Z., & Abas, F. (2020). Potentially bioactive metabolites from pineapple waste extracts and their antioxidant and α-glucosidase inhibitory activities by 1H NMR. *Foods*, *9*(2).

[9] Namrata, Y. S., & Sharma, T. (2017). Anti-microbial, antioxidant activity and phytochemical screening of polyphenolic flavonoids isolated from peels of *Ananas comosus*. *International Journal of Engineering Research & Technology*, *6*(9) 285-298.

[10] Li, T., Shen, P., Liu, C., Liang, R., Yan, N., & Chen, J. (2014). Major polyphenolics in pineapple peels and their antioxidant interactions. *International Journal of Food Properties*, *17*(8), 1805–1817.

[11] Unanma, H. C., Anaduaka, E. G., Uchendu, N. O., Ononiwu, C. P., & Ogugua, V. N. (2021). *Ananas comosus* and *Citrus sinensis* peels ameliorate CCl4-induced liver injury in Wistar rats. *Scientific African, 14*.

[12] Morais, D. R., Rotta, E. M., Sargi, S. C., Schmidt, E. M., Bonafe, E. G., Eberlin, M. N., Sawaya, A. C. H. F., & Visentainer, J. V. (2015). Antioxidant activity, phenolics, and UPLC-ESI(-)-MS of extracts from different tropical fruits parts and processed peels. *Food Research International*, *77*, 392–399.

[13] Alam, M. N., Bristi, N. J., & Rafiquzzaman, M. (2012). Review on in vivo and in vitro methods evaluation of antioxidant activity. *Saudi Pharmaceutical Journal*, *21*(2), 143–152.

[14] Jovanović, M., Milutinović, M., Kostić, M., Miladinović, B., Kitić, N., Branković, S., & Kitić, D. (2018). Antioxidant capacity of pineapple (*Ananas comosus* (L.) Merr.) extracts and juice. *Lekovite Sirovine*, *38*, 27–30.

[15] Zaki, N. A. M., & Ismail, S. F. (2018). Quality retention of microwave-dried pineapple peels and core. *Malaysian Journal of Chemical Engineering & Technology*, *1*, 1–7.

[16] Rajurkar, N., & Hande, S. M. (2011). Estimation of phytochemical content and antioxidant activity of some selected traditional Indian medicinal plants. *Indian Journal of Pharmaceutical Sciences*, *73*(2), 146–151.

[17] Fidrianny, I., Virna, V., & Insanu, M. (2018). Antioxidant potential of different parts of bogor pineapple (*Ananas comosus* [L.] Merr. Var. Queen) cultivated in West Java-Indonesia. *Asian Journal of Pharmaceutical and Clinical Research*, *11*(1), 129–133.

[18] Rathnakumar, K., Lakshmi, K., & Anal, A. K. (2017). Microwave method-a novel green technique for the extraction of bioactive from the waste of pineapple by optimizing the conditions. *International Journal of Science, Environment, and Technology*, *6*(5), 2992–3001.

[19] Oso, B., Olaoye, I., Ekpo, E., & Akhigbe, G. (2022). Antioxidant potentials and anti-inflammatory properties of methanol extracts of ripe and unripe peels of *Ananas comosus* (L.) Merr. *Ovidius University Annals of Chemistry*, *33*(1), 94–98.

[20] Putri, D. A., Ulfi, A., Purnomo, A. S., & Fatmawati, S. (2018). Antioxidant and antibacterial activities of *Ananas comosus* peel extracts. *Malaysian Journal of Fundamental and Applied*

https://scilett-fsg.uitm.edu.my/
Vol. 17(2) JUNE 2023

ISSN: 1675-7785
eISSN: 2682-8626

DOI: 10.24191/sl.v17i2.19501

Sciences, *14*(2), 307–311.

[21] Liu, S. H., Liu, Y. G., & Zhang, X. M. (2018). Extraction conditions and antioxidant activities of the extract of pineapple peel by ultrasonic. *IOP Conference Series: Earth and Environmental Science*, *186*(4).

[22] Kalaiselvi, M., Ravikumar, G., Gomathi, D., & Uma, C. (2012). In vitro free radical scavenging activity of *Ananus comosus* (L.) Merrill peel. *International Journal of Pharmacy and Pharmaceutical Sciences*, *4*(2), 604–609.

[23] Kuppusamy, S., Venkateswarlu, K., & Megharaj, M. (2020). Examining the polyphenol content, antioxidant activity, and fatty acid composition of twenty-one different wastes of fruits, vegetables, oilseeds, and beverages. *SN Applied Sciences*, *2*(4), 1–13.

[24] Okafor, O. Y., Erukainure, O. L., Ajiboye, J. A., Adejobi, R. O., Owolabi, F. O., & Kosoko, S. B. (2011). Modulatory effect of pineapple peel extract on lipid peroxidation, catalase activity, and hepatic biomarker levels in the blood plasma of alcohol-induced oxidative stressed rats. *Asian Pacific Journal of Tropical Biomedicine*, *1*(1), 12–14.

[25] Erukainure, O. L., Ajiboye, J. A., Adejobi, R. O., Okafor, O. Y., & Adenekan, S. O. (2011). Protective effect of pineapple (*Ananas cosmosus*) peel extract on alcohol-induced oxidative stress in brain tissues of male albino rats. *Asian Pacific Journal of Tropical Disease*, *1*(1), 5–9.

[26] Erukainure, O. L., Ajiboye, J. A., Okafo, O. Y., Kosok, R. S. B., Owolab, O. F. O., & Adenekan, I. S. O. (2011). Antioxidant effect of pineapple (*Ananas cosmosus*) peel extract on alcohol-induced oxidative stress in splenic tissues of male albino rats. *Journal of Food Biochemistry*, *36*(6), 643–647.

[27] Erukainure, O. L., Ajiboye, J. A., Okafor, O. Y., Okoro, E. E., Asieba, G., Sarumi, B. B., Adenekan, S. O., & Zaruwa, M. Z. (2016). Alcoholic lung injury: Pineapple peel extract modulates antioxidant enzymes and attenuates lipid peroxidation in rat models. *Clinical Phytoscience*, *2*(14).

[28] Emmanuel, E. U., Onagbonfeoana, E. S., Adanma, O. C., Precious, O. C., Faith, A.-I., & Ndukaku, O. Y. (2016). In vivo and vitro antioxidant and hypolipidemic activity of methanol extract of pineapple peels in Wistar rats. *International Journal of Biosciences (IJB)*, *8*(6), 64–72.

[29] Saravanan, N., & Nalini, N. (2007). Antioxidant effect of *Hemidesmus indicus* on ethanol-induced hepatotoxicity in rats. *Journal of Medicinal Food*, *10*(4), 675–682.

[30] Dwivedi, D., Dwivedi, M., Malviya, S., & Singh, V. (2017). Evaluation of wound healing, the anti-microbial and antioxidant potential of *Pongamia pinnata* in Wistar rats. *Journal of Traditional and Complementary Medicine*, *7*(1), 79–85.

[31] Andrés Juan, C., Manuel Pérez de la Lastra, J., Plou, F. J., Pérez-Lebeña, E., & Reinbothe, S. (2021). Molecular Sciences The Chemistry of Reactive Oxygen Species (ROS) Revisited: Outlining Their Role in Biological Macromolecules (DNA, Lipids and Proteins) and Induced Pathologies. *Int. J. Mol. Sci*, *22*, 4642.

[32] Khan, H., Ullah, H., Tundis, R., Belwal, T., Devkota, H. P., Daglia, M., Cetin, Z., Saygili, E. I., Campos, M. da G., Capanoglu, E., Du, M., Dar, P., & Xiao, J. (2020). Dietary Flavonoids in the Management of Huntington's Disease: Mechanism and Clinical Perspective. *EFood, 1*(1), 38–52.