Sains Malaysiana 53(6)(2024): 1281-1293
http://doi.org/10.17576/jsm-2024-5306-05

Antioxidant and Alpha-Glucosidase Inhibitory Activity of *Durio zibethinus* L. Clone 175 (Durian Udang Merah) Shell and UHPLC-Orbitrap-MS Profiling of the Extract

(Aktiviti Perencatan Antioksidan dan Alfa-Glukosidase Kulit Klon 175 *Durio zibethinus* L. (Durian Udang Merah) dan Pemprofilan Ekstrak UHPLC-Orbitrap-MS)

WAN MUHD HATIM WAN ZAIN[1], AHMED MEDIANI[2], NUR KHALEEDA ZULAIKHA ZOLKEFLEE[3], PEI LOU WONG[1] & FARIDAH ABAS[1,*]

[1]*Department of Food Science, Faculty of Food Science and Technology, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor, Malaysia*

[2]*Metabolomics Research Laboratory, Institute of Systems Biology (INBIOSIS), Universiti Kebangsaan Malaysia, 43600 UKM Bangi, Selangor, Malaysia*

[3]*Natural Medicines and Products Research Laboratory, Institute of Bioscience, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor, Malaysia*

Received: 4 March 2024/Accepted: 14 May 2024

ABSTRACT

Durio zibethinus or 'durian' is a well-known seasonal fruit of Southeast Asia and has been called the 'King of Fruit'. The popularity of durian has led to large production of this crop in Malaysia, consequently creating a huge agricultural waste including the shell. Despite illness remedies from various parts of durian, the information on phytochemical constituents and bioactivities of durian shells remained scarce. Therefore, this study aimed to evaluate the total phenolic content (TPC), antioxidant, and α-glucosidase inhibitory activities of *D. zibethinus* shell extracted with different ethanol percentage (0%, 50%, and 100%). Results showed that the 100% ethanolic extract exhibited the highest 2,2-dipheny-1-picrylhydrazyl (DPPH) free radical scavenging activity with an IC_{50} value of 96.91 ± 1.09 µg/mL. Furthermore, the 50% ethanol extract exhibited the highest TPC with 130.57 ± 1.92 mg GAE/g crude extract, and nitric oxide (NO) scavenging activity with an IC_{50} value of 435.30 ± 3.41 µg/mL. Both 50% and 100% ethanolic extracts of *D. zibethinus* shell exhibited great potential in α-glucosidase inhibitory activity with IC_{50} values of 1.99 ± 0.90 and 4.53 ± 0.21 µg/mL, respectively. Thus, the bioactive compounds in 100% ethanolic extract of *D. zibethinus* were profiled by ultra-performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS) analysis. A total of 20 compounds were tentatively identified, including flavonoids, alkaloids, benzofurans, terpenoids, pentose phosphate, organosulfur compounds, organooxygen compounds, polyketides, carotene, carboxylic acid, coumarin, and stigmasterol. In conclusion, durian shell exhibits potential for future applications driven by its inherent pharmacological benefits, consequently contributing to waste reduction.

Keywords: Antioxidant; *Durio zibethinus* shell; UHPLC-MS/MS; α-glucosidase inhibitory activity

ABSTRAK

Durio zibethinus atau durian adalah buah bermusim yang terkenal di Asia Tenggara dan turut dikenali sebagai Raja Buah. Kepopularan durian telah menyebabkan pengeluaran besar-besaran tanaman ini di Malaysia, seterusnya menghasilkan sisa pertanian yang banyak termasuk kulit. Walaupun pelbagai bahagian durian telah digunakan untuk rawatan penyakit, maklumat kandungan fitokimia dan bioaktiviti ekstrak kulit durian masih terhad. Oleh itu, kajian ini bertujuan untuk menilai jumlah kandungan fenol (TPC), aktiviti antioksidan dan perencatan α-glukosidase ekstrak kulit *D. zibethinus* yang diekstrak dengan nisbah etanol yang berbeza (0%, 50% dan 100%). Hasil menunjukkan bahawa ekstrak 100% etanol menunjukkan aktiviti pemerangkap radikal bebas 2,2-difenil-1-pikrilhidrazil (DPPH) tertinggi dengan nilai IC_{50} sebanyak 96.91 ± 1.09 µg/mL. Tambahan pula, ekstrak 50% etanol menunjukkan TPC tertinggi dengan 130.57 ± 1.92 mg ekstrak kasar GAE/g, dan aktiviti pemerangkapan nitrik oksida (NO) dengan nilai IC_{50} 435.30 ± 3.41 µg/mL. Kedua-dua ekstrak 50% dan 100% etanol daripada kulit *D. zibethinus* menunjukkan potensi

besar dalam aktiviti perencatan α-glukosidase dengan nilai IC_{50} masing-masing 1.99 ± 0.90 dan 4.53 ± 0.21 µg/mL. Oleh itu, sebatian bioaktif dalam ekstrak 100% etanol *D. zibethinus* telah diprofilkan menggunakan kromatografi cecair berprestasi tinggi ultra spektrometri jisim (UHPLC-MS/MS). Sebanyak 20 sebatian telah dikenal pasti secara tentatif termasuk flavonoid, alkaloid, benzofuran, terpenoid, pentosa fosfat, sebatian organosulfur, organooksigen, poliketida, karotena, asid karboksilik, kumarin dan stigmasterol. Kesimpulannya, kulit durian mempunyai potensi untuk aplikasi masa hadapan yang didorong oleh faedah farmakologi yang wujud, seterusnya menyumbang kepada pengurangan sisa.

Kata kunci: Antioksidan; kulit *Durio zibethinus*; perencatan aktiviti α-glukosidase; UHPLC-MS/MS

Introduction

A high positive impact and a reduction in the risk of chronic diseases were recognized through the consumption of an antioxidant-rich diet. A previous study reported that 62 fruits, 56 vegetables, 223 medicinal plants, and 50 fruit wastes were found to be higher in antioxidant activities (Xu et al. 2017). Among the foods, food wastes and medicinal plants tested strong antioxidant activities were reported in fruit wastes, such as grape seed, longan peel, mango peel, Chinese olive peel, sweetsop peel, and hawthorn peel extracts (Xu et al. 2017). The amount of waste is worsened when the yearly production of durian in Malaysia is taken into account which is approximately 350 thousand metric tons (MT) per year (Suntharalungam et al. 2018). This large amount of waste generated from food commodities may contribute to a serious environmental problem such as the release of greenhouse gases during decomposition (Sagar et al. 2018). However, the by-products of horticulture are a rich source of phenolic compounds, pigments, and dietary fibers (Sagar et al. 2018).

Durio zibethinus known as the King of Fruit or 'durian' is a native fruit of Southeast Asia and a seasonal fruit (Ketsa 2018). Generally, durian is consumed fresh as fruit or processed into jam, snack, and cake (Mariod, Saeed Mirghani & Hussein 2017). Typically, a single durian produces 60-70% of waste from inedible shells and seeds, potentially serving as a source of valuable bioactive compounds (Sagar et al. 2018). Therefore, more research should be done on each part of durian, especially the shell waste on its nutraceutical value and to show the possible bioactive compounds. This has also opened great opportunities for us to improve environmental health through the reduction of agricultural wastes and utilization of the waste for use in pharmaceutical sectors as well as benefiting human health. Traditionally, durian leaves and roots have been used as antipyretic decoction, febrifuge and anti-malarial agents by Asians (Nurul Arneida et al. 2018). While durian fruit pulp was reported to have potential as a fertility-enhancing agent in patients with polycystic ovarian syndrome (PCOS) (Nurul Arneida et al. 2018). The durian shells were used externally in skin disease treatment while the bark of *D. oxyleyanus* was used in malaria treatment in Sumatra (Brown 1997). Previous studies conducted on rats showed a reduction of 50.19% of the glucose levels and 35.82% of the cholesterol level in rats with high cholesterol when fed with a dose of 500 mg/kg bw of durian shell extracts for 14 days (Muhtadi et al. 2016). Constituents such as flavanones (hesperetin and hesperidin), and flavones (luteolin and apigenin), and flavonols (morin, quercetin, rutin, kaempferol, myricetin) were the major flavonoids identified in arils of durian (A. Aziz & Abbe Maleyki 2019). Meanwhile, the derivatives from hydroxycinnamic acid (caffeic, *p-coumaric*, ferulic, *p-anisic acid*) and hyroxybenzoic acid (gallic and vanillic acid) were the phenolic acids found in durian (A. Aziz & Abbe Maleyki 2019). Presently, the available research on the antioxidant, phytochemical and antidiabetic activities of durian is only on the arils, leaves, and bark, and limited data on the durian shell. Besides, most of the research done was on the Thailand durian variety such as '*Monthong*' and '*Chanee*', and Malaysia varieties such as 'Durian kampung', '*Yah Kang*' and '*Caher Phoy*' (A. Aziz & Abbe Maleyki 2019). A relatively few studies were conducted on the variety of 'Udang merah' which is a variety that originated from Malaysia for its precious bioactive compounds, antioxidants, and antidiabetic activities (Nurul Arneida et al. 2018). Thus, in the present study, the shell waste of the variety 'Udang merah' was investigated for its antioxidants and antidiabetic properties. The objectives of this study were to evaluate the antioxidant and α-glucosidase inhibitory activities of *D. zibethinus* shell extracted with different

ethanol percentage and profile the bioactive compounds in the most active *D. zibethinus* shell extract by using ultra-high performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS).

Materials and Methods

Chemical Reagent

2,2-Diphenyl-1-picrylhdrazyl (DPPH), *ρ-nitrophenyl-α-D-glucopyranoside* (PNPG), *N*-(1-naphthyl) ethylenediamine dihydrochloride (NED), quercetin hydrate, phosphate-buffered saline (PBS), gallic acid and phosphoric acid were obtained from Sigma Aldrich (St. Louis, USA). Sodium carbonate was supplied by Nacalai Tesque (Kyoto, Japan). Sulphanamide was supplied from BDH Laboratory Supplies (Poole, England). The Folin-Ciocalteu reagent was supplied by Merck (Darmstadt, Germany). The sodium nitroprusside (SNP) was supplied by Bendosen Laboratory Chemicals (Bendosen, Norway). The α-glucosidase enzyme was obtained from Megazyme (Bray, Ireland). Glycine was obtained from R & M Chemicals (Petaling Jaya, Malaysia). The absolute ethanol was supplied by Fisher Scientific (Shah Alam, Malaysia) while dimethyl sulfoxide (DMSO) was from Systerm (Shah Alam, Malaysia).

Sample Preparation

Twenty *D. zibethinus* fruits of the clone D175 or 'Udang Merah' weighing approximately 2 kg per fruit were obtained from a farm in Selangor. The shells were obtained through the removal of the arils and seeds. The shells were cut into small pieces and subjected to drying. The drying process was done according to the previous method (Suganya et al. 2019). The durian shells were subjected to oven drying at 40 °C for 3 days until completely dried (constant weight). The drying was conducted in a laboratory cabinet dryer (Smoke Master, Tokyo, Japan). Dried durian shells were then ground into a fine powder, sieved to uniform particle size and kept in an airtight container. The samples were stored in a chiller at 4 °C until further use. Extraction of the bioactive compound from dried ground *D. zibethinus* powder was done through the ultrasound-assisted extraction (UAE) method (Azmir et al. 2013) with three different ethanol concentrations of 0, 50, and 100% ethanol/water. A weight of 10 g of sample was weighed and mixed with 400 mL of each solvent and subjected to extraction using ultrasound sonication at a controlled temperature (below 40 °C) for 2 h and the extraction was done in two cycles (200 mL ethanol and 1 h of sonication for each cycle). Whatman filter paper No. 1 was used in filtrating the solution before being concentrated using a rotary evaporator (IKA HB10, Staufen, Germany) to yield concentrated crude extract. The crude extract was further subjected to freeze drying and stored in a chiller until further use.

Total Phenolic Content (TPC)

The Folin-Ciocalteu method was used in evaluating TPC of durian shell extracts in a 96-well microplate, according to the procedure with several modifications (Lee et al. 2014). A 100 µL of Folin-Ciocalteu reagent was added to 20 µL of sample into each well and kept in the dark for 5 min. Next, 80 µL of 7.5% sodium carbonate was added into each well and the plate was incubated for 30 min in the dark. The absorbance was then measured at 750 nm using a microplate reader (Tecan Trading AC, Männedorf, Switzerland). The sample was prepared at a stock concentration of 1000 µg/mL, using DMSO as the solvent, and each analysis was performed in triplicate. Gallic acid was used as a standard and subjected to the same procedure. The stock concentration for the standard was prepared at 1000 µg/mL and from the stock solution, six serial dilutions (0, 6.25, 12.5, 25, 50, and 100 µg/mL) were prepared and analyzed to get the standard curve. The obtained results were expressed in mg GAE/g dry weight basis of the sample.

2,2-Diphenyl-1-picryhydrazyl (DPPH) Free Radical Scavenging Activity

The radical scavenging potential of the durian shell extract was determined based on the described DPPH free radical scavenging assay (Lee et al. 2014). The assay was conducted in a 96-well microplate with 50 µL of the test compounds prepared in 7 serial dilutions (1000, 500, 250, 125, 62.5, 31.25 and 15.625 µg/mL) from a 3000 µg/mL stock concentration and DMSO was used as the solvent. Then, 100 µL of the DPPH solution was added into the well and incubated for 30 min in the dark. The absorbance was then measured at 517 nm against a reagent blank by using a microplate reader (Tecan Trading AC, Männedorf, Switzerland). The same procedure was used for quercetin as a positive control, which was prepared in 7 serial dilutions (100, 50, 25, 12.5, 6.25, 3.125 and 1.56 µg/mL) from a 1000 µg/mL stock concentration. The analysis was performed in triplicate.

The scavenging capacity (SC) was calculated as SC % = [(Ao -As)/Ao] × 100, where Ao is the absorbance of the reagent blank and As is the absorbance of the test samples. The results were expressed in IC_{50} values, which denote the concentration of the sample required to scavenge 50% DPPH free radicals.

NITRIC OXIDE (NO) SCAVENGING ACTIVITY

NO scavenging activity was conducted according to the previous method (Nur Ashikin et al. 2018). The assay was performed in a 96-well microplate with 60 µL test samples prepared in 7 serial dilutions (1000, 500, 250, 125, 62.5, 31. 25 and 15.625 µg/mL) from a-3000 µg/mL-stock concentration. A 60 µL of 10 mM SNP was mixed with 60 µL of durian shell extracts. The well plate was incubated for 150 min in the room. The mixture was then mixed with 60 µL of freshly prepared Griess reagent. Finally, the absorbance was read at 550 nm by using a microplate reader (Tecan Trading AC, Männedorf, Switzerland). Quercetin was used as a positive control and the results were expressed in IC_{50} values.

α-GLUCOSIDASE INHIBITORY ACTIVITY

The assay of α-glucosidase inhibitory activity was performed as described (Lee et al. 2014). The PNPG which was used as the substrate and the α-glucosidase enzyme was dissolved in 50 mM sodium phosphate buffer pH 6.5. The durian shell extract was prepared at 3000 µg/mL stock solution and 7 serial dilutions (150, 75, 37.5, 18.75, 9.375, 4.687 and 2.34 µg/mL). Exactly 10 µL of the enzyme was mixed with the test sample in the well plates and incubated for 5 min. Then, 50 µL of PNPG was added to each well of the test sample and negative control, while 50 µL of 30 mM sodium phosphate buffer was loaded to the blank sample. The mixture was incubated again for 15 min at room temperature. Next, 50 µL of 2M glycine (pH 10) as a stopping agent was added to each well of the blank sample, test sample, and negative control to stop the reaction. The absorbance was measured at 405 nm using a microplate reader. The percentage of α-glucosidase inhibitory activity was calculated as [(An – As) / An] × 100%, where An is the absorbance of the negative control; and As is the difference in absorbance of the test sample and blank sample. The same procedure was used for quercetin as a positive control and data were also shown in IC_{50} values.

ULTRAHIGH-PERFORMANCE LIQUID CHROMATOGRAPHY-TANDEM MASS SPECTROMETRY (UHPLC-MS/MS)

The UHPLC-MS/MS procedure was performed according to the report (Azliana et al. 2017). Each sample was separated using a C18 reversed-phase ACQUITY UHPLC® HSS T3 columns with 150 mm length, 2.3 mm internal diameter (ID) and 1.7 µm particle size (Waters, Dublin, Ireland) at 35 °C (thermostated column compartment) on a UHPLC system equipped with a binary pump, vacuum degasser, temperature-controlled autosampler and diode array detector (DAD) recorded from 200-600 nm (Thermo Fisher Scientific, Bremen, Germany). The mobile phase used was water containing 0.1% formic acid (solvent A) and acetonitrile with 0.1% formic acid (solvent B). The method was applied using gradient elution completed in 38 min and 50 s. The injection volume was 2 µL with a constant flow rate of 0.4 mL/min. The MS analysis was performed on the Q ExactiveTM Focus Orbitrap LC-MS/MS system (Thermo Fisher Scientific, Bremen, Germany) with a heated electrospray ionization (HESI-II) source. The ionization parameters were set as follows: capillary voltage±4 kV, heated capillary temperature 350 °C, sheath and auxiliary nitrogen gas flow 45 and 10 units. The total ion chromatograms (TIC) were recorded at *m/z* 150 - *m/z* 1500. A data-dependent program (dd-MS2) was used for further MS/MS analysis. The Xcalibur 4.0 software was used for data analyses.

STATISTICAL ANALYSIS

The results obtained were expressed as the mean ± standard deviation of three replicates. The analysis of significant differences was carried out using ANOVA and correlation analysis was done by Pearson Test. Microsoft Office Excel and Minitab software (Version 18, Minitab Inc., State College, PA, USA) were used to conduct the statistical analysis.

RESULTS AND DISCUSSION

YIELD OF EXTRACTION

The plant sample was extracted by using three different solvent concentrations which were 0, 50, and 100% ethanol and the yield was expressed as a percentage of dry weight of crude extract per dry weight basis of sample. The extraction yield of durian shells at different ethanol percentage can be perceived in Figure 1. The

sample extracted using 50% ethanol yielded 15.13 ± 1.15% (%w/w) crude extract, followed by the 0% ethanol with 13.26 ± 0.15% (%w/w) crude extract. Meanwhile, the extraction using absolute ethanol yielded a very low percentage of crude extract which is 5.13 ± 0.40% (%w/w). Besides, the result also showed a significant difference ($p < 0.05$) between the extraction yield of samples at all ethanol percentage. Previous studies on the extraction of bioactive compounds by using UAE with a ratio of 1:9 of durian peel using 70% ethanol obtained a lower percentage yield which was 12.77 ± 0.16% compared to all ethanolic extracts of the current study (Kunarto & Sani 2018). This probably indicated the significant effects of ethanol concentration and extraction time on the percentage yield of crude extract. Another study on durian shell discovered that the use of a conventional method (cold maceration) and a solvent mixture of 96% ethanol:acetone at a ratio of 4:1 resulted in a 16.93% (%w/w) crude extract yield (Muhtadi et al. 2016). When compared to the current study, it was found that the extraction yield obtained from the maceration method using different types of solvent (ethanol:acetone) was higher than all the extraction yields obtained using the UAE method at each ethanol concentration. This disparity could be attributed to the differing extraction efficiencies of the two methods and the specific solvents used due to its mechanism of action which is the intensification of mass transfer and accelerated entree of solvent into the cells of plant parts (Azmir et al. 2013).

TOTAL PHENOLIC CONTENT (TPC) OF *D. zibethinus* SHELL EXTRACTS

The TPC of different *D. zibethinus* shell ethanolic extracts are shown in Figure 2. Based on the results obtained, the 50% ethanol extract exhibited the highest TPC value with 130.57 ± 1.92 mg GAE/g crude extract, while the lowest TPC value was in the 100% ethanol extract with 63.89 ± 2.91 mg GAE/g crude extract. As for the sample extracted using water as the solvent had a TPC value of 74.20 ± 1.02 mg GAE/g crude extract. The result obtained showed a significant difference ($p < 0.05$) between the TPC of all the ethanolic extracts thus indicating the significant influence of the ethanol concentration used for extraction on the TPC value of the durian shell extracts. A slightly different result was reported whereby, 70% ethanol durian shell extracted using UAE showed a TPC value of 63.30 ± 0.08 mg GAE/g which was lower than 50% ethanol extract but showed a similarity to the 100% ethanol extract in the current study (Kunarto & Sani 2018). Another report stated that the TPC was obtained from the antioxidant study on *D. zibethinus* Murr. was 33.77 ± 1.77 mg GAE/g methanolic extract (Li & Wang 2011). This showed a relatively lower phenolic content in the methanolic extract of *D.*

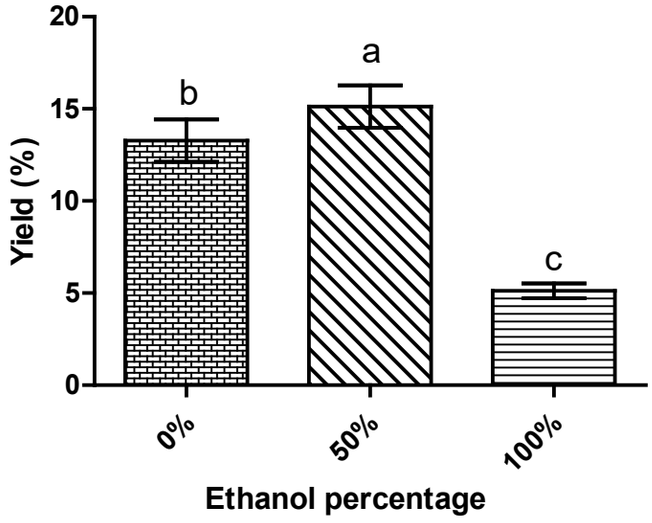

FIGURE 1. The extraction yield of *D. zibethinus* shell at different ethanol percentage

zibethinus shell compared to water and ethanolic extracts presented in this study. Studies on phenolics in almond hulls (*Prunus amygladus* L.) and pine sawdust (*Pinus pinaster* L.) found that extraction of phenolics or any bioactive compounds was more suitable by using ethanol, as methanol was more selective toward polyphenolics extraction (Altemimi et al. 2017). This finding suggests that the application of ethanol, water, or a mixture of both in the extraction of phenolic compounds in durian shell is a better option than using methanol as the solvent. Moreover, this also implies that the TPC of plant extract can be significantly affected by the solvent used during extraction due to differences in solvent polarities (Laoufi et al. 2017). The varying solvent polarity will selectively attract different hydrophobic or hydrophilic phenolic compounds in the sample (Ngo et al. 2017). Therefore, extraction solvents play an important role in the extraction of phenolic compounds in specific plant samples. It can be concluded that 50% ethanol is the best solvent for the extraction of phenolic compounds in durian shells.

DPPH RADICAL SCAVENGING ACTIVITY OF *D. zibethinus* SHELL EXTRACTS

The ethanolic extracts of durian shell were first screened for their DPPH scavenging activity (Table 1). The 50% ethanol and water extracts did not surpass a 50% inhibition which are 40.13 ± 1.70 % and 36.8 ± 1.476%, respectively. Besides, the percentage inhibition between these extracts showed no significant difference ($p > 0.05$), while both were significantly different from 100% ethanolic extract with a value of 77.97% ± 3.55. This indicated the potential of 100% ethanolic extract as a DPPH free radical scavenger. Furthermore, the IC_{50} value for 100% ethanolic extract was identified due to its effectiveness in scavenging the radicals and was compared to the quercetin standard. The result obtained shows that the IC_{50} value of 100% ethanolic extract is 96.91 ± 1.09 µg/mL compared to the standard which was 4.57 ± 0.72 µg/mL. Earlier studies also reported the methanolic extract of *D. zibethinus* obtained from Guangzhou, China had an IC_{50} value of 102.37 ± 1.98 µg/mL (Li & Wang 2011). Moreover, the use of solvent for extraction between the extracts which is absolute ethanol and methanol may have no significant influence on the DPPH radical scavenging activity. However, the extraction of durian shell with 70% ethanol by using UAE for 20 min had a lower IC_{50} value of 38.33 ± 0.12 µg/mL (Kunarto & Sani 2018). Their IC_{50} value of the 70% ethanolic extract was far lower than those two ethanolic extracts indicating an unusual data trend between the two studies. This study showed that the 100% ethanolic extract of durian shell has a substantial DPPH free radical scavenging property thus it is suggested as a better option solvent for extraction.

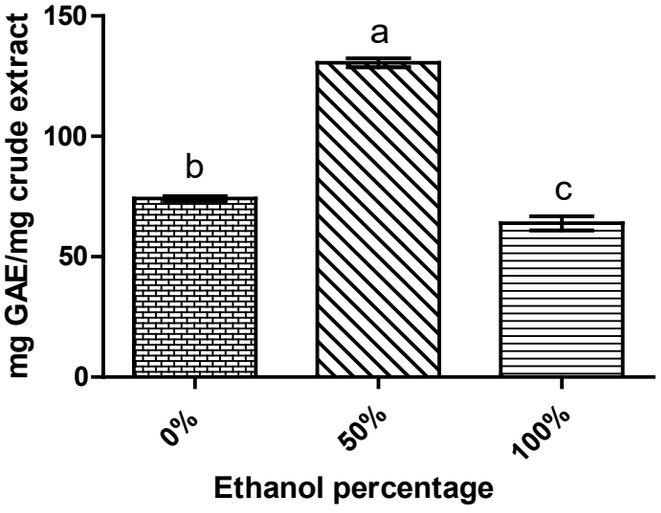

FIGURE 2. Total phenolic content of *D. zibethinus* shell extracts

TABLE 1. Biological activity of *D. zibethinus* shell extracted with different ethanol percentage

Bioactivities	Ethanol percentage (%)	Percentage of inhibition at 1000 µg/mL	IC_{50} values (µg/mL)
DPPH free radical scavenging	0	36.86 ± 1.47[b]	ND
	50	40.13 ± 1.70[b]	ND
	100	77.97 ± 3.55[a]	96.91 ± 1.09
NO scavenging	0	53.72 ± 0.92[ab]	ND
	50	56.62 ± 1.63[a]	435.30 ± 3.41
	100	50.87 ± 1.42[b]	ND
α-glucosidase inhibitory	0	74.73 ± 2.55[b]	ND
	50	99.83 ± 2.70[a]	1.99 ± 0.90
	100	99.49 ± 2.86[a]	4.53 ± 0.21

Values are the means ± standard deviation (n=3). Different superscript letters indicate significant differences ($p < 0.05$) among different ethanol percentage for the same assay
ND = not determined

NITRIC OXIDE (NO) SCAVENGING ACTIVITY OF *D. zibethinus* SHELL EXTRACTS

Table 1 shows that the 50% ethanolic extract had the highest percentage of NO scavenging activity which is 56.62 ± 1.63% followed by the 0% ethanolic extract which is 53.72 ± 0.92%. The lowest percentage of inhibition was achieved by the 100% ethanolic extract which is 50.87 ± 1.42%. The percentage of inhibition between 50% and 100% ethanolic extracts was determined to be significantly different ($p < 0.05$). Meanwhile, the 0% ethanolic extract of durian shell showed no significant difference ($p > 0.05$) towards the 50% and 100% ethanolic extracts. The IC_{50} value was further determined for the 50% ethanolic extract and compared with the standard quercetin. The IC_{50} of the 50% ethanolic extract and quercetin standard were 435.30 ± 3.41 µg/mL and 4.76 ± 1.05 µg/mL, respectively. The IC_{50} value obtained showed that the 50% ethanolic extract of the durian shell is a very weak NO scavenger. There is still insufficient data reported on the NO scavenging activity of different parts of durian plant thus comparative analysis between literature could not be done on the same species. However, a study previously reported that the chloroform and ethyl acetate fractions of durian shell have a strong inhibitory activity on the NO production in RAW 264.7 induced by LPS (lipopolysaccharide) with the IC_{50} values of 32.98 ± 2.85 µg/mL and 28.70 ± 1.35 µg/mL, respectively (Feng et al. 2016).

α-GLUCOSIDASE INHIBITORY ACTIVITY OF *D. zibethinus* SHELL EXTRACTS

The results for the α-glucosidase inhibitory activity of *D. zibethinus* shell extracts are shown in Table 1. All the extracts were screened at 1000 µg/mL to proceed with the determination of IC_{50} value. The results showed that the percentage of inhibition of α-glucosidase activity was the highest in the 50% and 100% ethanolic extracts. The percentage inhibition for these two samples was very high and approximately close to a complete inhibition on all the α-glucosidase activity which were 99.83 ± 2.70% and 99.49 ± 2.86% for 50 and 100% ethanolic extracts, respectively. In contrast to 0% ethanolic extract, the inhibition of α-glucosidase activity was lower which was 74.73 ± 2.55%. The IC_{50} values for the 50 and 100% ethanolic extracts were analyzed due to their substantial α-glucosidase inhibitory properties and the values obtained were 1.99 ± 0.90 µg/mL and 4.53 ± 0.21 µg/mL, respectively. When compared to the IC_{50} value obtained from the standard quercetin which is 6.89 ± 1.96 µg/mL, the 100% and 50% ethanolic extracts had much lower IC_{50} values and therefore indicated a greater α-glucosidase inhibitory activity. Research on the α-glucosidase

inhibitory activity by n-hexane and ethyl acetate of durian leaf extract was reported to have IC_{50} values of 35.83 µg/mL and 38.18 µg/mL, respectively (Aruan et al. 2019). A lower α-glucosidase inhibitory activity was shown by the n-hexane and ethyl acetate extracts of durian leaves compared to the 50 and 100% ethanolic extract of durian shell. However, when compared to 50% and 100% ethanolic durian shell extracts, a substantial inhibitory activity of α-glucosidase was shown by the water extract of durian leaves with an IC_{50} value of 9.79 µg/mL (Aruan et al. 2019). Thus, this finding showed the anti-diabetic potential of the durian leaves and shell extracts and also suggested that the extracts of the durian shells may contain bioactive components that can inhibit the action of α-glucosidase onto the PNPG. Furthermore, the phytochemical responsible for the potent α-glucosidase inhibitory activity of durian leaves water extract was identified to be the tannins and glycosides as the other compounds such as alkaloids, saponins, flavonoids, terpenoids, and glycosides were absence in the extract (Aruan et al. 2019). Meanwhile, terpenoids were the only phytochemicals identified in the n-hexane extract of durian leaves. This probably indicated the tannins and glycosides as potential α-glucosidase inhibitors in the extract. As for the ethanolic extract of durian leaves, flavonoids, terpenoids and glycosides were present in it (Aruan et al. 2019). The ethanolic extract of durian shell from the current study had stronger inhibitory activity than the water leaves extract probably due to two other compounds (flavonoids and glycosides) that are present in the shell extract and absent in the leaves extract. Other studies stated that excellent inhibitory activity of α-glucosidase was shown by the compounds from group terpenes, alkaloids, flavonoids, and phenols (Laoufi et al. 2017). Commercial acarbose which is an anti-diabetic drug also known as α-glucosidase inhibitor had an IC_{50} value of 2.154 µg/mL which indicated a very high inhibitory activity towards the α-glucosidase enzyme (Sulistiyani, Safithri & Sari 2016). This also proved the substantial anti-diabetic properties of 50% and 100% ethanolic extracts of durian and a possible therapy for diabetics in the future. A previous study conducted on rats showed a reduction of 50.19% in glucose levels and 35.82% in cholesterol levels in rats when fed with a dose of 500 mg/kg bw of durian shell extracts for 14 days (Muhtadi et al. 2016). Durian shells contain bioactive compounds that have potential anti-diabetic properties. These compounds can act as α-glucosidase inhibitors, which may help regulate blood sugar levels. Further research is needed to fully understand and explore the anti-diabetic potential of durian shell extracts.

Based on the Pearson test, the TPC of 0% ethanolic extract of durian shell had a positive correlation with the DPPH (R=0.316) and α-glucosidase (R=0.046) inhibition, respectively. However, a negative correlation was observed between TPC and NO inhibition of 0% ethanolic extract. Therefore, this indicated that the phenolic compound presence in the 0% ethanolic extract had contributed to the DPPH and α-glucosidase inhibition but not to the NO inhibition. Meanwhile, for 50% ethanolic extract, negative correlation was identified between TPC and DPPH inhibition (R=-0.968), and positive correlations were shown between TPC with NO inhibition (R=0.025) and α-glucosidase inhibition (R=0.646). Furthermore, a positive correlation was shown between TPC and NO inhibition (R=0.939) of the 100% ethanolic extract, while negative correlations between TPC with DPPH inhibition (R=-0.994) and α-glucosidase inhibition (R=-0.994). Therefore, this indicated that the phenolic compounds were not the contributor to the DPPH inhibition in 50% and 100% ethanolic extracts. The phenolic compound was indeed the contributor to the α-glucosidase inhibition for 50% ethanolic extract but not for the 100% ethanolic extract.

IDENTIFICATION OF COMPOUNDS IN 100% ETHANOLIC EXTRACT OF *D. zibethinus* SHELL USING UHPLC-MS/MS

In view of better antioxidant and α-glucosidase inhibition potentials demonstrated in the 100% ethanolic extract of *D. zibethinus*, this extract was selected for further identification by UHPLC-MS/MS to profile the bioactive compounds and tabulated in Table 2. The UHPLC-MS/MS had tentatively identified 20 compounds in *D. zibethinus* shell extract, and the peak was labeled according to the order of their retention time (Figure 3). Compounds were tentatively identified based on the exact mass measurement and fragmentations. The identification of metabolites was further confirmed by comparing the retention time and MS/MS spectra with literature or matching accurate mass and fragment information with Metabolomics workbench (http://www.metabolomicsworkbench.org/), MetFrag (https://msbi.ipb-halle.de/MetFrag/), METLIN (http://metlin.scripps.edu), GNPS (https://gnps.ucsd.edu/), ReSpect (http://spectra.psc.riken.jp/) and HMDB (http://www.hmdb.ca/) databases.

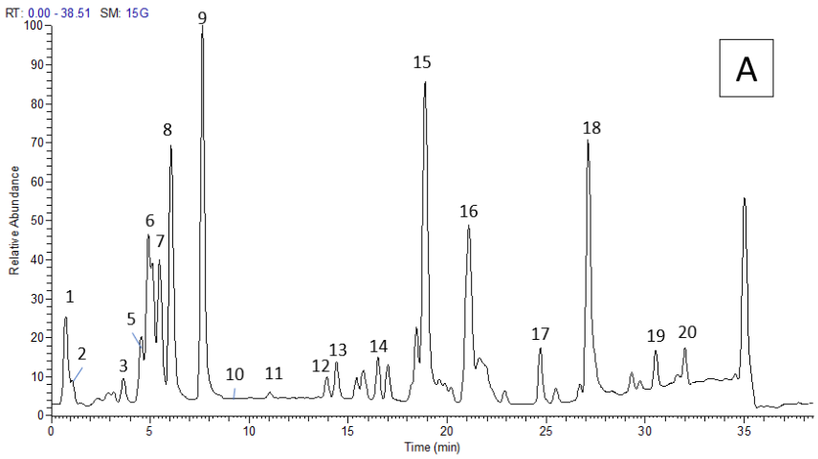

FIGURE 3. Total ion chromatogram (TIC) of 100% ethanolic extract of *D. zibethinus* shell. For Peak Assignment, see Table 2

TABLE 2. Tentative identification of compounds present in the 100% ethanolic extract of *D. zibethinus* shell

Peak No.	t_R (min)	$[M+H]^+$ (*m/z*)	$[M-H]^-$ (*m/z*)	Fragment ions (*m/z*)	Tentatively identified compounds	References
1	0.74	381.0789		218, 189, 133	Pteroside B	Yannai (2003)
2	1.08	294.1543		278, 248, 232	Dehydronuciferine	Yannai (2003)
3	3.66	287.0731		270, 136, 58	Kaempferol	A. Aziz & Abbe Maleyki (2019)
4	3.78	-	165.0578	139, 108, 95	Isomintlactone	Yannai (2003)
5	4.57	209.0441		194, 181, 165	Fraxetin	Feng et al. (2016)
6	4.92	319.0786		303, 271, 153, 136	Evofolin B	Feng et al. (2016)
7	5.51	195.1014		178, 165, 148	Ferulic acid	A. Aziz & Abbe Maleyki (2019)
8	6.07	453.3329		435, 407, 309	Torvanol A	Yannai (2003)
9	7.65	340.2588		294, 182, 128	5-Amino-1-(5-phospho-*D*-ribosyl)imidazole-4-carboxylate	Wishart et al. (2018)
10	9.57	218.9837		172, 156, 129	1-Isothiocyanato-8-(methylthio) octane	Yannai (2003)
11	11.03	371.1121		325, 267, 161, 149	Digalacturonate	Pinsorn et al. (2018)
12	13.93	343.2951		297, 241, 229, 183	13-Hydroxy-9-methoxy-10-oxo-11-octadecenoic acid	Yannai (2003)
13	14.36	335.2187		279, 219, 173, 147	1,5-Dibutyl methyl hydroxycitrate	Yannai (2003)
14	18.89	537.3386		494, 425, 361, 332	Alpha-Carotene	A. Aziz & Abbe Maleyki (2019)
15	21.08	429.2391		235, 220, 191, 165	Heteroflavanone B	Yannai (2003)
16	21.59	443.3333		400, 342, 271	Uvaol	Marquez-Martin et al. (2006)
17	24.69	546.4873		528, 511, 339, 137	Doxorubicinol	DiFrancesco et al. (2007)
18	27.11	414.8843		397, 302, 83	Beta-sitosterol	Illing, Hammado & Yusiranna (2017)
19	30.53	665.4222		647, 498, 401, 135	Phytolaccasaponin G	Yannai (2003)
20	32.00	473.3438		455, 442, 412, 272	Maslinic acid	Rudiyansyah, Lambert & Garson (2010)

Peak **1** (tR=0.74 min) was identified as pteroside B based on literature (Yannai 2003). The peak exhibited protonated molecular ion $[M+H]^+$ at *m/z* 381.0789 with three fragment ions in the MS/MS analysis at *m/z* 218, 189 and 133. The *m/z* 218 $[M+H-163]^+$ with loss of hydroxyethyl trimethyl indanone while the *m/z* 189 $[M+H-192]^+$ was identified as dehydrated vinyl hexopyranoside. The *m/z* 133 $[M+H-248]^+$ was identified as the ethyl hyroxyoxopropanoate. Peak **2** (tR=1.08 min) was identified as dehydronuciferine based on literature (Yannai 2003). The peak exhibited protonated molecular ion $[M+H]^+$ at *m/z* 294.1543 with three fragment ions in the MS/MS analysis at *m/z* 278, 248 and 232 from the loss of methane $[M+H-16]^+$, formaldehyde $[M+H-30]^+$ and loss of two methoxy groups $[M+H-62]^+$, respectively. Peak **3** (tR=3.87 min) was identified as kaempferol based on previously reported data (Aziz & Jalil 2019). The peak exhibited protonated molecular ion $[M+H]^+$ at *m/z* 287.0731 with three fragmentation ions in the MS/MS analysis at *m/z* 270 with the loss of OH $[M+H-17]^+$, *m/z* 136 $[M+H-150]^+$ was identified as hydroxyvinylphenol and *m/z* 58 $[M+H-150]^+$ was identified as glyoxal. Peak **4** (tR=3.66 min) showed deprotonated molecular ion $[M-H]^-$ at *m/z* 165.0578 was identified as isomintlactone. Three fragmented ions were produced in MS/MS analysis at *m/z* 139 from the loss of methylpropylfuranone unit $[M-H-26]^-$, *m/z* 108 from the loss of butyl $[M-H-57]^-$, and *m/z* 95 from the loss of pentene $[M-H-70]^-$ (Yannai 2003). Peak **5** (tR=4.57 min) was identified as frexitin based on a comparison with the literature (Feng et al. 2016). The peak exhibited molecular ion $[M+H]^+$ at *m/z* 209.0441 which later produced three fragmentation ions in the MS/MS analysis at *m/z* 194 from the loss of CH_3 $[M+H-15]^+$, *m/z* 181 from the loss of carbon monoxide $[M+H-28]^+$and *m/z* 165 from the loss of carbon dioxide $[M+H-44]^+$. Peak **6** (tR=4.92 min) was identified as evofolin B based on the reported data (Feng et al. 2016). The peak exhibited molecular ion $[M+H]^+$ at *m/z* 319.0786 which later produced four fragmentation ions in the MS/MS analysis at *m/z* 303 from the loss of CH_3 $[M+H-15]^+$, *m/z* 271 from the loss of formaldehyde and hydroxide $[M+H-30-17]^+$, *m/z*153 from the loss of hydroxymethoxyphenyl ethanal $[M+H-166]^+$ and *m/z* 136 from the loss of formaldehyde, methoxyphenol and carbon monoxide $[M+H-30-124-28]^+$. Peak **7** (tR=5.51 min) was identified as ferulic acid based on previous data (Aziz & Jalil 2019). The peak exhibited molecular ion $[M+H]^+$ at *m/z* 195.1014 with three fragmentation ions in the MS/MS analysis at *m/z* 178, 165 and 148. The *m/z* 178 indicated the loss of OH $[M+H-17]^+$ and the *m/z* 165 indicated the loss of formaldehyde $[M+H-30]^+$. Meanwhile, the *m/z* 148 indicated the loss of formic acid $[M+H-46]^+$. Peak **8** (tR=6.07 min) was identified as torvanol A based on literature (Yannai 2003). The peak exhibited molecular ion $[M+H]^+$ at *m/z* 453.3329 which later produced four fragmentation ions in the MS/MS analysis at *m/z* 435, 407 and 309 with loss of water $[M+H-18]^+$, formic acid $[M+H-46]^+$, and formic acid and sulfuric acid unit $[M+H-144]^+$, respectively. Peak **9** (tR=7.65 min) was identified as 5-amino-phosphoribosyl imidazole carboxylate based on the fragmentation information provided by established data (Wishart et al. 2018). The peak exhibited molecular ion $[M+H]^+$ at *m/z* 340.2588 which later produced three fragmentation ions in the MS/MS analysis at *m/z* 294 with loss of formate ion $[M+H-45]^+$, *m/z* 182 with loss of glycolaldehyde phosphate $[M+H-140]^+$ and water $[M+H-18]^+$ and *m/z* 128 showed the presence of aminoimidazole carboxylic acid unit $[M+H-212]^+$. Peak **10** (tR=9.57 min) was identified as 1-isothiocyanate-8-(methylthio)octane based on literature (Yannai 2003). The peak exhibited molecular ion $[M+H]^+$ at *m/z* 218.9837 which later produced three fragmentation ions in the MS/MS analysis at *m/z* 172, 156 and 129. The *m/z* 172 resulted from the loss of thioformaldehyde $[M+H-46]^+$, the *m/z* 156 resulted from the loss of dimethyl sulfide $[M+H-62]^+$ and *m/z* 129 resulted from the loss of isothiocyanatoethane $[M+H-87]^+$. Peak **11** (tR=11.03 min) was identified as digalacturonate based on the previous data reported (Pinsorn et al. 2018). The peak exhibited molecular ion $[M+H]^+$ at *m/z* 371.1121 which later produced three fragmentation ions in the MS/MS at *m/z* 325, 267, 161 and 149. The *m/z* 325 has resulted from the loss of formic acid $[M+H-46]^+$, *m/z* 267 $[M+H-44-60]^+$ with the loss of CO_2 and ethanediol and *m/z* 161 $[M+H-192-18]^+$ with loss of two units which were galactarolactone and water. The *m/z* 149 was identified to be the dihydroxy oxopentanoic acid. Peak **12** (tR=13.93 min) was identified as 13-hydroxy-9-methoxy-10-oxo-11-octadecenoic acid based on literature (Yannai 2003). The peak exhibited molecular ion $[M+H]^+$ at *m/z* 343.2951 which later produced four fragmentation ions in the MS/MS at *m/z* 297, 241, 229 and 183. The *m/z* 297 resulted from the loss of carbon monoxide $[M+H-28]^+$ while the *m/z* 241 was due to the loss of pentanoic acid $[M+H-102]^+$. As for *m/z* 229, it has resulted from the loss of hexenoic acid $[M+H-114]^+$. The *m/z* 183 $[M+H-128-32]^+$ resulted from the loss of two units which were heptenoic acid and methanol. Peak **13** (tR=14.36 min) was identified as 1,5-dibutyl methyl hydroxycitrate based on literature

(Yannai 2003). The peak exhibited molecular ion $[M+H]^+$ at *m/z* 335.2187 which later produced four fragmentation ions in the MS/MS at *m/z* 279, 219, 173 and 147. The *m/z* 279 resulted from the loss of butene $[M+H-56]^+$ while *m/z* 219 resulted from the loss of water and butyl acetate $[M+H-116]^+$. The *m/z* 173 was due to the loss of butyl glyoxylate $[M+H-130]^+$ and *m/z* 147 $[M+H-56-132]^+$ resulting from further losses of butyl glycolate from *m/z* 279. Peak **14** (tR=18.89 min) was identified as α-carotene based on previous data reported (Aziz & Jalil 2019). The peak exhibited molecular ion $[M+H]^+$ at *m/z* 537.3386 which later produced four fragmentation ions in the MS/MS at *m/z* 494 with loss of C_3H_7 $[M+H-43]^+$, *m/z* 425 $[M+H-56-56]^+$ with loss of two isobutene units and *m/z* 361 with the loss of butenyltrimethylcyclohexene $[M+H-178]^+$ while the *m/z* 332 $[M+H-15-190]^+$ was resulted from the loss of CH_3 and trimethylmethyl-butadienyl-cyclohexene. Peak **15** (tR=21.08 min) was identified as heteroflavanone B based on literature (Yannai 2003). The peak exhibited molecular ion $[M+H]^+$ at *m/z* 429.2391 which later produced four fragmentation ions in the MS/MS at *m/z* 235, 219, 191 and 165. The *m/z* 235 has resulted from the loss of the trimethoxystyrene $[M+H-194]^+$. Meanwhile, the *m/z* 219 $[M+H-194-16]^+$ was due to the loss of trimethoxystyrene and methane. The *m/z* 191 $[M+H-196-42]^+$ with the loss of trimethoxybenzaldehyde and ethenone and *m/z* 165 was identified to be the dimethoxyvinylbenzene $[M+H-264]^+$. Peak **16** (tR=21.59 min) was identified as uvaol based on literature (Marquez-Martin et al. 2006). The peak exhibited molecular ion $[M+H]^+$ at *m/z* 443.3333 which later produced three fragmentation ions in the MS/MS at *m/z* 400, 342 and 271. The *m/z* 400 $[M+H-28-15]^+$ from the loss of two ethylene and methyl radical, *m/z* 342 $[M+H-28-56-17]^+$ has resulted from the loss of ethylene, butene and hydroxide units and *m/z* 271 $[M+H-140-31]^+$ resulted from the loss of trimethylcyclohexenol and methoxy. Peak **17** (tR=24.69 min) was identified as doxorubicinol based on the data reported (DiFrancesco et al. 2007). The peak exhibited molecular ion $[M+H]^+$ at *m/z* 546.4873 which later produced four fragmentation ions in the MS/MS at *m/z* 528, 511, 339 and 137. The *m/z* 528 has resulted from the loss of water $[M+H-18]^+$. The *m/z* 511 has resulted from further losses of hydroxide $[M+H-17]^+$ from *m/z* 528. The *m/z* 339 $[M+H-147-60]^+$ resulted from the loss of aminotrideoxyhexopyranose and ethanediol. The *m/z* 137 was identified as methoxybenzaldehyde $[M+H-409]^+$. Peak **18** (tR=27.11 min) was identified as β-sitosterol based on previous data reported (Illing, Hammado & Yusiranna 2017). The peak exhibited molecular ion $[M+H]^+$ at *m/z* 414.8843 which later produced three fragmentation ions in the MS/MS at *m/z* 397 from the loss of water $[M+H-18]^+$, *m/z* 302 from the loss of ethylmethylpentene $[M+H-112]^+$ and *m/z* 83 was identified as methylpentadiene $[M+H-331]^+$. Peak **19** (tR=30.53 min) was identified as phytolaccasaponin G based on literature (Yannai 2003). The peak exhibited molecular ion $[M+H]^+$ at *m/z* 665.4222 which later produced four three fragmentation ions in the MS/MS at *m/z* 647 due to loss of water $[M+H-18]^+$, *m/z* 498 $[M+H-150-17]^+$ due to loss of ribose and hydroxide, *m/z* 401 hydroxide $[M+H-44-150-70]^+$ due to acetaldehyde, ribose and isobutenal, and *m/z* 135 $[M+H-530]^+$ was identified as deoxyribose. Peak **20** (tR=32.00 min) was identified as maslinic acid based on previous data reported (Rudiyansyah, Lambert & Garson 2010). The peak exhibited molecular ion $[M+H]^+$ at *m/z* 473.3438 which later produced four fragmentation ions in the MS/MS at *m/z* 455 due to loss of water $[M+H-18]^+$, *m/z* 442 due to loss of methoxide $[M+H-31]^+$, *m/z* 412 from the loss of water and methyl carbonyl $[M+H-18-43]^+$ and The *m/z* 272 due to loss of formate ions and the $C_9H_{16}O_2$ unit $[M+H-45-156]^+$.

A study conducted on *Eulophia herbacea* and *Eulophia ochreata* showed that β-sitosterol possesses strong radical scavenging, reducing power and a positive relationship was also observed between antioxidant properties and β-sitosterol (Manisha, Chandrashekhar & Raghunath 2018). Besides, the presence of higher β-sitosterol concentration was associated with antidiabetic properties, hypercholesterolemia prevention and anticancer (Manisha, Chandrashekhar & Raghunath 2018). Moreover, a study on maslinic acid extracted from *Plumeria rubra* leaves had high scavenging activity in DPPH radical scavenging activity (Nur & Al-Jasabi 2017). In addition, kaempferol which was also identified in durian shell extracts (Chandramohan et al. 2015) has been reported to reduce blood glucose levels in STZ-induced diabetic rats by lowering glycoprotein levels in the liver, increasing insulin production and improving glucose utilization. Another metabolite identified in the same extract, heteroflavanone B, exhibited dose dependent inhibition towards prostaglandin production in lipopolysaccharide-induced human whole blood with IC_{50} value of 0.8 μM (Masuri Kama et al. 2016). The presence of these metabolites could potentially contribute to the bioactivity of durian shell extract.

Conclusion

The current study found that using different ethanol concentrations for the extraction of *D. zibethinus* shell had a significant effect on the crude extract yield. In addition, the 50% ethanolic extract of durian shell contained the maximum phenolic concentration. The 100% ethanolic extracts significantly inhibited α-glucosidase enzyme and scavenged DPPH radicals. Furthermore, 20 chemicals were tentatively identified by UHPLC-MS/MS profiling, including flavonoids, alkaloids, benzofurans, terpenoids, pentose phosphate, organosulfur compounds, organooxygen compounds polyketides, carotene, carboxylic acid, and stigmastanes. The study suggests that the antioxidants and α-glucosidase inhibitors found in the durian shell could be beneficial for future use. Utilizing the trash formed by the durian shell may help to reduce the massive quantity of agricultural waste produced by this crop while also preserving the environment. In addition, *in vivo* testing and clinical studies should also be conducted to unveil the potential use of *D. zibethinus* shell as a natural therapeutic agent and to incorporate it as part of functional food or nutraceutical products.

Acknowledgments

The authors wish to thank Universiti Putra Malaysia (UPM) for the grant (GP-IPS/2021/9699000) provided under Putra Graduates Initiative Grant Scheme.

References

A. Aziz, N.A. & Abbe Maleyki, M.J. 2019. Bioactive compounds, nutritional value, and potential health benefits of indigenous durian (*Durio zibethinus* Murr.): A review. *Foods* 8(3): 96.

Azliana Abu-Bakar-Sajak, Ahmed Mediani, Maulidiani, Nur Sumirah Mohd-Dom, Chandradevan Machap, Muhajir Hamid, Amin Ismail, Alfi Khati & Faridah Abas. 2017. Effect of *Ipomoea aquatica* ethanolic extract in streptozotocin (STZ) induced diabetic rats via ^{1}H NMR-based metabolomics approach. *Phytomedicine* 36: 201-209.

Altemimi, A., Lakhssassi, N., Baharlouei, A., Watson, D.G. & Lightfoot, D.A. 2017. Phytochemicals: Extraction, isolation, and identification of bioactive compounds from plant extracts. *Plants* 6(4): 42.

Aruan, D.G.R., Barus, T., Haro, G., Siburian, R. & Simanjuntak, P. 2019. Phytochemical screening and antidiabetic activity of N-hexane, ethyl acetate and water extract from durian leaves (*Durio zibethinus* L.). *Oriental Journal of Chemistry* 35(1): 487-490.

Azmir, J., Zaidul, I.S.M., Rahman, M.M., Sharif, K.M., Mohamed, A., Sahena, F., Jahurul, M.H.A., Ghafoor, K., Norulaini, N.A.N. & Omar, A.K.M. 2013. Techniques for extraction of bioactive compounds from plant materials: A review. *Journal of Food Engineering* 117(4): 426-436.

Brown, M.J. 1997. Durio - A bibliographic review. In *International Plant Genetic Resources Institute*. 1st ed., edited by Arora, R.K., Ramanatha Rao, V. & Rao, A.N. New Delhi: International Plant Genetic Resources Institute.

Chandramohan, G., Al-Numair, K.S., Alsaif, M.A. & Veeramani, C. 2015. Antidiabetic effect of kaempferol a flavonoid compound, on streptozotocin-induced diabetic rats with special reference to glycoprotein components. *Progress in Nutrition* 17(1): 50-57.

DiFrancesco, R., Griggs, J.J., Donnelly, J. & DiCenzo, R. 2007. Simultaneous analysis of cyclophosphamide, doxorubicin and doxorubicinol by liquid chromatography coupled to tandem mass spectrometry. *Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences* 852(1-2): 545-553.

Feng, J., Wang, Y., Yi, X., Yang, W. & He, X. 2016. Phenolics from durian exert pronounced NO inhibitory and antioxidant activities. *Journal of Agricultural and Food Chemistry* 64(21): 4273-4279.

Illing, I., Hammado, N. & Yusiranna. 2017. Identification of secondary metabolism compounds from the septum of durian (*Durio zibethinus*). In *Proceeding International Conference on Natural and Social Science (ICONS)*. B640-45.

Ketsa, S. 2018. Durian - *Durio zibethinus*. In *Exotic Fruits Reference Guide*, 1st ed., edited by Rodrigues, S., de Oliveira Silva, E. & de Brito, E.S. London: Academic Press. pp. 169-180.

Kunarto, B. & Sani, E.Y. 2018. Antioxidant activity of extract from ultrasonic-assisted extraction of durian peels. *Journal of Applied Food Technology* 5(2): 25-29. https://doi.org/10.17728/jaft.3309

Laoufi, H., Benariba, N., Adjdir, S. & Djaziri, R. 2017. *In vitro* α-amylase and α-glucosidase inhibitory activity of *Ononis angustissima* extracts. *Journal of Applied Pharmaceutical Science* 7(2): 191-198.

Lee, S.Y., Mediani, A., Nur Ashikin, A.H., Azliana, A.B.S. & Abas, F. 2014. Antioxidant and α-glucosidase inhibitory activities of the leaf and stem of selected traditional medicinal plants. *International Food Research Journal* 21(1): 165-172.

Li, X. & Wang, L. 2011. Antioxidant activity of durian (*Durio zibethinus* Murr.) shell *in vitro*. *Article in Asian Journal of Pharmaceutical and Biological Research* 1(4): 542-521.

Manisha, P., Chandrashekhar, P. & Raghunath, M. 2018. Phytochemical investigation and validation of antioxidant potential of β-sitosterol from tubers of *Eulophia herbacea* and *Eulophia ochreata*. *International Journal of Pharmacognosy and Phytochemical Research* 10(9): 309-316.

Mariod, A.A., Saeed Mirghani, M.E. & Hussein, I. 2017. *Durio zibethinus* (Durian). In *Unconventional Oilseeds and Oil Sources*, 1st ed. London: Elsevier Science. pp. 187-197.

Marquez-Martin, A., De La Puerta, R., Fernandez-Arche, A., Ruiz-Gutierrez, V. & Yaqoob, P. 2006. Modulation of cytokine secretion by pentacyclic triterpenes from olive pomace oil in human mononuclear cells. *Cytokine* 36(5-6): 211-217.

Muhtadi, M., Haryoto, H., Sujono, T.A. & Suhendi, A. 2016. Antidiabetic and antihypercholesterolemia activities of rambutan (*Nephelium lappaceum* L.) and durian (*Durio zibethinus* Murr.) fruit peel extracts. *Journal of Applied Pharmaceutical Science* 6(4): 190-194.

Ngo, T.V., Scarlett, C.J., Bowyer, M.C., Ngo, P.D. & Vuong, Q.V. 2017. Impact of different extraction solvents on bioactive compounds and antioxidant capacity from the root of *Salacia chinensis* L. *Journal of Food Quality* 2017: 9305047.

Nur Ashikin Abdul-Hamid, Maulidiani Maulidiani, Ahmed Mediani, Ummul Izzatul Izzah Yahya, Intan Safinar Ismail, Chau Ling Tham, Khalid Shadid & Faridah Abas. 2018. Physicochemical characteristics, nutritional composition, and phytochemical profiles of nine Algerian date palm fruit (*Phoenix dactylifera* L.) varieties. *Journal of Food Biochemistry* https://doi.org/10.1111/jfbc.12663

Nur, N.M. & Al-Jasabi, S.A.M. 2017. Antioxidant properties of maslinic acid extracted from *Plumeria rubra* leaves. *International Journal of Contemporary Research and Review* 8(7): 20178-20183.

Nurul Arneida Husin, Sadequr Rahman, Rohini Karunakaran & Subhash Janardhan Bhore. 2018. A review on the nutritional, medicinal, molecular and genome attributes of durian (*Durio zibethinus* L.), the king of fruits in Malaysia. *Bioinformation* 14(06): 265-270.

Pinsorn, P., Oikawa, A., Watanabe, M., Sasaki, R., Ngamchuachit, P., Hoefgen, R., Saito, K. & Sirikantaramas, S. 2018. Metabolic variation in the pulps of two durian cultivars: Unraveling the metabolites that contribute to the flavor. *Food Chemistry* 268: 118-125.

Rudiyansyah, Lambert, L.K. & Garson, M.J. 2010. Lignans and triterpenes from the bark of *Durio carinatus* and *Durio oxleyanus*. *Journal of Natural Products* 73(10): 1649-1654.

Sagar, N.A., Pareek, S., Sharma, S., Yahia, E.M. & Lobo, M.G. 2018. Fruit and vegetable waste: Bioactive compounds, their extraction, and possible utilization. *Comprehensive Reviews in Food Science and Food Safety* 17(3): 512-531.

Masuri Kama Kamaruddin Shah, Hasnah Mohd Sirat, Shajarahtunnur Jamil, and Juriyati Jalil. 2016. Flavonoids from the bark of *Artocarpus integer* var. *silvestris* and their anti-inflammatory properties. *Natural Product Communications* 11(9): 1275-1278.

Suganya Murugesu, Zalikha Ibrahim, Qamar Uddin Ahmed, Bisha Fathamah Uzir, Nik Idris Nik Yusoff, Vikneswari Perumal, Faridah Abas, Khozirah Shaari & Alfi Khatib. 2019. Identification of α-glucosidase inhibitors from *Clinacanthus nutans* leaf extract using liquid chromatography-mass spectrometry-based metabolomics and protein-ligand interaction with molecular docking. *Journal of Pharmaceutical Analysis* 9(2): 91-99.

Sulistiyani, Safithri, M. & Sari, Y.P. 2016. Inhibition of α-glucosidase activity by ethanolic extract of *Melia azedarach* L. leaves. *IOP Conference Series: Earth and Environmental Science* 31: 012025.

Suntharalungam, C., Jamaludin, J.A., Athirah, N.F., Mustaffa, R. & Safari, S. 2018. *Durian as new source of Malaysia's Agricultural Wealth.* FFTC Agricultural Policy Platform (FFTC-AP). https://ap.fftc.org.tw/article/1321

Wishart, D.S., Feunang, Y.D., Marcu, A., Guo, A.C., Liang, K., Vázquez-Fresno, R., Sajed, T., Johnson, D., Li, C., Karu, N., Sayeeda, Z., Lo, E., Assempour, N., Berjanskii, M., Singhal, S., Arndt, D., Liang, Y., Badran, H., Grant, J., Serra-Cayuela, A., Liu, Y., Mandal, R., Neveu, V., Pon, A., Knox, C., Wilson, M., Manach, C. & Scalbert, A. 2018. HMDB 4.0: The human metabolome database for 2018. *Nucleic Acids Research* 46(D1): D608-D617.

Xu, D.P., Li, Y., Meng, X., Zhou, T., Zhou, Y., Zheng, J., Zhang, J.J. & Li, H.B. 2017. Natural antioxidants in foods and medicinal plants: Extraction, assessment and resources. *International Journal of Molecular Sciences* 18(1): 96.

Yannai, S. 2003. *Dictionary of Food Compounds with CD-ROM*. 2nd ed. Boca Raton: CRC Press.

*Corresponding author; email: faridah_abas@upm.edu.my