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Article

Exploration of Wendan Pomelo Peel from Four Different Growing Regions by LC-MS and Bioactivity Analysis

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Abstract: Wendan (a type of pomelo), as a popular fruit in China, is less known in other countries. Its peel is widely used in food and traditional medicine. Four different origins of Wendan pomelo were selected, and crude extracts were obtained by the Soxhlet extraction method. The composition of Wendan peel was analyzed by high-performance liquid chromatography-mass spectrometry (HPLC-MS) in positive ion mode. The compounds were identified by searching the Metabolite Link (METLIN), Spectral Database for Organic Compounds (SDBS) and referring to literature reports. A total of 20 compounds were identified among the samples from the four origins, of which 8 compounds were common. The majority of the compounds belonged to the flavonoid and coumarin classes, Meranzin hydrate was identified for the first time in pomelo peel. In vitro antioxidant activity experiments showed that samples from Taizhou, Zhejiang exhibited the highest antioxidant activity in the DPPH, ABTS, and FRAP assays, with values of 0.59 mg/mL, 97.06 $\mu\text{mol TE/g}$, and 60.62 $\mu\text{mol Fe}^{2+}/\text{g}$, respectively. Samples from Zhangzhou, Fujian showed antioxidant activity second only to the samples from Taizhou, Zhejiang. The sample from Zhangzhou, Fujian Province, showed excellent inhibitory activity in the α -glucosidase inhibition assay ($\text{IC}_{50}=7.99 \text{ mg/mL}$).

Keywords: Wendan pomelo peel; chemical components; antioxidant; α -glucosidase

1. Introduction

Citrus maxima (Burm.) Merr, commonly known as pomelo, is an evergreen tree belonging to the Rutaceae family. Its fruit has a smooth surface with small oil glands and is typically round or pear-shaped. The flesh of the fruit can be either white or red, with a few variants exhibiting a creamy yellow color. Pomelo cultivation can be found in various Southeast Asian regions such as Malaysia, Thailand, and Vietnam [1,2]. In China, it is primarily cultivated in Guangdong, Guangxi, Fujian and Zhejiang [2].

Pomelo has been widely used in food and cosmetic industry due to its special aroma, nutritional value and pharmacological activity [3]. Pomelo, in China, is used traditionally as functional food with the potential to balance insulin and glucose levels, thereby contributing to the management of diabetes [4]. Furthermore, pomelo products could be processed into pectin, essential oils and dried pomelo peel. [5]. In recent years, the pomelo processing industrial products, such as beverages, canned foods and wines have been developing rapidly.

The pulp portion of pomelo is used as fresh food to supplement the nutrients such as vitamins. The peel, accounting for approximately 30% of the whole pomelo, is consumed directly in the form of sweets, tea and medicine by locals on the southeast coast of China [2]. The bioactivities and phytochemistry of pomelo have been reviewed, including flavonoids, essential oils, coumarin classes, and triterpenes. The antioxidation, antibacterial, anticancer, and alleviation of depression have been reported [6–9]. However, there is relatively limited research on the classification of different species of pomelo.

The main pomelo species in China can be divided into three categories: Wendan pomelo, Shatian pomelo, and inter-specific pomelo [2]. Especially Wendan pomelo is well-known for its crisp and tender flesh, large size, and rich flavor. It was first cultivated in Zhangzhou, Fujian and later introduced to other regions. Currently, the most famous Wendan pomelo species in China are Yuhuan Wendan from Taizhou, Zhejiang, Duwei Wendan from Putian, Fujian, and Madou Wendan from Tainan, Taiwan. With the widespread cultivation of Wendan pomelo, there has been a continuous increase in its production. However, there is a lack of systematic research on Wendan pomelo peel, especially in terms of comparing the chemical composition and biological activities of Wendan pomelo peel from different cultivation regions.

Therefore, the present work was to investigate the composition and antioxidant activity of Wendan pomelo peel grown in China from four different origins.

2. Materials and Methods

2.1. Plant Materials

The Wendan (*Citrus maxima* cv. *Wentan Buntan*) peels were obtained from four different regions of China (Table 1, Figure 1), including Xuzhou (Jiangsu), Taizhou (Zhejiang), Zhangzhou (Fujian), Meizhou (Guangdong). These materials were identified by Professor Chun-lin Long (College of Life and Environmental Sciences, Minzu University of China) and the Flora of China, and then the fresh Wendan peels were dried, crushed and stored at cool place.

The extractions were carried out by the Soxhlet extraction method. The ground peel of Wendan pomelo (6.0g) was tightly wrapped in filter paper and placed into a Soxhlet extractor, which was then placed in a round-bottom flask (500ml) containing 70% ethanol solution to obtain the extract. The extract was subjected to vacuum filtration, with the addition of 25% ethanol solution for washing. The resulting filtrate was transferred to a rotary evaporator and distilled under reduced pressure at 60°C until no alcohol odor remained. Finally, the extract was dried in a fume hood.



Figure 1. Jiangsu, Zhejiang, Fujian and Guangdong Province are represented by the colors green, pink, orange and purple respectively. Samples collection site are the red dot.

Table 1. Characteristics and information of samples.

Accessions collected	Main geographical distribution	Longitude and Latitude	Traditional Name	Thickness of peels (mm)
W1	Xuzhou, Jiangsu	N:34°12'36" E:118°17'14"	Suqianmiyou	1~2
W2	Taizhou, Zhejiang	N:28°06'44" E:121°14'25"	Yuhuanwendan	2~3
W3	Zhangzhou, Fujian	N:24°25'22" E:117°28'16"	Pingheyong	2~3
W4	Meizhou, Guangdong	N:24°14'22" E:116°31'10"	Jiaxingmiyou	1~2

2.2. HPLC-Q-TOF-MS/MS analysis

The analysis [10] was conducted using the Agilent 1260 Infinity system (Agilent, USA) and the 1200 HPLC 6520 Q-TOF-MS (Agilent, USA). The samples were separated on a Hypersill Gold C18 column (250 mm × 4.6 mm, 5 μm, SN10609405, Thermo Scientific, USA). The injection sample volume and flow rate were set at 2 μL and 1 mL/min, respectively. The gradient conditions were as follows: solvent A (H₂O-CH₂O₂, 1%) and solvent B (acetonitrile, C₂H₃N 99%). The initial setting was 0-5 min with a linear gradient of 10% B, followed by 5-35 min with 30% B, 35-45 min with 100% B, and then held at 10% B for 5 min to allow column equilibration. The detection range was set from 200 nm to 600 nm using nitrogen gas as the carrier. Mass spectrometry conditions included electrospray ionization (ESI) source, with an ion source temperature of 300°C, positive ion detection, a scanning range of m/z 80-2000 Da, and a cone voltage of 30V.

2.3. Nuclear Magnetic Resonance

¹H and ¹³C NMR spectra (one-dimensional) were obtained on a Bruker Avance DRX-600 (Bruker, Germany) spectrometer with a 5 mm TCI cryoprobe and a 14.1 T magnetic field. The chemical shifts of ¹H and ¹³C were referenced according to the peak of the DMSO (C₂H₆OS) solvent used to solubilize the samples.

2.4. DPPH (2, 2-diphenyl-1-picrylhydrazyl)-Assay

The DPPH free radical scavenging activity was assessed in accordance with a modified version of a known protocol [11]. The extract solutions were diluted with methanol to obtain a series of concentrations ranging from 10 to 500 μg/mL. The 0.06 mM DPPH solution was prepared by dissolving DPPH in methanol. The 100 μL aliquot of the sample was mixed with 100 μL of the DPPH solution and kept in the dark at room temperature. After 30 minutes, the absorbance of the solution was measured at 517 nm. BHT was used as a positive control, and methanol served as the blank control, following the same experimental procedure. The radical scavenging activity was calculated using the equation:

$$SC_{50} (\%) = [1 - (A_1 - A_2) / A_0] \times 100\%$$

Where A₀ represents the absorbance of the blank control (methanol and DPPH solution), A₁ is the absorbance of the sample with DPPH solution, and A₂ is the absorbance of the sample solution with methanol. The results were expressed as SC₅₀ (mg/mL), and each batch of samples was tested in triplicate.

2.5. ABTS (2, 2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) assay

The ABTS free radical scavenging activity was determined with slight modifications based on a previously described method [12]. The ABTS solution was prepared by mixing equal volumes of potassium persulfate (2.45 mM) and ABTS stock solution (7 mM), and allowing the mixture to react

in the dark at room temperature for 12-16 hours. The ABTS radical solution was then diluted with methanol to achieve an absorbance of 0.70 ± 0.02 at 734 nm. The Trolox ($C_{14}H_{18}O_4$) standard solution (10 mM) was prepared using methanol and further diluted with methanol to obtain a series of concentrations ranging from 0.1 to 0.7 mM. For the assay, 20 μ L of Trolox was added to 180 μ L of the ABTS solution and incubated in the dark at room temperature. After 10 minutes, the absorbance of the solution was measured at 734 nm. The same procedure was followed for the sample analysis. The standard curve was constructed using the Trolox standard solution, with the absorbance as the ordinate and the Trolox concentration as the abscissa. The absorbance value obtained from the sample was then substituted into the standard curve to calculate the ABTS antioxidant activity. Each batch of samples was tested in triplicate, and the results were expressed as Trolox equivalent (μ mol TE/g).

2.6. Ferric Reducing Antioxidant Power (FRAP) assay

The FRAP assay was conducted with slight modifications based on a previously described method [13]. The working solution was prepared by combining 300 mM/L acetate buffer (pH 3.6), 10 mM/L TPTZ (tripyrindyltriazine) solution in 40 mM/L HCl, and 20 mM/L $FeCl_3 \cdot 6H_2O$ solution in a volume ratio of 10:1:1. Prior to analysis, the FRAP solution was incubated in a 37 °C water bath. The samples were diluted with methanol, and 20 μ L of the diluted sample solution was added to react with 180 μ L of the FRAP solution at 37 °C in the dark. After 30 minutes, the absorbance at 593 nm was measured. A standard curve was constructed using the Fe^{2+} concentration as the abscissa and the absorbance as the ordinate to calculate the FRAP antioxidant activity. Each batch of samples was tested in triplicate, and the results were expressed as Fe^{2+} equivalent (μ mol Fe^{2+} /g).

2.7. α -Glucosidase inhibitory assay

The α -glucosidase inhibitory assay was conducted with slight adjustments based on a previously described method [14]. The 1 U/mL α -glucosidase solution was prepared using phosphate buffer (0.1M, pH 6.8). For the assay, 10 μ L of the sample diluted in DMSO at various concentrations and 30 μ L of α -glucosidase solution were mixed in 80 μ L of potassium phosphate buffer and incubated for 5 minutes at a 37 °C water bath. Then, 30 μ L of 20 mM PNPG (p-Nitrophenyl- β -D-Galactopyranoside) was added to initiate the reaction, which was further incubated in a 37 °C water bath for 30 minutes. The reaction was terminated by adding 40 μ L of Na_2CO_3 solution (2M), and the absorbance was measured at 405 nm. Acarbose was used as a positive control. The inhibition ratio was calculated using the following equation:

$$\text{Inhibition (\%)} = [1 - (A_1 - A_0) / (A_3 - A_2)] \times 100\%$$

Where A_0 represents the absorbance of the sample blank (phosphate buffer instead of PNPG), A_1 is the absorbance of the sample, A_2 is the absorbance of the control blank (phosphate buffer instead of the sample and PNPG), and A_3 is the absorbance of the control (phosphate buffer instead of the sample). The results were expressed as IC_{50} (mg/mL), and each batch of samples was tested in triplicate.

3. Results and Discussion

3.1. Identification Components of Wendan pomelo peel

The ion chromatograms in positive ion mode obtained by HPLC-MS/MS for the pericarp of four different origins of Wendan pomelo peels are shown in Figure 2. The chemical composition results are presented in Table 2. A total of 20 compounds (Figure 3) were detected in the samples from the four origins, with 8 compounds common to all four samples and 2 compounds were identified but their names remain unknown. The major compounds were coumarins and flavonoids. The compound meranzin hydrate F13 (CPF13), which belongs to the coumarin compounds, exhibited the highest peak area in the chromatogram. This compound was first discovered in the root of *Prangos ferulacea* in 1972 [15] and is commonly studied in the context of Chaihu-Shugan-San [16]. It was the first time that this compound was discovered in the Wendan pomelo peel. The flavonoid compounds with higher peak areas in the chromatogram were identified as rutin (CP5), narirutin (CP10),

hesperidin (CP11), neohesperidin (CP12), and kaempferol (CP14). There were significant differences in peak areas among samples from different origins, with the proportions of coumarin compounds and flavonoid compounds in Zhangzhou samples being similar, while the coumarins were much more abundant than the flavonoids in the samples from Xuzhou and Meizhou.

The significant variations were observed in the chemical composition of samples from different origins. For instance, the sample from Zhejiang Taizhou (W3) exhibited the highest number of detected compounds with a total of 16 compounds. The sample from Guangdong Meizhou (WF4) had the lowest number of detected compounds, with 11 compounds identified only. For these compounds, CP2, CP3, CP6, and CP16 were exclusively found in the sample of Taizhou, while CP14 was detected only in the sample of Zhangzhou, and CP15 was present solely in the sample of Xuzhou, compound CP8 was not detected in the sample of Meizhou. Previous studies have suggested that variations in plant chemical composition may be attributed to ecological differences [17,18]. The chemical composition differences have been observed in samples of the same plant species collected from different regions or even different locations within the same region as described by Zhang et al. [19]

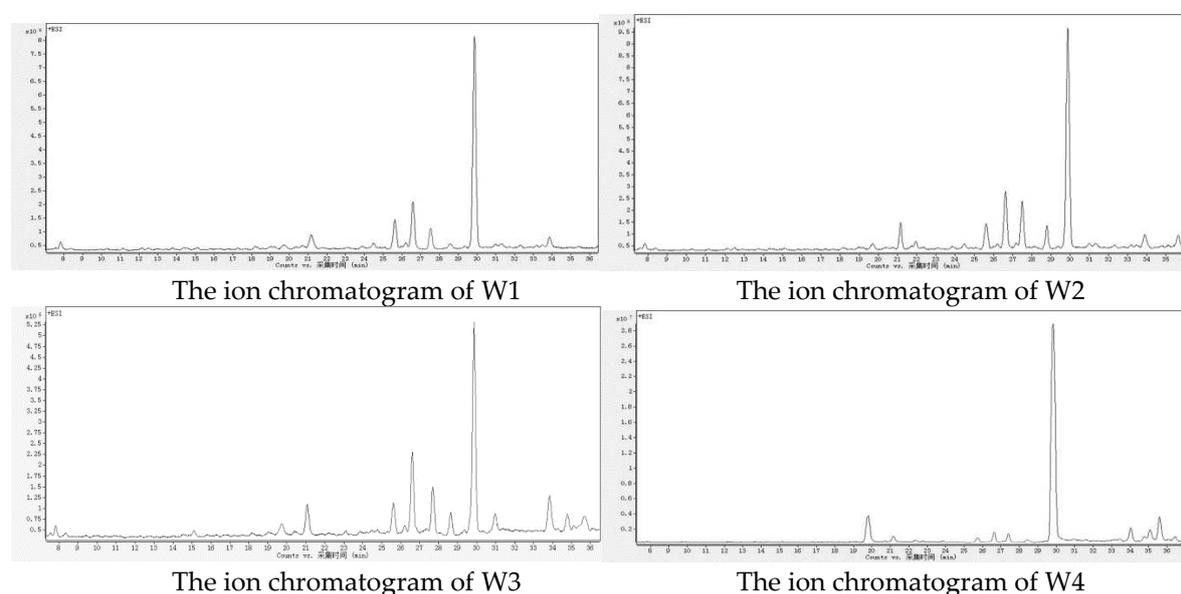


Figure 2. The ion chromatogram of Wendan pomelo peel from different regions.

Table 2. The chemical constituents of Wendan pomelo peel from four areas.

Number ¹	Rt (Min)	Molecular formula	Fragments (m/z)			Compound	W1	W2	W3	W4
			1 ^a	2	3					
CP1	7.81	C ₁₀ H ₈ O ₃	177.2405	133.1216	121.1081	7-methoxycoumarin [*]	+	+	+	-
CP2	12.13	C ₁₅ H ₁₆ O ₉	341.2512	323.1103	305.0924	Unknown	-	+	-	-
CP3	12.52	C ₁₅ H ₁₆ O ₉	341.0807	179.0340	151.0388	Esculetin-6-O-glucoside ^c	-	+	-	-
CP4	19.73	C ₁₆ H ₁₈ O ₉	355.1029	163.0392	145.0287	Chlorogenic acid ^c	+	+	+	+
CP5	21.17	C ₂₇ H ₃₀ O ₁₆	611.1611	465.1029	303.0501	Rutin [*]	+	+	+	+
CP6	21.95	C ₂₇ H ₃₀ O ₁₄	579.1710	433.1132	271.0603	Apigenin-O-(deoxyhexosyl)hexoside ^c	-	+	-	-
CP7	22.31	C ₂₁ H ₂₀ O ₁₀	433.1135	415.1034	397.0923	Isovitexin ^c	-	-	-	+
CP8	24.49	C ₂₈ H ₃₂ O ₁₆	625.2113	607.1564	589.3071	Lucenin-2 4'-methylether ^d	+	+	+	-
CP9	25.61	C ₂₃ H ₃₄ O ₁₅	573.1811	551.2143	227.1936	Genipin-β-gentiobioside ^e	+	+	+	+
CP10	26.68	C ₂₇ H ₃₂ O ₁₄	581.1881	419.1349	273.0763	Narirutin [*]	+	+	+	+
CP11	27.55	C ₂₈ H ₃₄ O ₁₅	611.1994	449.1457	303.0870	Hesperidin [*]	+	+	+	+
CP12	28.91	C ₂₈ H ₃₄ O ₁₅	611.1987	449.1447	303.0871	Neohesperidin [*]	+	+	+	+
CP13	29.87	C ₁₅ H ₁₈ O ₅	279.1243	261.1294	243.1027	Meranzin hydrate ^{*x}	+	+	+	+
CP14	30.88	C ₁₅ H ₁₀ O ₆	287.0553	258.0522	213.0543	Kaempferol ^{*c}	-	+	+	-
CP15	31.14	C ₁₁ H ₆ O ₃	187.0401	159.0444	143.0499	Angelicin ^c	+	-	-	-
CP16	31.36	C ₂₁ H ₂₀ O ₁₁	449.1078	303.0501	229.0495	Quercitrin ^c	-	-	+	-
CP17	32.08	C ₂₀ H ₂₄ O ₁₁	441.2495	352.3446	282.2769	Unknown	+	+	-	-

CP18	33.88	C ₂₁ H ₂₀ O ₁₂	465.4033	303.2861	274.3367	Isoquercitrin*	+	+	+	+
CP19	34.83	C ₂₈ H ₃₂ O ₁₅	609.1820	463.1244	301.1069	Diosmetin-7-O-rutinoside ^c	-	-	+	+
CP20	35.62	C ₁₅ H ₁₀ O ₇	303.0507	285.0409	257.0453	Quercetin ^c	-	+	+	+

¹Compound numbers are denoted as CPX (X = 1-20), a represents the main fragment ion [M+H]⁺, * indicates confirmation through standard compounds; "c-e" represents references [20–22]; x indicates determination through nuclear magnetic resonance analysis. "+" indicates the presence of the compound; "-" indicates the absence of the compound.

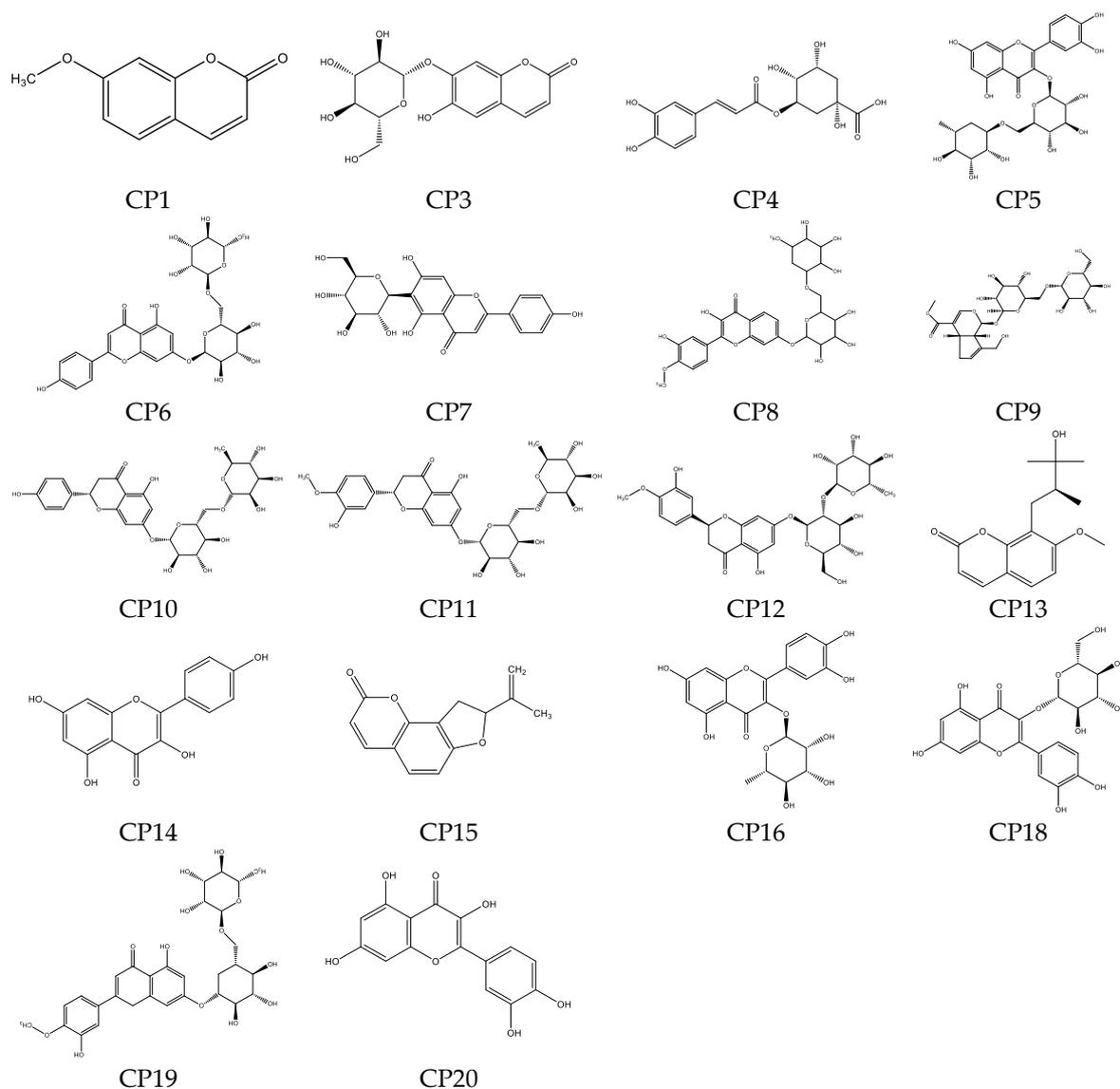


Figure 3. The structural formula of compounds.

3.2. NMR

The compound CP13 was characterized based on the analysis of ¹H NMR and ¹³C NMR spectra. In the ¹H NMR spectrum (Figure 4), methyl signals at δ 1.13 (s, H-17), 1.14 (s, H-18), and 3.87 (s, H-13) were observed on three carbon atoms. Additionally, four olefinic signals were detected at δ 6.24 (t, H-2), 7.95 (t, H-3), 7.53 (t, H-7), and 7.03 (t, H-8). Analysis of the ¹³C NMR spectrum (Figure 5) revealed a total of 15 carbon atoms in the compound, including three signals of CH₃, one signal of CH₂, five signals of CH, and six signals of C. The ¹H NMR and ¹³C NMR spectra displayed characteristic signals for a coumarin nucleus substituted on 7 by a methoxyl group. The molecular formula of CP13 was determined as C₁₅H₁₈O₅ based on the results obtained from MS, in conjunction with the analysis of the ¹H NMR and ¹³C NMR spectra. The compound was identified as a meranzin hydrate through structural elucidation. The compound meranzin hydrate, identified as a major

(CP11) exerts antioxidant effects by attenuating oxidative stress reactions [27]. Neohesperidin (CP12) has also been confirmed to possess excellent free radical scavenging abilities in both superoxide and hydroxyl radical tests [28]. These four compounds were detected in all samples, providing a comprehensive explanation for the observed antioxidant activity. However, the compound kaempferol (CP14) has been shown to possess antioxidant activity [29] and considering the differences in compound composition among samples and the potential synergistic effects between compounds [30], this may explain why some samples exhibit stronger antioxidant capacity while others show relatively weaker activity.

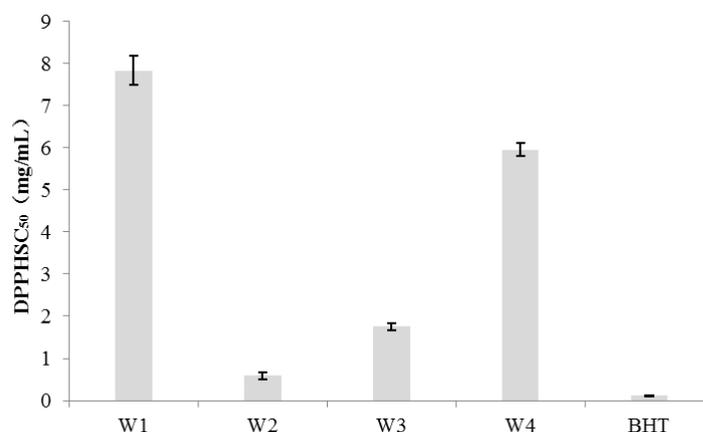


Figure 6. DPPH scavenging ability of samples from four regions.

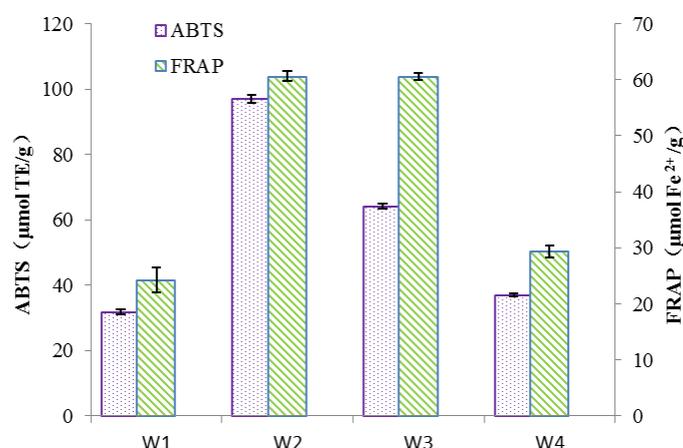


Figure 7. Antioxidant activities of samples from four regions in ABTS and FRAP assay.

3.4. α -Glucosidase inhibitory activity

The α -glucosidase inhibition activity, according to Table 3, was evaluated as a measure of hypoglycemic with lower values indicating stronger blood glucose-lowering ability. All samples from the four regions exhibited weaker activity compared to the positive control acarbose. But the samples of W3 ($I=7.99$ mg/mL) demonstrated the highest inhibitory activity in all samples, followed by W1 with a value of 11.86 mg/mL. Sample of W2 showed moderate activity with a value of 12.38 mg/mL, while W4 exhibited the weakest inhibitory activity.

The studies have indicated that quercitrin exhibits significant inhibitory effects on α -amylase and α -glucosidase, making it an ideal compound for targeting diabetes management [31,32]. Based on the obtained chemical composition and without considering synergistic effects, it was observed that the compound quercitrin (CPF16) detected in sample of W3 was not found in other samples.

Therefore, the presence of quercitrin in sample W3 may serve as a crucial indicator of its superior inhibitory activity compared to other samples.

Table 3. The α -Glucosidase inhibitory activities of samples from four regions.

Sample	I (mg/mL)
WF1	11.86±0.40
WF2	12.38±1.33
WF3	7.99±0.83
WF4	15.6±0.35
acarbose	0.96±0.07

4. Conclusions

This study compared the chemical composition and biological activities of Wendan peel samples collected from four different regions in China. The results revealed variations in the chemical composition of the samples from different origins. A total of 20 compounds, primarily flavonoids and coumarins, were detected among the four samples. The bioactivity assays demonstrated that the sample from Taizhou (W2) exhibited the highest antioxidant activity, followed by the sample from Zhangzhou (W3). These two samples could be considered as potential natural antioxidants. Additionally, the sample from Zhangzhou (W3) could be regarded as a promising source for the research and development of natural α -glucosidase inhibitors.

Author Contributions: Conceptualization, J.L.; methodology, J.L.; data curation, J.L.; writing—original draft preparation, J.L.; writing—review and editing, J.L. and W.W. All authors have read and agreed to the published version of the manuscript.

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