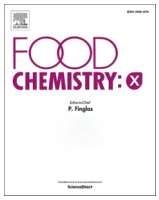
Food Chemistry: X 25 (2025) 102135

Contents lists available at ScienceDirect

Food Chemistry: X

journal homepage: www.sciencedirect.com/journal/food-chemistry-x



# New perspectives on djulis (*Chenopodium formosanum* Koidz.) and its potential application in functional food

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ARTICLE INFO

*Keywords:*
Djulis
*Chenopodium formosanum*
Phytochemical compounds
Functional properties
Applications

ABSTRACT

Djulis (*Chenopodium formosanum* Koidz.) is an endemic cereal plant to Taiwan that has been cultivated by Taiwanese aborigines for hundreds of years. Djulis Djulis is a well-known ruby cereal because it contains betanin and exhibits strong antioxidant activity. This review summarizes comprehensive information regarding proximate composition, phytochemical compounds, biological activities, and recent industrial applications. Djulis is rich in phytochemical compounds including flavonoids, phenolics, and betanin. Further assessment of cell and animal studies showed that djulis leaf, whole grain, hull, and seed extracts exhibited antioxidant, anti-aging, anti-diabetic, anticancer, anti-adipogenesis, hepatoprotective, anti-inflammatory, and gastric protective properties. Products incorporating djulis were also included in this review. This review provides new insights into the application of djulis in the development of new products.

## 1. Introduction

Djulis (*Chenopodium formosanum* Koidz.) in Paiwan or "Hong li" in Chinese, are plants endemic to Taiwan that have been cultivated by aborigines for more than 100 years (Li et al., 2020). Djulis is an herb crop belonging to the phylum Tracheophyte, class Magnoliopsida, order Caryophyllales, family Amaranthaceae, and genus Chenopodium (Liu, 1996). Djulis is a domesticated form of lambsquarter (*Chenopodium album* Linn) and a relative of *Chenopodium quinoa* (Jarvis et al., 2022). Djulis grows up to 2.5 m tall, where the stems are stout and branched, the petiole of the leaves is 3–5 cm long, the leaves are 6–12 cm long and 3–6 cm wide, and the seeds grow horizontally (Liu, 1996). Djulis is easy to cultivate, yielding 46 g of seeds per plant in a short harvest time (2.5 months), and its leaves are ready to harvest in 28 days (Chio et al., 2013).

According to the Ministry of Agriculture of Taiwan, djulis were considered an important food source for famine due to severe drought in the 19th century (Ministry of Agriculture, 2017). Djulis is considered a superfood because of its high fiber, starch, and essential amino acid contents. It is consumed and used as a wine starter and is incorporated into bakery and snack products, starchy desserts, and noodles (Kuo et al., 2021; Li et al., 2015; Li et al., 2021; Tsai et al., 2011). In addition, djulis also contain six phytosterols (34.73–59.48 mg/100 g) and triterpenes (30.56–57.47 mg/100 g), and five other unsaponifiable compounds (15.89–22.50 mg/100 g) (Huang, Chu, et al., 2019). The retail price of djulis seeds is approximately $ 30 per 600 g (Sui, 2016). The leaves of djulis are greatly enjoyed as delicacy during Chinese new year in Taitung, for example boiled djulis leaves sprinkled with peanut, fried in tempura batter, served with dongpo pork, or even as dumpling fillings (Tso, 2019). Djulis hulled seeds are usually cooked with rice or millet as a staple food in Taiwan or are used in gluten-free food product formulations (Lyu et al., 2022; Wang et al., 2022).

In 2013, the United Nations launched the International Day of Quinoa, promoting quinoa as the "superfood" (United Nations, 2013), which caused djulis to become popular in the domestic market (Liu, 2015). Nowadays, djulis has gained popularity as the aboriginal people grow djulis in their area as a new ecological tourism destination, where the beautiful red color of djulis can attract tourists and sell djulis-related

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https://doi.org/10.1016/j.fochx.2024.102135
Received 11 August 2024; Received in revised form 17 December 2024; Accepted 26 December 2024
Available online 27 December 2024

products (Ministry of Agriculture, 2017). Djulis is best planted from October to March, when the rainy season from July to September should be avoided (Ministry of Agriculture, 2017). Djulis are ready to be harvested after 100 days (spring and autumn) or 120 days (winter), when two-thirds of the hull changes color from green to red or yellow (Jhang et al., 2022; Ministry of Agriculture, 2017). The various colors of the djulis hull are shown in Fig. 1A. Djulis can be divided into three types: yellow, orange, and red (Ministry of Agriculture, 2017; Xie & Chen, 2021). Initially, the djulis hull is green (Fig. 1A-1) and then gradually turned greenish-red (Fig. 1A-2), and red (Fig. 1A-3), when completely mature. However, another strain of djulis exhibited a yellow to orange hull (Fig. 1A-4). Betalain pigment compositions, such as betacyanins (red-violet pigment) and betaxanthins (yellow-orange pigment), can determine the color of djulis. Parts of the entire djulis grain are shown in Fig. 1B.

Djulis is rich in dietary fiber and its major bioactive compounds are betanin, rutin, and kaempferol (Chyau et al., 2015; Lee, Chen, Xie, & Shih, 2019). Djulis hull contains high concentrations of dietary fiber and insoluble dietary fiber (75.21 ± 0.17 % and 71.54 ± 0.27 % dry weight, respectively) and has been demonstrated to significantly reduce blood glucose levels when consumed prior to meals (Li et al., 2021). The main pigments in djulis, betanin, and isobetanin, exhibit high FRAP and DPPH scavenging abilities, making them potential sustainable antioxidant agents for the food industry (Tsai et al., 2010). In addition to betanin, based on the result of *in vivo* study, rutin and kaempferol found in djulis water extract were also reported to provide hepatoprotective properties by attenuating oxidative stress (Chu et al., 2016). *In vitro* and *in vivo* studies of djulis water extract containing rutin and betanin showed potential antihypertensive activity (Chen et al., 2019). Interestingly, another study reported that in addition to these three major bioactive compounds, the ethanolic extract of djulis also contains quercetin, which can induce HepG2 cell apoptosis and significantly reduce tumor growth in nude mice, indicating its potential as a chemopreventive agent against the growth of hepatoma carcinoma cells (Chu et al., 2020). Other biological activities of djulis have also been reported, such as anti-aging, anti-diabetic, anticancer, anti-adipogenesis, anti-inflammatory, and gastric protective properties. These results suggest that, beyond its use as a daily dietary ingredient, djulis has potential for development as a functional food, biofunctional material, and cosmeceutical product.

In this literature review, studies focusing on djulis extracts, identification of bioactive compounds, and further development in various industries over the past 14 years were reviewed. Academic databases and search engines were employed to identify articles from SCI-indexed journals that focused on djulis proximate analysis, extraction methodologies, biological activities, and bioactive compound identification, as well as applications in various industries. Thus, the aim of this review is to provide compiled information on djulis from published studies to enhance the potential uses of underutilized djulis to boost its economic

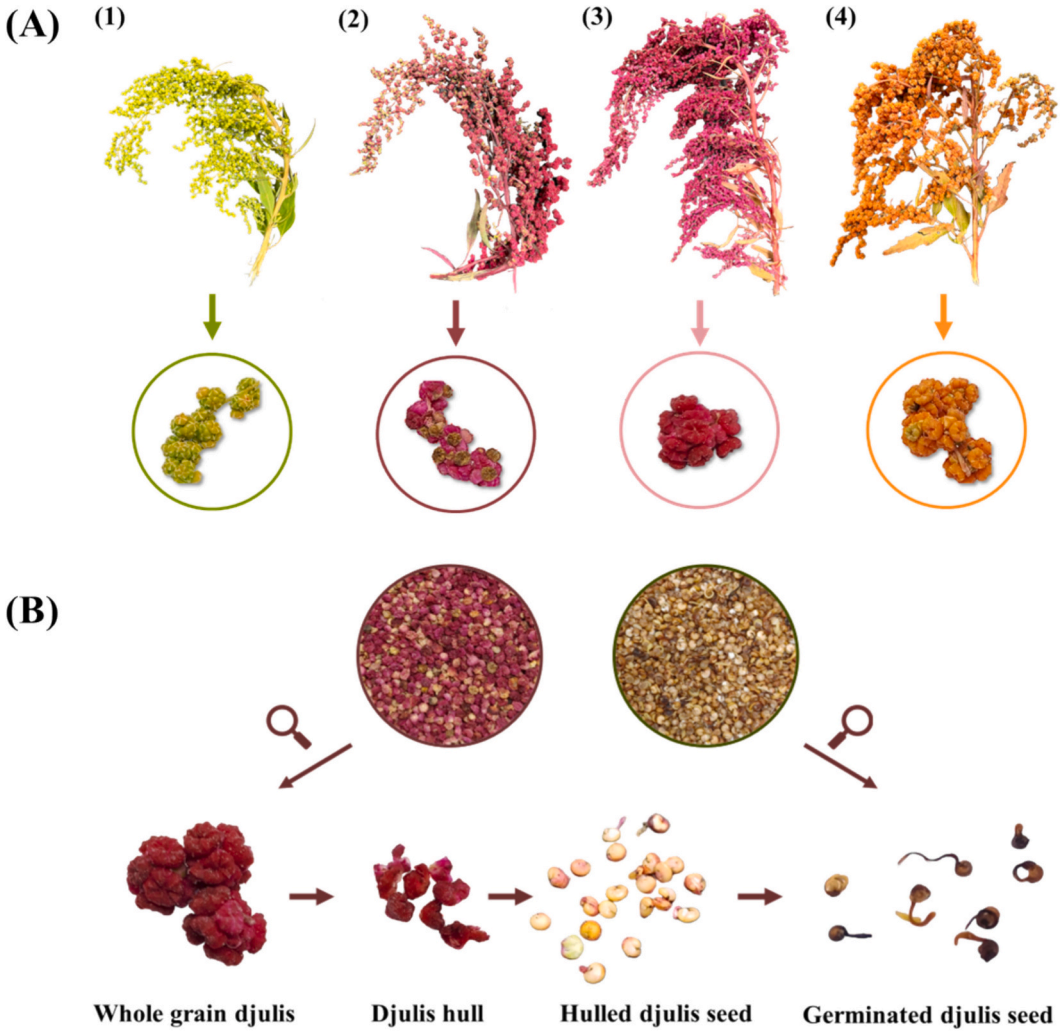


**Fig. 1.** (A) The appearance of whole grain djulis (*Chenopodium formosanum*) harvested in Yunlin county in various colors from the left is (1) green, (2) a combination of red and green, (3) red, and (4) orange; and (B) products of djulis whole grain, including hull, seeds, and germinated seeds. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

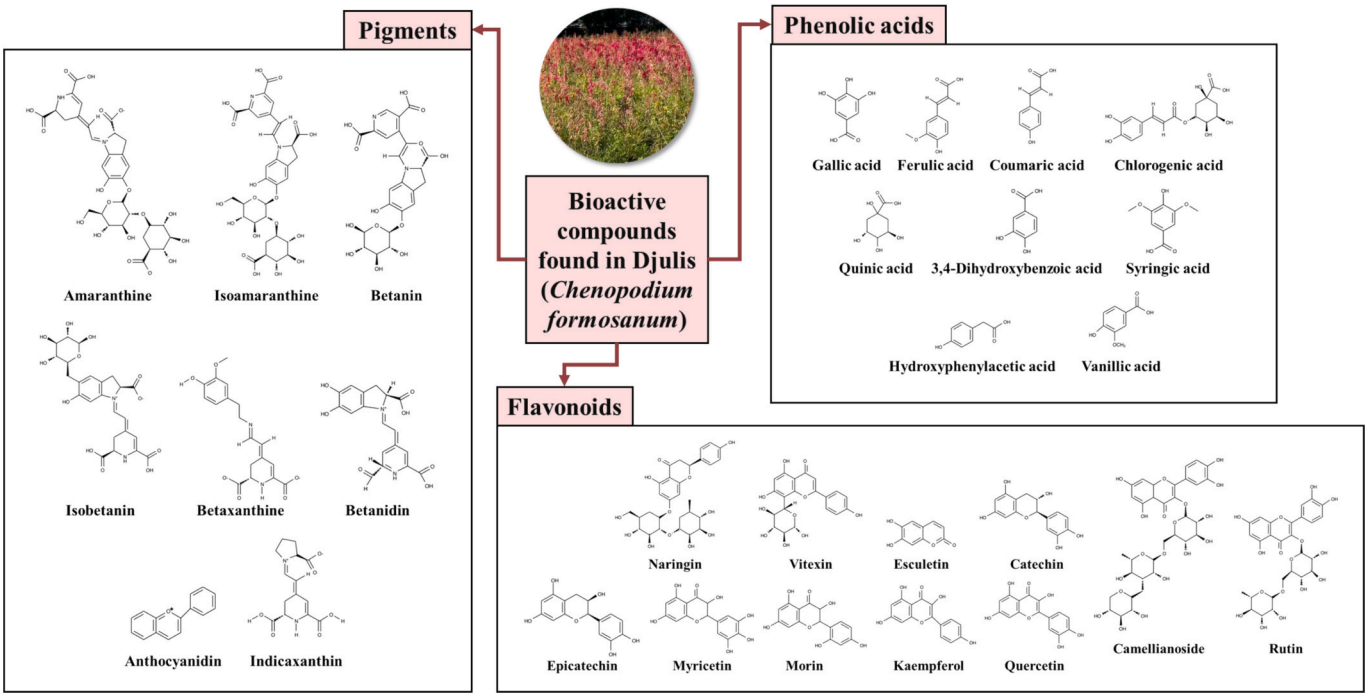


**Fig. 2.** Chemical structure of bioactive compounds found in djulis (*Chenopodium formosanum*).

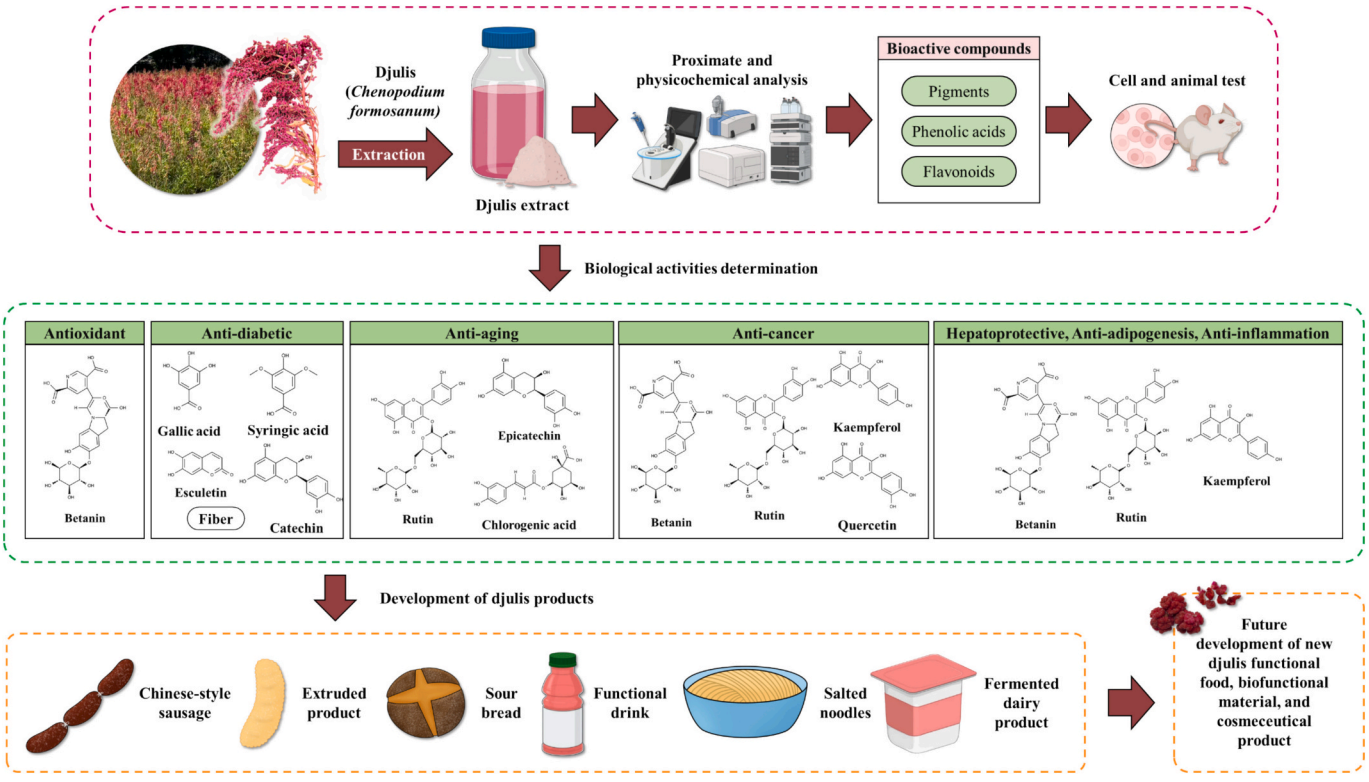


**Fig. 3.** Biological activities of djulis (*Chenopodium formosanum*), current developed product of djulis, and its potential in new product developments.

value.

## 2. Proximate composition of djulis: hulls and starch

Djulis hulls or the outer shell or coating of djulis are sometimes discarded during food processing because of their bitter taste and high microbial load ($10^5$ CFU/g) (Isnain et al., 2023; Sun et al., 2019; Tung, Zeng, Ho, Xu, Li, & Wu, 2021). However, djulis hull extract has been reported to have several health benefits, such as anti-nonalcoholic fatty liver disease (NAFLD) (Tung, Zeng, Ho, Xu, Li, & Wu, 2021), antioxidant (Li et al., 2020), and anti-glycation effects (Chen, Sridhar, & Tsai, 2021), decreased adipocyte size, and improved insulin sensitivity (Tung, Zeng,

Ho, Xu, Lin, & Wu, 2021). The proximate compositions of djulis hull and starch are listed in Table 1.

As shown in Table 1, the fiber content of the djulis hull was significantly higher than that of the quinoa hull, which was 75.21 ± 0.17 % and 5.60 ± 0.08 %, respectively. Consuming djulis hull containing a high amount of fiber before meals has been reported to reduce blood glucose levels (Li et al., 2021). However, it has been reported that at a dehulling rate of 8.6 %, the fiber content of quinoa is 28.90 % (Wu et al., 2020), which is still much lower than that of the djulis hull. It should be noted that the djulis hull can be considered a valuable fiber source. As can be seen in Table 1, in term of starch, djulis starch contains higher amylose content (22.14 ± 0.31–24.15 ± 0.28 %) than quinoa starch (9.46 ± 0.02–12.10 ± 0.13 %) (Jan et al., 2017; Lu et al., 2019). The amylose content of djulis starch is comparable to that of other common starch crops, including wheat, rye, barley, and potatoes (Sajilata et al., 2006).

## 3. Extraction method of djulis

### 3.1. Solvent extraction

Djulis was extracted with water, ethanol, methanol, and other solvents, such as ethyl acetate and butanol, to increase its phytochemical content. Djulis extraction using water is a commonly used extraction method. According to the method described in a previous study (Chen et al., 2019; Chu et al., 2021; Chyau et al., 2015), dried Djulis powder was extracted with boiling distilled water for a period of time (20 min to 2 h) with stirring, filtering, and re-extraction using the same method. The filtrate was freeze-dried to obtain a dehydrated powder. In addition to boiling, an alternative method for processing djulis involves soaking it for 24 h at 4 °C in the dark, followed by freeze-drying of the resulting filtrate (Hong et al., 2016). This method generated a water extract with a 10.6 % yield and demonstrated protective effects against UVB-induced skin damage based on experiments conducted using HaCaT cells and topical application in mice (Hong et al., 2016).

For ethanolic extraction, djulis extract was obtained by stirring the djulis powder in 50 % ethanol for 16 h at room temperature, filtered, and re-extracted using the same method (Chyau et al., 2018). Vacuum was used to remove ethanol from the combined filtrates, and the djulis extract was stored at 4 °C. In a previous study, ethanol-extracted red djulis hull extracts exhibited higher total sugar and flavonoid contents than the water extract; however, there was no significant difference in the phenolic content (Li et al., 2020). Red djulis hull ethanolic extract showed higher DPPH free radical scavenging activity (97.38 ± 0.04 %); however, higher DMPD radical scavenging activities were observed in the yellow djulis hull water extract (88.84 ± 0.01 %) (Li et al., 2020).

Various methanolic extraction methods have been reported in previous studies. Dried djulis and kernels were separately soaked in methanol for seven days at room temperature, decanted, filtered, concentrated in a rotary evaporator, and freeze-dried (Tung, Zeng, Ho, Xu, Li, & Wu, 2021). The major compound in djulis methanolic extract is rutin, which has been reported to be suitable for nonalcoholic fatty liver disease, obesity, and diabetes treatment (Tung, Zeng, Ho, Xu, Li, & Wu, 2021; Tung, Zeng, Ho, Xu, Lin, & Wu, 2021). Zhang et al. reported a shorter extraction period, in which dried samples were extracted with 80 % methanol at 70 °C for 2 h in a water shaker and centrifuged to obtain the supernatant, which was then filtered using filter paper (Zhang et al., 2020). Ethyl acetate and *n*-butanol have also been used as solvents to obtain djulis extract; however, these solvents affect HepG2 cell survival by decreasing cell viability compared to aqueous extracts (Chyau et al., 2015).

### 3.2. Additional treatments during djulis extraction

Enzymatic hydrolysis of djulis leaves and seeds was reported in a previous study using proteinase, and the results showed that enzymatically hydrolyzed djulis exhibited higher total phenolic content, especially esculetin (19-times), gallic acid, syringic acid, and catechin, leading to high anti-glycation and starch-hydrolyzing enzyme inhibition, indicating that djulis is suitable for glycation-associated diabetes (Chen, Sridhar, & Tsai, 2021). Non-thermal plasma treatment using nitrogen could significantly increase betacyanin, anthocyanin, and total phenolic content in djulis seeds owing to the generation of reactive nitrogen species. In addition, the antioxidant activity of djulis was not affected by non-thermal plasma treatment, and the djulis seed extract showed antioxidant and anti-inflammatory effects in THP-1 cells (Lu et al., 2021). Fermented djulis sprout (with *Rhizopus microsporus*) extract treatment of alveolar macrophages induced by PM2.5, resulted in ROS and p-NFκB reduction and restored cell viability due to gluconic acid, uridine, pantothenic acid, L-pyroglutamic acid, L-(−)-malic acid, and

**Table 1**
Comparison of chemical composition and properties of djulis (*Chenopodium formosanum)* parts summarized and compared with quinoa (*Chenopodium quinoa*) from previous reports.

| Parameter value (%) | Sample | | | | | |
|---|---|---|---|---|---|---|
| | Djulis bran (Ker et al., 2022) | Djulis hull (Li et al., 2021) | Djulis starch (Lu et al., 2019) | Quinoa bran (Przybylski et al., 1994) | Quinoa hull (Przybylski et al., 1994) | Quinoa starch (Jan et al., 2017) |
| Protein | 16.56 ± 0.43 | – | 0.22 ± 0.03 – 0.37 ± 0.07 | 20.40 ± 0.10 | 13.30 ± 0.10 | 0.89 ± 0.09– 0.95 ± 0.09 |
| Fiber | 6.14 ± 0.04 | 75.21 ± 0.17 | – | 5.00 ± 0.04 | 5.60 ± 0.08 | 0.10 ± 0.05– 0.13 ± 0.03 |
| Fat | 4.06 ± 0.06 | – | 0.75 ± 0.05 – 0.94 ± 0.04 | 11.60 ± 0.10 | 5.70 ± 0.10 | 0.32 ± 0.12– 0.40 ± 0.11 |
| Ash | 7.10 ± 0.06 | – | 0.11 ± 0.02 – 0.14 ± 0.03 | 3.90 ± 0.03 | 8.40 ± 0.13 | 0.18 ± 0.03– 0.22 ± 0.02 |
| Carbohydrate | 60.45 ± 0.76 | – | – | – | – | – |
| Alcohol insoluble solid | – | 84.27 ± 0.67 | – | – | – | – |
| Water insoluble solid | – | 81.17 ± 0.33 | – | – | – | – |
| Amylose | – | – | 22.14 ± 0.31 – 24.15 ± 0.28 | – | – | 9.46 ± 0.02– 12.10 ± 0.13 |
| Amylopectin | – | – | – | – | – | 87.9 ± 0.13– 90.54 ± 0.02 |
| Damaged starch | – | – | 2.12 ± 0.19 – 3.93 ± 0.27 | – | – | – |
| Moisture | – | – | 4.89 ± 0.21 – 6.35 ± 0.36 | 13.90 ± 0.05 | 11.30 ± 0.10 | – |

acetyl-L-carnitine (Hsieh et al., 2024). Moreover, soaking djulis seeds and germinating djulis increased GABA and polyphenol content and antioxidant capacity (Lu et al., 2024). In another study, high-pressure treatment was employed during djulis extraction using alcohol as a solvent, wherein treatment at 600 MPa for 5 min resulted in higher total phenolic and flavonoid content, with gallic acid and rutin reported as the primary phenolic and flavonoid compounds, respectively (Huang, Cheng, et al., 2019).

## 4. Bioactive compounds of djulis

### 4.1. Identification of djulis bioactive compounds

Djulis bioactive compounds, including pigments, phenolic acids, and flavonoids, can be identified using spectrophotometry and high-performance liquid chromatography (HPLC). Pigments, such as anthocyanidin, betaxanthin, and indicaxanthin, can be identified using spectrophotometry analysis conducted in dark conditions at ambient temperature (Ker et al., 2022; Lin, Tseng, et al., 2023). HPLC combined with different instruments has also been used to identify and quantify djulis bioactive compounds, such as HPLC coupled with liquid chromatography-mass spectrometry (HPLC-LC-MS) for betacyanin (Tsai et al., 2010), HPLC coupled with electrospray ionization-mass spectrometry (HPLC-ESI-MS) for pigments and phenolic acids (Chen et al., 2019), HPLC coupled with diode array detector and tandem mass spectrometry (HPLC-DAD-MS/MS) for phenolic acids and flavonoids (Hsu et al., 2017), and HPLC alone for specific compounds, such as gallic acid, chlorogenic acid, coumaric acid, rutin, vitexin, and naringin (Huang, Cheng, et al., 2019). The structures of the bioactive compounds found in djulis are shown in Fig. 2.

### 4.2. Pigments

As reported by Xie and Chen (Xie & Chen, 2021), djulis contain a highly water-soluble nitrogen-containing pigment called betalain. Detailed information on the pigments in djulis is presented in Table 2. Betalain is beneficial to human health because of its antimicrobial, anticancer, antilipidemic, hepatoprotective, neuroprotective, and anti-inflammatory properties (Sadowska-Bartosz & Bartosz, 2021). For the hull, the colored quinoa had a total betacyanin content of (0.0015 ± 0.0001–0.0523 ± 0.0023 mg/g) which is lower than djulis (2.36–4.27 mg/g) (Abderrahim et al., 2015; Lin, Tseng, et al., 2023; Tsai et al., 2011). Tsai et al. successfully purified betanin (47.8 %), isobetanin (30.0 %), amaranthine (13.6 %), and isoamaranthine (8.6 %) from red djulis. A higher amount of pigment was observed in djulis after extraction, along with a decrease in the particle size (Tsai et al., 2010; Tsai et al., 2011).

In previous studies, the pigment in djulis was found to be mainly betanin (Chen et al., 2019; Tsai et al., 2010; Tsai et al., 2011). Betanin (Fig. 1C), or betanidin-5-O-β-glucoside, is used as a natural red food colorant in cosmetic and pharmaceutical applications. It also acts as a scavenger of reactive oxygen species and induces endogenous antioxidant defense systems and phase II enzymes *via* gene regulatory mechanisms (Esatbeyoglu et al., 2015). Betanin can be retained using high-pressure processing (HPP) (2.1956–2.3612 mg/g) compared to conventional processing such as cooking and pasteurization (1.3295–1.8347 mg/g), indicating that djulis hull is suitable for food colorant or utilized as functional food (Sun et al., 2019).

Chyau et al. reported djulis water extract contained one more pigment other than betanin (68.33 mg/g), isobetanin (15.40 mg/g), amaranthine (20.02 mg/g), isoamaranthine (2.83 mg/g), which is betanidin (4.46 mg/g) (Chyau et al., 2015). However, lower amounts of pigments in djulis water extract, containing 8 ± 1 mg/g of betanin, 5 ± 1 mg/g of isobetanin, and 3 ± 1 mg/g of amaranthine, have also been reported (Chen et al., 2019). Lin et al. reported that fresh djulis contained anthocyanidin (21.3 ± 1.9–25.0 ± 0.3 ppm), sugar-free aglycone

**Table 2**
Bioactive compounds of of djulis (*Chenopodium formosanum)* summarized from previous reports.*

| Sample | Bioactive compound | Value | Ref. |
|---|---|---|---|
| Pigments | | | |
| Djulis | Anthocyanidin | 0.0213 ± 0.0019–0.025 ± 0.0003 mg/g | (Lin, Tseng, et al., 2023) |
| Djulis extract | Anthocyanidin | 0.3743 ± 0.034–0.3777 ± 0.0047 mg/g | |
| Djulis water extract | Amaranthine | 3 ± 1 mg/g | (Chen et al., 2019) |
| | Betanin | 8 ± 1 mg/g | |
| | Isobetanin | 5 ± 1 mg/g | |
| Djulis water extract | Amaranthine | 20.02 mg/g | (Chyau et al., 2015) |
| | Isoamaranthine | 2.83 mg/g | |
| | Betanidin | 4.46 mg/g | |
| | Isobetanin | 15.40 mg/g | |
| Djulis intact granule | Total betacyanin | 2.36 mg/g | (Tsai et al., 2011) |
| | Betanin | 1.13 mg/g | |
| | Isobetanin | 0.71 mg/g | |
| Djulis microparticles | Total betacyanin | 3.37 mg/g | |
| | Betanin | 1.61 mg/g | |
| | Isobetanin | 1.01 mg/g | |
| Djulis nanoparticles | Total betacyanin | 4.27 mg/g | |
| | Betanin | 2.04 mg/g | |
| | Isobetanin | 1.28 mg/g | |
| Red djulis grain extract | Amaranthine | 4.29 μM | (Tsai et al., 2010) |
| | Isoamaranthine | 2.12 μM | |
| | Betanin | 12.6 μM | |
| | Isobetanin | 5.8 μM | |
| Djulis bran | Betaxanthine | 99.1 ± 2.20 mg/g | (Ker et al., 2022) |
| | Indicaxanthin | 72.69 ± 3.20 mg/g | |
| Djulis seed water extract | Betanin | 16.43 mg/g | (Hong et al., 2016) |
| Phenolic acids | | | |
| Djulis bran | Total phenolic content | 19.50 ± 0.80 mg/g | (Ker et al., 2022) |
| Djulis | Polyphenols | 0.0698 ± 0.0011–0.09239 ± 0.002 mg/g | (Lin, Tseng, et al., 2023) |
| Djulis extract | Polyphenols | 1.054 ± 0.0167–1.6548 ± 0.0031 mg/g | |
| Djulis hull extract | Total phenolic | 451.5 ± 21.5 mg/g | (Huang, Cheng, et al., 2019) |
| | Gallic acid | 0.0422 ± 0.0019 mg/g | |
| | Chlorogenic acid | 0.0183 ± 0.0014 mg/g | |
| | Coumaric acid | 0.0093 ± 0.0007 mg/g | |
| Djulis hull extract + HPE | Total phenolic | 567.2 ± 18.2–642.4 ± 20.4 mg/g | |
| | Gallic acid | 0.0445 ± 0.0021–0.0532 ± 0.0022 mg/g | |
| | Chlorogenic acid | 0.0214 ± 0.0018–0.0234 ± 0.0018 mg/g | |
| | Coumaric acid | 0.0083 ± 0.0007–0.0112 ± 0.011 mg/g | |
| Djulis intact granule | Total phenol | 15.26 mg/g | (Tsai et al., 2011) |
| Djulis microparticles | Total phenol | 23.68 mg/g | |

(*continued on next page*)

**Table 2** (*continued*)

| Sample | Bioactive compound | Value | Ref. |
|---|---|---|---|
| Djulis nanoparticles | Total phenol | 26.11 mg/g | |
| Dehusk djulis ethanolic extract | Total phenolic acids | 2.11968 ± 0.04263 | (Hsu et al., 2017) |
| | Vanillic acid | 0.07066 ± 0.00699 | |
| | Vanillic acid hexoside | 0.04503 ± 0.00313 | |
| | Quinic acid | 0.037 ± 0.00439 | |
| | Caffeoyl-spermine-conjugate | 0.01311 ± 0.0028 | |
| | Caffeoyl-putrescine-derivative (1) | 0.0317 ± 0.00274 | |
| | Caffeoyl-putrescine-derivative (2) | 0.0115 ± 0.00078 | |
| | Hydroxyphenylacetic acid | 0.05542 ± 0.00488 | |
| | Hydroxyphenylacetic acid pentoside | 1.85526 ± 0.01692 | |
| Djulis seed water extract | Vanillic acid | 0.85 | (Hong et al., 2016) |
| | Chlorogenic acid | 0.65 | |
| | Gallic acid | 0.51 | |
| | Ferulic acid | 0.09 | |
| Whole djulis methanolic extract | Total phenolics | 5.2171 | (Lee, Chen, Xie, & Shih, 2019) |
| Djulis husk methanolic extract | Total phenolics | 10.7254 | |
| Djulis without husk methanolic extract | Total phenolics | 2.56959 | |
| Djulis leaf treated with hydrolysis | Gallic acid | 0.1364 ± 0.0096 | (Chen, Sridhar, & Tsai, 2021) |
| | 3,4-Dihydroxybenzoic acid | 0.0356 ± 0.0005 | |
| | Esculetin | 33.8956 ± 0.7948 | |
| | Syringic acid | 0.1138 ± 0.0237 | |
| | *p*-Coumaric acid | 0.2826 ± 0.0471 | |
| | Ferulic acid | 0.5984 ± 0.0157 | |
| | Estyl13,4-dihydroxybenzoate | 0.1106 ± 0.0005 | |
| | Ellagic acid | 0.4556 ± 0.0865 | |
| Flavonoids | | | |
| Djulis | Total flavonoid | 0.3946 ± 0.0542–0.4675 ± 0.0354 | (Lin, Tseng, et al., 2023) |
| Shelled djulis extract | Total flavonoid | 5.9557 ± 0.8181–8.2333 ± 0.6263 | |
| Djulis hull extract | Rutin | 0.0223 ± 0.0017 | (Huang, Cheng, et al., 2019) |
| | Vitexin | 0.0158 ± 0.0011 | |
| | Naringin | 0.0082 ± 0.0013 | |
| Djulis hull extract + HPE | Rutin | 0.0268 ± 0.0021–0.0342 ± 0.0005 | |
| | Vitexin | 0.0149 ± 0.0012–0.0221 ± 0.0007 | |
| | Naringin | 0.0097 ± 0.0012–0.0105 ± 0.0009 | |
| Djulis aqueous extract | Rutin | 150 ± 30 | (Chen et al., 2019) |
| | Quercetin derivatives | 36 ± 6 | |
| | Quercetin-3-O-rutinoside-7- O-rhamnoside | 45 ± 8 | |
| | Quercetin-3-O-deoxy-hexose-O- hexose-O-pentoside | 12 ± 2 | |
| | Camellianoside | 90 ± 20 | |
| | Kaempferol derivative | 9 ± 2 | |
| | Kaempferol 3-O-[6‴-p-coumaroyl- glucosyl-β-(1 → 4)-rhamnoside] | 17 ± 3 | |
| | Quercetin 3-O-2″-(6″-p-coumaroyl) glucosylrhamnoside | 40 ± 7 | |
| | 20-Hydroxyecdysone | 150 ± 30 | |
| | Kaempferol-3,7-di-O-rhamnoside | 13 ± 2 | |
| | Kaempferol-3-O-rutinoside | 5 ± 7 | |
| Dehusk djulis ethanolic extract | Total flavonoids | 0.79074 ± 0.10509 | (Hsu et al., 2017) |
| | Quercetin-acetyl-rutinoside hexoside (1) | 0.0238 ± 0.00303 | |
| | Quercetin-acetyl-rutinoside hexoside (2) | 0.02814 ± 0.00242 | |
| | Quercetin-acetyl-rutinoside (1) | 0.05729 ± 0.00592 | |
| | Quercetin-acetyl-rutinoside (2) | 0.04437 ± 0.00341 | |
| | Quercetin-3-O-(coumaroyl)-rutinoside pentoside (1) | 0.01993 ± 0.00229 | |
| | Quercetin-3-O-(coumaroyl)-rutinoside (1) | 0.03036 ± 0.0016 | |
| | Quercetin-3-O-(coumaroyl)-rutinoside deoxyhexoside | 0.03519 ± 0.00347 | |
| | Quercetin-3-O-(coumaroyl)-rutinoside pentoside (2) | 0.02515 ± 0.0097 | |
| | Quercetin-3-O-(coumaroyl)-rutinoside (2) | 0.07069 ± 0.00942 | |
| | Quercetin-acetyl-rutinoside hexoside glucuronide | 0.07278 ± 0.00792 | |
| | Quercetin-acetyl-glycoside | 0.02225 ± 0.00374 | |
| | Rutin-O-pentoside (1) | 0.06757 ± 0.00473 | |
| | Rutin-O-pentoside (2) | 0.2573 ± 0.00205 | |
| | Rutin (Quercetin-3-O-rutinoside) | 0.03592 ± 0.00276 | |
| Djulis intact granule | Rutin | 0.0338 | (Tsai et al., 2011) |
| Djulis microparticles | Rutin | 0.0484 | |
| Djulis nanoparticles | Rutin | 0.0562 | |
| Djulis seed water extract | Rutin | 0.033 | (Hong et al., 2016) |
| | Epicatechin | 0.0043 | |
| Whole djulis methanolic extract | Total flavonoids | 3.0988 | (Lee, Chen, Xie, & Shih, 2019) |
| Djulis husk methanolic extract | Total flavonoids | 7.4831 | |
| Djulis without husk methanolic extract | Total flavonoids | 1.10224 | |
| Djulis leaf treated with hydrolysis | Rutin | 1.4989 ± 0.0649 | (Chen, Sridhar, & Tsai, 2021) |
| | Vitexin | 1.9997 ± 0.0260 | |
| | Quercetin | 2.0712 ± 0.0229 | |

(*continued on next page*)

**Table 2** (*continued*)

| Sample | Bioactive compound | Value | Ref. |
|---|---|---|---|
| | Catechin | 1.5263 ± 0.2667 | |
| | Epicatechin | 0.4257 ± 0.0171 | |
| | Myricetin | 0.3759 ± 0.0395 | |
| | Morin | 1.2570 ± 0.1490 | |

* HPE: High-pressure Assisted Extraction.

of anthocyanin, but the number increased after extraction (374.3 ± 34.0–377.7 ± 4.7 ppm) (Lin, Tseng, et al., 2023). In addition, the reduction in particle size was reported to produce almost twice the betanin content; however, it also showed the most serious pigment degradation owing to its high surface area and susceptibility to oxidation (Tsai et al., 2011).

Betalains can be divided into two major groups based on their chemical constituents: betacyanins (red-violet pigments) and betaxanthins (yellow-orange pigments) (Xie & Chen, 2021). Aglycone of betacyanin, betanidin, is formed after the condensation of betalamic acid and cycloDOPA, whereas isobetanidin is the C15 epimer of betanidin (Xie & Chen, 2021). Betanidin has a glucoside, amaranthine has a glucuronosylglucoside, and isoamaranthine is its C15 epimer (Sarker & Oba, 2021). On the other hand, glycosylation on betalain forms betanin, betanin decarboxylation form 17-decarboxy-betanin, betanin dehydrogenation form neobetanin, but when betanin decarboxylation and dehydrogenation occurs in the same time will form 2,17-bidecarboxy-2,3-dehydro-neobetanin. Isobetanin is the C15 epimer of betanin (Gliszczyńska-Świgło et al., 2006).

### 4.3. Polyphenols

The phenolic compounds of djulis hull extract, such as gallic acid (0.0445 ± 0.0021–0.0532 ± 0.0022 mg/g), chlorogenic acid (0.0214 ± 0.0018–0.0234 ± 0.0018 mg/g), and coumaric acid (0.0083 ± 0.0007–0.0112 ± 0.0011 mg/g), were also increased with high-pressure assisted extraction compared to those without (0.0422 ± 0.0019, 0.0183 ± 0.0014, and 0.0093 ± 0.0007 mg/g, respectively) (Huang, Cheng, et al., 2019). Gallic acid, which can be found in djulis, is a promising candidate as a dietary supplement because of its anti-inflammatory, antitumor, and antioxidant activities as well as its therapeutic effects on gastrointestinal, cognitive, metabolic, and cardiovascular problems (Kahkeshani et al., 2019). In addition to gallic acid, esculetin, catechin, and syringic acid have also been reported as major phenolic acids in djulis hulls, leaves, and seeds; they exhibit anti-glycation activity, and their content could be increased by enzyme hydrolysis treatment (Chen, Sridhar, & Tsai, 2021).

Decreasing the particle size of djulis also led to a higher total phenol level of 15.26 to 26.11 mg/g (Tsai et al., 2011). Dehusked djulis extracts have been reported to have different phenolic compound profiles than djulis hull extracts, such as vanillic acid, vanillic acid hexoside, quinic acid, caffeoyl-spermine-conjugatecaffeoyl-putrescine-derivatives, hydroxyphenylacetic acid, and hydroxyphenylacetic acid pentoside, where the amount of hydroxyphenylacetic acid pentoside has been reported to be remarkably higher (1.85526 mg/g) (Hsu et al., 2017). The total phenolic content of djulis methanolic extracts was reported to be higher in husks (10.7254 mg/g) than in whole grains (5.2171 mg/g) and seeds (2.56959 mg/g) (Lee, Chen, Xie, & Shih, 2019).

### 4.4. Flavonoids

After extraction, the flavonoid content in djulis increased from 0.3946 ± 0.0542–0.4675 ± 0.0354 mg/g to 5.9557 ± 0.8181–8.2333 ± 0.6263 mg/g (Lin, Tseng, et al., 2023). Flavonoid compounds in djulis, such as rutin, vitexin, and naringin, also increased after extraction assisted by high pressure (Huang, Cheng, et al., 2019). Reducing the particle size of djulis before extraction was also reported to increase the rutin content from 3.38 to 5.62 mg/g (Tsai et al., 2011). Rutin and 20-hydroxyecdysone are the most abundant flavonoid compounds in djulis (150 ± 30 mg/g and 150 ± 30 mg/g, respectively) (Chen et al., 2019). Lee et al. reported that the total flavonoid content of djulis methanolic extracts was highest in the husk (7.4831 mg quercetin equivalent/g), compared to the whole grain (3.0988 mg quercetin equivalent/g) and seeds (1.10224 mg quercetin equivalent/g) (Lee, Chen, Xie, & Shih, 2019).

Various pharmacological activities of rutin have been reported, including antibacterial, antiprotozoal, antitumor, anti-inflammatory, anti-allergic, antiviral, cytoprotective, vasoactive, hypolipidemic, antiplatelet, antispasmodic, and antihypertensive properties (Patel & Patel, 2019), whereas 20-hydroxyecdysone has antioxidant, antidiabetic, anti-obesity, antihypertensive, anticancer, and anti-inflammatory properties (Zeng et al., 2019). In addition, rutin-O-pentoside (2) was reported to have the highest flavonoid content (0.2573 μg/g) in djulis ethanolic extract (Hsu et al., 2017). In addition, rutin and chlorogenic acid in djulis seed water extract have been reported to significantly increased cell viability and decreased interleukin-6 (IL-6) in UVB-irradiated HaCaT cells (Hong et al., 2016).

## 5. Biological activities of djulis extracts

Djulis possesses antioxidant, anti-aging, antidiabetic, anticancer, anti-inflammatory, hepatoprotective, anti-adipogenesis, and gastric-protective properties. The biological activities of specific bioactive compounds found in djulis are listed in Table 4.

### 5.1. Antioxidant capacity

Djulis also known as “ruby of cereals” because of its red colored nitrogenous pigments such as betanin (47.8 %), isobetanin (30.0 %), amaranthin (13.6 %), and isoamaranthine (8.6 %) which possess antioxidant capacity (Tsai et al., 2010; Tsai et al., 2022). In a previous study, betanin and isobetanin were reported to have antioxidant activities, as determined by DPPH (2,2-Diphenyl-1-picrylhydrazyl) and ferric reducing ability of plasma (FRAP) assays, indicating that djulis has physiological benefits in the human body (Chyau et al., 2015). Owing to its high nutritional value, various parts of the djulis plant have been incorporated into various functional food products. The addition of djulis seeds fermented with *Lactobacillus delbrueckii* subsp. *bulgaricus* and *Streptococcus salivarius* subsp. *thermophilus* to milk resulted in high antioxidant capacity and phenolic content and improved glucose utilization and glucose transporter expression in hepatocyte cells (FL83B) (Hou et al., 2022). Compared with djulis seeds, the betacyanin and antioxidant activities of djulis sprouts increased significantly, indicating that the germination process under stress can improve bioactive compounds and is suitable for the development of functional foods (Wang et al., 2022).

Previous studies have reported the antioxidant capacity of djulis extracts (Table 3). According to a previous report by Li et al., red djulis hull aqueous and ethanolic extracts and djulis root aqueous extracts exhibited stronger antioxidant activity than yellow djulis hull water, ethanolic extract, and djulis root ethanolic extract, as determined by TEAC, FRAP, DPPH, CUPRAC, and DMPD analyses (Li et al., 2020). In addition, DPPH and FRAP assays have shown that betanin has a significantly higher antioxidant capacity than amaranthine, isoamaranthine, and isobetanin (Tsai et al., 2010). Betanin has been reported to increase liver tissue antioxidant capacity, which is associated with the nuclear factor erythroid 2-related factor 2 (Nrf2)-mediated pathway, in a dose-dependent manner (Mousavi et al., 2022). High-pressure treatment with djulis extract inhibited intracellular ROS production in LPS-induced RAW 264.7 cells (Huang, Cheng, et al., 2019). Consumption of djulis functional drink for 8 weeks was reported to increase superoxide dismutase (9.5 %) and catalase (124.8 %), enzymes that protect cells from radical attack, when compared to placebo (Tsai et al., 2022).

**Table 3**
Antioxidant ability of djulis (*Chenopodium formosanum)* summarized from previous reports.

| Sample | Value | $EC_{50}$ | Ref. |
|---|---|---|---|
| Trolox Equivalent Antioxidant Capacity (TEAC) | | | |
| Ethanol extracted yellow djulis hulls (10 mg/mL) | 5.62 % | – | (Li et al., 2020) |
| Water extracted yellow djulis hulls (10 mg/mL) | 48.46 % | – | |
| Ethanol extracted red djulis hulls (10 mg/mL) | 72.23 % | – | |
| Water extracted red djulis hulls (10 mg/mL) | 94.67 % | – | |
| Ethanol extracted djulis roots (10 mg/mL) | 77.54 % | – | |
| Water extracted djulis roots (10 mg/mL) | – | – | |
| Kaohsiung djulis extract (10 mg/mL) | 79.9 ± 1.1 μmol TE | – | (Lin, Tseng, et al., 2023) |
| Pingtung djulis extract (10 mg/mL) | 45.2 ± 1.6 μmol TE | – | |
| Ferric Reducing Antioxidant Power (FRAP) | | | |
| Ethanol extracted yellow djulis hulls (500 μg/mL) | 0.167 ± 0.01 mM | – | (Li et al., 2020) |
| Water extracted yellow djulis hulls (500 μg/mL) | 0.495 ± 0.01 mM | – | |
| Ethanol extracted red djulis hulls (500 μg/mL) | 0.897 ± 0.09 mM | – | |
| Water extracted red djulis hulls (500 μg/mL) | 0.939 ± 0.01 mM | – | |
| Ethanol extracted djulis roots (500 μg/mL) | 0.574 ± 0.05 mM | – | |
| Water extracted djulis roots (500 μg/mL) | 0.396 ± 0.02 mM | – | |
| Kaohsiung djulis extract (500 μg/mL) | 22.5 ± 0.4 μM | – | (Lin, Tseng, et al., 2023) |
| Pingtung djulis extract (500 μg/mL) | 12.2 ± 0.9 μM | – | (Tsai et al., 2010) |
| Amaranthine (4.29 μM) | 35.35 μmol/L | – | |
| Isoamaranthine (2.12 μM) | 26.20 μmol/L | – | |
| Betanin (12.6 μM) | 128.87 μmol/L | – | |
| Isobetanin (5.8 μM) | 36.20 μmol/L | – | |
| Djulis intact granule | 517.24 μmol/L | – | (Tsai et al., 2011) |
| Djulis microparticle | 699.28 μmol/L | – | |
| Djulis nanoparticle | 713.92 μmol/L | – | |
| Cupric Reducing Antioxidant Capacity (CUPRAC) | | | |
| Ethanol extracted yellow djulis hulls (1000 μg/mL) | 0.045 ± 0.01 OD | – | (Li et al., 2020) |
| Water extracted yellow djulis hulls (1000 μg/mL) | 0.280 ± 0.01 OD | – | |
| Ethanol extracted red djulis hulls (1000 μg/mL) | 0.663 ± 0.05 OD | – | |
| Water extracted red djulis hulls (1000 μg/mL) | 0.733 ± 0.04 OD | – | |
| Ethanol extracted djulis roots (1000 μg/mL) | 0.337 ± 0.07 OD | – | |
| Water extracted djulis roots (1000 μg/mL) | 0.279 ± 0.03 OD | – | |
| 2,2-Diphenyl-1-Picrylhydrazyl Radical Scavenging Assay (DPPH) | | | |
| Ethanol extracted yellow djulis hulls (1000 μg/mL) | 19.62 ± 0.04 % | 1004.1 ± 6.22 μg/mL | (Li et al., 2020) |
| Water extracted yellow djulis hulls (1000 μg/mL) | 45.76 ± 0.01 % | 2511.5 ± 7.42 μg/mL | |
| Ethanol extracted red djulis hulls (1000 μg/mL) | 92.48 ± 0.01 % | 291.9 ± 9.89 μg/mL | |
| Water extracted red djulis hulls (1000 μg/mL) | 77.02 ± 0.01 % | 443.0 ± 8.98 μg/mL | |
| Ethanol extracted djulis roots (1000 μg/mL) | 74.94 ± 0.01 % | 579.6 ± 8.28 μg/mL | |
| Water extracted djulis roots (1000 μg/mL) | 39.53 ± 0.01 % | 1166.1 ± 8.77 μg/mL | |
| Kaohsiung djulis extract (1000 μg/mL) | 84.8 ± 1.4 % | – | (Lin, Tseng, et al., 2023) |
| Pingtung djulis extract (1000 μg/mL) | 85.5 ± 3.7 % | – | |
| Amaranthine (4.29 μM) | 16.97 % | – | (Tsai et al., 2010) |
| Isoamaranthine (2.12 μM) | 9.60 % | – | |
| Betanin (12.6 μM) | 52.84 % | – | |
| Isobetanin (5.8 μM) | 22.69 % | – | |
| Djulis intact granule | 46.42 % | – | (Tsai et al., 2011) |
| Djulis microparticle | 60.98 % | – | |
| Djulis nanoparticle | 65.68 % | – | |
| *N*,*N*-Dimethyl-P-Phenylendiamine (DMPD) | | | |
| Ethanol extracted yellow djulis hulls (1000 μg/mL) | 5.42 ± 0.02 % | 406.4 ± 13.5 μg/mL | (Li et al., 2020) |
| Water extracted yellow djulis hulls (1000 μg/mL) | 88.84 ± 0.01 % | 8921.5 ± 10.2 μg/mL | |
| Ethanol extracted red djulis hulls (1000 μg/mL) | 17.80 ± 0.01 % | 2883.6 ± 14.7 μg/mL | |
| Water extracted red djulis hulls (1000 μg/mL) | 77.92 ± 0.01 % | 560.3 ± 10.8 μg/mL | |
| Ethanol extracted djulis roots (1000 μg/mL) | 32.44 ± 0.02 % | 1483.7 ± 8.98 μg/mL | |
| Water extracted djulis roots (1000 μg/mL) | 71.36 ± 0.01 % | 643.8 ± 9.20 μg/mL | |
| Ferrous Ion Chelating Ability (FICA) | | | |
| Djulis intact granule | 7.68 % | – | (Tsai et al., 2011) |
| Djulis microparticle | 8.17 % | – | |
| Djulis nanoparticle | 10.31 % | – | |

### 5.2. Anti-aging

A previous study (Lin et al., 2021) reported that unhulled djulis extracts tested on CCD-966SK cells showed increased repairing ability of skin cells, skin-barrier-related genes, and antioxidant-related gene expression, which can also inhibit advanced glycation end products (AGEs) and melanin formation owing to its ability to increase collagen-related genes, indicating that djulis extract can be applied in anti-aging skin care products, cosmetics, or functional beverages. Epicatechin has been reported to contribute to the anti-aging properties of djulis leaves (Lin, Chung, et al., 2023). Methanolic extract of djulis leaves fermented with *A. oryzae* was reported to have anti-aging activity, with $IC_{50}$ of 113.5 ± 9.2, 137.4 ± 16.2, 106 ± 7.6, 176.4 ± 13.8 mg/L for collagenase, elastase, hyaluronidase, and MMP-1 activity, respectively (Lin, Chung, et al., 2023). In addition, rutin and chlorogenic acid in djulis seed water extract exhibited anti-photoaging effects against UV-induced damage in HaCaT cells by reducing interleukin-6 (IL-6), matrix metalloprotease (MMP-1), and reactive oxygen species (ROS) (Hong et al., 2016).

### 5.3. Anti-diabetic

Hsu et al. reported the potential of djulis as an anti-diabetic functional food ingredients for diabetes type 2 patients, because djulis water extract can significantly increase glucose uptake in 3 T3-L1 adipocytes owing to its synergistic effect with insulin (Hsu et al., 2018). A previous study reported that djulis contains abundant dietary fiber (75.21 ± 0.17 % dry weight), and patients with diabetes type 2 consuming djulis powder 30–60 min before meals can reduce blood glucose content significantly compared with patients at the same postprandial times who did not consume it (Li et al., 2021). Lin et al. reported that djulis extract

**Table 4**
Summary of the specific bioactive compounds in djulis (*Chenopodium formosanum*) and their biological activity.

| Bioactive compounds | Specific compound(s) | Sample | Biological activity | Key finding(s) | Ref. |
|---|---|---|---|---|---|
| Pigments | Betanin and isobetanin | Djulis water extract | Antioxidant | • Betanin and isobetanin accounted for more than 70 % of the FRAP reducing power or DPPH scavenging capacity. | (Tsai et al., 2010) |
| Phenolic acids<br>Flavonoids<br>Others | Caffeic acid, 3,4-dihydroxyphenylacetate<br>Quercetin, 7-O-α-L-rhamnoside 3-O-rutinoside<br>Guanosine, 20-Hydroxyecdysone, and adenine | Unhulled red djuis water extract | Anti-aging | • Enhanced skin cell repair ability, increased TGM1, KRT1, KRT10, SOD2, and COL1A2 expression, and decreased MMP9 expression.<br>• Increased collagen and inhibited AGEs formation and melanin. | (Lin et al., 2021) |
| Flavonoids | Quercetin and epicatechin | Fermented djulis leaf extract | Anti-aging<br>Skin whitening | • Exhibited anti-collagenase, anti-elastase, anti-hyaluronidase, and anti-MMP-1 activities.<br>• The $IC_{50}$ value of *in vivo* antityrosinase activity was 33.2 mg/L | (Lin, Chung, et al., 2023) |
| Flavonoid<br>Phenolic acid | Rutin<br>Chlorogenic acid | Djulis seed water extract | Protection from UVB-induced skin damage (Anti-photoaging) | • Exhibited higher HaCaT cell viability and reduced interleukin (IL-) 6, matrix metalloprotease (MMP-) 1, and reactive oxygen species (ROS) under UVB-irradiated conditions.<br>• In animal models, mice supplemented with djulis extract showed a thinner epidermis and lower IL-6 levels in the skin layer. | (Hong et al., 2016) |
| Phenolic acid<br>Flavonoids | Gallic acid and syringic acid<br>Esculetin catechin | Djulis hull, seed, and leave enzymatic hydrolysis | Anti-glycation | • Djulis enzymatic hydrolysis showed a strong inhibitory effect on advanced glycation end products (AGEs), methylglyoxal, α-amylase, and α-glucosidase. | (Chen, Sridhar, & Tsai, 2021) |
| Others | Fiber | Djulis hull fiber | Hypoglycemic (Anti-diabetic) | • Consuming djulis hull 30 and 60 min before a meal significantly lowered blood glucose levels compared to those who did not consume it at the same postprandial times. | (Li et al., 2021) |
| Pigment<br>Flavonoid | Betanin<br>Rutin, kaempferol, quercetin | Djulis ethanolic extract | Anticancer | • Djulis extract induced apoptosis accompanied by Sub-G0 phase arrest, ROS generation, loss of mitochondrial membrane potential (ΔΨm), increase in Bax/Bcl-2 ratio, caspase-3 activation, and PARP cleavage.<br>• Djulis extract significantly reduced tumor growth in nude mice. | (Chu et al., 2020) |
| Pigment<br>Flavonoid | Betanin<br>Rutin, kaempferol | Djulis water extract | Hepatoprotective | • Djulis extract protects rat liver from $CCl_4$-treated liver injury by lowering aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels, attenuating histopathological changes, inhibiting lipid peroxidation, restoring glutathione (GSH), enhancing superoxide dismutase (SOD), and reducing DNA damage. | (Chu et al., 2016) |
| Pigment<br>Flavonoid | Betanin<br>Rutin, kaempferol | Djulis ethanolic extract | Anti-adipogenesis | • Djulis extract downregulated the gene expression of PPARγ, C/EBPα, and SREBP-1c, leading to inhibition of adipose tissue formation and adipocyte function. | (Chyau et al., 2018) |

ameliorates TNF-α-induced insulin resistance, indicating that it has the potential to control insulin resistance, diabetes, and obesity (Lin, Tseng, et al., 2023). Djulis hulls, leaves, and seedlings treated with enzyme hydrolysis have been reported for their potential to prevent glycation-associated diabetes owing to their high inhibitory effects on advanced glycation end products (65.04 %–72.77 %), methylglyoxal (80.01 %–90.70 %), α-amylase (86.37 %–93.50 %), and α-glucosidase (35.50 %–38.16 %) (Chen, Sridhar, & Tsai, 2021). These results indicate that djulis contains fiber, phenolic compounds, and antioxidants that are suitable for the development of functional foods for diabetes prevention.

### 5.4. Anticancer

In a previous study, bioactive compounds in the ethanolic extract of djulis, mainly quercetin, showed anti-proliferative activity in $HepG_2$ cells (human hepatoma cells) and significantly reduced tumor growth in nude mice in tumor xenografts of $HepG_2$ cells, indicating that djulis could be developed as an anti-hepatoma cell (Chu et al., 2020). In another study, bioactive compounds in djulis water extract also showed protective effects against oxidative damage and cytoprotective effects against t-BHP-induced $HepG_2$ cells by decreasing reactive oxygen species (ROS) generation, thiobarbituric acid reactive substance (TBARS) formation, caspase-3 activity, nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor alpha (IκB-α), and poly (ADP-ribose) polymerase (PARP) degradation (Chyau et al., 2015). Combined with *Lactobacillus acidophilus*, djulis has anticancer potential in inflammation-associated colon carcinogenesis, where it regulates colon cancer biomarkers by inhibiting cell proliferation and inflammation and promoting apoptosis (Lee, Chen, Chien, et al., 2019). Moreover, djulis methanolic extract, which contains high levels of phenolic compounds and flavonoids, could prevent colon cancer progression in rats with colon carcinogenesis induced with 1,2-dimethylhydrazine by regulating anti-apoptotic, pre-apoptotic, and proliferation-related proteins (Lee, Chen, Xie, & Shih, 2019).

### 5.5. Anti-inflammation and hepatoprotective

Djulis hull extract is high in rutin and has an anti-nonalcoholic fatty liver disease (NAFLD) effect in C57BL/6 J mice fed a high-fat diet. The results showed that oral administration of djulis extract decreased the inflammatory response (PPARγ, IL-6, and TNF-α) and modulated oxidative damage, which can reduce the progression of NAFLD (Tung, Zeng, Ho, Xu, Li, & Wu, 2021). Bioactive compounds in djulis water extract, including rutin, kaempferol, and betanin, have been reported to be responsible for the hepatoprotective effect of carbon tetrachloride-treated liver injury in rat liver by attenuating oxidative stress (Chu

et al., 2016). Rutin is a naturally occurring flavonoid that can control the metabolism of fatty acids, lower the level of malondialdehyde in hepatocytes, and increase superoxide dismutase activity. It can also suppress the autophagic activity of liver tissues by suppressing important autophagy biomarkers such as TNF-α and IL-1β (Liu et al., 2017). Mice with alcoholic liver injury treated with kaempferol have been reported to show lower oxidative stress, lipid peroxidation, and expression levels and activity of hepatic cytochrome 21 (CYP2E1) but increased antioxidative defense activity (Wang et al., 2015).

### 5.6. Anti-adipogenesis

Ethanolic djulis extract contains bioactive compounds such as rutin, kaempferol, and betanin, which inhibit lipid accumulation by downregulating the expression of peroxisome proliferator-activated receptor-γ (PPARγ), CCAAT/enhancer binding protein-α (C/EBPα), and SREBP-1c (fatty acid synthetic proteins) (Chyau et al., 2018). The anti-adipogenic activity of rutin is mediated by downregulation of key adipogenic transcription factors (PPARγ and C/EBPα) (Choi et al., 2006). In zebrafish, kaempferol inhibits the early stages of lipid accumulation by suppressing the mTOR signaling pathway (Lee et al., 2015). Betanin can also induce fat browning and regulate lipid metabolism *via* the adenosine monophosphate-activated protein kinase (AMPK)-mediated pathway in 3 T3-L1 cells by inhibiting lipogenesis and enhancing lipolysis and fatty acid oxidation (Lee et al., 2023). These findings indicate that djulis is a suitable anti-obesity treatment.

In another study, 9, 12-octadecadienoyl chloride was a linoleoyl chloride also found at low concentrations in *Colocasia esculenta* extract (Eleazu, 2016), and it has antispermatogenic and antitubercular properties (Kalaivani et al., 2012). Ethyl linoleate was also found in *Consolida ajacis* seed extract as its major compound and has been reported to be lethal against the diamondback moth (*Plutella xylostella*) (Peng et al., 2023). Methyl oleate, an unsaturated methyl ester present in fatty acid methyl ether, has been reported to exhibit insecticidal effects against *Aedes aegypti* larvae (Neto et al., 2023). These studies indicate that djulis leaf and seed extracts can be considered as new ingredients for natural insecticides.

### 5.7. Gastric protection

The ethanolic extract of djulis hull was reported to exhibit gastric protection in C57BL/6 J mice with indomethachin-induced stomach injury by regulating antioxidant status and inhibiting proinflammatory signaling pathways (Isnain et al., 2023). A previous study reported that betanin administration in rats with ethanol-induced gastric ulcers lowered reactive oxygen stress (ROS) levels, which mitigated lymphocyte infiltration and inhibited inflammatory responses by downregulating target genes associated with inflammation in gastric tissues (Karampour et al., 2019). This result indicates that djulis hull is suitable for development as a functional food for gastric ulcer prevention and protection owing to its higher content of betanin, flavonoids, and phenolic compounds than its seeds (Alghamdi, 2023).

## 6. Application as functional food, drink, and health product

Djulis has the potential to be developed into a functional food. Djulis fermented with *Lactobacillus casei* BCRC 10697 has a Trolox equivalent antioxidant capacity (TEAC) of 6.82 mmol/kg, which is 63 % higher than that of unfermented bread, and the substitution of wheat flour with fermented djulis in sour bread can increase its phenolic (18 %) and flavonoid (40 %) content, as well as hardness, chewiness, shelf life, and acceptability (Chen, Hsieh, et al., 2021). Salted noodles supplemented with djulis flour (5–15 %) positively influenced its sensory value (Li et al., 2015). Increased djulis flour decreases the departure time, stability, arrival time, and extensibility of dough; however, the maximum resistance to extension increases (Li et al., 2015). The addition of djulis to Chinese-style sausage increased its antioxidant activity with a 62.368 % DPPH inhibitory rate, indicating that djulis can slow down the organoleptic degradation of sausages (Chung et al., 2023). In addition to food, djulis extract has been incorporated into functional drinks, along with apple juice, fructose, high-methoxyl pectin, citric acid, apple flavor, and water. The results showed that 8 weeks of consumption had protective effects against oxidative stress-induced damage, delayed skin aging, and improved skin conditions (Tsai et al., 2022). Djulis extract (2 %) was also used in supplement drink formulations with fish collagen (12 %), apple juice (8 %), green caviar (1 %), and water, and its consumption led to improvements in moisture, elasticity, gloss, spots, wrinkles, roughness, smoothness, pores, collagen, and erythema in the skin (Chang et al., 2021). The incorporation of fermented djulis into dairy products has increased the free radical scavenging abilities of DPPH (752.35 ± 29.29 μg) and ABTS (771.52 ± 3.79 μg TE/g), free phenol content (169.90 ± 14.59 mg gallic acid/g), the total flavonoid (3.05 ± 0.03 mg quercetin/g), and gamma-aminobutyric acid content (3.07 ± 0.94 mg/g) (Hou et al., 2022). A recent study demonstrated that an extrudate snack produced from djulis exhibited high antioxidant activity, which potentially contributed to the regulation of blood glucose levels in an animal model of diabetic cardiomyopathy (Cheng et al., 2024). The biological activities of djulis and the currently developed djulis products are shown in Fig. 3. These findings suggest that djulis has the potential for wider healthy product development.

## 7. Djulis extract patents

In 2012, Tsai et al. patented the active substance of djulis for hyperlipidemia and hypercholesterolemia medication or health products (US20120171315A1) by inhibiting cholesterol absorption, improving cholesterol metabolism, increasing anti-oxidation, and reducing LDL cholesterol in vessel walls (Tsai & Chaung, 2012). In addition, in 2017, Su et al. patented djulis extract to enhance collagen secretion and prevent cutaneous aging (US9687438B2) in food products, skincare, and cosmetic development (Su et al., 2017).

## 8. Conclusions

Djulis (*Chenopodium formosanum*), a cereal plant endemic to Taiwan, contains pigments (betanin), phenolic acids (syringic acid and gallic acid), and flavonoids (rutin, kaempferol, quercetin, catechin, and epicatechin) as the main bioactive compounds. Djulis exhibits high antioxidant activity, which leads to various biological properties, such as antioxidant, anti-aging, anti-diabetic, anticancer, anti-adipogenesis, hepatoprotective, anti-inflammatory, and gastric protective properties. Djulis extracts can be obtained through different solvent extractions, and additional treatments, including enzymatic hydrolysis, sprouting, non-thermal plasma, reduction of particle size, fermentation, and high pressure, have been applied to increase its bioactive compounds. Compared to leaves, hulls, seeds, and whole grains are more commonly studied and utilized. Djulis has been incorporated as a functional ingredient in food and drinks, including sour dough bread, salted noodles, sausages, fermented dairy products, extrudate snacks, and functional drinks, as well as in cosmetics as an anti-aging ingredient. Further development of products containing djulis is recommended to promote nutritional intake and health benefits.

## CRediT authorship contribution statement

**Amanda Tresiliana Mulio:** Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Chien-Shan Chiu:** Funding acquisition, Methodology, Project administration, Resources, Software. **Yung-Jia Chan:** Supervision, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Wen-Chien Lu:** Supervision, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Po-Hsien Li:** Writing – review & editing,

Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

## Acknowledgments

This research was financially supported by Taichung Veterans General Hospital/Providence University Joint Research Program, (TCVGH-PU-1138102), Taiwan.

## Data availability

The data that has been used is confidential.

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