Biological and Biomedical Journal

Journal homepage: https://bbj.journals.ekb.eg

Evaluation of the protective effects of passion fruit (*Passiflora edulis*) against cisplatin-induced neurotoxicity in rats

Elsayed Elbadrawy *, Hala Elkewawy, Dina Adel

Nutrition and Food Science, Home Economics Department, Faculty of Specific Education, Mansoura University, Egypt.

ARTICLE INFO

Received: 29/6/2025
Revised: 31/7/2025
Accepted: 25/8/2025

Corresponding author:
Elsayed Elbadrawy, Ph. D
E-mail: s_elbadrawy@mans.edu.eg
Mobile: (+2)01001123699

P-ISSN: 2974-4334
E-ISSN: 2974-4342
DOI:
10.21608/BBJ.2025.399047.1114

ABSTRACT

Neurotoxicity is a significant side effect of chemotherapy. This study evaluated the nutritional benefits and protective effects of passion fruit against cisplatin-induced neurotoxicity in rats. A total of 30 rats were involved in the experiment. Six of these rats served as a negative control group. The remaining rats were injected intraperitoneally (i.p.) with cisplatin (2.3 mg/kg) for five consecutive days. Among the four neurotoxic groups, one served as a positive control, while the others received different forms of passion fruit: one group was administered passion fruit juice (PFJ) orally via a stomach tube, another received passion fruit peel powder (PFP), and the last group received a combination of PFJ and PFP for 45 days. Blood samples were collected, and the rats' brains were isolated to examine various parameters, including antioxidants, anti-inflammatory markers, neurotransmitters, and some hormones. The results indicated that the treated groups had lower levels of malondialdehyde, nitric oxide, and β-amyloid in their brains. Additionally, they showed increases in total antioxidant capacity and higher levels of serotonin, dopamine, and acetylcholinesterase compared to the positive control group. Furthermore, serum levels of C-reactive protein, tumor necrosis factor-alpha, and cyclooxygenase-2 significantly decreased in the treated groups. Histopathological analysis revealed fewer inflammatory cells and normal nerve fibers in the treated rats compared to the positive control group. The study recommends using a combination of passion fruit pulp and peel powder to help mitigate the neurotoxic effects associated with cisplatin, highlighting the potential benefits of passion fruit in reducing the side effects of chemotherapy.

Keywords: Antioxidants, Anti-inflammatory, Histopathology, Passion fruit, Rats

1. Introduction

Neurotoxicity is the state in which the nervous system is exposed to harmful substances (neurotoxicants), whether they occur naturally or are man-made, resulting in a disruption of the normal functioning of the neurological system. Only a small number of these neurotoxins have a direct effect on brain cells, whereas others significantly disrupt metabolic processes that depend largely on the neurological system. Neurotoxicity may arise as a consequence of chemotherapy, drug treatments, radiation therapy, organ transplantation, susceptibility to heavy metals like mercury and lead, specific foods, pesticides, industrial items, and solvents utilized in cosmetic cleaning, as well as pharmaceutical drugs. Signs of intoxication can either emerge immediately upon exposure or have a delayed onset. These symptoms may consist of encephalopathy, numbness or limb weakness, behavioral and cognitive deficits (Bilge, 2022; Constantinescu et al., 2025). Antineoplastic agents, including platinum-based drugs, may induce systemic neuronal damage, resulting in diffuse, bilateral

degenerative alterations in peripheral sensitivity. This affects how individuals perceive pain, heat, and cold. As a result, the quality of life significantly and frequently permanently declines for many cancer patients due to cisplatin (Cis)-induced peripheral neuropathy. This condition typically manifests as shooting, burning, or electric-shock-like pain (Cioroiu and Weim, 2017; Seddiek et al., 2025). Cis is one of the most commonly prescribed chemotherapy medications. The body's natural antioxidant defense system, which includes antioxidant enzymes and exogenous antioxidants derived from fruits and vegetables, regulates oxidative stress. Key exogenous antioxidants include vitamins E and C, as well as compounds like flavonoids and carotenoids (Poljsak et al., 2013; Chouikh et al., 2025). Since endogenous antioxidants neutralize free radicals, numerous studies have highlighted the health benefits of dietary antioxidants (Mangge, 2014; Montezano et al., 2015). Given the issues linked to inflammation and oxidative stress in individuals experiencing neurotoxicity, the scientific community has increasingly focused on the importance of incorporating natural antioxidants into the diet and their potential effects on health maintenance and recovery. Fruits are a vital component of the human diet and are highly regarded for their ability to improve health. In addition to acting as the primary source of phytoestrogens, anti-inflammatory substances, and antioxidants, they also contribute vitamins and minerals to the diet regularly (Rekhy and McConchie, 2014). *Passiflora edulis* (Passion fruit), often referred to as "the king of fruits," is commonly found worldwide in tropical and subtropical areas (He et al., 2020). This plant contains approximately 110 phytochemical components, primarily consisting of triterpenoids and flavonoids. Diverse fruit juices, extracts, and isolated chemicals obtained from passion fruit have demonstrated a range of biological activities and health benefits, including hypolipidemic, antidiabetic, anti-tumor, antioxidant, and anti-hypertensive properties. Additionally, passion fruit is non-toxic and considered safe for daily consumption in typical amounts (He et al., 2020; Dos Santos et al., 2025). Passion fruit is rich in several nutritionally beneficial substances, including vitamin C, dietary fiber, B vitamins, niacin, phosphorus, and iron. Various pharmacological studies, both in *vivo* and in *vitro*, have revealed a range of promising bioactivities associated with passion fruit. These include anti-inflammatory, anti-hypertensive, anti-diabetic, antimicrobial, antioxidant, hepatoprotective, and lung-protective effects, as well as sedative, antidepressant, and anxiolytic-like properties (Silva et al., 2015; Dzotam et al., 2015; Zhang et al., 2016 and Panelli et al., 2018; Fonseca et al., 2025). The pharmacological actions are thought to be primarily mediated by bioactive components such as polyphenols, triterpenes, and polysaccharides (El-Badrawy, 1999). Most of these effects resemble those attributed to passion fruit in traditional and folk medicine (Chowdhury et al., 2024). According to Weyya et al. (2024), active phytochemical substances with antioxidant characteristics can suppress oxidative damage and halt the development of inflammatory illnesses and disorders, including neurological ones. Neurotoxicity is a notable detrimental impact observed in patients undergoing a complete course of chemotherapy. Therefore, the objective of this investigation was to assess the protective properties of passion fruit against neurotoxicity induced by cisplatin in rats.

Materials and methods

Chemicals

All chemicals and biochemical analysis kits were obtained from Sigma-Aldrich Company.

Passion fruit and powder preparation

Passion fruit was obtained from the local market at Mansoura City, Egypt. The fruit was identified in the Department of Vegetables and Fruits at the Faculty of Agriculture, Mansoura University. The fresh passion fruits were washed with running water, and the peels were manually separated from the pulp. Then, the peels were carefully washed with running water and dried in an electric oven at 60°C to a constant weight, then crushed carefully to make powder. On the other hand, the pulp and seeds of the passion fruit were separated in a laboratory using a Kenwood Classic Blender

(1200 W, 220V, Japan) to extract juice, which was stored frozen until use.

Chemical analysis of passion fruit juice and peel

The mineral content of the samples was identified as mentioned by Chapman and Pratt (1979). The content of Zn, Fe, Na, Mg, K, Cu, and Ca was calculated using atomic absorption spectrophotometry according to the techniques described in A.O.A.C. (2010). In contrast, P content was measured using a spectrophotometer following Astem (1975). The titrimetric method for determining ascorbic acid (vitamin C) was outlined by Mazumdar and Majumder (2003), vitamin A determined by using spectrophotometric method according to Aremu and Nweze (2017), vitamin E was ascertained using the spectrophotometric technique outlined by Rutkowski and Grzegorczyk (2007) and vitamin K was determined by spectrophotometric method as described by Michale (1962), while, folic acid was calculated based on Ruengsitagoon and Hattanat (2012). Total phenols were estimated by Folin-Ciocalteu's reagent (FCR) spectrophotometrically at the absorbance of 765 nm, as mg gallic acid/g, following Limmongkon et al. (2017). Total flavonoids were determined as mg quercetin/g by using a colorimetric technique, according to Zhishen et al. (1999). Total anthocyanins were ascertained using the methodology outlined by Onayemi et al. (2006).

Experimental Animals

Thirty healthy adult male albino rats (Sprague Dawley), weighing 180 ± 5g, were sourced from the Faculty of Pharmacy at Mansoura University, Egypt. Handling of animals in this study adhered to the guidelines established by the scientific research ethics committee at Mansoura University, approval number: 38-10/2022.

Basal Diet

The modified Reeves et al. (1993) diet was used, which contains the following ingredients: 3% cellulose, 49.7% maize starch, 20% casein, 5% corn oil, 10% sugar, 2% vitamin combination, 10% minerals, and 0.3% DL-methionine.

Experimental design

Thirty adult male albino rats, each weighing 180±5 g, were acclimatized by being fed a basal diet for one week before the experiment. The animals were housed separately under regulated illumination (a 12-hour cycle of light and darkness) and at a temperature of 25°C, with unrestricted access to food and water. After acclimatization, the rats were split up into five groups (6 rats each), one of which remained fed on the basal diet during the experiment period and served as a negative control (group 1). The rest rats were given a daily intraperitoneal injection of 2.3 mg/kg body weight of Cis to induce neurotoxicity disease for 5 days according to Zhang et al. (2020). One of the injured groups received the basal diet for only forty-five days and served as the positive control group (group 2). The other three groups were treated as follows:

Group 3: rats with neurotoxicity that were treated orally with passion fruit juice (20 ml/kg b.wt.) *via* a stomach tube (PFJ). Group 4: rats with neurotoxicity treated with passion fruit peel powder (30 g/kg diet) (PFP). Group 5: rats with neurotoxicity treated with a mix of passion fruit juice (10 ml/kg b.wt.) orally by stomach tube and peel powder (15 g/kg diet) (PFJ+PFP).

Blood and brain samples collection

After forty-five days, blood samples were taken from the rats following anesthesia *via* the ocular vein of each rat. These samples were placed in sterile, dry tubes for clotting at room temperature. After that, the tubes were centrifuged for ten minutes at 5000 rpm to separate the serum. The brains of all the rats were then isolated after euthanasia. Both the serum and the brains were stored in a deep freezer until further use. The brains were homogenized as described by Herron et al. (2022). Additionally, the sciatic nerves were separated and preserved in formalin for histopathological examination.

Biochemical assays in brain tissues and blood

Nitric oxide (NO) was determined in brain tissue according to Montgomery and Dymock (1961). Malondialdehyde (MDA) concentration in brain tissue was determined by Ohkawa et al. (1979). Total antioxidant

activity (TAC) was determined according to the colorimetric technique of Koracevic et al. (2001). The manufacturer's protocol provided by Ray Biotech, Canada, was followed to quantify β-amyloid (Aß40 and Aß42) in the hippocampus using a sandwich ELISA. As per Doungue et al. (2018), the absorbances were promptly measured at 450 nm using an ELISA reader. Acetylcholinesterase (AchE) activity was estimated spectrophotometrically according to the methods of Ellman et al. (1961) and Knedel and Boottger (1967). Measurement of brain tissue serotonin was carried out by using kits of the double-antibody sandwich Enzyme-Linked Immunosorbent Assay (ELISA), as described by Behiry et al. (2019). Dopamine in partial brain tissue samples was analyzed as mentioned by Lai et al. (2022) using ELISA (Dopamine Research ELISA kit, Labor Diagnostic Nord, Germany). The determination of tumor necrosis factor-alpha (TNF-α) was performed according to the method described by Brouckaert et al. (1993). The level of cyclooxygenase-2 (COX-2) was determined according to Kulmacz and Lands (1983). The serum C-reactive protein (CRP) level was analyzed according to Friedman and Young (2001).

Histopathological analysis

The sciatic nerve samples were used to create paraffin blocks, which were subsequently cut into slices of 4-micron thickness. The obtained tissue slices were gathered, deparaffinized, and stained with hematoxylin and eosin on glass slides; the tissue blocks were ready for histopathological analysis under a light microscope (Bancroft and Stevens, 1990).

Statistical analysis

The data were presented as the mean ± SD. One-way analysis of variance (ANOVA) was employed to conduct statistical comparisons among experimental groups, and Tukey's Honestly Significant Difference (HSD) post-hoc test was employed to evaluate pairwise differences at $p>0.05$. IBM SPSS Statistics (Version 29.0, IBM Corp., USA, 2022) was used in data analysis.

3. Results

Minerals, vitamins and polyphenols contents of Passion fruit

Minerals have a significant influence on establishing the nutritional content of fruits. Results of some minerals, including calcium (Ca), potassium (K), phosphorus (P), sodium (Na), magnesium (Mg), zinc (Zn), iron (Fe), and copper (Cu), were recorded in Table (1). It was found that potassium and phosphorus contents recorded 1197.13±4.82 and 118.22±2.57 mg/100 g, in passion fruit pulp, while its Ca and Na contents were 59.18±1.03 and 31.74±1.22 mg/100 g, respectively. However, passion fruit peel powder had the highest values of K, Ca, Na, and Mg content with values of 2217.84±4.19, 316.20±1.08, 74.57±0.92, and 110.21±0.14 mg/100 g, respectively, while it recorded the lowest values of P (69.10±1.56 mg/100 g). Passion fruit peel powder had a higher content of Fe (6.77±0.08 mg/100 g) and Cu (2.94±0.05 mg/100 g), while pulp contains 2.34±0.05 and 0.11±0.02 mg/100 g of Fe and Cu, respectively. As for the zinc content, it was found that passion fruit pulp recorded a high value of 1.26±0.04 mg/100 g, while the Zn value of Passion fruit peel powder was 0.74±0.03 mg/100 g. The fruit pulp has the following vitamins per 100 g: vitamin A (817±5.00 IU), vitamin C (31.84±0.27 mg), vitamin E (0.027±0.01 mg), vitamin K (0.64±0.03 µg), and folic acid (11.98±0.2 µg). In comparison, the vitamin content in passion fruit peel is as follows: vitamin A (1112±7.00 IU), vitamin C (34.16±0.18 mg), vitamin E (0.03±0.01 mg), vitamin K (0.71±0.05 µg), and folic acid (13.14±0.23 µg) per 100 g. In the pulp, the values of total phenols recorded were 41.73 ± 1.22 mg/100 g, the flavonoids were 3.74 ± 0.50 mg/100 g, and the anthocyanins were 0.21 ± 0.03 mg/100 g. In contrast, the peel of the passion fruit contained significantly higher concentrations: 192.61 ± 0.93 mg/100 g of total phenols, 48.11 ± 0.46 mg/100 g of flavonoids, and 106.68 ± 0.11 mg/100 g of anthocyanins.

Table 1. Minerals, vitamins, and polyphenol compounds in fresh pulp and dry peel of passion fruit.

	Fresh pulp	Dry peel
Ca (mg/100 g)	59.18±1.03	316.20±1.08
K (mg/100 g)	1197.13±4.82	2217.84±4.19
P (mg/100 g)	118.22±2.57	69.10±1.56
Na (mg/100 g)	31.74±1.22	74.57±0.92
Mg (mg/100 g)	89.37±0.160	110.21±0.14
Zn (mg/100 g)	1.26±0.04	0.74±0.03
Fe (mg/100 g)	2.34±0.05	6.77±0.08
Cu (mg/100 g)	0.11±0.02	2.94±0.05
Vitamin A (IU/100 g)	817±5.00	1112±7.00
Vit. C (mg/100 g)	31.84±0.27	34.16±0.18
Vit. E (mg/100 g)	0.027±0.01	0.03±0.01
Vit. K (µg/100 g)	0.64±0.03	0.71±0.05
Folic acid (µg/100 g)	11.98±0.200	13.14±0.23
Total phenol (mg/100 g)	41.73±1.22	192.61±0.93
Total flavonoid (mg/100 g)	3.74±0.50	48.11±0.46
Anthocyanin (mg/100 g)	0.21±0.03	106.68±0.11

Results are presented as means ± SD

Effect of passion fruit juice and peel powder on oxidative stress markers in brain tissues of rats with neurotoxicity

The data in Table 2 revealed that the indicators of oxidative stress, MDA and NO, increased significantly in the cisplatin control group (positive control), which reached 1184±56.42 nmol/g and 45.52±4.54 nmol/g in contrast to the normal control, 728±31.61 nmol/g and 19.57±0.851 nmol/g for MDA and NO, respectively. Also, the positive control group showed a notable decline in TAC (209.7±12.06 µmol/g) compared to the normal control (272±6.25 µmol/g). The two treatment groups that received passion fruit juice and peel powder showed a notable reduction in brain levels of MDA and NO. The juice group showed decreases of 29.63% in MDA and 23.66% in NO, while the peel powder group demonstrated reductions of 20.52% in MDA and 25.04% in NO compared to the positive control. Additionally, a notable increase in TAC was observed in the passion fruit juice group, with an increase of 13.97%. The peel powder group achieved a slightly higher rise in TAC at 15.55% compared to the positive control. There was no discernible difference between the juice and peel powder groups regarding these measurements. Notably, the mixed group that received both passion fruit juice and peel powder showed the most significant reductions in MDA and NO levels, with decreases of 29.58% and 41.43%, respectively. This group also recorded the highest increase in TAC at 21.50% in contrast to the positive control.

Effect of passion fruit juice and peel powder on neurotransmitter parameters in brain tissues of rats with neurotoxicity

Table 3 showed substantial decreases in brain serotonin, dopamine, and AChE in the positive control group than those of the normal control by 71.21, 72.70, and 75.07%, respectively, while β-amyloid levels increased significantly by 682.71%. The results indicate that groups treated with passion fruit juice, passion peel powder, or their combination exhibited a significant rise in serotonin, dopamine, and AChE levels, along with a notable decrease in β-amyloid relative to the positive control. The increased percentages for serotonin, dopamine, and AChE concentration in the passion fruit juice group were 114.80%, 129.67%, and 140.99%, respectively, when compared to the positive control group. In the peel powder group, the percentages were 113.44%, 132.01%, and 139.75%, respectively. Additionally, the peel powder group revealed a notable decline in brain β-amyloid levels of

23.87%, while the juice group exhibited a decrease of 23.48%. Notably, the rats treated with a combination of passion fruit juice and peel powder showed the greatest improvement in serotonin, dopamine, and AChE levels, as well as the most significant reduction in β-amyloid levels.

Table 2. Effect of passion fruit juice and peel powder on oxidative stress parameters in brain tissues of rats with neurotoxicity

Groups	MDA (nmol/g)	NO (nmol/mg)	TAC (µmol/g)
Normal control	728^{c}±31.61	19.57^{c}±0.851	272^{a}±6.245
Positive control	1184^{a}±56.41*	45.52^{a}±4.544*	209.7^{c}±12.06*
PFJ	939.7^{b}±48.54**	34.75^{b}±2.328**	239^{b}±2.646**
PFP	941^{b}±55.07**	34.12^{b}±2.462**	242.3^{b}±3.512**
Mix group (PFJ+PFP)	833.7^{bc}±20.5**	26.66^{bc}±3.641**	254.7^{ab}±8.145**

The results are shown as means ± standard deviation (SD) and percentage of change. Different superscript letters in the same column indicate significant change at $p<0.05$. (*) % of change compared to the normal group. (**) % of change compared to the positive control. PFJ: Passion Fruit Juice, PFP: Passion Fruit Peel.

Table 3. Impact of passion fruit juice and peel powder on neurotransmitter parameters in brain tissues of rats with neurotoxicity

Groups	Serotonin (ng/mg)	Dopamine (ng/mg)	AChE (ng/mg)	β-amyloid (µg/g)
Normal control	4.317^{a}±0.067	1.563^{a}±0.067	4.227^{a}±0.097	45.7^{d}±3.045
Positive control	1.243^{d}±0.115*	0.4267^{c}±0.031*	1.054^{c}±0.131*	357.7^{a}±12.77*
PFJ	2.67^{c}±0.056**	0.98^{b}±0.123**	2.54^{b}±0.288**	273.7^{b}±8.737**
PFP	2.653^{c}±0.093**	0.99^{b}±0.132**	2.527^{b}±0.365**	272.3^{b}±9.684**
Mix group	2.94^{b}±0.095**	1.191^{b}±0.182**	2.953^{b}±0.129**	233.1^{c}±9.439**

The results are shown as means ± standard deviation (SD) and percentage of change. Different superscript letters in the same column indicated a significant change at $p<0.05$. (*) % of change compared to the normal group. (**) % of change compared to the positive control. PFJ: Passion Fruit Juice, PFP: Passion Fruit Peel.

Impact of passion fruit juice and peel powder on inflammatory markers in the serum of rats with neurotoxicity

The findings in Table 4 indicated that all the inflammatory parameters, CRP, TNF-α, and COX-2, significantly increased in the serum of the positive control group compared to the normal control group. The treated groups exhibited significant decreases in all these parameters relative to the positive control. It was observed that the effect of peel powder was more potent in reducing CRP, TNF-α, and COX-2 levels than passion fruit juice. There was no discernible change between the two samples in reducing the anti-inflammatory parameters. Regarding the cisplatin group treated with the mixture of passion fruit juice and peel powder, a greater reduction in serum anti-inflammatory parameters, 66.34%, 35.93%, and 40.49% for CRP, TNF-α, and COX-2, respectively, was observed, indicating that the mixture is more effective in reducing inflammation. In terms of serum CRP levels, a significant increase of 55.4% was observed in the positive control group relative to the normal control group. However, the three treated groups with the pulp juice, peel powder, and their mixtures showed a notable drop in serum CRP levels with percentages of 61.61, 63.05, and 66.35%, respectively, relative to the positive control.

Table 4. Impact of passion fruit juice and peel powder on inflammatory markers in the serum of rats with neurotoxicity

Groups	CRP (µg/ml)	TNF-α (pg/ml)	COX-2 (ng/ml)
Normal control	92.85^{b} ±.6.12	8.387^{d}±0.277	24.13^{c}±1.27
Positive control	144.3^{a}±7.622*	15.78^{a}±0.433*	89.88^{a}±5.60*
PFJ	55.4^{c}±6.222**	12.33^{b}±0.737**	66.04^{b}±4.46**
PFP	53.27^{c}±5.42**	12.22^{b}±0.709**	65.6^{b}±7.05**
Mix group (PFJ+PFP)	48.55^{c}±6.503**	10.11^{c}±0.705**	53.49^{b}±4.88**

The results are shown as means ± standard deviation (SD) and percentage of change. Different superscript letters in the same column indicated a significant change at $p<0.05$. (*) % of change compared to the normal group. (**) % of change compared to the positive control. PFJ: Passion Fruit Juice, PFP: Passion Fruit Peel.

Histopathological examination of the sciatic nerve

The sciatic nerve slices of rats in the normal control group yielded specimens, well-organized nerve fibers ,and no structure (Fig. 1a). At the same time, the samples taken from the animals' sciatic nerve slices in the cisplatin control (positive group) demonstrated congested blood vessels (red arrow), and many inflammatory cell aggregations in the epineural sheath (black arrows) (Fig.1b). Moreover, the specimens isolated from sciatic nerve sections of rats in cisplatin-treated rats treated with passion fruit juice showed fewer inflammatory cell aggregations in the epineural sheath (black arrows) (Fig.1c). The specimens isolated from sciatic nerve sections of rats in cisplatin-treated rats treated with passion peel powder showed congested blood vessels (red arrow) (Fig.1d). The specimens isolated from sciatic nerve sections of rats in cisplatin rats treated with the mix of passion fruit juice and peel powder showed normal well organized nerve fibers and no structure (Fig.1e).

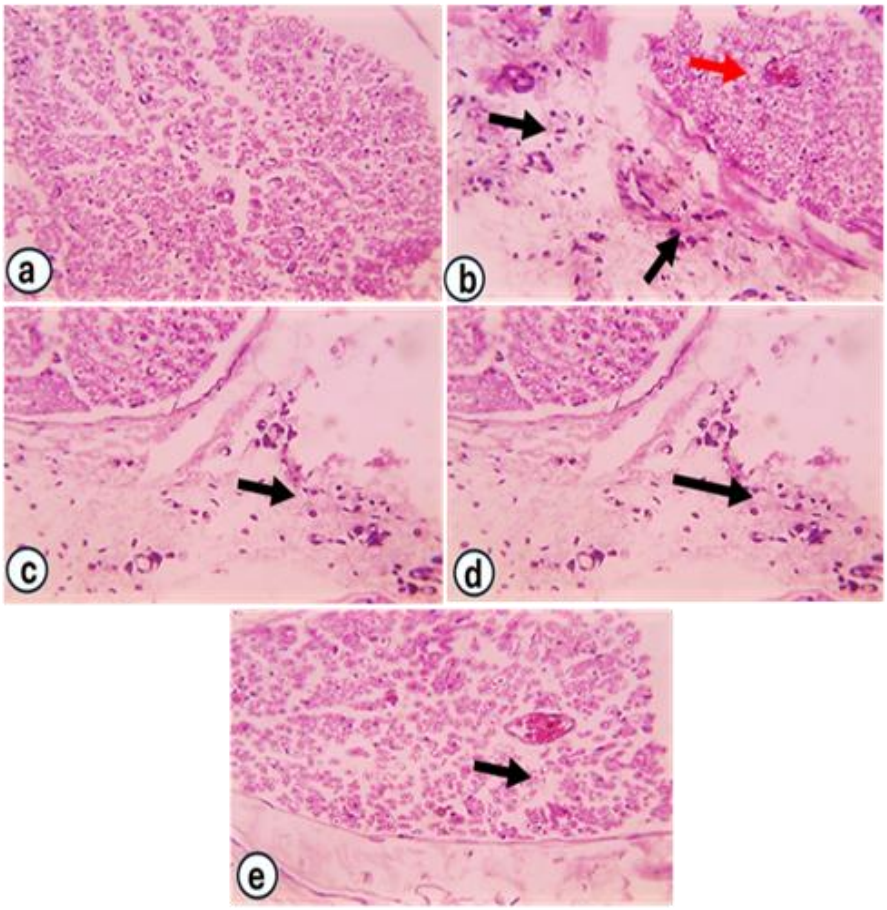

Fig. 1. Normal, well-organized nerve fibers and no structure defect show in the control group (a), congested blood vessels (red arrow), many inflammatory cells aggregate in the epineural sheath (black arrows) in the positive group (b), fewer inflammatory cells aggregation in epineural sheath (black arrows) in Cis group treated with passion fruit juice (c), Congested blood vessels (red arrow) in the Cis group treated with passion peel powder (d), and normal well-organized nerve fibers and no structure defect in Cis group treated with passion fruit juice and peel powder (e) (X: 400; scale bar: 50 μm).

4. DISCUSSION

The passion fruit is one of the most exquisite plants that has been used for medicinal purposes. Consequently, many evaluations must be carried out before they are available for human consumption. They typically serve as components of a supplementary diet to promote health and prevent diseases. Minerals play a crucial role in assessing nutritional value. The estimated elements in passion fruit pulp and peel were found to be sufficient for children, adults, pregnant women, and nursing mothers, and they were also found to be of acceptable quality and quantity (Fonseca et al., 2025; Dos Santos et al., 2025). Potassium is the most prevalent mineral in passion fruit, as it is in many other fruits. A notable source of K is found in passion fruit, which is essential for preserving the acid-base equilibrium and regulating blood pressure (Martin, 1997; Wardlaw, 2003). Phosphorus provides strength and rigidity to teeth and bones and is essential to the basic metabolic processes occurring within the body (Wardlaw, 2003). Magnesium is a vital element in a balanced human diet, serving as a cofactor in numerous enzyme systems and working with calcium to influence muscle excitability and neurochemical transmission (Martin, 1997; Wardlaw, 2003). Eating passion fruits may help support normal bodily functions and blood clotting. Additionally, passion fruit is an excellent source of plant-based (non-heme) iron, which is crucial for the production of red blood cells. Therefore, pregnant women and children need to include passion fruit in their diets, as it is essential for their health

(Babasaheb, 2000; Oluyemi et al., 2006). According to Bello et al. (2008) and Dimari and Hati (2010), for men aged 19 to 30, 8 mg of iron should be consumed daily, for women it is 18 mg, and for pregnant women it is 27 mg. Since Zn is associated with the immune system, it is a crucial element for human health (Taboada, 2017).

Minor minerals found in passion fruit seeds include iron, copper, manganese, zinc and others. These minerals are essential components for physiological functions in humans. Our results agreed with those mentioned by Adeyeye and Aremu (2017) and De Toledo et al. (2018), who demonstrated that purple passion fruit pulp contains minerals such as Na, K, Ca, Mg, Zn, Fe, Mn and P. The peel of passion fruit is rich in vitamins, as mentioned earlier. Its high vitamin C content is particularly beneficial because vitamin C is a powerful water-soluble antioxidant. Vitamin C-rich fruits increase the body's resistance to viral infections, such as those that cause the flu, and also help eliminate detrimental free radicals that promote inflammation (Morton, 1987). Additionally, Vit. A is necessary for keeping skin and mucous membranes healthy. According to Adeyeye and Aremu (2017), vitamins C and A are abundant in passion fruit juice. Interestingly, the outer peel of the passion fruit has even higher concentrations of these vitamins. Our findings align with the research conducted by Dos Reis et al. (2018) and the USDA (2019). Dos Reis et al. (2018) found that phenolic compound in purple passion fruit was 788.93 and 1570.80 mg/100 g DW in pulp and peel, respectively, while total flavonoid was 229.79 mg/100 g dry weight in passion pulp and the content of anthocyanin was 103.69 mg/100 g DW in passion peel. Also, Septembre-Malaterre et al. (2016) researched the total flavonoid content of passion fruit pulp and discovered that it contains 70.10 mg quercetin equivalent/100 g. Viera et al. (2022) reported that gulupa (purple passion fruit) had 1.64 mg gallic acid g^{-1} polyphenols and 0.45 mg quercetin g^{-1} flavonoids. Eating natural fruits high in flavonoids and vitamin A can shield humans from cancers of the oral and lungs (Morton, 1987).

Our analysis of the bioactive compounds revealed that passion fruit is rich in phenolic compounds, which possess significant biological activities. Cis is a commonly utilized platinum-based chemotherapeutic agent known for its effectiveness in treating various malignancies. However, its clinical utility is often limited by significant side effects, among which neurotoxicity is prominent. Cis-induced neurotoxicity primarily manifests as peripheral neuropathy, characterized by sensory disturbances such as tingling, numbness, and loss of proprioception, predominantly affecting the extremities. According to the current results, the passion fruit juice and peel powder group showed significant decreases in brain MDA and NO. Our findings are consistent with those of Ibrahim (2022), who observed a notable decrease in NO and MDA levels in the blood of all treated groups receiving varying amounts of passion fruit juice, in contrast to the positive control group. Additionally, there was an increase in TAC. Our results provide strong evidence that passion fruit, including both its juice and peel, helps counteract neurotoxicity caused by Cis. This effect is linked to mechanisms related to reducing oxidative stress, modulating inflammation, and regulating neurotransmitters. Previous studies have already emphasized the antioxidant potential of Passiflora edulis (Kandandapani et al., 2015; Rotta et al., 2019). Our study highlights the neuroprotective impacts of certain substances in the context of chemotherapy. Notably, the peel of the passion fruit was found to be more effective in reducing oxidative damage compared to the pulp. This can be attributed to its higher phenolic content, with 192.61 mg of phenolics per 100 g for the peel, compared to 41.73 mg per 100 g for the pulp. Additionally, previous research (Silva et al., 2015) has linked the anti-inflammatory impacts of passion fruit to its polysaccharide content. However, this finding contrasts with those of De Toledo et al. (2018), who reported lower phenolic levels in tropical varieties of the fruit. We propose that differences in regional growing conditions or extraction methods could explain this discrepancy, an aspect that is often overlooked

in phytochemical studies. The synergistic effect of PFJ and PFP in reducing MDA by 29.58%, NO by 41.43% and raising TAC by 21.46% underscores the combinatorial advantage of utilizing both fruit components, as they may target distinct oxidative pathways. According to Briguglio et al. (2018), dopamine is necessary for humans to be able to coordinate their movements, be motivated, and respond to rewards. On the other hand, serotonin (5-HT) pathways in the central nervous system regulate behavior, eating, and sleep, while in the gut, they control gastrointestinal motility. An enzyme called acetylcholine esterase breaks down the neurotransmitter acetylcholine, which is associated with short-term memory, and it is used to identify cholinergic neurons. Our results showed that rats given passion fruit juice and peel powder for 45 days had much higher levels of serotonin, dopamine, and AChE in the brain. This result is in line with that of Doungue et al. (2018), who found that the passion fruit juice improved cognitive function by inhibiting AChE activities and reducing neuroinflammatory markers. Many diseases are linked to free radicals due to their harmful effects on cells. Phenolic compounds found in plants may protect cells from oxidative stress caused by these free radicals by acting as scavengers. The anti-inflammatory effects observed were also significant. The impressive reduction in TNF-α levels from passion fruit peel may be attributed to its flavonoid profile, which might inhibit nuclear factor kappa B (NF-κB) signaling a hypothesis that needs further molecular validation. Additionally, the three treated groups, which received pulp juice, peel powder, and their mixtures, showed a significant decrease in serum CRP levels compared to the positive control group. The phytochemicals present in passion fruit may be responsible for its beneficial effects (Phama et al., 2019). Histopathological analysis of the sciatic nerve in the positive control group showed congested blood vessels and numerous inflammatory cell aggregations in the epineural sheath. In contrast, rats treated with passion fruit juice, peel powder, or their mixture exhibited fewer inflammatory cells and displayed normal, well-organized nerve fibers. Doungue et al. (2018) reported that in the hippocampus CA1 region, co-administration of *Passiflora edulis* fruit extract and flavonoid fraction dramatically reduced the degenerative and morphological alterations of the pyramidal cells caused by $AlCl_3$. The bioactive compounds in passion fruit may significantly contribute to its neuroprotective effects.
2025).

Conclusion

It can be concluded that the passion fruit contains many different soluble nutrients and phytochemicals, including vitamins A, C, E, K, and folic acids, minerals (Ca, P, K, Na, Mg, Zn, Fe, and Cu), besides phenolic acids, flavonoids, and anthocyanins. The pulp juice and peel powder of passion fruit demonstrated antioxidant and anti-inflammatory effects against cis-induced neurotoxicity in rats. They improved the levels of serotonin, dopamine, acetylcholine esterase, and β-amyloid in the brain of the rats with neurotoxicity. The histopathological examination of the sciatic nerve demonstrated significant improvement in the groups treated with passion fruit juice, pulp, or their mixture. The results indicated that the combination of passion fruit pulp juice and peel powder was the most effective in reducing Cis-induced toxicity in rats, likely due to their synergistic effects. Therefore, it is recommended to use a mixture of passion fruit pulp and peel powder in the treatment of neurotoxicity and to help mitigate the side effects of Cis, which is commonly used in cancer treatment.

References

A.O.A.C. (2010). Official Methods of Analysis of the Association of Official Analytical Chemists. 18th Edition, Washington, DC.

Adeyeye, E. I., & Aremu, M. O. (2017). Chemical composition of the raw fruit coat, seed and pulp of passion fruit (*Passiflora edulis*). Journal Trends in Science & Technology, 2, 334-341.

Aremu S. O. & C. C. Nweze (2017). Determination of vitamin A content from selected Nigerian fruits using the spectrophotometric method. Bangladesh J. Sci. Ind. Res. 52(2): 153-158.

Astem S, 1975. Annual book of American Society of Testing Materials standard water. Part 31 Dsis -72. Philadelphia, PA.

Babasaheb BD, 2000. Handbook of Nutrition and Diet. Marcel Dekker Inc., New York.

Bancroft JD, Stevens A, 1990. Theory and Practice of Histological Techniques. Churchill Livingston, Edinburgh, London, Melbourne and New York: 21–119.

Behiry EG, Maha Z, Mohamed M, Mohamed A, 2019. Diagnostic significance of serum serotonin levels in prediction of esophageal and fundal varices in cirrhotic patients. Med. J. Cairo Univ. 87: 4413-4419.

Bello MO, Falade OS, Adewusi SR, Olawole NO, 2008. Studies on the chemical compositions and anti-nutrients of some lesser-known Nigeria fruits. Afr. J. Biotechnol. 7: 3972-3979.

Bilge S, 2022. Neurotoxicity, types, clinical manifestations, diagnosis and treatment. In: Neurotoxicity – new advances.

Briguglio M, Dell'Osso B, Panzica G, Malgaroli A, Banfi G, Zanaboni Dina C, Galentino R, Porta M, 2018. Dietary neurotransmitters: a narrative review on current knowledge. Nutrients. 10: 591.

Brouckaert P, Libert C, Everaerdt B, Takahashi N, Cauwels A, Fiers W, 1993. Tumor necrosis factor, its receptors and the connection with interleukin 1 and interleukin 6. Immunobiology. 187: 317-329.

Chapman HD, Pratt PF, 1979. Methods of Analysis for Soils, Plants and Waters. 2nd ed. Univ. California Press, Berkeley, CA, USA: 12-19.

Chouikh A, Chenguel A, Ali AB, 2025. Understanding the role of free radicals, oxidative stress, and antioxidants: a comprehensive review. Lett. Appl. NanoBioSci. 14: 66.

Chowdhury MM, Sikder MI, Islam MR, Barua N, Yeasmin S, Eva TA, Islam A, Rasna IJ, Hossain MK, 2024. A review of ethnomedicinal uses, phytochemistry, nutritional values, and pharmacological activities of Hylocereus polyrhizus. J. Herbmed Pharmacol. 13: 353-365.

Cioroiu C, Weimer LH, 2017. Update on chemotherapy-induced peripheral neuropathy. Curr. Neurol. Neurosci. Rep. 17: 1-8.

Constantinescu AM, Karzi VE, Docea AO, Tsitsimpikou C, Nosyrev AE, Tsatsakis A, Hernández AF, Bogdan C, 2025. Neurobehavioral effects of low dose exposure to chemical mixtures: a review. Arch. Toxicol. 99: 1-17.

De Toledo NMV, De Camargo AC, Ramos PBM, Button DC, Granato D, Canniatti-Brazaca SG, 2018. Potentials and pitfalls on the use of passion fruit by-products in drinkable yogurt: physicochemical, technological, microbiological, and sensory aspects. Beverages. 4: 47.

Dimari GA, Hati SS, 2010. Vitamin C composition and mineral content of some Nigerian packaged juices drinks. J. Life Phys. Sci. 3: 129-134.

Dos Reis LCR, Facco EMP, Salvador M, Flôres SH, de Oliveira Rios A, 2018. Antioxidant potential and physicochemical characterization of yellow, purple and orange passion fruit. J. Food Sci. Technol. 55: 2679-2691.

Dos Santos OV, Ramos ADS, Soares SD, Miki KSL, Teixeira SML, Teixeira-Costa BE, 2025. Passion fruit. In: Minor Fruits. Apple Academic Press: 109-142.

Doungue HT, Kengne APN, Kuate D, 2018. Neuroprotective effect and antioxidant activity of Passiflora edulis fruit flavonoid fraction, aqueous extract, and juice in aluminum chloride-induced Alzheimer's disease rats. Nutrire. 43: 1-12.

Dzotam JK, Touani FK, Kuete V, 2015. Antibacterial and antibiotic-modifying activities of three food plants (Xanthosoma mafaffa Lam., Moringa oleifera (L.) Schott and Passiflora edulis Sims) against multidrug-resistant Gram-negative bacteria. BMC Complement. Altern. Med. 16: 1-8.

El–Badrawy EEY, 1999. Hypoglycemic effect of the glycan isolated from guava fruit (Psidium guajava). VDLUFA–Schriftenreihe. 52: 203-206.

Ellman GL, Courtney KD, Andres V Jr, Featherstone RM, 1961. A new and rapid colorimetric determination of acetylcholinesterase activity. Biochem. Pharmacol. 7: 88-95.

Fonseca AM, Silvestre AJ, Rocha SM, 2025. From physicochemical characteristics variability to purple passion fruit (Passiflora edulis f. edulis) powders nutritional value: on the

path of zero-waste. J. Sci. Food Agric. 105: 3306-3316.

Friedman RB, Young DS, 2001. Effects of disease on clinical laboratory tests. 4th ed. AACC Press. Clin. Chem. 48: 682-683.

He X, Luan F, Yang Y, Wang Z, Zhao Z, Fang J, Wang M, Zuo M, Li Y, 2020. Passiflora edulis: an insight into current research on phytochemistry and pharmacology. Front. Pharmacol. 11: 617.

Herron S, Delpech JC, Madore C, Ikezu T, 2022. Using mechanical homogenization to isolate microglia from mouse brain tissue to preserve transcriptomic integrity. STAR Protoc. 3: 101670.

IBM Corporation, 2022. IBM SPSS Statistics for Windows, Version 29.0. Armonk, NY: IBM Corp.

Ibrahim RIT, 2022. Biological activities of passion fruit (Passiflora edulis) in impediment of alloxan-induced cataract in rats. Res. J. Specific Educ., Faculty of Specific Education, Mansoura Univ. 71: 1-26.

Kandandapani S, Balaraman AK, Ahamed HN, 2015. Extracts of passion fruit peel and seed of Passiflora edulis (Passifloraceae) attenuate oxidative stress in diabetic rats. Chin. J. Nat. Med. 13: 680-686.

Knedel M, Boetteger R, 1967. Kinetic method for determination of pseudocholinesterase (acylcholine acylhydrolase) activity. Wien. Klin. Wochenschr. 45: 325-327.

Koracevic D, Koracevic G, Djordjevic V, Andrejevic S, Cosic V, 2001. Method for the measurement of antioxidant activity in human fluids. J. Clin. Pathol. 54: 356-361.

Kulmacz RJ, Lands WEM, 1983. Requirements for hydroperoxide by the cyclooxygenase and peroxidase activities of prostaglandin H synthase. Prostaglandins. 25: 531-540.

Lai WD, Tung TH, Teng CY, Chang CH, Chen YC, Huang HY, Lee HC, Huang SY, 2022. Fish oil ameliorates neuropsychiatric behaviors and gut dysbiosis by elevating selected microbiota–derived metabolites and tissue tight junctions in rats under chronic sleep deprivation. Food Funct. 13: 2662-2680.

Limmongkon A, Janhom P, Amthong A, Kawpanuk M, Nopprang P, Poohadsuan J, Somboon T, Saijeen S, Surangkul D, Srikummool M, Boonsong T, 2017. Antioxidant activity, total phenolic, and resveratrol content in five cultivars of peanut sprouts. Asian Pac. J. Trop. Biomed. 7: 332-338.

Mangge H, Becker K, Fuchs D, Gostner JM, 2014. Antioxidants, inflammation and cardiovascular disease. World J. Cardiol. 6: 462.

Martin E, 1997. Principles of Human Nutrition. Chapman and Hall, London.

Mazumdar BC, Majumder K, 2003. Methods on Physico-chemical Analysis of Fruits. Daya Publishing House, Delhi.

Michalek JE, 1962. A method for the determination of vitamin K_S in fruits and vegetables.

Montezano AC, Dulak-Lis M, Tsiropoulou S, Harvey A, Briones AM, Touyz RM, 2015. Oxidative stress and human hypertension: vascular mechanisms, biomarkers, and novel therapies. Can. J. Cardiol. 31: 631-641.

Montogomery H, Dymock J, 1961. The determination of nitrite in water: colorimetric method of nitric oxide assay. Analyst. 86: 414.

Morton J, 1987. Passionfruit. In: Fruits of Warm Climates. Julia F. Morton, Miami, FL: 320-328.

Ohkawa H, Ohishi N, Yagi K, 1979. Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. Anal. Biochem. 95: 351-358.

Oluyemi EA, Akinlua AA, Adenuga AA, Adebayo MB, 2006. Mineral contents of some commonly consumed Nigerian foods. Eur. J. Sci. Res. 6: 11-15.

Onayemi OO, Neto CC, Heuvel JEV, 2006. The effect of partial defoliation on vine carbohydrate concentration and flavonoid production in cranberries. Hort. Sci. 41: 607-611.

Panelli MF, Pierine DT, De Souza SLB, Ferron AJT, Garcia JL, Santos KCD, Corrêa CR, 2018. Bark of Passiflora edulis treatment stimulates antioxidant capacity and reduces dyslipidemia and body fat in db/db mice. Antioxidants. 7: 120.

Phama DC, Vua NH, Samhaberb WM, Nguyena MT, 2019. Physicochemical characteristics and aroma analysis of passion fruit juice and guava juice concentrated by a novel evaporation concept. Chem. Eng. 75: 43-48.

Poljsak B, Šuput D, Milisav I, 2013. Achieving the balance between ROS and antioxidants:

when to use the synthetic antioxidants. Oxid. Med. Cell. Longev. 2013: 956792.

Reeves PG, Nielsen FH, Fahey Jr GC, 1993. AIN-93 purified diets for laboratory rodents: final report of the American Institute of Nutrition ad hoc writing committee on the reformulation of the AIN-76A rodent diet. J. Nutr. 123: 1939-1951.

Rekhy R, McConchie R, 2014. Promoting consumption of fruit and vegetables for better health. Have campaigns delivered on the goals? Appetite. 79: 113-123.

Rotta EM, Rodrigues CA, Jardim ICSF, Maldaner L, Visentainer JV, 2019. Determination of phenolic compounds and antioxidant activity in passion fruit pulp (Passiflora spp.) using a modified QuEChERS method and UHPLC-MS/MS. LWT. 100: 397-403.

Ruengsitagoon W, Hattanat N, 2012. Simple spectrophotometric method for determination of folic acid. The 4th Annual Northeast Pharmacy Res. Conf., Fac. Pharma. Sci., Khon Kaen Univ., Thailand.

Rutkowski M, Grzegorczyk K, 2007. Modifications of spectrophotometric methods for antioxidative vitamins determination convenient in analytical practice. Acta Sci. Pol. Technol. Aliment. 6: 17-28.

Seddiek H, Hanna M, Hamoud AEM, Elbaset MA, Akabawy AM, Kotb MZ, Khalifa MM, 2025. Deferiprone ameliorates cisplatin-induced peripheral neurotoxicity via ferritinophagy adjustment. Sci. Rep. 15: 4485.

Septembre-Malaterre A, Stanislas G, Douraguia E, Gonthier MP, 2016. Evaluation of nutritional and antioxidant properties of the tropical fruits banana, litchi, mango, papaya, passion fruit and pineapple cultivated in Réunion, French Island. Food Chem. 212: 225-233.

Silva RO, Damasceno SR, Brito TV, Dias JM, Fontenele AM, Braúna IS, Júnior JS, Maciel JS, de Paula RC, Ribeiro RA, Barbosa AL, 2015. Polysaccharide fraction isolated from Passiflora edulis inhibits the inflammatory response and the oxidative stress in mice. J. Pharm. Pharmacol. 67: 1017-1027.

Taboada N, 2017. El Zinc y el Cobre: Micronutrientes Esenciales para la Salud Humana. Acta Med. Centro. 11: 79-89.

U.S. Department of Agriculture, 2019. Food Data Central. Agric. Res. Serv. Available at: http://fdc.nal.usda.gov [Accessed 26 Apr. 2020].

Viera W, Shinohara T, Samaniego I, Sanada A, Terada N, Ron L, Suárez-Tapia A, Koshio K, 2022. Phytochemical composition and antioxidant activity of Passiflora spp. germplasm grown in Ecuador. Plants. 11: 328.

Wardlaw GM, 2003. Contemporary Nutrition. McGraw-Hill, New York.

Weyya G, Belay A, Tadesse E, 2024. Passion fruit (Passiflora edulis Sims) by-products as a source of bioactive compounds for non-communicable disease prevention: extraction methods and mechanisms of action. A systematic review. Front. Nutr. 11: 1340511.

Zhang M, Du W, Acklin S, Jin S, Xia F, 2020. SIRT2 protects peripheral neurons from cisplatin-induced injury by enhancing nucleotide excision repair. J. Clin. Invest. 130(6): 2953-2965.

Zhang YJ, Zhou T, Wang F, Zhou Y, Li Y, Zhang JJ, Zheng J, Xu DP, Li HB, 2016. The effects of Syzygium samarangense, Passiflora edulis and Solanum muricatum on alcohol-induced liver injury. Int. J. Mol. Sci. 17(10): 1616.

Zhishen J, Mengcheng T, Jianming W, 1999. The determination of flavonoid contents in mulberry and their scavenging effects on superoxide radicals. Food Chem. 64(4): 555-559.