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BIOACTIVE COMPOUNDS IN *Cucumis melo* L. AND ITS BENEFICIAL HEALTH EFFECTS: A SCOPING REVIEW

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ABSTRACT

Cucumis melo L. possesses numerous medicinal and nutritive functions due to the rich sources of biological active compounds. However, *Cucumis melo* L. processing generate by-products that threaten the environment. This study aims to explore the bioactive compounds present in different melon parts and the fruit's beneficial health effects. A methodological framework proposed by Arksey and O'Malley was used to conduct the scoping review. An electronic database search for English academic articles was conducted using PubMed, Scopus and ScienceDirect encompassing years between 1999 and 2019. All types of studies, excluding systematic review or review papers were eligible for inclusion. Out of 602 studies identified, a total of 18 studies were included. Both peels and seeds were rich in phenolic compounds. The seed oil contained rich sources of tocopherols, while β-carotene and vitamin C were found in the flesh. Next, the main beneficial health effects included antioxidant, anti-inflammatory, anti-ulcer, anti-angiogenic, anti-diabetic, anti-bacterial and anti-hypothyroidism activities, which were attributable to the presence of bioactive compounds. In summary, *Cucumis melo* L., particularly its seeds and peels exhibited various health benefits. This was an indicative of the potential of incorporating these by-products into various food and nutraceutical applications to create novel functional food or dietary supplements.

Key words: Bioactive compounds, *Cucumis melo* L., health

INTRODUCTION

Melon, which is also known as *Cucumis melo* L., belongs to the Cucurbitaceae family that is inclusive of several fruit species, such as watermelon (*Citrullus lanatus* L.); squash (*Cucurbita maxima* L.); cucumber (*Cucumis sativus* L.); and cantaloupe (*Cucumis melo* L.) (Ismail e*t al.,* 2010; Ritschel *et al.,* 2004). Melon is one of the most widely cultivated and consumed fruits worldwide. It is the main plant of this particular family (Gill *et al.,* 2011) and grows well in all tropical and subtropical regions in the world, such as Europe, Asia and Africa (Mallek-Ayadi *et al.,* 2018), with preference for hot weather (Milind & Kulwant, 2011). *Cucumis melo* L. is comprised of various fruit groups, which include orange flesh cantaloupes, green flesh honeydew, and mixed melons (Ibrahim & El-Masry, 2016). Various studies have reported that *Cucumis melo* L. is a delicious and juicy fruit offering numerous medicinal and nutritive functions (Milind & Kulwant, 2011; Vishwakarma *et al.,* 2017). It contains polyphenols, organic acids, lignans and other polar compounds that are beneficial to human health (Rodríguez-Pérez *et al.,* 2013).

The processing of melon can generate a huge amount of waste materials and by-products, such as its seeds and skin (Mallek-Ayadi *et al.,* 2016). These residues can threaten the environment. Therefore, the environmental view underlines that it is vital for these generated by-products to be re-used in the food or nutraceutical industry for waste production reduction and environmental protection (Ibrahim & El-Masry, 2016). These wastes contain rich sources of biological active compounds, such as polyphenols, vitamins, enzymes, and dietary fibers (Sagar *et al.,* 2018). Hence, it is of great interest as there is an increased demand for natural compound

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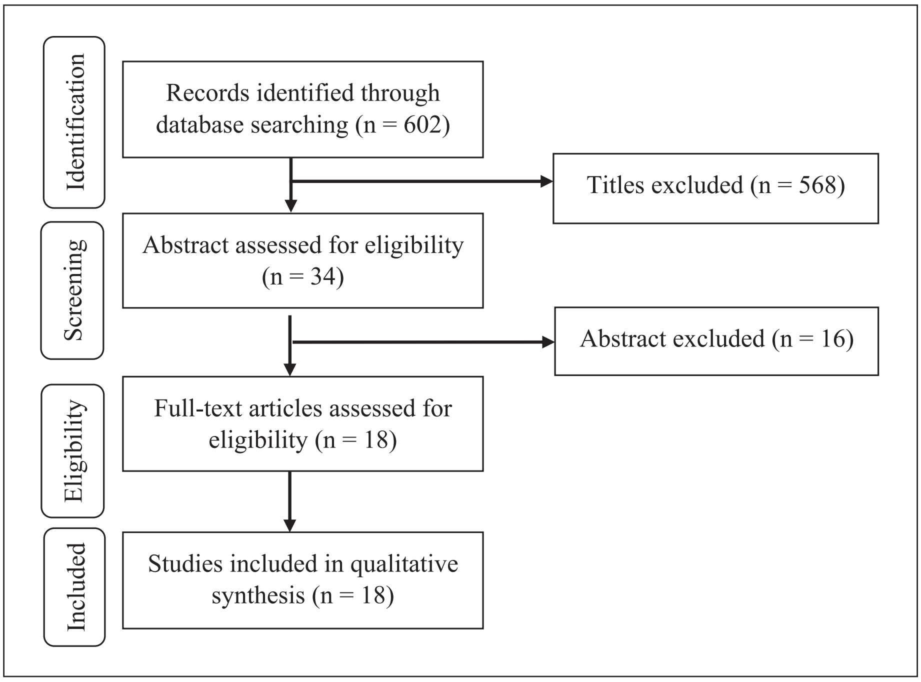

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow diagram of study selection.

beneficial towards human health (Silva *et al.,* 2018). Thus, the use of such waste to produce various functional ingredients in food products or supplements is an initial step towards sustainable development. This scoping review aims to examine the bioactive compounds obtained from the different parts of *Cucumis melo* L. and its beneficial health effects.

MATERIALS AND METHODS

The present study was designed as a scoping review in identifying the bioactive compounds of *Cucumis melo* L. and its beneficial health effects. The five-stage methodological framework outlined by Arksey and O'Malley (2005) was used as a guideline for the scoping review, which consisted of: (1) identifying the research questions; (2) identifying relevant studies; (3) selecting studies; (4) charting the data; and (5) collating, summarizing and reporting the results. Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow diagram illustrates the flow of the process from article search to its final selection as shown in Figure 1 (Moher *et al.,* 2009).

Identifying the research questions

The review questions were: (1) what are the bioactive compounds present in the different parts of *Cucumis melo* L.? and (2) what are the beneficial health effects of *Cucumis melo* L.?

Identifying relevant studies

Academic journals (in English) published from year 1999 to 2019 were identified by conducting electronic database search using PubMed, Scopus, and ScienceDirect. All types of studies, excluding systematic reviews or review papers were included in the search. Titles, abstracts and keywords were examined independently for their eligibility by the researchers. A total of 18 studies were included in this review out of 602 studies identified through the electronic databases. The key search terms used to search the articles are displayed in Table 1.

Selecting studies

Identified studies were eligible for inclusion in this review if they met the following inclusion criteria: (1) fruits involved were of cantaloupe, *Cucumis melo* L., or melon; (2) reported only single data on the concentration of each bioactive

Table 1. Key search terms in the scoping review

- Cantaloupe AND Health
- *Cucumis melo* L. AND Health
- Melon AND Health
- Cantaloupe AND Bioactive compounds
- *Cucumis melo* L. AND Bioactive compounds
- Melon AND Bioactive compounds
- Cantaloupe AND Biological activity
- *Cucumis melo* L. AND Biological activity
- Melon AND Biological activity

compounds; and (3) evaluated the beneficial health effects of *Cucumis melo* L.

Charting the data

The data presented according to author(s), year of publication, country, bioactive compounds, amount, and health benefits.

Collating, summarizing and reporting the results

The findings of the review on the bioactive compounds in *Cucumis melo* L. and its beneficial health effects were presented accordingly.

RESULTS

Study characteristics

As per Table 2, 11 studies investigated the *Cucumis melo* L. seeds, three studies examined the *Cucumis melo* L. peels, one study explored the *Cucumis melo* L. flesh, while three studies evaluated the *Cucumis melo* L. peel, seeds and flesh collectively. Five studies were conducted in India (Arora *et al.,* 2011; Gill *et al.,* 2011; Mehra *et al.,* 2015; Parmar & Kar, 2009; Sood *et al.,* 2011), three in Tunisia (Mallek-Ayadi *et al.*, 2016; Mallek-Ayadi *et al.,* 2017; Mallek-Ayadi *et al*., 2018) and two in Malaysia (Ismail *et al.,* 2010; Norrizah *et al.,* 2012), China (Azhari *et al.,* 2014; Siddeeg & Alsir, 2014) and Egypt (Al-Sayed & Ahmed, 2013; Ibrahim & El-Masry, 2016) respectively. Only one study was undertaken in the United States of America (USA) (Laur & Tian, 2011), South Korea (Chen & Kang, 2013), Bulgaria (Petkova & Antova, 2015), and Iran (Rasouli *et al.,* 2017) respectively.

Bioactive compounds in *Cucumis melo* L. peel

Mallek-Ayadi *et al.* (2016) reported that 18 individual phenolic compounds were identified in *Cucumis melo L.* (*maazoun* cultivar) peel extract using high-performance liquid chromatography (HPLC). Among them, nine classes of the phenolic compounds were recognized, namely hydroxy-benzoic acids, phenylethanoid, phenolic alcohol, hydroxycinnamic acids, flavones, flavanone glycosides, secoiridoids, benzeneacetic acid, and lignan. 3-hydroxybenzoic acid constituted the major phenolic compounds with 33.45±0.37 mg/100g, followed by apigenin-7-glycoside (29.34±0.17 mg/100g), isovanillic acid (23.70±0.04 mg/100g), m-coumaric acid (19.91±0.37 mg/100g), oleuropein (18.88±0.29 mg/100g), and luteolin-7-glycoside (16.51±0.15 mg/100g). Besides, notable amounts of flavone (13.51±0.32 mg/100g), gallic acid (12.07±0.12 mg/100g), naringenin (11.58±0.11 mg/100g), and tyrosol (11.35±0.03 mg/100g) were also present in the melon peel extract.

Next, HPLC analysis on *Cucumis melo* L. var. *cantalupensis* peel extract revealed the four phenolic compounds of 4-hydroxybenzoic acid (326.2 µg/g dry weight), vanillin (197.4 µg/g dry weight), coumaric acid (81.1 µg/g dry weight), and chlorogenic acid (65.9 µg/g dry weight) (Ibrahim & El-Masry, 2016). Another study investigated the phenolic compounds present in sharlyn melon peel powders, whereby four phenolic compounds were detected: 4-hydroxybenzoic acid (958.3 µg/g dry weight), vanillin (851.8 µg/g dry weight), coumaric acid (8.8 lg/g dry weight), and chlorogenic acid (66.2 µg/g dry weight) (Al-Sayed & Ahmed, 2013).

Bioactive compounds in *Cucumis melo* L. seed

A total of 15 phenolic compounds were identified in *Cucumis melo* L. (*maazoun* cultivar) seed extract in which phenolic acids, flavonoids, phenolic monoterpene, secoiridoid and stilbenoid were among the phenolic classes detected. The highest concentration of phenolic compounds was found in naringenin-7-O-glycoside (4.30±0.00 mg/100g), followed by gallic acid (4.24±0.03 mg/100g), vanillic acid (3.87±0.02 mg/100g), and 4-hydroxybenzoic acid (3.28±0.03 mg/100g) (Mallek-Ayadi *et al.*, 2018). Meanwhile, the chemical analysis of tocopherol composition for three varieties of melon (i.e. honeydew, dessert 5, and hybrid 1) seed oils revealed the presence of α-tocopherol, β-tocopherol, γ-tocotrienol, and γ-tocopherol. Among these three melon varieties, γ-tocopherol showed the highest concentration that ranged from 71.4±0.3% to 91.5±0.5% (Petkova & Antova, 2015).

Besides, Azhari *et al*. (2014) found that the *Cucumis melo* L. var. *tibish* seed oil contained the highest concentration of δ- tocopherol (27.40±0.53 mg/100g oil), followed by γ-tocopherol (13.10±0.41 mg/100g oil), and α-tocopherol (2.70±0.17 mg/100g oil). However, β-tocopherol was not identified in this study. Next, Mallek-Ayadi *et al*. (2017) examined the phenolic compounds found in *Cucumis melo* L. (*maazoun* cultivar) seed oil and identified 11 phenolic compounds. The highest content was found in amentoflavone (32.80±0.21 µg/g fresh weight), which was followed by luteolin-7-O glycoside (9.60±0.01 µg/g fresh weight), naringenin (4.72±0.01 µg/g fresh weight), and gallic acid (7.26±0.02 µg/g fresh weight). The tocopherol composition in the seed oils was dominated by β+γ-tocopherols (18.13±0.41 mg/100 g), followed by δ-tocopherol (6.09±0.53 mg/100 g) and α-tocopherol (2.85±0.17 mg/100g).

Table 2. Bioactive compounds and beneficial health effects

Author, year	Country	Fruit part	Bioactive compounds	Amount	Health benefits
(Mallek-Ayadi *et al.*, 2018)	Tunisia	*Cucumis melo* L. (*maazoun* cultivar) seeds	Naringenin-7-O-glycoside Gallic acid Vanillic acid 4-hydroxybenzoic acid	4.30±0.00 mg/100g extract 4.24±0.03 mg/100g extract 3.87±0.02 mg/100g extract 3.28±0.03 mg/100g extract	ND
(Mallek-Ayadi *et al.*, 2017)	Tunisia	*Cucumis melo* L. (*maazoun* cultivar) seed oil	Amentoflavone Gallic acid Protocatechuic acid Caffeic acid Rosmarinic acids Luteolin-7-O glycoside α-tocopherol β+γ-tocopherols δ-tocopherol	32.80±0.21 µg/g fw7.26±0.02 µg/g fw0.89±0.01 µg/g fw3.13±0.00 µg/g fw2.91±0.04 µg/g fw9.60±0.01 µg/g fw2.85±0.17 mg/100g oil 18.13±0.41 mg/100g oil 6.09±0.53 mg/100g oil	ND
(Rasouli *et al.*, 2017)	Iran	*Cucumis melo* L. seed	ND	ND	Anti-angiogenic effect of purified trypsin inhibitor on three dimensional cultures of human umbilical vein endothelial cells
(Mallek-Ayadi *et al.*, 2016)	Tunisia	*Cucumis melo* L. (*maazoun* cultivar) peels	3-Hydroxybenzoic acid Apigenin-7-glycoside Isovanillic acid m-coumaric acid Oleuropein Luteolin-7-glycoside Gallic acid Tyrosol Naringenin Flavone	33.5±0.37 mg/100g extract 29.3±0.17 mg/100g extract 23.7±0.04 mg/100g extract 19.9±0.37 mg/100g extract 18.9±0.29 mg/100g extract 16.5±0.15 mg/100g extract 12.1±0.12 mg/100g extract 11.4±0.03 mg/100g extract 11.6±0.11 mg/100g extract 13.5±0.32 mg/100g extract	ND
(Ibrahim & El-Mesry, 2016)	Egypt	*Cucumis melo* L. var. *cantalupensis*			Antioxidant activity (DPPH)
		Skin	4-hydroxybenzoic acid Vanillin Chlorgenic acid Coumaric acid	326.2 µg/g dw 197.4 µg/g dw 65.9 µg/g dw 81.1 µg/g dw	91.73±0.35%
		Seed	ND	ND	48.55±0.84%
		Flesh	ND	ND	66.36±0.95%

Table 2 continued...

(Mehra *et al*., 2015)	India	Musk melon (*Cucumis melo* L.) seeds	ND	ND	Antioxidant activity (FRAP: 5.63 µg BHTE/mg)
(Petkova & Antova, 2015)	Bulgaria	*Cucumis melo* L. seed oil			
		Honeydew	α-tocopherol β-tocopherol γ- tocopherol γ-tocotrienol	2.9±0.1% 1.7±0.1% 91.5±0.5% 3.9±0.1%	ND
		Dessert 5	α-tocopherol β-tocopherol γ- tocopherol γ-tocotrienol	19.7±0.3% ND 71.4±0.3% 8.9±0.5%	ND
		Hybrid 1	α-tocopherol β-tocopherol γ- tocopherol γ-tocotrienol	6.2±0.2% ND 78.5±0.5% 15.3±0.3%	ND
(Azhari *et al*., 2014)	China	*Cucumis melo* L. var. *tibish* seed	δ- tocopherol γ-tocopherol α-tocopherol	27.40±0.53 mg/100g oil 13.10±0.41 mg/100g oil 2.70±0.17 mg/100g oil	Antioxidant activity ABTS: 23.30 mg/mL DPPH: 25.25 mg/mL
(Siddeeg & Alsir, 2014)	China	*C. melo* L. var. *tibish* seeds	Hexenal	ND	Antibacterial activity against Gram-positive bacteria and Gram-negative bacteria
(Al-Sayed & Ahmed, 2013)	Egypt	Sharlyn melon (*Cucumis melo* L.) peels	4-hydroxybenzoic acid vanillin coumaric acid chlorogenic acid	325.3 µg/g dw 199.2 µg/g dw 80.8 µg/g dw 66.2 µg/g dw	ND
(Chen & Kang, 2013)	South Korea	*C. melo* L. var. *makuwa Makino* seed	Unsaturated fatty acid: palmitic acid, oleic acid and linoleic acid	ND	Antidiabetic activity by inhibiting α-glucosidase by 35.3% and α-amylase by 61.8%

Table 2 continued...

(Norrizah *et al.*, 2012)	Malaysia	*Cucumis melo* L. cultivars			Antioxidant activity (DPPH: SC_{50})
		Glamour flesh Champion flesh Honeymoon flesh	β-carotene	$5.2x10^{-5}$% $3.4x10^{-4}$% $9.5x10^{-4}$%	ND
		Glamour skin Champion skin Honeymoon skin	ND	ND	320 µg/ml 390 µg/ml 500 µg/ml
		Glamour seed Champion seed Honeymoon seed	ND	ND	250 µg/ml 270 µg/ml 450 µg/ml
(Arora *et al.*, 2011)	India	*Cucumis. melo* L. var. *agrestis* seeds	ND	ND	Anti-inflammatory activity in which the paw edema was reduced by 61.6% at 300 mg/kg Analgesic activity was 70.6% using acetic acid induced writhing method Antioxidant activity DPPH: 24.01±7.1% to 75.59±6.7% Hydrogen peroxide: 45.23±5.4% to 69.86±4.0%
(Gill *et al.*, 2011)	India	*Cucumis melo* L. var. *agrestis* seed	ND	ND	Anti-inflammatory activity in which the paw edema was reduced by 56.5% at 300 mg/kg Antioxidant activity DPPH: 52.8±0.28% to 74.9±0.76% Hydrogen peroxide: 35.2±0.02% to 58.9±0.01%

Table 2 continued...

(Laur & Tian, 2011)	USA	Cantaloupe			
		Oro Rico (CA, USA) Durango (CA, USA) Caribbean Gold (Honduras) Cantaloupe unknown variety (Guatemala)	β-carotene	3138±228.1 µg/100g fw 2448±291.8 µg/100g fw 3633±322.7 µg/100g fw 3861±559.7 µg/100g fw	ND
		Honeydew			
		Emerald (CA, USA) Vanessa (CA, USA) Saturno(CA, USA) Santa Fe (CA, USA) Summer Dew (Honduras) Honeydew unknown variety (Mexico)		124.1±49.7 µg/100g fw 63.1±11.0 µg/100g fw 118.7±31.9 µg/100g fw 109.1±8.3 µg/100g fw 99.0±27.6 µg/100g fw 172.9±50.6 µg/100g fw	ND
(Sood *et al.*, 2011)	India	*Cucumis melo* L. var. *agrestis* seeds	Triterpenoids, sterols	ND	Antiulcer activity through three models: pyloric ligation, water immersion stress, and indomethacin induced ulcer models. Antioxidant activity (DPPH: 52.8±0.28% to 74.9±0.76%)
(Ismail *et al.*, 2010)	Malaysia	*Cucumis melo* L. Flesh Seed Skin	ND	ND	Antioxidant activity DPPH RSA (mg/ml) / Hydroxyl RSA (g DMSOE/g extract) 11.9±1.00 / 67.19±8.90 25.44±2.83 / 37.37±2.42 9.58±0.37 / 39.11±2.91
(Parmar & Kar, 2009)	India	*Cucumis melo* L. peel	ND	ND	Protect against hypothyroidism

Bioactive compounds in *Cucumis melo* L. flesh

β-carotene and vitamin C content in cantaloupe and honeydew melons were examined in a study conducted by (Laur & Tian, 2011). It was observed that the cantaloupe melons possessed higher β-carotene and vitamin C content compared to honeydew melons. Next, three rock melon cultivars viz Honeymoon, Champion and Glamour were explored in terms of their β-carotene content. The highest content was found in Honeymoon with 9.5×10-4%, followed by Glamour (5.2×10-5%) and Champion (3.4×10-4%) (Norrizah *et al.,* 2012).

Antioxidant activity

Five studies examined the anti-oxidant activity of *Cucumis melo* L., which was evaluated using various assays like 2,2-diphenyl-1-picrylhydrazylradical radical scavenging activity (DPPH RSA); hydroxyl radical scavenging activity (HRSA); ferric reducing antioxidant power (FRAP); hydrogen peroxide RSA; and 2,2'-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid) radical scavenging activity (ABTS RSA). First, Ibrahim and El-Masry (2016) reported that the DPPH RSA of *Cucumis melo* L. var. *cantalupensis* extract was 91.73±0.35%, 66.36± 0.95% and 48.55±0.84% for skin, flesh and seed, respectively. Next, the DPPH assay conducted on the three varieties of seed and skin of rock melon cultivars (i.e. Glamour, Champion and Honeymoon) demonstrated SC50 that ranged from 250 to 500 μg/mL, whereby Glamour seed exhibited the greatest RSA at the lowest concentration (Norrizah *et al.,* 2012). Besides, another study evaluated the DPPH RSA and HRSA of methanolic extract of the flesh, seed and skin of *Cucumis melo* L. The IC50 of DPPH RSA ranged from 9.58±0.37 mg/mL to 25.44±2.83 mg/mL, while the HRSA ranged from 37.37±2.42 dimethyl sulfoxide equivalents (DMSOE)/g extract to 67.19±8.90 g DMSOE/g extract (Ismail *et al.,* 2010).

In addition, the FRAP of *Cucumis melo* L. seeds was 5.63 μg butylated hydroxytoluene (BHTE)/mg sample as reported by Mehra *et al*. (2015). The anti-oxidant activity of Seinat (*Cucumis melo* L. var. *tibish*) seed oil was also examined using ABTS assay and DPPH assay, with IC_{50} of 23.30 mg/mL and 25.25 mg/mL in comparison with BHT (10.52 mg/mL and 14.05 mg/mL), respectively (Azhari *et al.,* 2014). Moreover, three studies examined the *Cucumis melo* L. var *agrestis* seed extract, whereby both studies conducted by Gill *et al*. (2011) and Sood *et al*. (2011) exposed the *Cucumis melo* L. var *agrestis* seed extract to DPPH and its RSA. They ranged from 52.8±0.28% to 74.9±0.76% with the extract concentration of 100 μg/mL to 300 μg/mL. Besides, another DPPH assay performed on the same seed extract as previous study revealed the RSA of 24.01±7.1% to 75.59±6.7%, with extract concentration ranging from 50 μg/mL to 300 μg/mL. Meanwhile, 200 μg/mL to 400 μg/mL of extract showed 45.23±5.4% to 69.86±4.0% of hydrogen peroxide RSA (Arora *et al.,* 2011). Last but not least, the hydrogen peroxide RSA of seed extract concentration ranging from 25 μg/mL to 200 μg/mL was 35.2±0.02% to 58.9±0.01% (Gill *et al.,* 2011).

Anti-inflammatory and analgesic activity

Gill *et al*. (2011) tested the anti-inflammatory activity of *Cucumis melo* L. var *agrestis* seed extract using carrageenan-induced paw edema in rats. Its analgesic activity was also examined using tail immersion and tail flick methods in mice. Significant reduction in paw edema of 43.4% and 56.6% was observed at the dose of 200 mg/kg and 300 mg/kg of seed extract, respectively, whereby higher dose resulted in significant pain alleviation. Next, another study conducted by Arora *et al*. (2011) evaluated the analgesic activity of the seed extract (same as previous study) using acetic-acid induced jerking response in albino mice and tail immersion method in albino rats accordingly. The anti-inflammatory activity was also investigated using the same method as the previous study, which yielded results reporting that the rat paw edema was inhibited by 61.6% at the dose of 300 mg/kg of seed extract. Besides, at the dose of 300 mg/kg, the analgesic activity was at 70.6% using acetic acid-induced writhing method, and significant increment of pain threshold was observed after 60 min when using the tail immersion method.

Anti-bacterial activity and anti-ulcer activity

An *in vitro* study was conducted in China to explore the anti-bacterial activity of essential oil extracted from Seinat (*Cucumis melo* L. var. *tibish*) seeds against three strains of Gram-positive bacteria (i.e. *Streptococcus pyogenes, Staphylococcus aureus* and *Bacillus subtilis*) and three strains of Gram-negative bacteria (*Salmonella typhimurium, Shigella dysenterae* and *Escherichia coli*). The outcomes of this study consequently concluded that the extracted essential oil exhibited anti-bacterial activity against all bacteria, especially Gram-positive bacteria, with a minimum inhibitory concentration that varied from 0.5 to 5 mg/mL of sample (Siddeeg & Alsir, 2014). Similarly, the anti-ulcer activity of methanolic extract of *Cucumis melo* L. seeds was tested against gastric ulcerations using pyloric ligation, water immersion stress and non-steroidal anti-inflammatory drugs (NSAIDs) (i.e. indomethacin)-induced ulcer models. The findings concluded that the seed extract suppressed the ulcers in pyloric ligation, water immersion stress, and NSAIDs-induced ulcer models by 57.6%, 67.6%

and 61.9%, respectively, upon administration at the dose of 300 mg/kg (Sood *et al.,* 2011).

Anti-hypothyroidism, anti-angiogenic and anti-diabetic activity

An *in vivo* study conducted on both healthy normal and propylthiouracil-induced hypothyroid Wistar albino male rat demonstrated significant increments in thyroid hormone (i.e. T3 and T4) levels following the administration of 100 mg/kg *Cucumis melo* L. peel extracts. This implied that the peel extracts possessed thyroid stimulatory properties (Parmar & Kar, 2009). Meanwhile, an *in-vitro* study was undertaken to examine the anti-angiogenic effect of trypsin inhibitor purified from *Cucumis melo* L. seeds on the three-dimensional culture of human umbilical vein endothelial cells. The finding revealed that the trypsin inhibitor can suppress the angiogenesis (Rasouli *et al.,* 2017). Chen and Kang (2013) investigated the role of oriental melon (*Cucumis melo* L. var. *makuwa Makino*) seed on α-glucoside and α-amylase suppression. The results found that hexane extract inhibited the α-glucoside and α-amylase by 35.5% and 61.8%, respectively.

DISCUSSION

Different fruit parts contain different bioactive compounds and have varying concentrations. The qualitative and quantitative profile of the bioactive compounds in different fruit parts will inevitably affect their functional properties (Silva *et al.,* 2018; Torres-León *et al.,* 2016). From the findings, the bioactive compounds found in *Cucumis melo* L. peel consisted of 3-hydroxybenzoic acid, apigenin-7-glycoside, isovanillic acid, vanillin, m-coumaric acid, chlorogenic acid, oleuropein, luteolin-7-glycoside, chlorogenic acid, flavone, gallic acid, naringenin and tyrosol. Meanwhile, the bioactive compounds present in *Cucumis melo* L. seed included naringenin-7-O-glycoside, gallic acid, vanillic acid, 4-hydroxybenzoic acid, amentoflavone, luteolin-7-O glycoside, α-tocopherol, β-tocopherol, γ-tocopherol, δ-tocopherol and γ-tocotrienol. For *Cucumis melo* L. flesh, β-carotene and vitamin C were observed. In terms of the abundance of phenolic compounds, 3-hydroxybenzoic acid was the most abundant phenolic compounds present in *Cucumis melo* L. peels, while narigenin-7-O-glycoside was the predominant phenolic compounds in *Cucumis melo* L. seeds and amentoflavone was the major phenolic compounds in *Cucumis melo* L. seed oils.

A study reported that 3-hydroxybenzoic acid possesses anti-mutagenic, anti-microbial and anti-fungal properties. Isovanillic acid also manifests anti-oxidant and anti-bacterial effects (Khadem & Marles, 2010). Besides, chlorogenic and coumaric acids also play an important role in preventing cancer and cardiovascular disease (Bendini *et al.,* 2007). Similarly, gallic acid and tyrosol exhibit anti-inflammatory and anti-cancer properties (Soong & Barlow, 2006), as well as free radical scavenging and antibacterial activities against the intestinal flora (Ismail *et al.,* 2012). Another study reported that gallic acid possesses anti-cancer, anti-mutagenic and anti-inflammatory properties (Jabri-Karoui *et al.,* 2012), while apigenin-7-glycoside, naringenin-7-O-glycoside, and luteolin-7-glycoside display anti-inflammatory, anti-oxidant, anti-tumor and free radical scavenging activities (Bhujbal *et al.,* 2010; Kim *et al.,* 2006). Oleuropein is yet another phenolic compound that exhibits a potent anti-oxidant activity (Rodríguez-Morató *et al.,* 2015). Lastly, amentoflavone as the main flavone identified in *Cucumis melo* L. seed oil demonstrates anti-oxidant capacity (Mallek-Ayadi *et al.,* 2017).

Furthermore, seed oils are good sources of vitamin E (i.e. tocopherols and tocotrienols) (Silva *et al.,* 2018). These compounds possess antioxidant properties and are consequently vital in controlling the quality of vegetables oils via preventing poly-unsaturated fatty acids (PUFA) oxidation (Atanasov *et al.,* 2018; Huang *et al.,* 2002; Mallek-Ayadi *et al.,* 2017). Vitamin E could also protect the biological system from reactive oxygen species and prevent chronic diseases, such as cardiovascular diseases, Alzheimer disease, and cancer (Castelo-Branco & Torres, 2009; Nyam *et al.,* 2009). Evidence suggested that γ and α-homologues are the major forms of tocopherols and tocotrienol present in the fruit seed oils (Górnaœ *et al.,* 2015), while α-tocopherol was revealed in a study to exert beneficial effects on human nutrition due to its higher biological activity compared to other tocopherols (Saloua *et al.,* 2009). Meanwhile, γ-tocopherol is considered as the best antioxidant (Dias *et al.,* 2013; O'Brien, 2009), which is due to its lipid oxidation suppressing abilities in food via stabilizing hydroperoxy and other free radicals that could influence the oil flavor quality (Mallek-Ayadi *et al.,* 2017). By looking at *Cucumis melo* L. flesh, a study reported that orange-fleshed fruits contain the highest amount of γ-carotene and exhibit high antioxidant activities (Truong *et al.,* 2007).

Various evidence stated that the antioxidant activity of the fruit extract is highly attributable to the concentration of phenolic compounds found in the fruit itself (Ismail *et al.,* 2010; Norrizah *et al.,* 2012; Rolim *et al.,* 2018). The findings of DPPH assay proposed that the phenolic compounds present in the fruit extract could scavenge the free radicals via electron- or hydrogen-donating mechanisms. Subsequently, it could prevent the initiation of detrimental free radical-mediated chain reactions (Ibrahim & El-Masry, 2016). Since free radicals could induce pain stimulation, anti-oxidants play a crucial role in reducing the pain and contributing to its analgesic effect (Gill *et al.,* 2011). Thus, *Cucumis melo* L. exhibited its analgesic effect by inhibiting free radical generation, whereby such free radicals could also lead to inflammation. This occurred via increased gene activity in the production of pro-inflammatory cytokines, such as interleukin-6, tumor necrosis factor, and interferons (Fischer & Maier, 2015). Similarly, anti-inflammatory properties of *Cucumis melo* L. was also observed in Carrageenan-induced rat edema. Carrageenan stimulated the accumulation of leukocytes in the pleural space and increased the leukotriene B4 (LKB4) level in the pleural exudate after inflammatory stimulation. The migration of neutrophils to the affected area would release the toxic oxygen free radicals into extracellular space, which contributed to the pro-inflammatory condition. Additionally, *Cucumis melo* L. could suppress the leukocyte influx and increase the LTB4 levels (Gill *et al.,* 2011).

A study had suggested that the presence of hexenal in the essential oil of Seinat (*Cucumis melo* L. var. *tibish*) seeds was attributed as the active compound responsible for anti-bacterial activity (Kubo *et al.,* 2004). Interestingly, Gram-positive bacteria are more vulnerable compared to Gram-negative bacteria due to their lower resistance (Siddeeg & Alsir, 2014). Moreover, *Cucumis melo* L. peel extract induced T4 production at the glandular level and peripheral mono deiodination of T4 (main source of T3 synthesis), which exerted its anti-hypothyroidism activity (Peeters & Visser, 2017). Besides, the anti-angiogenic activity of *Cucumis melo* L. could be due to the suppression of several important steps in tumor growth, which was capable of interrupting angiogenesis and tumor progression (Rasouli *et al.,* 2017).

Furthermore, the anti-diabetic effect of *Cucumis melo* L. was exhibited through the suppression of α-glucosidase and α-amylase. The inhibition of these two enzymes could delay the oligosaccharide liberation from starch, which resulted in slower glucose absorption in the small intestine for achieving better postprandial blood glucose control (Apostolidis *et al.,* 2011). Multiple evidence also suggested that unsaturated fatty acids such as palmitic acid, oleic acid and linoleic acid play a role in inhibiting the α-glucosidase and α-amylase (Chen & Kang, 2013; Paul *et al.,* 2010). Last but not least, the anti-ulcer activity of *Cucumis melo* L. may be attributed to the presence of triterpenoids and sterols, which resulted in the reduction of vascular permeability, free radical synthesis, lipid peroxidation, and the strengthening of mucosal barriers (Sood *et al.,* 2011).

This scoping review discerned some shortcomings, namely all prior studies have been conducted to assess the biological activities of melon by-products that took place *in vitro* and *in vivo*. Thus, more human studies should be conducted to further confirm their therapeutic effects in relation to several diseases. Besides, only English and full text were included, while the literature search was also limited to three electronic databases. Therefore, a more thorough search should be conducted to obtain more related articles. Finally, the safety issues of the bioactive compounds were not investigated and further study should be undertaken to explore the safety issues.

CONCLUSION

Cucumis melo L., particularly its by-products (seeds and peels), exhibited various health benefits. Thus, there is a potential of incorporating these by-products into various food and nutraceutical applications to create novel functional food or dietary supplements. The bioavailability of the bioactive compounds and the sensory aspects of the new food products should be investigated when developing the products to ensure efficacy and sustainability. This can enhance human health and well-being by improving their quality of life. Concurrently, the food waste that emerged as a major issue could be overcome through utilizing *Cucumis melo* L. by-products.

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