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Phytochemistry, Nutritional Composition, Health Benefits, Applications and Future Prospects of *Momordica Charantia* L.: A Comprehensive Review

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Abstract

Momordica charantia L., commonly known as bitter melon (BM) or bitter gourd, has great nutritional value and versatile properties. BM is consumed directly as a traditional vegetable or used for pickling, and has also been made into uniquely flavored canned products, tea, compound beverages, and wine. Various extracts, juices and isolated compounds show a wide range of health effects and biological activities, such as antioxidant, anti-inflammatory, antitumor, antidiabetic, anti-obesity, antifungal, neuroprotective, and blood cholesterol-reducing effects. In this review, we not only review the phytochemical properties of BM but also highlight the potential of Chia seeds for food applications and the use of all parts as a source of ingredients for medicines and cosmetics that promote health and well-being. This will provide theoretical support for the integrated use of such natural products.

Keywords: *Momordica charantia* L., nutritional value, comprehensive application, bioactivity, safety

1. Introduction

The genus *Momordica* is an herbaceous vine in family Cucurbitaceae. The major species, *Momordica charantia* L., commonly recognized as bitter melon (BM) or bitter gourd, and is additionally referred to as cundeamor in South America or karela in India (Çiçek S S, 2022). BM is cultivated throughout the world, including the tropical regions of Asia, the Amazon River Basin, East Africa and the Caribbean, where it is used both as a vegetable and in traditional folk medicine practices (Dandawate P R et al., 2016).

BM is similar in appearance to a cucumber, usually oblong and still green when eaten, with a relatively thin layer of pulp around its large, flesh-filled and flattened seeds (Saeed F et al., 2011; Vijayalakshmi B, Kumar G S & Salimath P V, 2009). All parts of BM, including the fruit, have a bitter taste, and in cooking BM fruit is often sautéed with a variety of vegetables, stuffed, or added in small quantities to soups or legumes to introduce subtle bitterness and texture. Various components of BM (such as fruits, flowers and shoots) are used as flavor enhancers in a range of traditional Asian cuisines, with shoots and leaves cooked and eaten as vegetables and fruit extracts used in tea production (Dandawate P R et al., 2016).

BM has a long history of medicinal use and has been recommended in Ayurveda (traditional Indian medicine) for centuries as a beneficial dietary supplement for the treatment and amelioration of diabetes and its associated complications (Nerurkar P & Ray R B, 2010). In recent decades, significant efforts have been dedicated to the pharmacological study of BM. Various extracts and isolated compounds, including triterpenoids, glycosides,

triterpenoid saponins, phenols, flavonoids, and certain protein fractions (Li Z et al., 2020), have exhibited a wide spectrum of biological activities, such as antioxidant (Chen F & Huang G, 2019; Wang F et al., 2023), anti-inflammatory (Wang F et al., 2023), antitumor (Fang E F et al., 2019), antidiabetic (Oyelere S F et al., 2022; Chang C I et al., 2021), anti-obesity (Cortez-Navarrete M et al., 2021), antifungal (Wang S et al., 2016), neuroprotective (Zhan K, Ji X & Luo L, 2023) and blood cholesterol-reducing (Naz R et al., 2016) effects. In recent years, many reviews have been published on the nutritional value, phytochemistry, and pharmacology of BM (Zheng J et al., 2023; Sun L et al., 2021). However, there are few reviews on the potential uses of all BM fruit fractions (peel, pulp, and seeds) and the phytochemical properties and associated biological activities of these fractions.

In this review, we systematically summarize the phytochemistry, nutrient composition, health effects, applications and future perspectives regarding BM. This will provide theoretical support for the comprehensive utilization of such natural products.

2. Nutritional Value and Chemical Composition of BM

A wide range of nutrients including vitamins, fatty acids, minerals, proteins, phenolic compounds and flavonoids are present in *Momordica* plants, and the nutritional value and chemical composition of BM are shown in Tables 1 and 2.

2.1 Minerals

The species of *Momordica* are important vegetable crops in the Cucurbitaceae family, rich in minerals in their pulp, peel, and seeds (Kandangath Raghavan A, Garlapati Phani K & Nallamuthu I, 2015). Mineral contents in various parts of the fruit show higher levels of K and Ca in the whole fruit, followed by Mg and P in the endocarp, and Na in the epicarp, whereas the seeds contained the lowest amounts of these macro-minerals. Conversely, BM seeds were identified as a significant source of micro-minerals such as Fe, Zn, Cu, and Mn (Singla D et al., 2023). Minerals are vital to the body's metabolism and their importance is often underestimated because people only need trace amounts. Therefore, it is beneficial to include BM in a healthy diet because it contains essential minerals that support overall health.

2.2 Vitamins

BM fruits are also an excellent source of vitamin E (tocopherols) and vitamin A (Tuan P A et al., 2011; Saini R K & Keum Y S, 2017). According to the USDA Food Composition Database, BM has a high proportion of vitamin A (426 IU). BM is a potential neuroprotectant including vitamin E as probable active components for the prevention for PAHs-induced neurotoxicity (Pattarachotanant N, Prasansuklab A & Tencomnao T, 2021). Vitamin C content (5.2 mg/g) in the BM extract is close to that in strawberry (5.9 mg/g) (Nguyen T-V-L et al., 2020).

2.3 Polysaccharides

The polysaccharides predominantly found in BM consist of rhamnose, xylose, galactose, and arabinose. They are important pharmacological active ingredients, water-soluble, with an average molecular weight of 4-900 kDa (Zhan K, Ji X & Luo L, 2023; Yang X, Chen F & Huang G, 2020). The antioxidant activity of BM polysaccharides, extracted via aqueous methods and precipitated with ethanol, is markedly increased *in vitro* following carboxymethylation and acetylation modifications. Notably, the carboxymethylated derivatives demonstrate superior antioxidant activity, potentially due to the incorporation of carboxyl groups. This modification results in the formation of a negatively charged, hydrophilic surface structure in the bitter melon polysaccharides, which enhances their water solubility and consequently augments their antioxidant efficacy (Chen F & Huang G, 2019). Therefore, BM polysaccharides have the potential to act as antioxidants.

2.4 Fatty Acids and Amino Acids

α-Eleostearic acid, belonging to the conjugated linolenic acid (CLNA) family, is primarily found in seeds and to a lesser extent in flesh. In the oils extracted from seeds of 10 different BM varieties, α-Eleostearic acid (α-ESA; *cis*-9, *trans*-11, *trans*-13- isomer of CLNA) accounted for 30-60% of the total fatty acids (Bialek A et al., 2016; Chen G-C et al., 2016). Elevated fatty acid concentrations are essential to increase the utilization of BM as a functional food ingredient, providing new perspectives and opportunities for the treatment of obesity.

The amino acid composition of BM varies in different tissues and at different stages of growth. To date, 17 amino acids have been identified in BM, and the contents of Asn, Asp, Thr, Ser, Gln, Glu, Gle, Pro, Gly, Ala, Leu, Tyr, Phe, Met, His, Lys, and Arg vary in different tissues and stages of maturation. The Tyr content in ripe pericarp measures 59.4 mg/g, contrasting with 56.5 mg/g in immature pericarp, and a notably lower 41.1 mg/g in ripe seeds (Horax R et al., 2010). Crucially, essential amino acids comprise approximately 36.58% of the total amino acid content, adequately meeting human nutritional needs.

Table 1. Nutritional compositions of *Momordica*

Nutrients	Species	Part	Content (mg/100g)	Ref.
Minerals				
Ca	*Momordica charantia* Linn. (Goj karela)	Seed	38.35 DW	(Karaman K et al., 2018)
	Momordica charantia Linn. (Guti karela)		41.16 DW	
	Momordica charantia Linn. (Majhari karela)		44.01 DW	
	Momordica sp. (PAUBG-232)	Fruit	71.39 DW	(Singla D et al., 2023)
	Momordica sp. (PAUBG-407)	Peel	67.68 DW	
	Momordica sp. (Black King)		62.33 DW	(Mahwish M et al., 2018)
	Momordica sp. (Black King)	Fruit	70.33 DW	
	Momordica sp. (BG-20)	Seed	2.66 DW	
Cu	*Momordica charantia* Linn. (Goj karela)		0.35 DW	(Karaman K et al., 2018)
	Momordica charantia Linn. (Guti karela)		0.29 DW	
	Momordica charantia Linn.(Majhari karela)		0.33 DW	
	Momordica sp. (PAUBG-407)	Seed	525.45 DW	(Singla D et al., 2023)
	Momordica sp. (PAUBG-407)	Peel	452.41 DW	
	Momordica sp. (PAUBG-407)	Fruit	411.22 DW	
	Momordica sp. (PAUBG-119)	Peel	24.54 DW	
Fe	*Momordica charantia* Linn.(Goj karela)	Seed	4.11 DW	(Karaman K et al., 2018)
	Momordica charantia Linn.(Guti karela)		4.26 DW	
	Momordica charantia Linn. (Majhari karela)		4.50 DW	
	Momordica sp. (PAUBG-195)		6.14 DW	(Singla D et al., 2023)
	Momordica sp. (PAUBG-93)		5.49 DW	
	Momordica sp. (PAUBG-328)		5.48 DW	
	Momordica sp. (PAUBG-146)	Peel	0.72 DW	
	Momordica sp. (Black King)		3.27 DW	(Mahwish M et al., 2018)
	Momordica sp. (GHBG-1)	Fruit	4.03 DW	
	Momordica sp. (KHBG-1)	Seed	4.91 DW	
Zn	*Momordica charantia* Linn. (Goj karela)		1.24 DW	(Karaman K et al., 2018)
	Momordica charantia Linn. (Guti karela)		1.35 DW	
	Momordica charantia Linn. (Majhari karela)		1.29 DW	
	Momordica sp. (PAUBG-88)		2.64 DW	(Singla D et al., 2023)
	Momordica sp. (Black King)	Peel	0.94 DW	(Mahwish M et al., 2018)
		Fruit	0.97 DW	
		Seed	3.52 DW	
P	*Momordica charantia* Linn. (Goj karela)		14.24 DW	(Karaman K et al., 2018)
	Momordica charantia Linn. (Guti karela)		13.65 DW	
	Momordica charantia Linn. (Majhari karela)		13.47 DW	
	Momordica sp. (PAUBG-88)	Peel	98.24 DW	(Singla D et al., 2023)
	Momordica sp. (PAUBG-88)	Fruit	84.83 DW	
	Momordica sp. (PAUBG-407)	Peel	59.37 DW	
	Momordica sp. (PAUBG-146)	Seed	8.56 DW	
	Momordica spp (Black King)	Peel	125.00 DW	(Mahwish M et

	Momordica spp (Black King)	Fruit	128.67 DW	al., 2018)
	Momordica sp. (KHBG-1)	Seed	28.67 DW	
K	*Momordica* sp. (PAUBG-407)	Fruit	483.49 DW	(Singla D et al., 2023)
	Momordica sp. (PAUBG-130)	Fruit	416.14 DW	
	Momordica sp. (PAUBG-119)	Seed	7.24 DW	
	Momordica sp. (Black King)	Peel	326.33 DW	(Mahwish M et al., 2018)
		Fruit	397.00 DW	
		Seed	37.33 DW	
Mg	*Momordica* sp. (PAUBG-335)	Peel	101.70 DW	(Singla D et al., 2023)
	Momordica sp. (PAUBG-222)	Seed	1.04 DW	
	Momordica sp. (Black King)	Peel	56.33 DW	(Mahwish M et al., 2018)
		Fruit	64.66 DW	
		Seed	4.63 DW	
Na	*Momordica* sp. (PAUBG-232)	Peel	18.56 DW	(Singla D et al., 2023)
	Momordica sp. (PAUBG-351)	Peel	17.65 DW	
	Momordica sp. (PAUBG-351)	Seed	0.45 DW	
	Momordica sp. (FSD Long)	Fruit	91.00 DW	
	Momordica sp. (BG-20)	Seed	3.1 DW	
	Momordica sp. (KHBG-1)	Peel	83.33 DW	
Mn	*Momordica* sp. (PAUBG-407)	Seed	179.05 DW	
	Momordica sp. (PAUBG-119)		46.92 DW	
Vitamins				
Vitamin C	*Momordica charantia* L.	Pulp	11.57 FW	(Hercos G F D et al., 2021)
	Momordica charantia L.	Seed	10.42 FW	
	Momordica sp. (PG)	Pulp	11.73 FW	(Zhang Y et al., 2023)
	Momordica sp. (JLZ)		12.16 FW	
	Momordica sp. (BFM)		5.67 FW	
	Momordica sp. (RB)		12.58 FW	
	Momordica sp. (CB)		12.66 FW	
	Momordica sp. (LJ)		6.53 FW	
	Momordica sp. (LBS)		6.31 FW	
Vitamin E	*Momordica* sp.	Fruit	4.29 FW	(Saini R K, Keum Y S, 2017)
Organic acids				
Oxalic acid	*Momordica* sp. (PG)	Pulp	2061 FW	(Zhang Y et al., 2023)
	Momordica sp. (JLZ)		3419 FW	
	Momordica sp. (BFM)		2211 FW	
	Momordica sp. (RB)		2555 FW	
	Momordica sp. (CB)		3023 FW	
	Momordica sp. (LJ)		3658 FW	
	Momordica sp. (LBS)		1642 FW	
Succinic acid	*Momordica* sp. (PG)		441.9 FW	
	Momordica sp. (JLZ)		266.8 FW	
	Momordica sp. (BFM)		265.0 FW	

	Momordica sp. (RB)		303.0 FW	
	Momordica sp. (CB)		631.0 FW	
	Momordica sp. (LJ)		204.7 FW	
	Momordica sp. (LBS)		167.9 FW	
Malic acid	*Momordica* sp. (PG)		8535 FW	
	Momordica sp. (JLZ)		22,140 FW	
	Momordica sp. (BFM)		10,927 FW	
	Momordica sp. (RB)		8000 FW	
	Momordica sp. (CB)		21,218 FW	
	Momordica sp. (LJ)		13,432 FW	
	Momordica sp. (LBS)		5940 FW	
Citric acid	*Momordica* sp. (PG)		410.2 FW	
	Momordica sp. (JLZ)		1862 FW	
	Momordica sp. (BFM)		1072 FW	
	Momordica sp. (RB)		438.4 FW	
	Momordica sp. (CB)		1084 FW	
	Momordica sp. (LJ)		689.0 FW	
	Momordica sp. (LBS)		377.8 FW	
Other compositions				
Soluble protein	*Momordica* sp. (PG)	Pulp	0.05 FW	(Zhang Y et al., 2023)
	Momordica sp. (JLZ)		0.13 FW	
	Momordica sp. (BFM)		0.05 FW	
	Momordica sp. (RB)		0.06 FW	
	Momordica sp. (CB)		0.12 FW	
	Momordica sp. (LJ)		0.06 FW	
	Momordica sp. (LBS)		0.13 FW	
Cellulose	*Momordica* sp. (PG)		2.99 DW	
	Momordica sp. (JLZ)		2.85 DW	
	Momordica sp. (BFM)		3.99 DW	
	Momordica sp. (RB)		2.75 DW	
	Momordica sp. (CB)		3.72 DW	
	Momordica sp. (LJ)		3.18 DW	
	Momordica sp. (LBS)		2.87 DW	

2.5 Phenolic Compounds

Bitter melon is rich in bioactive compounds (especially phenolic compounds), which are widely used in both medicinal and culinary fields. Phenolic compounds in the *Momordica* plant have been reported to come mainly from the pericarp, pulp and seeds. The immature stage of BM showed higher polyphenol levels compared to the ripe stages, with the seeds containing a higher polyphenol content than the peel (Lee J J & Yoon K Y, 2021).

The distribution of phenolic compounds in various parts of ripe BM fruits (pulp, rind, and seeds) as well as in whole immature fruits was quantified using UPLC-MS/MS. The highest total content of phenolic compounds was observed in both pulp of mature and immature fruits, measuring 964.00±15.64 mg/g and 918.63±18.22 mg/g, respectively. The phenolic content of the peel and seeds of mature BM was 898.15±14.88 mg/g and 598.57±16.14 mg/g, respectively (Lopes A et al., 2020). Therefore, the pulp of BM ripe fruits is a promising source of phenolic compounds. It deserves to be further explored in future studies, especially in the development of nutraceutical products, functional ingredients, foods and pharmaceuticals.

2.6 Flavonoid Compounds

Flavonoids usually refer to a class of compounds with a C6-C3-C6 structure in which the two benzene rings (A and B rings) are linked together by a central three-carbon chain, and have a variety of pharmacological properties such as antitumor, anti-inflammatory, antioxidant, antiviral and cardioprotective effects (Zhang H et al., 2022). The flavonoid content of bitter melon roots is low, whereas the flavonoid content of leaves and flowers is high. For example, the content of rutin in roots was only 37.04 μg/g (DW), while the content of rutin in leaves was as high as 3970.83 μg/g (DW). Figure 1 shows the major phenylalanine and flavonoid biosynthetic pathways in BM (Cuong D M et al., 2018).

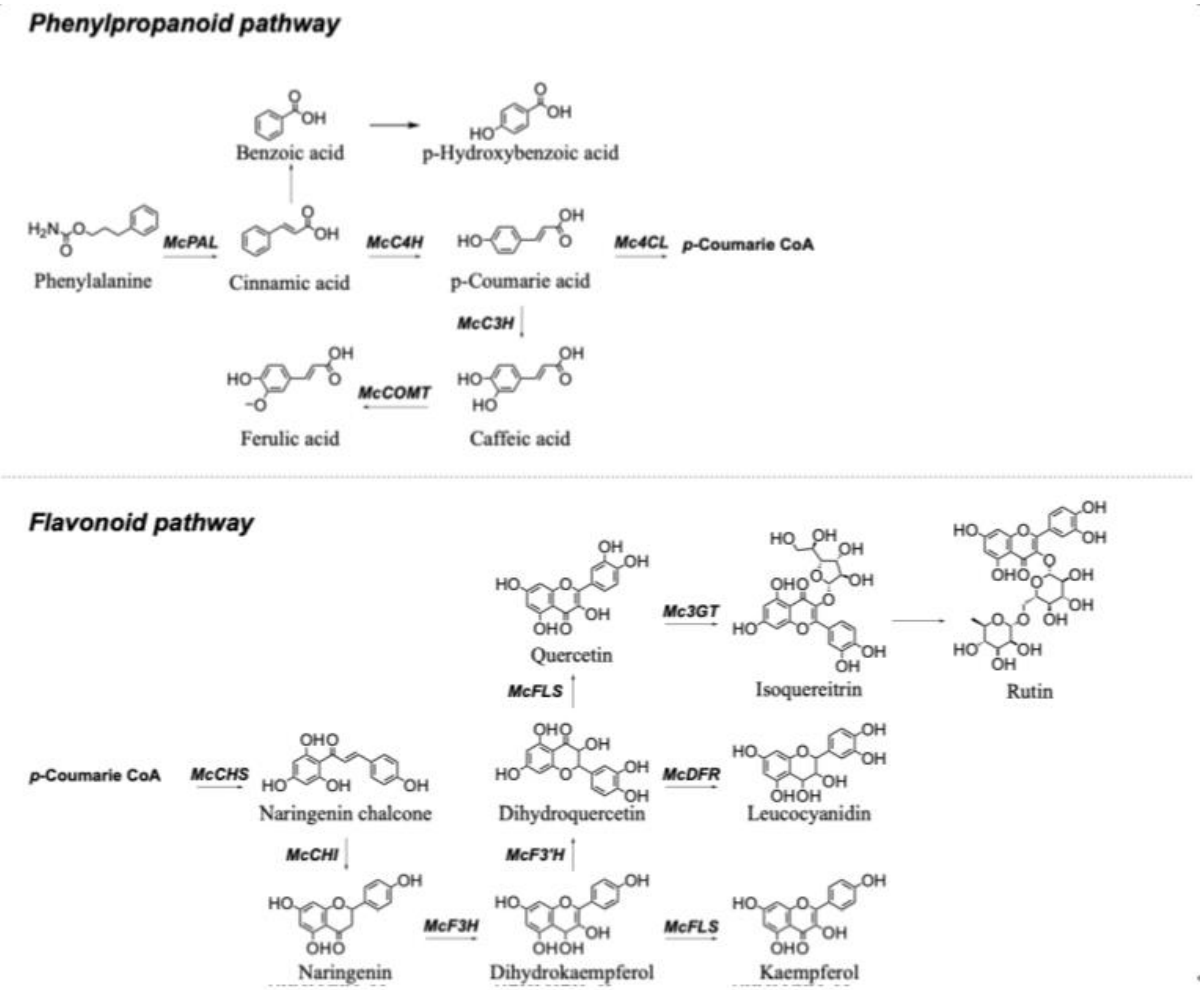

Figure 1. Structures of the main phenylpropanoid and flavonoids of *Momordica* plant, along with their corresponding biosynthetic pathway

Note: PAL: phenylalanine ammonia-lyase; C4H: cinnamate 4-hydroxylase; C3H: coumarate 3-hydroxylase; COMT: caffeic acid 3-*O*-methyltransferase; 4CL: 4-coumaroyl CoA ligase; CHS: chalcone synthase; CHI: chalcone isomerase; F3H: flavanone 3-hydroxylase; F3'H: flavonoid 3-hydroxylase; FLS: flavonol synthase; DFR: dihydroflavonol-4 reductase; 36T: flavonoid 3-*O*-glucosyltransferase.

2.7 Alkaloid Compounds

The total alkaloid content of BM seeds was significantly higher at 0.98% ± 0.02% compared to the whole fruit (0.65% ± 0.03%), pulp (0.53% ± 0.02%) and peel (0.52% ± 0.03%). Dietary intake of various parts of BM significantly reduced blood glucose concentrations, and among these parts, the seeds, which are rich in a large number of alkaloids, showed excellent ability to regulate blood glucose levels (Mahwish et al., 2023).

2.8 Saponin Compounds

The saponin compounds in BM are generally divided into two main groups: oleanoid and cucurbitane triterpenoids (Popovich D G, Li L & Zhang W, 2010). More than 100 saponins extracted from the fruit, stem and

leaves of BM have been isolated and characterized. Among them, bittersweet, a natural triterpenoid from the Cucurbitaceae family present in the fruit, leaves and seeds of BM, has potential hypoglycemic activity. The saponin content was significantly higher in male flowers (15.11 ± 1.45 μg/g) compared to female flowers (1.55 ± 0.08 μg/g), stems (0.14 ± 0.01 μg/g), young leaves (4.82 ± 0.53 μg/g) and mature leaves (6.58 ± 0.87 μg/g) (Cuong D M et al., 2017). Seven BM saponins, namely momordicoside L, 3*β*,7*β*,25-trihydroxycucurbita-5,23(*E*)-dien-19-al, momordicoside K, momordicine I, momordicoside I, momordicoside F_2, and momordicoside F_1, were determined using the UPLC-ESI-MS/MS (Liu Y-J et al., 2020). Furthermore, momordicoside U (Namsa N D et al., 2011), kuguaglycoside G (Tambor M et al., 2016), 3-hydroxycucurbita-5, 24-dien-19-al-7, 23-di-*O*-*β*-glucopyranoside (Aziz M, Karboune S, 2018), momordicine I (Sabourian R et al., 2016), 3*β*, 7*β*, 25-tri-hydroxycucurbita-5, 23 (*E*)-dien-19-al (Puri R et al., 2011), momordicine II (Pandit S et al., 2016) had also been isolated.

2.9 Volatile Components

More than 30 structurally distinct volatile constituents were isolated from BM flowers, of which laurene was the predominant compound, followed by methyl jasmonate and 1-octadecanol (Sarkar N, Mitra S & Barik A, 2017). Volatile compounds in leaves and fruits obtained by water distillation were identified by HS-SPME and GC-MS, and 18 compounds were found in mature fruits and 21 compounds in leaves. Benzaldehyde, linalool and *β*-cyclocitral were identified by both analytical methods. Linalool was found to be the major compound in both cases (Ferreira Almeida N et al., 2024).

Table 2. Chemical compounds identified in different parts of the *Momordica* plant

Chemical compounds	**Plant sources**	**Part**	**Extraction solvents**	**Characterization or analysis methods**	**Ref.**
Phenolic acids and phenols					
Quinic acid	Apucarana, Brazil	Pulp, peel, seed	Ethanol/water (80:20, *v/v*)	UPLC–MS/MS	(Lopes A P et al., 2018)
4-Hydroxybenzoic acid		Pulp, peel, seed			
Trans-cinnamic acid		Pulp, peel, seed			
p-Coumaric acid		Pulp, peel, seed			
Caffeic acid		Pulp, peel, seed			
Gallic acid		Pulp, peel, seed			
Quercetin		Pulp, peel, seed			
Rutin		Peel			
Ferulic acid	Apucarana, Brazil	Pulp, peel	Ethanol	UPLC–MS/MS	(Lopes A et al., 2020)
Synaptic acid		Pulp, peel, seed			
Chlorogenic acid		Peel			
Vanillic acid		Pulp, peel, seed			
Apigenin		Pulp, peel, seed			
Catechin		Pulp, peel			
Crisin		Pulp, peel, seed			
Kaempferol		Pulp, peel, seed			
Tannic Acid	Gyeongsan, Korea	Peel	Ethanol	HPLC	(Lee J J et al., 2021)
Epicatechin		Peel	Ethanol		
Syringic acid		Leave	Choline chloride-acetic acid, water, methanol, ethanol		
Quercetin-3-glucoside		Leave			
Salicylic acid		Leave			
Luteolin-3',7-di-*O*-glucoside	Târgu Mureş,	Stem, leave	Ethanol/water (80:20, *v/v*)	UPLC	(Laczko-Zold E et al.,

Luteolin-7-*O*-glucoside	Romania	Stem, leave, fruit				2023)
4-*O*-Feruoylquinic acid,	Santa Cruz area, Trinidad	Fruit		Ethanol/water (80:20, *v/v*)	HPLC/MS	(Svobodova B et al., 2017)
Quercetin-*O*-dihexoside		Fruit				
5-*O*-Feruoylquinic acid		Fruit				
Quercetin-*O*-pentosylhexoside		Fruit				
Quercetin-3-*O*-rutinoside		Fruit				
Kaempferol-*O*-pentosylhexoside		Fruit				
Quercetin-*O*-acetylhexoside		Fruit				
Kaempferol-3-*O*-rutinoside		Fruit				
Kaempferol-3-*O*-glucoside		Fruit				
Isorhamnetin-3-*O*-glucoside		Fruit				
Kaempferol-*O*-acetylhexoside		Fruit				
Isorhamnetin-*O*-acetylhexoside		Fruit				
Ellagic acid	India	Fruit		Methanol, ethanol and *n*-butanol	HPTLC	(Yadav R et al., 2016)
Flavonoids and their derivatives						
Herbacetin	Shandong and Hebei Province, China	Fruit		70% Methanol	UPLC-MS/MS	(Zhang, et al., 2022)
Isolhamnetin-3,7-*O*-diglucoside		Fruit				
Isorhamnetin-3-*O*-(6″-acetyl) glucoside		Fruit				
Isorhamnetin-3-*O*-rutinoside		Fruit				
Kaempferol-3-*O*-neohesperidoside		Fruit				
Kaempferol-4'-*O*-glucoside		Fruit				
Kaempferol-3-*O*-(6″-malonyl) glucoside		Fruit				
Kaempferol-3-*O*-glucoside-7-*O*-rhamnoside		Fruit				
Kaempferol-6,8-di-*C*-glucoside		Fruit				
Dihydro kaempferol-7-*O*-glucoside		Fruit				
Quercetin-3-*O*-(6″-acetyl) galactoside		Fruit				
Quercetin-3-*O*-(6″-malonyl) galactoside		Fruit				

Quercetin-7-*O*-(6″-malonyl) glucoside		Fruit			
Sakuranin		Fruit			
Sexangularetin-3-*O*-glucoside-7-*O*-rhamnoside		Fruit			
Saponarin-4′-*O*-glucoside		Fruit			
Aromadendrin-7-*O*-glucoside		Fruit			
Tricin-7-*O*-glucoside		Fruit			
Limocitrin-3-*O*-arabinoside		Fruit			
Limocitrin-7-*O*-glucoside		Fruit			
Rutin	Soure, Brazil	Leave	Ethanol, ethyl acetate	LC-HRMS	(Muribeca A d J B et al., 2022)
Kaempferol-*O*-glucoside-*O*-pentoside		Leave	Ethanol		
Luteolin-*O*-rutinoside		Leave	Ethanol, ethyl acetate		
Kaempferol-*O*-glucoside		Leave	Ethanol, ethyl acetate		
Isorhamnetin-*O*-glucoside		Leave	Ethanol		
Quercetin-*O*-acetylpentoside		Leave	Ethanol, ethyl acetate		
Catechin hydrate	Beijing, China	Flower	80% Ethanol	HPLC	(Cuong D M et al., 2018)
Benzoic acid		Root, stem, leave, flower			

Note: HPLC-MS: high-performance liquid chromatography-mass spectrometry; UPLC-MS: ultra performance liquid chromatography mass spectrometry; HPLC: high-performance liquid chromatography; HPTLC: high-performance thin layer chromatography; LC-HRMS: liquid chromatography, high resolution mass spectrometry.

3. Health Benefits

Herein, the potential health benefits of *Momordica* plants and some of their potential mechanisms are summarized in **Table 3** and **Figure 2**.

3.1 Antioxidant Activity

Several studies have been carried out to verify the *in vitro* antioxidant activity of *Momordica* plants through $ABTS^+$ radical scavenging capability, NO radical inhibition ability and DPPH radical scavenging capability (Nguyen T-V-L et al., 2020; AkyÜz E et al., 2020; Hani N M et al., 2017).

In recent years, the quest for appropriate natural antioxidants has emerged as a significant research field due to the suspected role of synthetic antioxidants, such as butyl hydroxyanisole (BHA) and butyl hydroxytoluene (BHT), in liver damage and carcinogenesis. Several studies have confirmed that plant polysaccharides exhibit significant antioxidant activity, which can be further enhanced through chemical modifications (Liu Y, Sun Y & Huang G, 2018). The antioxidant activity of polysaccharides derived from BM was found to be significantly enhanced through carboxymethylation, a structural modification technique. This enhancement can be attributed to the introduction of negatively charged carboxyl groups, which create a negatively charged hydrophilic surface structure for the polysaccharide. As a result, the water solubility of the polysaccharide is greatly improved, leading to enhanced antioxidant activity (Chen F & Huang G, 2019).

As a vital active ingredient in BM, polysaccharide has been shown to significantly elevate the levels of superoxide dismutase (SOD) and catalase (CAT) in the serum of mice. High doses of polysaccharides (300 μg/g) increased SOD and CAT levels in serum by 47.4% and 63.1%, respectively. Furthermore, high doses of polysaccharides (300 μg/g) increased malondialdehyde (MDA) levels in the brain by 57.0%, thereby

demonstrating its antioxidant and anti-aging properties (Huang H et al., 2020).

In addition, it is widely recognized that aging is related to oxidative stress. BM saponins produce anti-oxidative stress and anti-aging effects through the IIS (insulin/insulin-like growth factor-1 signaling) pathway associated with sir-2.1 and hlh-30 (Zhang J et al., 2022); The intake of BM polysaccharides reduces D-galactose-induced spatial memory dysfunction and improves telomerase activity in aged rats through the Nrf2/β-catenin signaling pathway (Yue J et al., 2023). BM active extracts play a crucial role in alleviating aging caused by oxidative stress damage and reversing the decline in learning and memory abilities.

Table 3. Biological activity and mechanism of action of *Momordica* components or extracts

Extracts or components	Observation or methods	Effects	References
Antioxidant activity			
M. charantia fruit extracts (seed, pulp and peel)	DPPH and $ABTS^+$ assay	The peel exhibited the most noteworthy DPPH radical scavenging activity (EC_{50}=245.0 μg/mL). Moreover, the $ABTS^+$ assay demonstrated that the peel possessed the most potent antioxidant capacity, ($EC_{50=}$262.67 μg/mL).	(Mishra S et al., 2021)
Polysaccharide	DPPH radical, hydroxyl radical and superoxide radical	The polysaccharide exhibited scavenging capacities of 60% at 0.5 mg/mL against DPPH radicals, 50% at 0.8 mg/mL against superoxide radicals, and 33% at 0.9 mg/mL against hydroxyl radicals.	(Mei X et al., 2020)
M. charantia powder	$ABTS^+$, FRAP and DPPH assay	The *M. charantia* powder extract demonstrated remarkable antioxidant capacity at concentrations ranging from 0.25 to 1.0 mg/mL.	(Tan S P et al., 2014)
M. charantia methanol extract	ROS and MTT assay	The methanol extract of *Momordica charantia* significantly decreased SNP-induced ROS production and H_2O_2-induced cytotoxicity in HaCaT cells in a dose-dependent manner ranging from 0 to 200 μg/ml.	(Park S H et al., 2019)
Phenolic compounds of *M. charantia* by different solvents	DPPH and ORAC assay	The highest antioxidant capacity by DPPH assay was observed in ethanol/water (80:20, *v/v*) for peel (7.20±0.09 mg ET/g). In the ORAC assay, the highest antioxidant capacity was noted in ethanol/water (80:20, *v/v*) for seeds (4.93±0.04 mg ET/g).	(Lopes A P et al., 2018)
M. charantia extract by different solvents	DPPH radical, $ABTS^+$ radical and NO radical	The pulp extracted with deionized water exhibited the highest DPPH radical scavenging activity of 153.36±11.86 mg TEAC/g extract. The water extract of the inner tissue extracted with 60% ethanol demonstrated the highest ABTS radical inhibition activity of 244.39±12.81 mg TEAC/g extract. The inner tissue showed the highest NO radical inhibition activity of 6201.75±157.04 mg TEAC/g extract.	(Trakoolthong P et al., 2022)
Anti-inflammatory activity			
Triterpenoid (TCD) from vines and leaves	*In vitro*, RAW 264.7 cells	TCD (20-50 μM) dose-dependently inhibited LPS-induced iNOS expression.	(Chou M C et al., 2022)
Lignans and saponins from *M. cochinchinensis* seeds	*In vitro*, RAW 264.7 cells	Lignans and saponins could inhibit the release of NO and TNF-α in RAW 264.7 cells induced by LPS.	(Wang M et al., 2019)
Triterpenoids from	*In vitro*, FL83B	The two triterpenes dose-dependently inhibited	(Cheng H-L et

fruit	cells	the expression of iNOS, with IC_{50} values of 19.8 μM and 25.7 μM, respectively.	al., 2017)
BM (*M. charantia* Linn. var. *abbreviata Ser.*) fruit EA extract	*In vitro*, THP-1 cells	The BM EA extract not only decreases IL-8 levels, but also reduces TNF-α and IL-1*β* production in *P. acnes*-stimulated THP-1 cells, while also exhibiting an inhibitory effect on MMP-9 levels.	(Hsu C et al., 2012)
BM (*M. charantia* L. var. *abbreviate Seringe*) fruit	*In vivo*, sepsis mice	The diet containing 10% wild BM significantly inhibited the expression of iNOS protein, reduced the formation of the inflammatory mediator NO, and decreased the production of the inflammatory mediator PGE_2 by downregulating the expression of COX-2 protein.	(Chao C-Y et al., 2014)
BM fruit power extract	*In vitro*, RAW 264.7 cells	The extract decreased the LPS-induced expression of genes linked to the formation of inflammatory vesicle complex (NF-κB, NLRP3, Pycard, Casp1).	(Perez J L et al., 2021)
Crude BM extract	*In vivo*, colitis model	The crude BM extract significantly decreased colitis-induced weight loss and alleviated the colonic damage score of colitis, accompanied by a noteworthy elevation in serum anti-inflammatory cytokine IL-10 levels.	(Ünal N G et al., 2019)
Charantadiol A	*In vivo*, periodontitis model	Charantadiol A significantly suppressed *P. gingivalis*-stimulated IL-6 and TNF-α mRNA levels in gingival tissues of mice.	(Tsai T-H et al., 2021)
α-Eleostearic acid	*In vivo*, spinal cord injury (SCI) model	BM extract inhibits SCI-induced up-regulation of GFAP, IL-1*β*, and IL-6 mRNA and attenuates IL-4 and CISD2 mRNA down-regulation.	(Kung W-M et al., 2020)
Antitumor activity			
Methanol extracts from BM fruit	*In vitro*, HT-29 and SW480 cells	Methanol extracts demonstrated a dose-dependent inhibition of HT-29 and SW480 cell proliferation, with IC_{50} values of 57 μg/mL and 85 μg/mL, respectively.	(Kwatra D et al., 2013)
Momordicine-I	*In vitro*, Cal27, JHU022 and JHU029 cells	Momordicine-I markedly inhibited C-Met signaling and its downstream effectors, resulting in a substantial reduction in the expression of phosphorylated STAT3 (Tyr-705).	(Sur S et al., 2021)
Antidiabetic activity			
Polysaccharides	*In vivo*, STZ-induced rats	The polysaccharides successfully normalized hyperglycemia levels in diabetic rats. Furthermore, they exhibited an increase in the expression levels of Ins1, Jagged1, Pdx1, and Hes1 genes, along with a decrease in the expression levels of Notch1 and Dll4.	(Sajadimajd S et al., 2022)
Saponins	*In vivo*, STZ-induced mice	The total content of saponins in BM was 18.24 μg/mg. Diabetic mice treated with saponins at doses of 100 and 200 mg/kg body weight daily for a duration of 30 days exhibited significant reductions in BG levels of 12.63% and 26.47%, respectively (p<0.05).	(Deng Y et al., 2023)
Aqueous extract of seeds of BM	*In vitro*, adipocytes	Aqueous extract of BM seeds reduced glucose levels in diabetic adipocytes and significantly increased glycogen content and glucose-6-phosphate dehydrogenase activity.	(Saxena M et al., 2022)

BM juice	*In vivo*, STZ-induced rats	It induced a significant increase in serum insulin levels (3.41 ± 0.08 and 3.28 ± 0.08 vs. 2.39 ± 0.27 μIU/mL), HDL-cholesterol, total antioxidant capacity, *β*-cell function percentage, and pancreatic reduced GSH content, and it ameliorated histopathological changes in the pancreas.	(Mahmoud M F et al., 2017)
Charantin and vicine	*In vivo*, hyperglycemic rat model	When administered at a dosage of 300 mg/kg of whole fruit, it led to a 31.64% reduction in BG levels and a 27.35% elevation in insulin levels in hyperglycemic rats.	(Mahwish et al., 2021)
BM seed protein hydrolysate	*In vivo*, STZ-induced rats	The hydrolysates induced a reduction in levels of BG, glycated hemoglobin (HbA1c), and glycogen, as well as a decrease in serum lipid markers (cholesterol, high-density lipoproteins, low-density lipoproteins, and total cholesterol) in spontaneous diabetic rats in a dose-dependent fashion.	(Yuguda A Y, 2023)
Antibacterial activity			
Flavonoids from BM leaves	*In vitro*	The MIC of the ethyl acetate phase derived from the leaf extract of BM against *K. pneumoniae* is determined to be 156.2 μg/mL. In contrast, the MIC of the ethanol extract against *P. mirabilis* is measured at 312.5 μg/mL, and against both *K. pneumoniae* and *S. aureus*, it is quantified at 625 μg/mL.	(Muribeca A d J B et al., 2022)
BM seed oil	*In vitro*	The oil exhibited the greatest activity against *S. typhi* and *K. pneumoniae*, displaying a MIC of 15.63 mg/mL. The antimicrobial inhibition zones of the oil were 21.0±1.41 mm against *S. typhi*, 18.0±0 mm against *E. coli*, 15.0±1.41 mm against *R. stolonifer* and *A. niger*, and 17.0±1.41 mm against *C. albicans*.	(Zubair M F et al., 2018)
Fruit extracts from three different stages of cultivation	*In vitro*	The immature dried fruit extract in 80% and 100% methanol exhibited promising antibacterial activities, with a>18.5±0.21 mm zone of inhibition against *S. aureus*, whereas the extract from mature dried fruit in 80% methanol demonstrated a 18.4±0.17 mm zone of inhibition against *E. coli.*	(Naqvi S A R et al., 2020)
Seed extract	*In vitro*, liquid dilution method	The ethyl acetate fraction exhibits a MBC against *S. epidermidis*, with an MBC value of 40%.	(Rahmi M, Sari T M, Despanita, 2021)
Fruit ethanolic extract	*In vitro*, microdilution in broth method	*E. coli*, *P. aeruginosa*, *S. aureus*, *C. albicans*, *C. glabrata*, *C. guilliermondii*, *C. krusei*, *C. parapsilosis*, and *C. tropicalis* were all sensitive to the extracts, with their MIC and MBC/MFC being less than 0.125 mg/mL.	(Lucena Filho J H et al., 2015)
Antiviral activity			
M. balsamina leaf extract	*In vitro*, MTT assay	*M. balsamina* leaf extract inhibits HIV-1 infection by more than 50% at concentrations of 0.02 mg/mL and higher, while exhibiting no toxicity within its inhibitory range (0-0.5 mg/mL).	(Coleman M I et al., 2022)
BM fruit extract	*In vitro*	BM extract-derived antiviral protein exhibits a dose-dependent inhibitory effect on the H1N1	(Pongthanapisith V et al., 2013)

		subtype. When the concentration is 1.401 mg/mL, this protein shows significant inhibitory effect on the H1N1 virus.	
Balsamin	*In vitro*, growth curves and single-round assay	Balsamin significantly inhibits HIV-1 replication in T cell lines and primary $CD4^+$ T cells, achieving over 99% inhibition in growth curve assays.	(Kaur I et al., 2013)
BM powder extract	*In vitro*, MTT assay and *in vivo*, HTLV-1 infected mice	The IC_{50} values for ethanol and aqueous extract were 38.33 μg/mL and 29.09 μg/mL, respectively. Additionally, both solutions demonstrated significant inhibitory effects on the HTLV-1 infected mice group.	(Ahmadi Ghezeldasht S et al., 2023)
BM leaf extract	*In vitro*	The BM leaf extract exhibited significant antiviral activity against human herpesvirus-3 (HHV-3), with the MIC values of the ethanolic and aqueous extract being 250 and 62.5 μg/mL, respectively.	(Angamuthu D et al., 2019)
Cardiovascular protection effect			
BM fruit extract	*In vivo*, high sucrose and high fat diets rat	The maximum reduction in total cholesterol was: 6.60% for the peel, 6.04% for the pulp, and 6.70% for the whole fruit; the maximum reduction in low-density lipoprotein was 5.55% for the peel, 6.81% for the pulp, and 6.60% for the whole fruit, and the high-density lipoprotein levels improved.	(Mahwish et al., 2017)
BM aqueous extract	*In vivo*, dahl salt-sensitive (DSS) rats	BM aqueous extract can significantly prevent the increase in blood pressure, blood urea nitrogen, creatinine, and the urine protein-to-creatinine ratio in DSS rats.	(Zeng L et al., 2022)

Note: ROS: reactive oxygen species; ORAC: oxygen radical absorbance capacity; DPPH: 2,2-diphenyl-1-picrylhydrazyl; ABTS: 2,2′-azino-bis (3-ethylbenzthiazoline-6-sulphonic acid); NO: nitric oxide; CISD2: CDGSH iron sulfur domain 2; GSH: glutathione; MIC: Minimum inhibitory concentration; MBC: Minimum bactericidal concentration; MFC: Minimum fungicidal concentration.

3.2 Anti-Inflammatory Activity

Cucurbitane-type triterpenoids isolated from the vines and leaves of BM showed anti-inflammatory activity *in vivo* and *in vitro*, it inhibited LPS-induced phagocytosis and the expression of iNOS, NO, TNF-α, and IL-6 in a macrophage model, and also ameliorated ear oedema in an animal model, the mechanism of which may be the inhibition of IKK/ NF-κB pathway (Chou M C et al., 2022). Triterpenes isolated from the fruit of BM were found to inhibit other TNF-α-induced proinflammatory signals, such as the activation of the inhibitor-κB kinase complex, phosphorylation of NF-κB inhibitors, and activation of c-Jun *N*-terminal kinase. Additionally, triterpenes exhibited significant inhibition of 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced ear edema in mice (Cheng H-L et al., 2017).

Hsu et al. assessed the inhibitory impact of an ethyl acetate extract from BM (*M. charantia* Linn. var. *abbreviata Ser.*) fruit on *Propionibacterium acnes*-induced inflammation. The findings revealed the extract's efficacy in suppressing the levels of pro-inflammatory cytokines and matrix metalloproteinase (MMP)-9 in *P. acnes*-stimulated THP-1 cells *in vitro*. Moreover, intradermal injection in mice led to a reduction in *P. acnes*-induced granulomatous inflammation and ear swelling (Hsu C et al., 2012). The ethanol extract of BM demonstrated the most substantial reduction in LPS-induced prostaglandin E_2 (PGE_2) production, showing a 35% decrease at an ethanol extract concentration of 25 μg/mL. The butanol extract of BM placenta downregulated the expression of inflammatory genes induced by LPS, such as IL-1*α*, IL-1*β*, TNF-α, G1p2, and Ccl5. Furthermore, it reduced NF-κB DNA binding activity, as well as the phosphorylation levels of p38, JNK, ERK, and MAPKs (Dandawate P R et al., 2016). Rich in anti-inflammatory ingredient, BM can be an excellent option as a natural source of anti-inflammatory compounds.

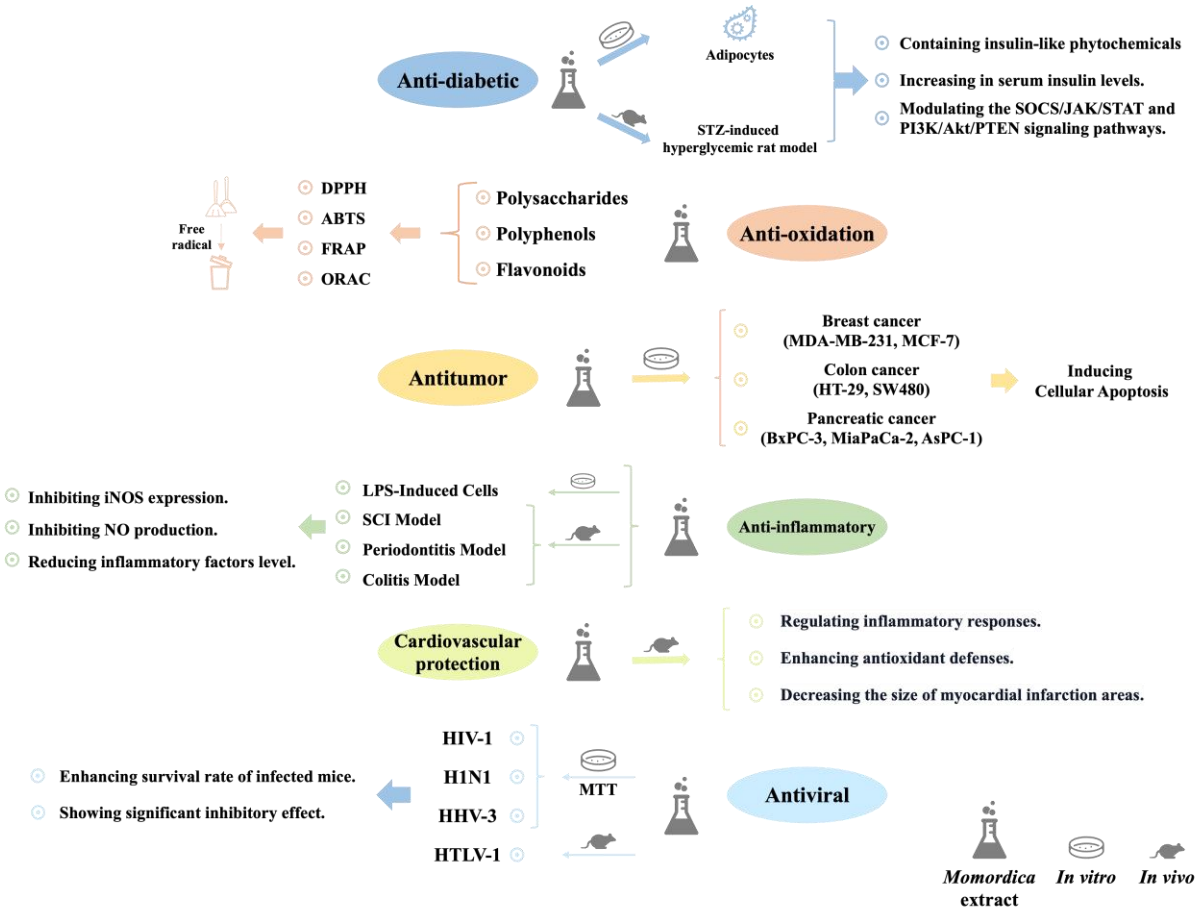

Figure 2. The potential health benefits of *Momordica*

The anti-diabetic, anti-inflammatory as well as antiviral activities of *Momordica* and its extracts have been validated by *in vivo* and *in vitro* studies. Among them, the LPS-induced RAW 264.7 inflammation model was mostly used in studies of anti-inflammatory activity. The cardiovascular protective effects of *Momordica* and its extracts are primarily utilized as a supplementary treatment for diabetes.

3.3 Antitumor Activity

The antitumor activity of BM extract was first reported in 1983, and several studies over the past decade have demonstrated its efficacy in inhibiting the proliferation of breast (MDA-MB-231, MCF-7), colon (HT-29, SW480) and pancreatic cancer cell lines (BxPC-3, MiaPaCa-2, AsPC-1) (Fang E F et al., 2019).

The mechanism of antitumor activity of BM extracts varies depending on the type of extract, cell type, and method of preparation of the extract. BM vesicles extract (BMVE) obtained from juice extraction was found to inhibit the proliferation of MCF-7 and 4T1 cells. In addition, it was observed that BMVE induced ROS generation played an important role in tumor cell apoptosis, and the cell scratch assay showed that BMVE inhibited the migration of tumor cells (Feng T et al., 2023). Momordicine-I, a secondary metabolite of BM, was procured via aqueous extraction and segregation from seedless whole fruits through the use of a common household juicer operated at ambient temperature (Sur S et al., 2021).

In addition, both apoptosis and autophagy have been shown to be pathways of BM mediated tumor cell death. Kuguacin J extracted from BM is able to inhibit the proliferation of prostate cancer cells through multiple mechanisms. It effectively blocks the expression of the active forms of MMP-9 and MMP-2 and disrupts cell cycle progression, ultimately leading to apoptosis (Pitchakarn P et al., 2012). The methanolic extract derived from BM effectively suppresses colon cancer stem cells by modulating energy homeostasis and autophagy (Kwatra D et al., 2013).

3.4 Antidiabetic Activity

As a traditional food and medicinal plant, BM is extensively utilized in the management of hyperglycemia by decreasing blood glucose (BG) levels in diabetic individuals, with several clinical studies showcasing its

beneficial effects on patients (Peter E et al., 2019). The raw BM can help regulate BG levels in diabetic patients by positively influencing their intestinal flora. Recent study has demonstrated that BM powder has the potential to promote the restoration of gut flora and the production of intestinal metabolites. This mechanism, in turn, can influence obesity-related inflammatory reactions, consequently mitigating insulin resistance induced by high-density lipoprotein cholesterol (Bai J, Zhu Y, Dong Y, 2018). Furthermore, the BM fruit juice (250 mg/2 ml water) significantly decreased fasting BG levels in normal rats (p<0.05 at 120 min) (Xu B et al., 2022).

BM contains a variety of phytochemicals with potential hypoglycemic effects, such as charantin, insulin-like peptides, vicine, polypeptide-p, sterol glycosides, triterpenoids, saponins, polysaccharides, alkaloids, water-soluble crude peptides, flavonoids, and phenols (Gao Y et al., 2023). Aqueous extract of BM was discovered to elevate tissue glycogen, serum insulin, and Glucagon-like peptide (GLP-1) levels in diabetic Wistar rats, consequently facilitating glucose-dependent insulin secretion from pancreatic β-cells, while concurrently reducing fasting BG and glycated hemoglobin (Bhat G A et al., 2018). In INS-1 cells and rat pancreatic islets, the methanol extract of green fruit BM and its ethyl acetate fraction were found to significantly increase ATP content, enhance insulin secretion in a dose-dependent manner, elevate serum insulin levels following glucose challenge, and substantially reduce BG levels (Shimada T et al., 2022). In STZ-induced diabetic rats, BM leaf nanoparticles (50 mg/kg) alleviate diabetic nephropathy by modulating the SOCS/JAK/STAT and PI3K/Akt/PTEN signaling pathways. Specifically, the levels of Akt, PI3K, TGF-β, JAK2, and STAT3 are downregulated, while the expressions of PTEN, SOCS3, and SOCS4 are upregulated (Elekofehinti O O et al., 2021).

Recent studies have also indicated that BM or its extracts may ameliorate diabetes-induced inflammation, ulcers, retinopathy, and reproductive dysfunction resulting from altered reproductive parameters. (Rosyid F N et al., 2022; Soliman G A et al., 2020; Liu J et al., 2023).

3.5 Antibacterial

Studies have ascertained that BM harbors a plethora of bioactive compounds, including flavonoids, phenolic substances, and cucurbitane-type triterpenoids, which exhibit significant antimicrobial therapeutic potential. The incorporation of these compounds within BM endows it with antimicrobial attributes and efficacy against bacterial pathogens (Villarreal La Torre V et al., 2020). Among them, various parts of BM have inhibitory effects on a wide range of bacteria.

For instance, the methanolic extract of the leaves exhibited a MIC value of 100 mg/mL against *P. aeruginosa* (Leelaprakash G & Rose C, 2011), while the stem extract showed a MIC value of 250 μg/mL against *E. faecalis* (Saengsai J et al., 2015). Furthermore, the chloroform extract derived from the fruits demonstrated a MIC value of 200 μg/mL against both *B. subtilis* and *E. coli* (Nguyen T et al., 2019). Lastly, the ethanol extract obtained from the seeds displayed a MIC value of 125 μg/mL against *C. krusei* (Lucena Filho J H et al., 2015). While BM has demonstrated the presence of potent antimicrobial metabolites, further investigation is required to elucidate its specific antimicrobial mechanism of action.

3.6 Antiviral Activity

The discovery of antiviral proteins in the seeds of *Momordica* plant has been reported and the antiviral activity in the seed extracts has been attributed to various small molecules and antiviral proteins. These molecules irreversibly inhibit viral translation, thereby inhibiting the spread of infection (Ramalhete C et al., 2016; Yao X et al., 2011). Several ribosome-inactivating proteins (RIPs) have been identified, including *Momordica* anti-HIV protein (MAP30) and α-, β-, and γ-momorcharin (MMC). These proteins have been shown to inhibit the replication of herpes simplex virus-1 (HSV-1), poliovirus type I in Hep2 cells, and human immunodeficiency virus type 1 (HIV-1) (Liu S et al., 2012). A single-round infectivity assay has also concluded that balsamin, a type of RIP, may exert its activity at the translation step of viral replication, specifically between the reverse transcription of the incoming viral genome and the release of newly produced viral particles (Kaur I et al., 2013). The research on the antiviral activity of BM protein extracts offers a novel approach and insightful ideas for the development of antiviral drugs. It also serves as a valuable reference for exploring the medicinal properties of other extracts and plants.

3.7 Anti-Parasitic Activity

BM contains various plant components, such as momordicin, momordin, momordicoside, karavilagenin, karaviloside, and kuguacin, all of which contribute to its restorative properties, including antibacterial, antiviral, and antiparasitic effects (Poolperm S & Jiraungkoorskul W, 2017). After treatment with concentrations of 25, 50, and 100 mg/mL of BM leaf extract, the mortality rates of the gastrointestinal nematodes *A. galli*, *Heterakis gallinae*, and *Capillaria spp*. in chickens were 22%, 70%, and 90%, respectively (Alam M et al., 2014). In addition, BM leaf extract also affects the embryonic development of *Fasciola hepatica* eggs in mammals (Pereira C A d J et al., 2016). BM seed extract induces paralysis in Indian adult earthworm (*Pheretima posthuma*)

within 3 minutes and results in death within 8 minutes (Ankalabasappa V et al., 2015). BM exhibits notable anti-parasitic activity and may serve as a potential anthelmintic, particularly for poultry and livestock.

3.8 Cardiovascular Protection Effect

BM extract has been found to help reduce cardiac damage and improve cardiac function by modulating inflammatory responses, enhancing antioxidant defenses, and reducing the size of myocardial infarcts, suggesting that BM may be beneficial to cardiovascular health (Czompa A et al., 2017). Ethanol extract of BM can significantly reduce LDL cholesterol in cholesterol-fed rats and alleviate cholesterol-induced myocardial degeneration and aortic damage (Innih S O, Eze I G & Omage K, 2021). BM (*M. balsamina*) leaf extract can significantly reduce BG concentration and improve erythropoietin secretion in STZ-induced diabetic mice, thereby significantly increasing erythropoiesis in diabetic animals. BM can also significantly improved hemoglobin concentration and moderately increased erythrocyte indices, particularly mean corpuscular volume, mean corpuscular hemoglobin concentration, and mean corpuscular hemoglobin (Ludidi A et al., 2019).

4. Uses-Economic Botany

4.1 Use in Foods

In addition to being consumed directly as a traditional vegetable or used for pickling, BM can also be made into uniquely flavored canned products, processed into tea, compound beverages, and wine (Yan J-K et al., 2019).

Various products made from BM, such as BM tea — an herbal tea made from dried BM slices, also known as Gohyah — are gradually becoming popular herbal remedies (Jia S et al., 2017).

In addition, emerging nano-encapsulation technologies can help to improve the stability of various bioactive compounds extracted from BM, ensuring that their activities remain essentially unchanged under the different acidic, alkaline, and thermal conditions that may be experienced during the processing of food or beverages (Gayathry K S & John J A, 2022).

4.2 Use in Cosmetics

The fruit of BM is its main edible part, while the seeds, leaves and other parts of BM are usually discarded. Some Chinese scholars have found that the seeds, leaves and other parts of BM show great potential for cosmetic applications and are worthy of in-depth study and further development. The oil components in BM seeds have potential medicinal value for preventing skin-related diseases, microbial infections, skin inflammation and skin aging. In addition, bitter melon seeds have the potential to be used in the production of natural antiseptic soaps (Zubair M F et al., 2018).

Study have shown that the water and ethanol extracts of BM fruits and seeds exhibit significant whitening and anti-wrinkle properties, making BM extract a highly potential and effective cosmetic ingredient (Kim H-W et al., 2015). BM leaves are also used to make a high-quality skin care and cosmetic cream, which is a crumbly white cream with the distinctive odor, pseudoplastic thixotropy and plastic thixotropy of BM, and is homogeneous and stable in texture (Hajard I & Pratami D, 2020). The antioxidant and 5α reductase inhibitory properties of BM extracts make them ideally suited for the formulation of functional microemulsions that have the potential to be further developed into cosmetic or pharmaceutical products aimed at controlling hair loss (Trakoolthong P et al., 2022).

4.3 Use in Traditional Medicines

Momordica plant is rich in a variety of active compounds such as polyphenols and flavonoids and is widely used in traditional medicine. In Asia, South Africa, Nigeria and Senegal, *Momordica* is commonly used for the treatment of fever, pain relief, gastrointestinal disorders, parasitic infections, diabetes, malaria and to promote wound healing. The pharmacological effects of these natural active ingredients are well-documented and validated in the traditional healing practices of these regions (Ramalhete C et al., 2022; Stuper-Szablewska K et al., 2023).

BM leaves were mixed with other medicinal substances to make a potion to relieve symptoms such as fever in children by the indigenous people of Kaluppini (Nurbaya & Chandra, 2020). Due to the excellent anti-diabetic activity of the fruits of the *Momordica* plant, it is widely used in the Ayurvedic system of medicine as an adjunct therapy for the treatment of diabetes (Pahlavani N et al., 2019).

4.4 Other Uses

A recent study reported that BM aqueous extract can be involved in the preparation of silver nanoparticles, giving the material enhanced antibacterial, antioxidant and in vitro antitumor activities, while the synthesis method is environmentally friendly (Palanisamy S et al., 2024). Hydroxyapatite nanoparticles were synthesized using *Momordica charantia* as a templating agent, with potential applications in bone and dental repair, as well as other orthopedic uses (Abraham A et al., 2023).

Activated carbon derivatives from BM fruit peels can also be used as supercapacitor electrode materials to improve charge storage performance (Aparna M L, Rao G R & Thomas T, 2022). BM leaf powder can absorb methyl orange dye and Cr (VI) metal ions from wastewater, making it a low-cost bio-adsorbent (Shahab M R et al., 2023). The innovative carbon dot fluorescence sensing system, utilizing fresh BM as the sole precursor, demonstrates efficacy in the detection of Pd^{2+} and Fe^{3+} present in tap and environmental water sources (Dong Y et al., 2021).

5. Safety

BM is generally not harmful to human health under normal conditions, but variations in intake and other related conditions may result in adverse reactions of varying degrees. Studies have shown that after 12 weeks of continuous consumption of BM powder capsules, some diabetic patients may experience adverse reactions such as anorexia, nausea, abdominal discomfort, diarrhea, constipation, foamy urine, and skin rashes, but not serious adverse reactions (Kim S K et al., 2020). Momordicines I isolated from BM leaves may have harmful effects on normal cells at concentrations higher than 10 μM (Chou M-C et al., 2022). Vicine-like compounds in BM seeds may induce heart and blood diseases (Khan M F et al., 2019). When the daily intake is controlled within 6 g, BM products have not been clearly proven to pose significant health risks. However, based on research results from animal experiments, bitter melon may have potential effects on the blood system and reproductive health. It is especially important to note that certain enzyme components in it may increase the risk of miscarriage. Therefore, it is recommended that pregnant or nursing women avoid using BM products. BM products are also not suitable for people with glucose-6-phosphate dehydrogenase (G6PD) deficiency to prevent possible health problems (Khan M F et al., 2019; Demmers A et al., 2022). It was found that mice developed nephrotoxicity after administration of 4 g/kg of BM for more than a week (Mardani S et al., 2014). In summary, BM is generally considered safe, but it is important to be aware of its potential toxicity and side effects to ensure its safe use in daily life.

6. Pesticide Residues and Food Safety

Trace pesticide residues in BM pose some potential threat to human health and create many uncertainties in food processing. Currently, commonly used pesticide includes abamectin, imidacloprid and a range of organophosphorus insecticides such as acephate, chlorpyrifos, diazinon, dimethoate, fenitrothion, malathion, and quinalphos. The widespread use of these insecticides and the difficulty in detecting their residues have raised great concern about the safety of BM (Table 4). Therefore, the study of effective methods for the detection of pesticide residues in BM has become an important issue to ensure food safety.

In recent years, research on the impact of pesticide residues in BM on consumers' daily diets has increased. For example, the QuEChERS (Quick, Easy, Cheap, Effective, Rugged, Safe) UPLC-tandem mass spectrometry method was used for the detection of abamectin residues, and it was found that the pesticide residues in BM did not exceed 0.019 mg/kg (Luo X et al., 2022).

In another study, the dissipation model and half-life detection method of imidacloprid were developed by LC-MS, and it was found that the residues of imidacloprid dissipated below the limit of quantification (LOQ) (0.025 mg/kg) within 2.51 and 3.13 days at the concentrations of 20 and 40 g a.i ha^{-1} (a.i ha^{-1}: active ingredient per hectare), respectively. After washing with water, the pesticide residues were reduced by 42.37% and the lowest residue was only 0.06 mg/kg, which was much lower than the MRLs (Mawtham M M et al., 2022).

In another study, after extraction of biomaterial samples from BM by the QuEChERS method, the concentrated extracts were analyzed for organophosphorus pesticides using a Shimadzu Gas Chromatograph-2010 equipped with a FTD detector, and the residues of chlorpyrifos, dichlorvos, and dimethoate were found to be 0.056, 0.097, and 0.032 mg/kg, respectively, which exceeded the European Union's maximum residue limit (0.010). Although subsequent studies have shown little short-term health risk, some chronic risk remains (Kaium A et al., 2021).

In recent years, significant progress has been made in monitoring plant pests and diseases and in methods for detecting pesticide residues. For example, by creating a database of common diseases affecting biodiverse leaves, the types of pests and diseases can be predicted more accurately, with a prediction accuracy of 82%, allowing for more targeted pesticide use (Fusic S J et al., 2024). A simple, efficient and environmentally friendly Surface Enhanced Raman Spectroscopy (SERS) assay has also been developed, which uses silver-decorated cotton swabs as wipes for rapid detection of single and mixed pesticide residues in real samples (Kong L et al., 2020).

Traditional chemical pesticides are gradually being replaced by emerging biopesticides (e.g., metarhizium, beauveria, trichoderma) and natural extracts (e.g., Azadirachta indica), mainly because of the latter's significant advantage of lower health risk (Paudel S et al., 2020).

To summarize, it is important to research and develop green biopesticides and natural insect-resistant extracts, and use pesticides scientifically and rationally, while continuously improving pesticide residue detection methods and increasing the sensitivity of pesticide residue detection. The results of the research to date show that

the pesticide residues in bitter melon are far lower than the maximum residue limit standards set by the countries in the world, and that the BM can be consumed without fear or further processed into other additional products.

Table 4. BM registered for pesticide use in China and corresponding MRLs in various countries

Pesticides	Maximum residue limits (MRLs, mg/kg)							
	China	Canada	United States	Australia	Korea	European Union	Japan	Codex Alimentarius Commission
Abamectin	0.050	0.010	0.005	0.020	0.050	0.010	0.010	0.01
Imidacloprid	1.000	0.500	0.500	0.200	0.200	/	1.000	0.20
Acephate	0.020	/	/	0.020	/	0.01	0.100	/
Chlorpyrifos	0.020	0.050	0.050	/	0.500	0.01	1.000	/
Diazinon	0.050	0.250	0.750	/	0.030	0.01	0.100	/
Dimethoate	/	/	1.000	/	/	0.01	1.000	/
Fenitrothion	0.500	/	/	/	/	0.01	0.500	/
Malathion	0.100	/	/	/	0.050	0.02	0.200	/
Quinalphos	/	/	/	/	/	0.01	0.050	/

7. Conclusions and Perspectives

Momordica plants are widely appreciated by consumers globally for their unique flavor and nutritional benefits. BM is notably rich in various chemical and nutritional components, including polyphenols, polysaccharides, minerals, and vitamins. BM is consumed directly as a traditional vegetable or used for pickling, and has also been made into uniquely flavored canned products, tea, compound beverages, wine and so on. The pharmacological activities of these phytochemicals include antioxidant, anti-inflammatory, antitumor, antidiabetic, anti-obesity, antifungal, neuroprotective, and blood cholesterol-reducing effects.

However, there are still many issues that need to be further studied. Firstly, the research on active ingredients and functional activities of BM is not thorough enough. Most studies are focused on cell experiments, and there is little research on the absorption and mechanism of active ingredients in vivo. Secondly, research on the antitumor activity remains limited to in vitro studies, with only a few investigations delving into their mechanisms of action. The application in health food, medicine, and chemical industry focused on the functional activity of BM further development. Therefore, it should strengthen the depth and breadth of following 4 aspects: (1) Future antitumor research should concentrate on identifying the active compounds within the chemical constituents of Momordica plants and elucidating their mechanisms of action. (2) The second is to carry out targeted research and development of health food, medicine, beauty, and other products. (3) The third is to continuously explore techniques suitable for extracting active ingredients from BM, in order to obtain high-purity and high content active ingredients. With the deepening of research, BM is expected to develop more medicinal and nutritional values, in order to better serve health and clinical care. (4) While significant progress has also been made in the study of its antidiabetic activity, including the identification of the active ingredient, an in-depth study of the mechanism of action and potential synergies with other treatments. However, a number of studies have also emphasized the potential for adverse effects when used as an adjunctive therapy for diabetes. Therefore, there is a need for further in vivo studies and/or even clinical trials to confirm its efficacy and safety.

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