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Chapter

Phytochemical Profile and Antiobesity Potential of *Momordica charantia* Linn.

Pushpa Anantrao Karale, Shashikant Dhawale and Mahesh Karale

Abstract

Momordica charantia L. is growing in many tropical and subtropical regions; the fruits of bitter melon are also gradually becoming popular for treating diabetes and associated diseases. Over 248 compounds belonging to the lipids, phenolics and terpenoids class are reported by diverse studies. However, *M. charantia* L. appears to be an inimitable species that synthesizes a diverse range of natural products in the fruits, leaves, stems and roots. The cucurbitane types of triterpenes exist in the various tissues of the plant in their aglycone as well as glycosylated forms. The bitter melon seems to exert their lipid lowering and antiobesity effects via several mechanisms like PPARs, LXRs, SREBPs, and Sirts mediated fat metabolism in various tissues, prevent adipocyte hypertrophy and visceral fat accumulation. *M. charantia* L. has been comprehensively studied worldwide for its therapeutic properties to treat a number of diseases like diabetes, dyslipidaemia, obesity, and certain cancers. This chapter apparently displays an encompassing literature review on vast potential of bitter melon as antiobesity agent and assembles data on complex phytochemistry.

Keywords: obesity, phytochemicals, bitter melon, cucurbitane type terpenoids

1. Introduction

Momordica charantia L. or Bitter Melon, also known as balsam pear or Karela, is a vegetable and common food in Indian cuisine and has been used comprehensively in folk medicine. Momordica charantia L. is tropical or subtropical creeping belonging to family Cucurbitaceae and widely used as medicinal herb from ancient time (**Figure 1**). The Latin name Momordica means "to bite" referring to the serrated edges of the leaf, which appear as if they have been bitten. The major regions of M. charantia L. cultivation are Asia including China, India, Sri Lanka and Thailand, central and South America and North America [1]. In Ayurveda, the fruit is considered as tonic, stomachic, stimulant, emetic, antibilous, laxative and alterative. Bitter melon has been used in various Asian traditional medicine systems for a long time. It is well recognized, the plant is extensively in use in the Chinese, Indian Ayurvedic, and Indonesian systems of medicines as well as in Japan [2].

The therapeutic significance of the plant is symbolized by the fruits which contain about half a dozen seeds per gram of the fresh fruit. As the name implies, the fruits are bitter and bitterness enhance with the level of maturity and hence



The image describes plant parts of M. charantia L. unripe fruit; ripe fruit and seeds of plant.

earlier harvesting required to battle bitter taste. The leaves and young shoots of bitter melon recognized to be used in traditional medicine as an herbal tea. The range of pharmacological activities reported for bitter melon is rapidly increasing in recent years and its claimed uses and potential applications for cancer and other diseases have been extensively reviewed. Likewise, the range of medicinal claims range from diabetes, hypertension, obesity, cancer, as well as AIDS. *M. charantia* L. possesses various beneficial effects, including anti-cancer, anti-viral, antioxidant, antiulcer, anti-obesity, anti-HIV, cytotoxic, anti-inflammatory, reduction of cholesterol, inhibition of protein tyrosine phosphatase 1B, and anti-osteoporosis [3]. This chapter aims to highlight the complex phytochemistry and extensive review on antiobesity potential of bitter melon with possible targets.

2. Plant profile

2.1 Botanical description

Cucurbitaceae family is known to comprise some 101 accepted genera and the genus Momordica L. itself comprises of some 50 accepted species within the family [4]. *M. charantia* L. was known previously by several synonyms including the *Cucumis argyi* H. Lev., *Cucumis intermedius* M. Roem., *Momordica anthelmintica* Schumach. & Thonn., *Momordica charantia subsp. abbreviata* (Ser.) Greb., *Momordica charantia* var. *abbreviata* Ser., *Momordica charantia* f. *muricata* (Willd.)., *Momordica charantia* var. *muricata* (Willd.) Chakrav., *Momordica charantia* var. *pseudobalsamina* Griseb., *Momordica charantia* var. *zeylanica* Hitchc., *Momordica elegans* Salisb., *Momordica papillosa* Peckolt ex Rosenthal., *Momordica roxburghiana* G. Don., *Momordica senegalensis* Lam., *Momordica thollonii* Cogn., *Momordica zeylanica* Mill. The botanical description of different parts of the plant demonstrated in **Table 1**. The taxonomic hierarchy of bitter melon within the plant kingdom is as follow:

Kingdom: Plantae Subkingdom: Viridiplantae Superdivision: Embryophyta Division: Tracheophyta Subdivision: Spermatophytina Class: Magnoliopsida Super order: Rosanae Order: Cucurbitales

Plant parts	Description Broadly ovate to orbicular in outline, cordate, narrowly decurrent on to petiole, sparsely pubescent to densely villous on veins beneath, deeply palmately 3–7-lobed, lobes variously sinuate-dentate or lobulate. Leaf lamina 10 × 12.5 cm.		
Leaves			
Flowers	Flowers are monoecious and solitary. Male flowers: peduncle 0.3–5 cm long; bract 2–17 mm long, broadly ovate or reniform, sessile, cordate, amplexicaul, pedicel 2–9.5 cm long. Receptacle-tube 1–5 mm long; lobes 3- 7 mm long, ovate-lanceolate. Petals 1.0–2.5 cm long, pale to deep yellow, ovate to obovate. Female flowers: peduncle 0.2–5 cm long; bract 1–12 mm long; pedicel 1–10 cm long; ovary 8–11 × 2–4 mm, ovoid-rostrate to fusi-form, ridged, pilose on ridges, tuberculate;		
	receptacle-tube 1–3 mm long, lobes 2–5 mm long, lanceolate; petals 0.7–1.2 cm long.		
Fruits	Fruit 2.5–4.8 \times 1.5–2.3 cm, ovoid-rostrate or ellipsoid, longitudinally ribbed and tuberculate, bright orange-red, dehiscent into 3 valves; fruit-stalk 3.4–15 cm long.		
Seeds	Seeds 8–11, 4.5–8 \times 2–3.5 mm, enveloped in sticky red pulp, ovate-elliptic to oblong in outline; faces flattened, sculptured, with sinuate edges; margins grooved.		
Petiole	Petiole 0.5–7 cm long.		

Table 1.

Botanical description of Momordica charantia Linn.

Family: Cucurbitaceae **Genus:** Momordica Linn. **Species:** *Momordica charantia* L.-balsampear

2.2 Phytochemistry

The main constituents of bitter melon are triterpenoids, saponins, protein, polysaccharides, steroid, alkaloid, lipid, and phenolic compounds. Several bioactive compounds of *M. charantia* L. have been recorded and the literature shown that these were responsible for various pharmacological effects as depicted in **Table 2** [5].

2.2.1 Triterpenoids

The most abundant phytochemical components of bitter melon fruits are the triterpenoids class of secondary metabolites, and are well-known for their bitterness

Sr. No.	Bioactive compounds	Distribution	Pharmacological effects
1	Triterpenoids	Leaves, stem, fruits	Chemo protective, anticancer, antioxidant, antidiabetic
2	Peptides and proteins	Seed	Antiviral, anti-tumor, immune suppressant, antimicrobial
3	Phenolics	Fruit and seed	Antioxidant, anti-inflammatory, immunostimulant
4	Saponin	Fruit, root, seed	Antihyperglycemic, hypolipidemic, antiviral, bacteriostatic
5	Polysaccharide	All parts of plant	Antioxidant, antidiabetic, immune enhancement, neuroprotective, antitumor
6	Lipid	Seed	Anti-tumor, antioxidant
7	Steroids	Fruit and pericarp	Antimicrobial

Table 2.

Bioactive components of Momordica charantia Linn. And their pharmacological effects.

and toxicity. These were divided in two types primarily the cucurbitane-type and to a less extent oleane type which may occur either in their glycosylated or aglycone forms. The sugar monomers as β -D-glucopyranosyl, β -D-allopyranosyl, β -Dxylopyranosyl occur in cucurbitane-type triterpenes either by their own as O-linked glycosides, or in different combinations as disaccharides or polysaccharides. The rare glycoside in these compounds was the 3-keto-glucoside [6]. An extremely large and certainly exhibited 193 number of cucurbitane-type triterpenes isolated from bitter melon having various pharmacological effects (**Table 3**) [7]. The fruits are predominance source of terpenoids with great deal of structural diversity but the leaves, stems and roots have also been shown to be good sources of these compounds [8].

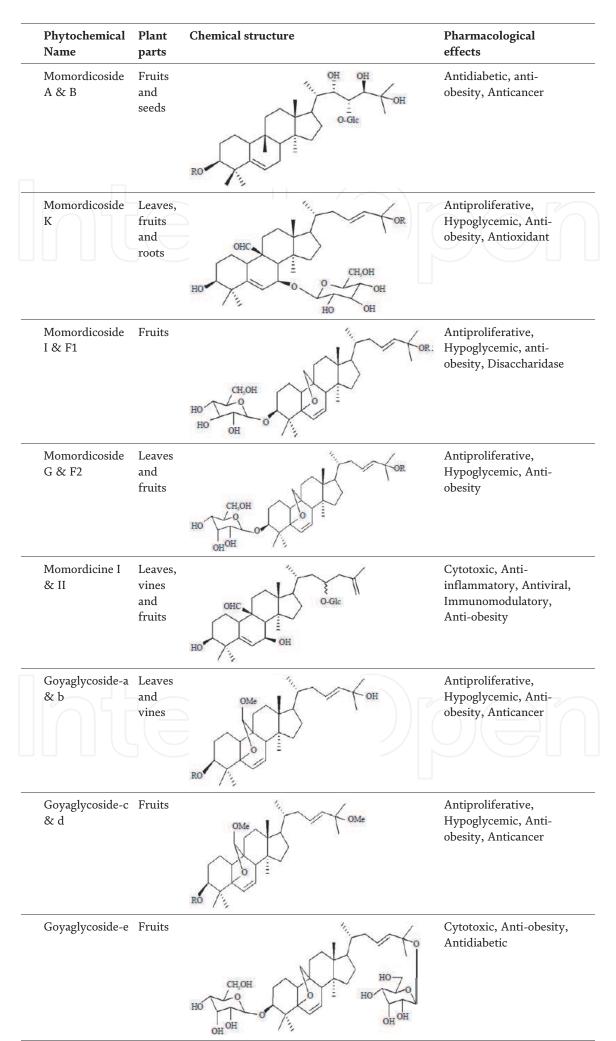
Momordicosides A and B were isolated firstly from the seeds of bitter melon fruits; While, Momordicosides C, D and E were isolated as minor components of the seeds [9]. The study on the fruits of *M. charantia* L. further added a Momordicosides F1, F2, G, I, K and L as novel compounds in previous one [10]. The Momordicosides I and Momordicosides M along with other compounds have also been isolated from the fruits of bitter melon [11]. Further additions of Momordicosides M-O as a new compound were confirmed by chemical examination of the fresh fruits [12]. The Vietnamese origin dried fruits of *M. charantia* had shown existence of an auxiliary three pioneering Momordicosides U, V and W. The cucurbitane-type triterpenes which are known to be responsible for the bitterness of the leaves and vines of the *M. charantia* L. are Momordicines. The Momordicine IV and the malonyl derivative of Momordicine II, Momordicine V was readily available in the leaves of bitter melon. The isolation of Momordicines VI, VII, and VIII were first confirmed from the stems and leaves of bitter melon [13].

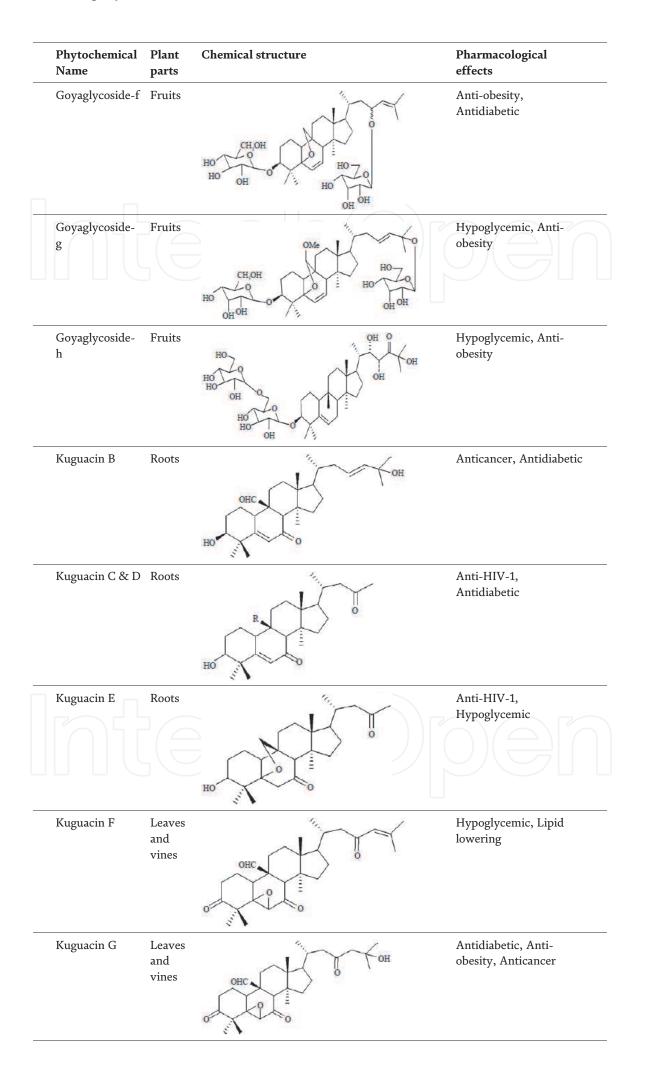
The Goyaglycosides-a, -b, -c, -d, -e, -f, -g, and -h were isolated from the fresh fruits of Japanese *M. charantia* L. A novel compound Goyaglycoside I was an additional triterpene isolated from the immature fruit of bitter melon [14]. The novel Cucurbitane-type triterpene called karavilagenins A-C and five new triterpene glycosides called karavilosides I-V were isolated from the dried fruit of *M. charantia* L. [15]. The three novel compounds that they names charantosides A, B and C were obtained from fruits of bitter melon. The methanol extracts of the fruits of Japanese *M. charantia* L. shown charantosides I, II, III-VI, VII and VIII, however charantoside IX and X were other novel compounds reported by the studies [16].

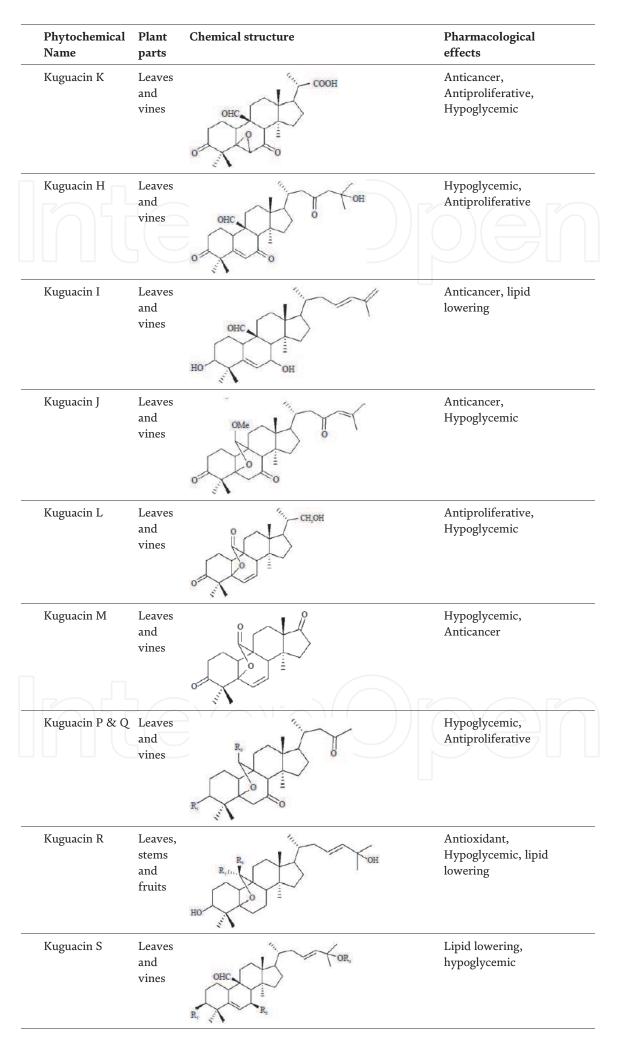
Another group of interesting triterpenoids are those known by their trivial names kuguacins. Kuguacins A-E and Kuguacins F-S were isolated from the roots and the leaves of bitter melon plant respectively [17]. Kuguacins II-VI was novel compounds isolated together with various other known compounds from the fruit of *M. charantia* L. From the aqueous ethanolic extracts of fresh fruits isolated eight novel cucurbitane-type glycosides that they named kuguasaponins A-H. The ethanolic extract of fruits of *M. charantia* L. identified 15 cucurbitane-type triterpene glycosides including 4 new compounds, kuguaosides A-D [18].

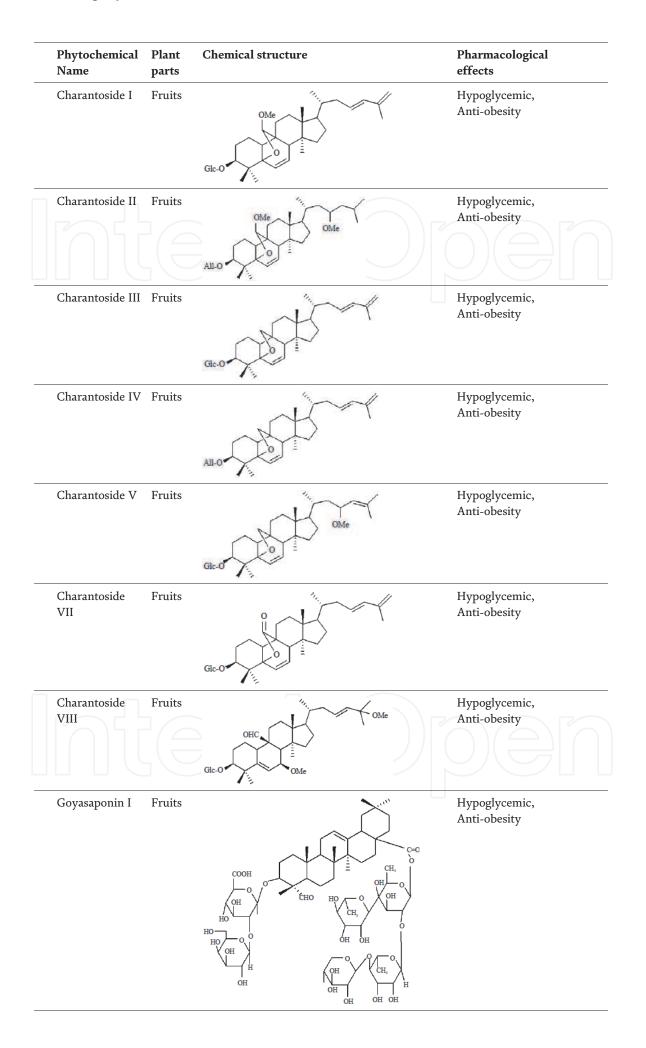
2.2.2 Flavonoids and phenolic compounds

A number of phenolic compounds with many biological activities have been isolated from bitter melon including, coumaric, caffeic, and ferulic acids as well as the caffeic acid ester, chlorogenic acid, Benzoic, gallic and gentisic acid. The major flavonoids and phenolic acids in the dried leaves of bitter melon were also analyzed and found to be rutin, gentisic acid and coumaric acid [19]. While the phenolic acids and flavonoids as well as their glycosides can be readily extracted by water, their non-polar derivatives may be present in the oil components of the plant.









Phytochemical Plant **Chemical structure** Pharmacological effects Name parts Goyasaponin II Fruits Hypoglycemic, Anti-obesity CH, COOH HO он ′сно OH н́с Goyasaponin III Fruits Hypoglycemic, Anti-obesity сно Karavilagenin C Fruits Antidiabetic Karaviloside I, Fruits Antiproliferative, II & III Antidiabetic, OR Hypolipidemic Kuguaglycoside Roots Cytotoxic, Antiproliferative, G Hypoglycemic, Anticancer Momordicinin Fruits Antidiabetic, Anti-obesity, lipid

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Table 3.

Pharmacological effects of cucurbitane type of triterpenoids of Momordica charantia.

lowering

2.2.3 Other components

Other than the bioactive compounds, unsaturated fatty acids, alkaloids, amino acids minerals and vitamins are also present in bitter melon. The extracts of bitter melon shows nine kinds of unsaturated fatty. It has also been demonstrated that 12, 13 and 12 carbon fatty acids are found in young, mature, and senescent leaves of *M. charantia* L. representing 87.3%, 95.25%, and 83.11% of the total fatty acids respectively. The contents of total amino acids and the free amino acids of *M. charantia* L. were 11.99% and 2.36% as determined by acid hydrolysis and amino acid analysis. In addition, bitter melon is a natural source of vitamins; ascorbic acid was detected in the range of 440–780 mg in the fruit fraction. Vicine is an alkaloidal agent that has been isolated from the seeds of bitter melon, which is responsible for hypoglycaemic activity [20].

3. Antiobesity and lipid lowering effects

The various experimental studies reported decrease in serum TC, TG and LDL-C concentrations and an increase in serum high density lipoprotein-cholesterol (HDL-C) for bitter melon by different authors. The action of bitter melon in lowering fat has been supported by plentiful studies, its effect on the level of serum FFAs have been contradictory with some authors showing reduction, some shown same level, and others reported an increased levels. For example, the serum FFAs concentration increased in obese rats treated with bitter melon shown by Chen et al. [21]. An increased level of TG and LDL-C in the serum that may arises due to either overproduction by the liver or defective removal from the circulation or the overall dyslipidaemia in diabetes. It is not clear why bitter melon increase the serum level of FFAs. It may facilitate fat mobilization due to the suppression of lipogenesis or lipid deposition. While other revealed *M. charantia* L. could lower the serum and liver TG levels [22].

The findings of experimental research conclude that, *M. charantia* L. may reduce the fasting insulin, TG, cholesterol and epididymal fat, which were increased by HFD. The dwindling of insulin resistance, improves glucose tolerance, and increases insulin signaling under HFD-induced insulin-resistance and elevated serum lipids may also shown by bitter melon. The administration of an aqueous extract of unripe fruits of bitter melon improved glucose and insulin tolerance together with inhibition of plasma apoB-100 and apoB-48. The animal study had shown that, the evidence of a potent inhibitor of apoB secretion and TG synthesis as well as the plasma lipid and VLDL effects of bitter melon juice [23]. Overall the studies on the fruits, seeds, and aerial parts of *M. charantia* Linn have been shown to reduce adiposity, lower serum insulin and normalize glucose tolerance in rats fed with a HFD. The body weight and visceral fat mass of bitter melon treated obese rats were shown to be lowered [24].

While further study revealed that, bitter melon supplementation into HFD notably suppressed the levels of fatty acid synthase (FAS), acetyl-CoA carboxylase-1 (ACC-1), lipoprotein lipase (LPL) and adipocyte fatty acid binding protein [25]. Water extract of *M. charantia* L. fruits at a dose 1 g/Kg body weight revealed to be effectual in improving the obesity-induced hyperglycaemia and hyperleptinemia [26]. This in progression propose that bitter melon can reduce insulin resistance, visceral fat accumulation and adipocyte hypertrophy probably by down-regulating the expression of key lipogenic genes or proteins in adipose tissues. Aqueous fruit extract of *M. charantia* L. significantly reduce the level of serum TG, TC, LDL and VLDL at a dose of 350 mg/Kg body weight in experimental rats [27]. Numerous

animal studies have been designated the efficacy of bitter melon in the amelioration of weight gain and regulation of lipid metabolism [28].

The methanolic extract of fruit of bitter melon showed antidiabetic and antihyperlipidemic action during different seasons of the year, this suggests that antidiabetic and hypolipidemic activity of *M. charantia* L. may fluctuate on quantity and quality of active constituents during different seasons of the year and reach the peak during spring [29]. The bitter melon seed oil had shown significantly decreased in body-weight, Lee's index, fat index and adipose size in the HFD mice. Meanwhile, the serum FFAs levels returned to normal at the dosage of 10 g/kg [30]. Momordica charantia L. extracts have anti-obesity effects and the ability to modulate lipid prolife of mice fed a HFD by suppressing body weight gain, visceral tissue weight, plasma and hepatic lipid concentrations, and lipid peroxidation along with increasing lipid metabolism. The plasma TG, TC, and LDL-C levels along with hepatic TG and TC concentrations considerably lowered in mice fed a HFD by Momordica charantia L. extracts. Also elevated plasma HDL-C levels and fecal TG concentration shown in animals treated with the extracts. The extracts comprise anti-obesity effects in mice fed a HFD by inhibiting lipid peroxidation whereas increasing lipid metabolism [31]. Bitter melon extract showed useful benefit on body weight gain and fat deposition.

Moreover, bitter melon reduced the lipid accumulation during differentiation from a pre-adipocyte to adipocyte and down-regulated PPAR [32]. PPAR is considered the master regulator of adipogenesis during differentiation of pre-adipocyte to adipocyte [33]. Bitter melon juice inhibited adipocyte differentiation by reducing PPAR, SREBP, and perilipin mRNA gene expression and by increasing lipolysis in primary human adipocyte [34]. Several transcriptional regulatory factors like AMPK, PPAR, and PGC-1 regulate the mitochondrial biogenesis, which would be a possible way of increasing lipid metabolism and utilization in energy demanding cells and tissues [35]. PGC-1 stimulates mitochondrial biogenesis and respiration in multiple cell types and modulates biological programs normally associated with increased oxidative metabolism. Also decreased plasma level of TGs, cholesterol, and FFA in plasma of rats fed a HF diet revealed by bitter melon supplementation due to up regulation and activation of PGC-1 [36].

Bitter melon affects on various body organs to treat obesity and diabetes as [37]:

1. Liver

- Increased β-oxidation
- Increased PPAR-α and PPAR-gamma expression
- Increased expression of the transcription coactivator PGC-1α
- Decreased fatty acid synthesis
- Decreased fat

2. Pancreas

- Increased insulin secretion
- Prevents cell damage
- Increased PPAR- α and PPAR- gamma expression in skeletal muscle

3. Fat cells

- Inhibited adipocyte hypertrophy
- Inhibited adipocyte differentiation
- Increased PPAR-gamma expression
- Increased expression of the transcription co-activator PGC-1α
- Decreased visceral fat mass

AMPK synchronized PPAR and PGC-1 activation encouraged most of the transcriptional signal to augment fatty acid oxidation and mitochondrial function [38]. Recent investigation also reported that increased hepatic AMPK p, AMPK, AMPK-2, and Sirt1 content in HF diet fed mice with supplementation of 1.2% bitter melon extract [39]. LXRs were first recognized as orphan members of the nuclear receptor plays an important role in lipid and cholesterol metabolism and oxidized derivatives of cholesterol act as ligands for the LXRs. A high cholesterol diet fed mice develop enlarged fatty livers, degeneration of liver cells, high cholesterol levels in liver, and impaired liver function by LXR knockout [40]. The *M. charantia* L. extract supplementation decreased hepatic LXR which was responsible for decreased serum TC and LDL-C, HDL-C in high cholesterol diet Wistar rats [41]. Bitter melon extract was a potent inhibitor of lipogenesis and stimulator of lipolysis in 3 T3-L1 pre-adipocyte shown by researcher [42].

4. Toxic effects

The severe adverse reactions were not reported during the short term studies while extensive data on the potential toxic effect of bitter melon are not available. Bitter melon fruits are edible and assumed to be well tolerated, at the same time toxicological evidences were reported to discover its therapeutic potential for diabetes. The two cases of acute intoxication reported after taking bitter melon tea [43]. The fruit and seeds demonstrated greater toxicity than the leaf or aerial parts of the plant. Abdominal pain as a side effect has also been reported in some studies [44]. The antifertility and abortifacient effects of the *M. charantia* L. reported in animals also value advance investigation. An acute disease favism characterized by hemolytic anemia, in individuals with a hereditary loss of the enzyme glucose-6-phosphatase has been shown by vicine found in fava bean. Consequently, the presence of vicine in bitter melon seeds was also suggested to put patients with glucose-6-phosphatase deficiency at risk [45]. Although there have been no reports on favism induced by bitter melon, individuals susceptible to the disease should avoid eating the fruit.

Several studies have been directed to reduce the bitterness of *M. charantia* L. preparations attributes to the triterpene compounds and increasing tolerability by the general public through various formulation approaches. Some recent studies used β -cyclodextrin at 0.25–2% concentrations to improve sensory quality, total phenolic content, antioxidant activity and antidiabetic potential of *M. charantia* L. juice [46]. Various encapsulation methods of bitter melon extracts along with optimized spray-drying techniques were also scrutinized to obtain the powder [47].

5. Conclusion

M. charantia L. has been broadly studied globally for its medicinal properties and to treat a number of diseases like diabetes, dyslipidaemia, obesity, and certain cancers. The extracts of fruits and different compounds seem to exert their beneficial effects via several mechanisms like PPARs, LXRs and SREBPs mediated fat metabolism in various tissues, reduces visceral fat accumulation and adipose hypertrophy. Isolated compounds from this plant like cucurbitane type of terpenoids, flavonoids and phenolic acids possesses antiobesity potential. These mechanisms will be directly related to controlling and treating diabetes mellitus, dyslipidaemia, obesity and related cardiovascular complications. Thus, further studies are required to conduct more double blind randomized trials with bitter melon extracts in obese population. In this chapter, we summarized phytoconstituents of bitter melon and its antiobesity potential. This compilation of phytochemicals and antiobesity activity of *Momordica charantia* L. will help the researchers in designing new untried strategies.

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