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Review

Phytochemical profile and biological activities of *Momordica charantia* L. (Cucurbitaceae): A review

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This study discusses the bioactive composition, supercritical fluid extraction and biological activities of *Momordica charantia* L. from the last five years. Numerous compounds that have been identified in the extracts of *M. charantia,* including phytosterols, terpenoids, fatty acids, phenolic compounds, phenolic acids and flavonoids were also discussed. Although, several studies reported the use of organic solvents in the extraction of these compounds, this review emphasized on supercritical fluid extraction (SFE), good selectivity, varied fractions in terms of mass yields and chemical composition obtained, in addition to providing a solvent-free extract. Moreover, the biological effects of *M. charantia* extracts, including their antidiabetic, neuroprotective, anti-obesogenic, antimalarial, antioxidant, anti-inflammatory, antimicrobial and allelopathic activities, were discussed. These biological effects of the extracts of *M. charantia* can directly affect human health. The findings of this review are important, as they can guide future studies related to obtaining bioactive compounds from *M. charantia* and its applications.

Key words: Bitter melon, supercritical fluid, bioactive compounds, biological activities.

INTRODUCTION

Momordica charantia L. belongs to the Cucurbitaceae family comprising of 47 species in Africa and 12 in Asia and Australia. All have unisexual flowers, and of the African species, 24 are dioecious, 23 monoecious, while all Asian species are dioecious (Schaefer and Renner, 2010; Dalamu et al., 2012; Rahman, 2013). This plant is known in English as: balsam pear, bitt gourd, African cucumber, wild cucumber, bitter cucumber, bitter melon, bitter apple, carilla fruit, carilla seed, leprosy gourd, basam apple, in Peru as: fun-kua, papailla Central america: cundeamor, balsamina, pepinillo, serosi, in Brazil as: melão de São caetano, melão de São Vicente,

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fruto de cobra, in Philippines as: ampalaya, apalia, palia, paria, pulia, saligun, apape, apapet, amargoso, margoso, in Malasya as: paria laut, duaun periok, in China as: ku gua, k'u hua, chin li chih, lai pu tao, in Japan as: nega-reishi, gôyâ, in Tibetan as: gser-gyi metog, in Mozambique as: nhadzumba, and in Congo as: lunbuzi, lubuzi-buzi, lumbuzi-busi (Quattrocchi, 1999; Abascal and Yarnell, 2005; Zhao et al., 2012). Although it originates from Asia, it is cultivated in several parts of the world, including Central and South America and Africa (Ji et al., 2012).

The São Caetano melon is widely used as a medicine and as food. It has several ethnopharmacological indications, such as antidiabetic (Rahmatullah et al., 2012), immunomodulatory (Deng et al., 2014), anti-dengue (Tang et al., 2012) and antioxidant activities (Aljohi et al., 2016), and has been shown to prevent hepatic fibrosis (Efird et al., 2014); in agriculture, it can be used to promote allelopathic activity (Singh, 2014).

In the Amazon, alternative medicine is very important for traditional communities, and the use of medicinal plants such as *M. charantia* has been widespread in the treatment of diseases such as malaria (Veiga and Scudeller, 2015). Bioactive compounds have been isolated from several parts of the plant, including the fruits, seeds and leaves (Choi et al., 2012; Yaldız et al., 2015). These biological activities are attributed to their complex chemical composition; they are rich in tannins, terpenoids, carbohydrates, resins, saponins, flavonoids, sterols, phylobatamins, anthraquinones, glycosides, amino acids, fatty acids and phenolic compounds (Sathya et al., 2012; Sood et al., 2012). The bioactive compounds are commonly obtained through conventional extraction techniques with many different types of organic solvents (Dar et al., 2014; Tan et al., 2014; Yeo et al., 2014), which may be toxic to human health. Therefore, other forms of extraction are necessary, for example, extraction with supercritical fluids. This extraction technique has great advantages over conventional methods, such as being selective depending on the operating conditions (temperature, pressure, and density) used during the extraction process. It is also considered a "green technique" for obtaining active compounds of plant origin (Coelho et al., 2012; Sánchez-Camargo et al., 2012; Oman et al., 2013). These benefits to human health make *M. charantia* a very important medicinal plant for use in alternative therapies worldwide (Urasaki et al., 2016), as has already been demonstrated in other previous literature reviews (Upadhyay et al., 2015; Tan et al., 2016; Zhang et al., 2016; Janagal et al., 2018).

BOTANICAL TAXONOMY OF THIS PLANT

M. charantia (*Cucurbitaceae*) is Liana or terrestrial creeper found throughout Brazil, and is characterized by the presence of simple, long and pubescent tendrils that present a thin, grooved, and green herbaceous stem. Mature fruits of the wild balsam-pear are 2 to 7 cm in length and 1.4 to 2 cm in width. The leaves are membranous, alternating, and simple with palmatipartite appearance and actinomorphic venation pattern with right lateral insertion, and are obtuse-quadrangular in cross section. They have a hairy surface, mucronate dentate margin, acute apex, lobed base and pubescent surface. The plant also produces pale or whitish yellow monocoic flowers and green berry-like fruits when immature that become yellow-orange when ripe. The seeds are wrapped in a reddish and edible substance. The species, *M. charantia* has diclinous flowers, with diurnal anthesis. The period it can last during flowering is 100 days. In the beginning of the flowering, the species presents dicogamy of the protandry type. The female flowers do not produce nectar, while the male flowers produce nectar during the entire period of anthesis. Fruit formation occurs through crossed-pollination and self-pollination. Figure 1 shows *M. charantia* with some fruits and flowers (Walters and Decker-Walters, 1988; Lenzi et al., 2005; Aguoru 2012; Dalamu et al., 2012; Singh et al., 2014; Giuliani et al., 2016).

PHYTOCHEMICALS PRESENT IN *M. CHARANTIA*

M. charantia contains a large number of bioactive compounds, which were identified and published in the last five years. Results of phytochemical analyses revealed the presence of alkaloids, tannins, saponins, flavonoids, cardiac glycosides and steroids (Mada et al., 2013; Oragwa et al., 2013). The biological activities of these substances are presented in this review.

Phytosterols

Phytosterols are group of sterols naturally found in plants. They are generally found in low concentrations, and have a total of up to 30 carbon atoms (Cherif, 2012). Articles on the identification of phytosterols in *M. charantia* are summarized in Table 1, and their chemical structures are shown in Figure 2. Phytosterols are known for lowering blood cholesterol levels, without altering the high-density lipoprotein or triglyceride levels (Yi et al., 2016). Other pharmacological effects attributed to phytosterols include anticancer, atherosclerotic, anti-inflammatory and antioxidant activities (Ramprasath and Awad, 2015; Uddin et al., 2015; Zhu et al., 2015).

Terpenoids

Terpenoids are diversified class of natural products that have various biological functions in the plant, and are responsible for the growth of the plant (Moses and Pollier, 2013).They also have anti-inflammatory and anticancer applications (Liu et al., 2012; Zhangetal, 2012).

Figure 1. *Momordica charantia* L. fruit and leaves.

Table 1. Phytosterols identified in *Momordica charantia* L. in the last five years.

Identified sterols	Reference
β-sitosterol and Daucosterol	Kim et al. (2013)
Campesterol, Stigmasterol and β-sitosterol	Yoshime et al. (2016)
β-sitosterol	Sen et al. (2012)
25ξ-isopropenylchole-5,(6)-ene-3-O-β-D-lucopyranoside	Liu et al. (2012)
Stigmasterol, β-sitosterol and Diosgenin	Agarwal and Kamal (2013)
Δ5–avenasterol and 25,26-dihydroelasterol	Daliborca et al. (2015)

The effects of six new cucurbitane-type triterpenoids (3-[(5β,19-Epoxy-19,25-dimethoxycucurbita-6,23-dien-3-yl)-2- oxoacetic acid; 3-[(5β,19-Epoxy-19,25-dimethoxycucurbita-6,23-dien-3-yl)oxy]- 3-oxopropanoic acid; 3-[(5-Formyl-7β-hydroxy-25-methoxycucurbita-5,23-dien-3-yl)- oxy]-3-oxopropanoic acid; 3-[(5-Formyl-7β-methoxy-7,23S-dimethoxycucurbita-5,23-dien3-yl)oxy]-3-oxopropanoic acid; 3-[(25-O-Methylkaravilagenin D-3-yl)oxy]-2-oxoacetic acid; 3-[(5-Formyl-7β,25-dihydroxymethoxycucurbita-5,23-dien-3-yl)- oxy]-3-oxopropanoic acid, isolated from the fruits of *M. charantia* on a typical proliferation of vascular smooth muscle cells (VSMCs) were analyzed, and in some cases up to 72.4% proliferation blockade were observed. In addition, these phytochemicals showed no cytotoxicity against the cultured cells studied; thus, *M. charantia* is a potential source of new active biomolecules for the treatment of cardiovascular diseases through the inhibition of VSMC proliferation (Tuan et al., 2017). The terpenoids that have been identified in *M. charantia* are summarized in Table 2, and their chemical structures are presented in Figure 3.

Fatty acids

Fatty acids are organic compounds with a carboxyl group (-COOH) bound to carbonic chains that can be saturated or unsaturated (Campen et al., 2015; Wood et al., 2016). Fatty acids, such as ω-3, can exert functions that are beneficial to human health, and can prevent or reduce the risk of developing cardiovascular diseases (Delgado-Lista et al., 2012). It is also reported that they may act as antimicrobial agents against bacteria (Alva-Murillo et al., 2012) and fungi (Urbanek et al., 2012). These biological activities justify new research on the extraction and applications of fixed oils of vegetable origin. *M. charantia* has high levels of fatty acids, as shown in Table 3. Some examples of their chemical structures are shown in Figure 4.

Phenolic compounds

Phenolic compounds are among the numerous secondary metabolites found in plants. They can be found in the form of simple phenols, phenolic acids, coumarins,

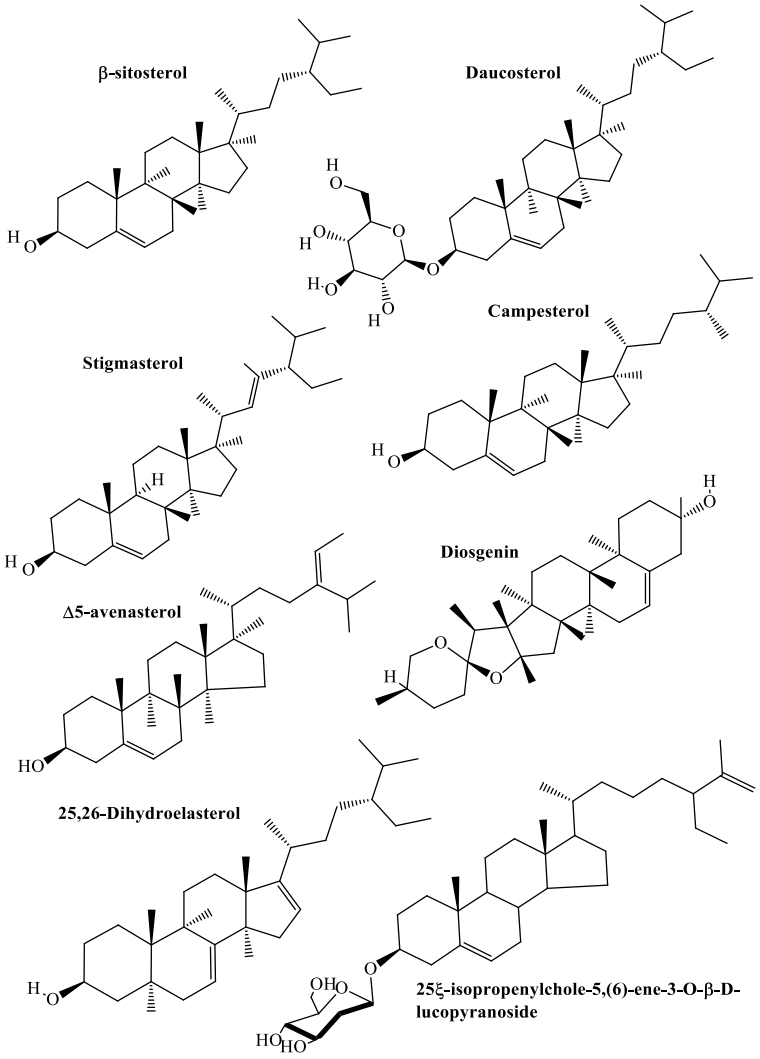

Figure 2. Chemical structures of phytosterols identified in *M. charantia* L. in the last five years.

tannins, lignins, lignans and flavonoids (Žilić et al., 2012; Khoddami et al., 2013). These compounds have several important effects, such as antioxidant, antimicrobial anti-HIV-1, and anticancer activities (Alves et al., 2013; Ghasemzadeh and Jaafar, 2013; Hu et al., 2013; Roby et al., 2013). Species such as *M. charantia* are a rich source of phenolic compounds, as shown in Table 4. The chemical structures of phenolic acids and flavonoids are represented in Figures 5 and 6, respectively.

EXTRACTION OF BIOMOLECULES OF *M. CHARANTIA* WITH SUPERCRITICAL FLUID

Active compounds of plant origin are generally extracted according to their chemical composition, biological activities, and the needs and purposes of the studies; however, some extraction methods can affect the quality of the extracts due to contamination from organic solvents, which can also increase the cytotoxicity of these extracts. In this scenario, supercritical fluid extraction (SFE) has been gaining interest in recent years, because in addition to being considered a "green" extraction method, it has other advantages (Poliakoff and Licence, 2015) such as fractionation selectivity (Chitra et al., 2015), higher yields of bioactive compounds as compared to those of conventional methods (Farías-Campomanes et al., 2013), and the fact that it can be performed at low temperatures, avoiding the degradation of thermosensitive substances. A supercritical fluid is any pure substance at a pressure and temperature above its critical point where distinct liquid and gas phases do not exist (Knez et al., 2014) (Figure 7). In addition, the SFE extraction method has other advantages over conventional methods, such as not using toxic organic solvents, and it usually works with a lower extraction

Table 2. Terpenoids identified in *Momordica charantia* L. in the last five years.

Identified terpenoids	Reference
Charantagenins D and charantagenins E	Wang et al. (2012)
4 new compounds, kuguaosides A−D (1−4), along with 11 known ones, charantoside A (5), momordicosides I (6), F1 (7), F2 (8), K (9), L (10), and U (11), goyaglycosides-b (12) and -d (13), 7β,25-dihydroxycucurbita-5,23(E)-dien-19-al 3-O-β-D-allopyranoside (14), and 25-hydroxy-5β,19-epoxycucurbita-6,23- dien-19-on-3β-ol 3-O-β-D-glucopyranoside (15).	Hsiao et al. (2013)
Phytol	Hsu et al. (2012)
Kuguacin J (Kuj)	Pitchakarn et al. (2012)
5β,19-epoxy-25- methoxy-cucurbita-6,23-diene-3b,19-diol (EMCD)	Cheng et al. (2012)
Charantin A (16), charantin B (17), momordicines I (18) and II (19), 3b,7b,25-trihydroxycucurbita-5,(23E)- dien-19-al (20), and momordicoside K (21)	Zhang et al. (2014)
3*β*,7*β*-dihydroxy-25-methoxycucurbita-5,23- diene-19-al (DMC)	Weng et al. (2013)
28-*O*-*β*-Dxylopyranosyl, (1→3)-*β*-D-xylopyranosyl, (1→4)-*α*-L-rhamnopyranosyl, (1→2)-[*α*-L-rhamnopyranosyl, (1→3)]-*β*-D-fucopyranosyl gypsogenin 3-*O*-*β*-D-glucopyranosyl, (1→2)-*β*-Dglucopyranosiduronic acid (C1) and 28-*O*-*β*-D-xylopyranosyl, (1→4)-*α*-L-rhamnopyranosyl, (1→2)-[*α*-L-rhamnopyranosyl, (1→3)]-*β*-D-fucopyranosyl gypsogenin 3-*O*-*β*-D-glucopyranosyl, (1→2)-*β*-D-glucopyranosiduronic acid (C2)	Ma et al. (2014)
5β,19‑epoxycucurbitane triterpenoids,	Liaw et al. (2015)
Karavilagenin F, karaviloside XII, karaviloside XIII, momordicine VI, momordicine VII, momordicine VIII	Zhao et al. (2014)

temperature, reducing the incidence of degradation of the product; in some cases subsequent purification steps are not necessary (Bagheri et al., 2014; Conde et al., 2014; Nguyen et al., 2015).

In the extraction process, a wide variety of fluids can be used as solvents as shown in Table 5. However, most of these compounds, such as light hydrocarbons, are generally flammable and toxic. On the other hand, carbon dioxide is the only compound that can be used as a "green solvent" and its critical properties are relatively low (Table 5). Carbon dioxide (CO_2) is particularly advantageous for the processing of food materials, because it is an inert gas, in other words, it reacts with the chemical compounds present in the extracts (Tabernero et al., 2012; Conde-Hernández et al., 2017). The critical properties of a pure substance may vary according to the interaction of the chemical bonds (intermolecular forces). As indicated in Table 5, molecules with the highest polarity have the highest critical properties (Pc) and (Tc) (Botelho et al., 2015).

In supercritical fluid extraction, temperature and pressure combinations are linked to the solubility of the compounds (Botelho et al., 2014). The control of pressure and temperature in supercritical fluids is one of the most important operating parameters because the density of the supercritical fluid increases with the pressure at constant temperature and decreases with temperature at constant pressure (Mantell et al., 2013). The density variation may lead to a possible change in the solubility of the compounds present in the raw material (Dias et al., 2012; de Oliveira et al., 2016).

Besides that, the mathematical models of mass transfer are important tool for SFE. These models exploit the kinetic behavior of the dynamic extraction period, and offer parameters such as mass transfer coefficient, diffusion coefficient and diffusivity in the solid phase (Sovová, 2012; Özkal and Yener, 2016). In addition, the modeling of the kinetic curves of extraction makes it possible to suggest scale-up methodology to predict the behavior of the extraction process on an industrial scale (Prado et al., 2012; Wüst Zibetti et al., 2013; Taher et al., 2014).

In this context, in recent years, several authors have used this technique to obtain bioactive

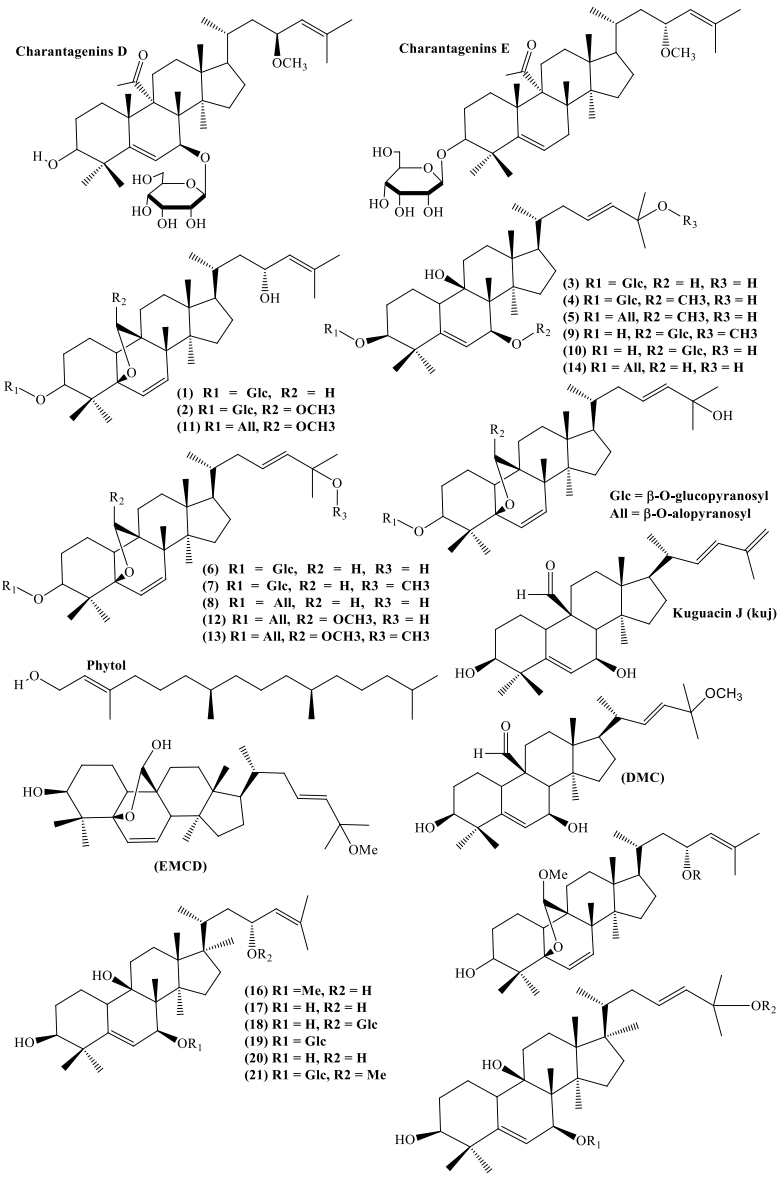

Figure 3. Chemical structures of some terpenoids identified in *Momordica charantia* L.

extracts of *M. charantia* (Ning-Ping, 2013). Supercritical carbon dioxide (SC-CO_2) with ethanol as co-solvent has been used to extract flavonoids from the *M. charantia* fruit, and the influence of parameters such as temperature, pressure and extraction time were verified (Shan et al., 2012). The experimental data showed that pressure, temperature and time had statistically significant effects on the extraction yield, indicating that extraction with SC-CO_2 and ethanol may be an alternative method for the selective extraction of flavonoids from *M. charantia*.

Bitter melon seed oil was extracted with SC-CO_2 to verify the best extraction operating conditions, and the highest yield was obtained at 250 bar/50°C in 100 min report, extraction with SC-CO_2 was performed to improve the efficiency and selectivity of fatty acid extraction, in which the authors found the presence of 42.60% of conjugated linolenic acid (ClNa, cis-9, trans-11, trans 13-18: 3) and 13.17% of conjugated linoleic acid (CLA, cis-9, trans 11-18: 2) (Xu et al., 2016).

BIOLOGICAL ACTIVITIES OF *M. CHARANTIA*

The biological activities of plants traditionally used in folk medicine or as functional foods are the primary motivator for further research (Sihoglu and Tepe, 2015; Heinrich et al., 2016). Several studies on the biological activity of this

Table 3. Chemical composition of fatty acids identified in *Momordica charantia* L.

Fatty acids	Reference
Palmitic, stearic, myristic, pentadecanoic, arachidic, α-linolenic, linoleic, oleic and palmitoleic acids.	Sarkar et al. (2013)
Capric, lauric, palmitic, stearic, oleic, linoleic and arachidic acids.	Ahmad et al. (2012)
Palmitoleic, arachidic, docosanoic, oleic, stearic, heneicosanoic, α-linolenic, myristic, nonadecanoic, lauric, decanoic, linoleic, tridecanoic and pentadecanoic acids.	Sarkar and Barik (2015)
Palmitic, stearic, oleic, linoleic, α-eleostearic, arachidic and gadoleic acids.	Gölükçü et al. (2014)
Decanoic, lauric, tridecanoic acid, myristic, pentadecanoic, palmitoleic, palmitic, heptadecanoic, α-linolenic, nonadecanoic, heneicosanoic, docosanoic and tetracosanoic acids.	Mukherjee and Barik (2014)
Tridecanoic, myristic, palmitic, stearic, oleic, arachidic, α-linolenic, henicosanoic, behenic and lignoceric acids.	Saini et al. (2017)
α-Eleostearic and stearic acids.	Yoshime et al. (2016)

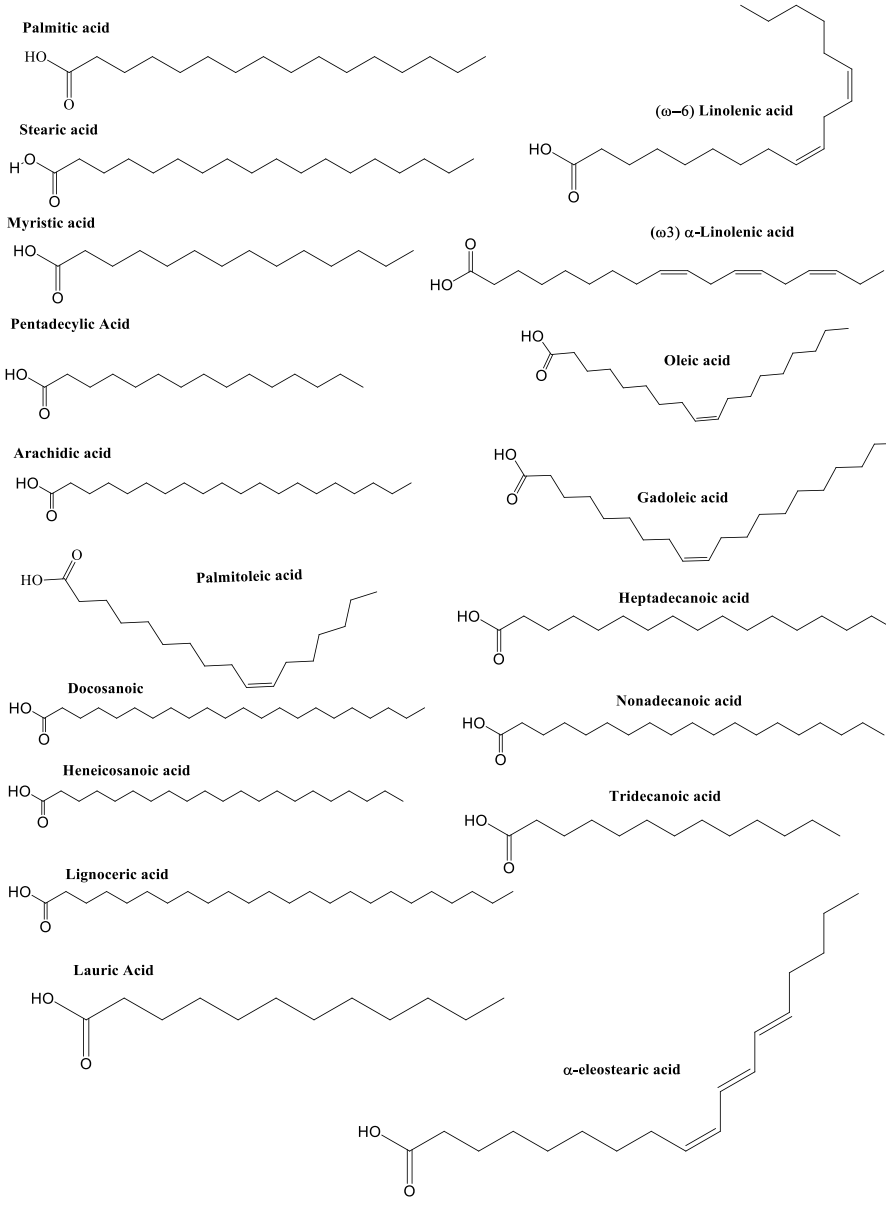

Figure 4. Chemical structures of fatty acids identified in *Momordica charantia* L.

Table 4. Chemical composition related to the phenolic compounds identified in *M. charantia* L.

Phenolic acids	Flavonoids	Reference
Gallic, chlorogenic, caffeic and ellagic acids.	Catechin, epicatechin, rutin, quercitrin, isoquercitrin, quercetin and kaempferol.	Shodehinde et al. (2016)
Gallic, protocatechuic, tannic, p-hydroxylbenzoic, vanillic, caffeic, chlorogenic, p-coumaric and ferulic acids.	Epigallocatechin, epicatechin, gallocatechin gallate, quercetin and kaempferol.	Choi et al. (2012)
Protocatechuic, gallic, chlorogenic, syringic, caffeic, ferulic, 3- coumaric and 4- coumaric acids.	Catechin, rutin, luteolin-7-O-glycoside, naringenin-7-O -glycoside, apigenin- 7-O –glycoside, myricetin, quercetin, kaempferol, luteolin and apigenin.	Kenny et al. (2013)
Gallic, chlorogenic, caffeic, *p*–coumaric, ferullic acids.	Catechin	Lee et al. (2016)
Caffeic, *p*-coumaric, ferulic, *o*-coumaric, chlorogenic, *m*-coumaric, *p*-hydroxybenzoic, gallic, protocatechuic, β-resorcylic, vanillic, syringic, gentisic, salicylic, veratric, *t*-cinnamic and homogentisic acids.	Myricetin, quercetin, kaempferol, catechin, rutin, hesperidin, naringenin, biochanin a, and naringin.	Thiruvengadam et al. (2014)

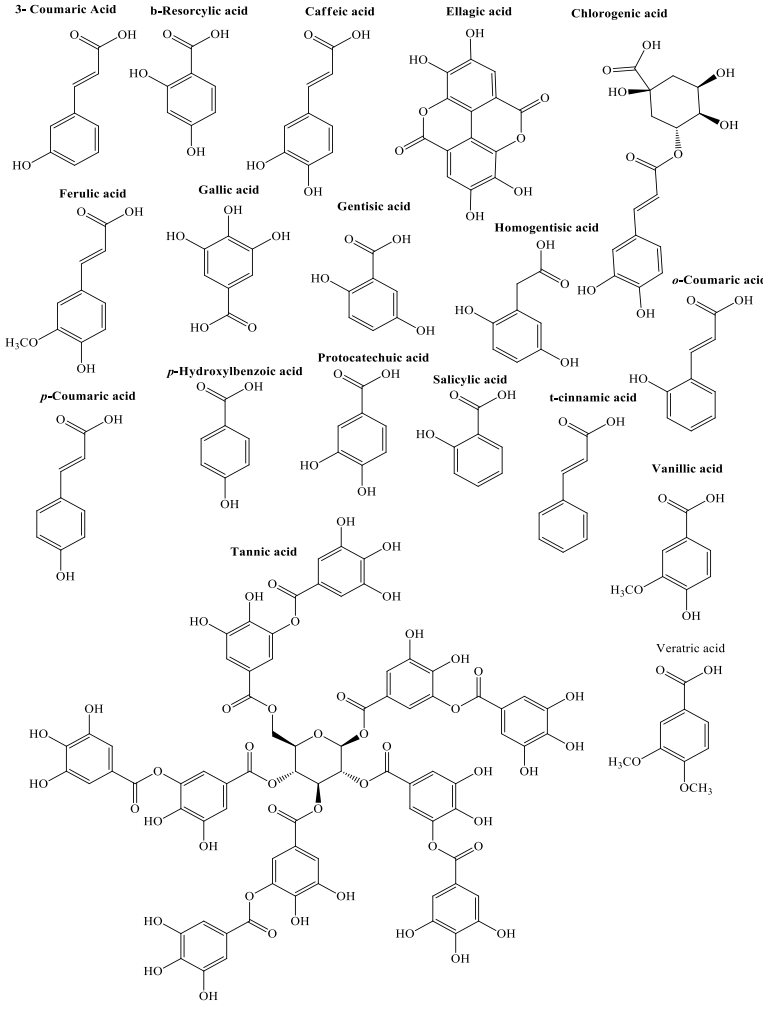

Figure 5. Chemical structures of phenolic acids identified in *Momordica charantia* L.

plant have been published. In this section, the main studies evaluating the biological activities of *M. charantia* were discussed.

Antidiabetic activity

Diabetes is defined as a group of metabolic diseases

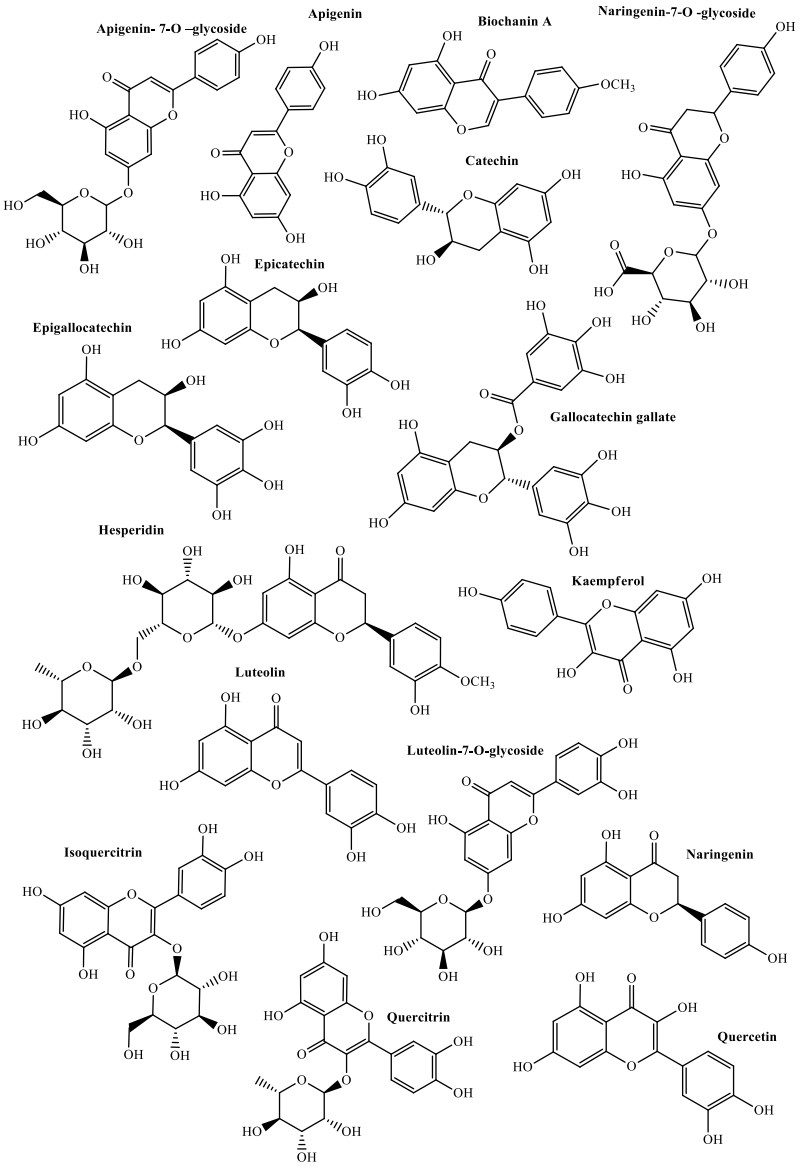

Figure 6. Chemical structures of flavonoids identified in *Momordica charantia* L.

characterized by hyperglycemia caused by defects in insulin secretion, insulin action or both. Chronic (Xu et al., 2014). In addition, the oils showed a high concentration of linolenic and stearic acids. In another hyperglycemia of diabetes is associated with long-term damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels (Freinkel et al., 2014; Lo et al., 2014). This disease is common throughout the world, and it is reported that people with this pathology seek alternative treatment with *M. charantia* and other medicinal plants to complement their therapy (Joseph and Jini, 2013).

The extract of *M. charantia* was shown to reduce blood glucose level in rats (Perumal et al., 2015). These results might be related to a study indicating that the extracts of *M*. *charantia* inhibited the activity of α-amylase and α-glucosidase, reducing blood glucose levels (Poovitha and Parani, 2016). These results can be corroborated by other numerous studies that report antidiabetic activity of the São Caetano melon (Blum et al., 2012; Chaturvedi, 2012; Hasan and Khatoon, 2012; Xu et al., 2015; Mishra et al., 2015; Tayyab and Lal, 2016; Yousaf et al., 2016). Thus, this medicinal herb could potentially be used to treat diabetes. In another scientific report, the effects of *M*. *charantia* on insulin resistance in diabetic rats were analyzed. The results show that the extract exerts its preventive effects on insulin resistance through the modulation of phospho-NF-κB and phospho-c-Jun N-

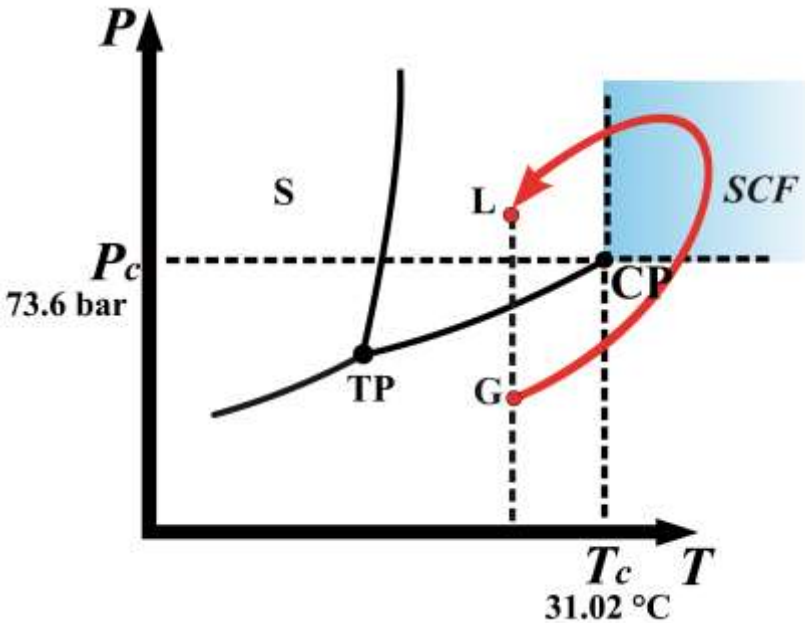

Figure 7. The *pV T* surface for equilibrium states of CO_2. The solid (S) line *GL* is a thermodynamic path where the continuous transformation of the gas (G) into a liquid (L) does not require the phenomenon of condensation to cross the liquid vapor coexistence curve at constant temperature, triple point (TC), critical pressure (Pc), critical temperature (Tc) and critical point (CP). Phase diagram of CO_2, adopted from Zappoli et al. (2015).

Table 5. Critical properties of different compounds. Adapted from Tabernero et al. (2012).

Critical properties of different compounds	Tc (°C)	Pc (bar)
Ethylene	9.35	51
Carbon dioxide	31.02	73.6
Ethane	32.45	49
n-Propane	93.85	43
Chlorotrifluoromethane	111.75	39
Ammonia	132.5	113
Methanol	240.55	79
Benzene	289.05	49
Water	374.45	221

terminal kinase (JNK) pathways (Yang et al., 2015).

Despite these results, there are some reports that *M. charantia* does not have sufficient effect on type 2 diabetes mellitus (Ooi et al., 2012). One study showed that *M. charantia* extract had hypoglycemic effects, and suggested that it has potential to increase insulin sensitivity in rats with type 2 diabetes, instead of protecting against β-cell dysfunction (Wang et al., 2014). However, the majority of studies analyzed in this review indicated that *M. charantia* may act as a complementary treatment for diabetes (Ahmad et al., 2012; Lo et al., 2013; Chhabra and Dixit, 2013; Singh et al., 2014; Duraiswamy et al., 2016; Ekezie et al., 2016; Mahmoud et al., 2017; Wang et al., 2017).

Neuroprotective activity

Cerebral ischemia usually occurs through an obstruction of the arteries in the brain. Although, therapies for restoring blood flow to brain tissues are effective, reperfusion in the ischemic brain leads to a series of pathophysiological changes (Hua et al., 2015), and is a significant cause of morbidity and mortality in patients with aneurysmal subarachnoid hemorrhage (ASAH) (da Costa et al., 2015). The immune response is a great

contributor to stroke pathology, and inflammation occurs due to the involvement of peripheral leukocytes and resident immune cells in the brain (Benakis et al., 2015).

A recent study showed that *M. charantia* could inactivate reactive oxygen species (ROS) present in the area damaged by intracerebral hemorrhage, significantly attenuating thrombin-induced neuronal death in primary hippocampal neurons (Duan et al., 2014). In addition, *M. charantia* inhibited the activation of c-Jun N-terminal kinase 3 caused by intracerebral hemorrhage. These results corroborate those obtained by Gong et al. (2015) who classified *M. charantia* as a plant that has neuroprotective activity, inhibiting the effects of c-Jun N-terminal kinase signaling during ischemia/reperfusion injury. These few scientific reports regarding the neuroprotective activity of *M. charantia* are very important to direct future work in the scientific community.

Obesity reduction

Obesity is considered a worldwide epidemic and is directly related to coronary diseases and diabetes (Yaghootkar et al., 2014; Scherer and Hill, 2016). It can also cause chronic inflammation of adipose tissue (Bluher, 2016). *M. charantia* is also known for its ability to reduce body weight gain (Bao et al., 2013). Therefore, it may be an alternative method for therapies in the control of obesity.

Wang and Ryu (2015a) analyzed the effects on obesity and lipid profile of rats fed fatty acid-rich extracts of *M. charantia*. They found that this plant was anti-obesogenic, and had the ability to modulate lipid proliferation, decrease body weight gain, visceral tissue weight, plasma and lipid concentrations, and lipid peroxidation in metabolism. The weight loss may be related to the increased energy of the rats, demonstrating that a diet rich in *M. charantia* extracts may aid in the treatment of obesity (Bian et al., 2016).

Recent clinical trials have shown that plant extracts, including the São Caetano melon extract, have therapeutic potential against diabetes and metabolic dysfunction related to obesity in animals (Chen et al., 2012; Alam et al., 2015). The effects of this plant on mitochondrial function, during the accumulation of liver fat associated with obesity, were identified by Xu et al. (2014). These authors suggested that *M. charantia* reduces inflammation and oxidative stress, modulates mitochondrial activity, suppresses the activation of apoptosis and inhibits the accumulation of lipids during the development of fat in the liver.

In this context, several articles have shown that *M. charantia* suppresses weight gain in animals, primarily rats (Zeng et al., 2012; Bin and Liu, 2013; Yu et al., 2013; Shih et al., 2014; Wang and Ryu, 2015b; Bai et al., 2016). Some results show that the extracts of *M. charantia* improve the oxidation of hepatic triacylglycerol, which may be one of the mechanisms involved in the decrease of body fat concentration (Senanayake et al., 2012).

Anticancer effect

In many parts of the world, cancer is a large public health problem and represents one of the leading causes of death. In the future, cancer deaths will likely overcome deaths caused by cardiovascular diseases (Siegel et al., 2015). Estimates indicate that one out of four deaths in the United States are due to cancer (Siegel et al., 2013). The main types of cancer are lung, breast and colorectal cancers, and those that cause death most are lung (1.6 million deaths), liver (745,000 deaths) and stomach (723,000 deaths) cancers (Ferlay et al., 2015). However, such deaths can be avoided if the cancer is diagnosed and treated early.

Cancer treatment is generally time-consuming, which risks patients' psychological and physical health (Stanton et al., 2015). In addition, there is risk of acquiring chemoresistance, a great obstacle in clinical management. Therefore, alternative therapies with the use of drugs obtained from medicinal plants including *M. charantia* are of great importance (Comhaire, 2014; Yung et al., 2016).

M. charantia is known to inhibit the growth of cancer cells by inducing of apoptosis (Dandawate et al., 2016). For example, the protein MAP30 present in São Caetano melon seeds, has an effect on liver cancer, HepG2 hepatocellular carcinoma models of human hepatoma and rat cells (Fang et al., 2012). The authors also suggested that the seeds would work as a relatively safe agent for prophylaxis and treatment of this cancer. Other studies also reported the anticancer activity of *M. charantia* (Brennan et al., 2012).

In other studies, the anticancer activity of São Caetano melon was linked to other chemical compounds such as triterpenoids. The effects of Kuguacin J (Kuj), a component of *M. charantia* obtained from the extract of its leaves, were evaluated, and the results showed that this secondary metabolite has a strong inhibitory effect on the growth of prostate cancer in PC3 cell line, with inhibition of up to 63% of cell growth, with no adverse effect on the patient (Pitchakarn et al., 2012). The anticancer activity of terpenoids and sterols found in *M. charantia* are also reported by other authors (Wang et al., 2012; Zhang et al., 2012; Weng et al., 2013). The literatures indicates that *M. charantia* inhibits many types of cancer, including hepatocellular carcinoma (Zhang et al., 2015), lung (Fan et al., 2015), bladder (Lin et al., 2016), colon (Dia and Krishnan 2016) and breast (L. yuan Bai et al., 2016) cancers. The mechanisms of action of bioactive compounds on cancer cells may be related to apoptosis through the regulation of enzymes with a cysteine residue capable of cleaving other proteins

(caspase) and mitochondria (Li et al., 2012; Manoharan et al., 2014; Minina et al., 2017).

Antioxidant activity

There is growing interest in antioxidants of natural origin because of their potential beneficial effect on human health (Gülçin, 2012). Natural antioxidants are very important for maintaining quality of life (Shahidi and Ambigaipalan, 2015), because the human body produces ROS, which can damage cellular structures such as carbohydrates, nucleic acids, lipids and proteins and alter their function, leading to the development of various degenerative diseases (Birben et al., 2012).

Therapeutic agents for the treatment of diseases caused by oxidative stress and metabolic disorders are well known. *Momordica* species have shown good results regarding their antioxidant activity (Nagarani et al., 2014) and may prevent oxidative stress (Sagor et al., 2015). In this way, they may also exert cardioprotective activity (Raish, 2017). Rammal et al. (2012) found that *M. charantia* has the capacity to eliminate ROS; they concluded that the consumption of 100 g of fruit can provide up to 145 ± 1.16 mg of a compound equivalent to vitamin C. Others analyzed the effects of *M. charantia* extracts on the $DPPH^+$ radical, and found an IC_{50} value of up to 0.46 mg/mL (Shan et al., 2012). The antioxidant activities of the extracts of *M. charantia* may be directly related to the method of extraction used to obtain the bioactive compounds. For example, extracts rich in phenolic compounds are shown to have antioxidant activity in different analytical methods: 2,2-diphenyl-1-picrylhydrazyl ($DPPH^+$); 2,2'-Azino-bis (3-ethylbenzthiazoline-6-sulfonic acid) ($ABTS^{\bullet+}$), and potential iron reducer (FRAP) (Choi et al., 2012; Hamissou et al., 2013; Kenny et al., 2013; An, 2014; Aljohi et al., 2016; Ri Lee, 2016; Hani et al., 2017). In addition to the phenolic compounds mentioned above, some polysaccharides present in *M. charantia* exert antioxidant activities (Liu et al., 2014; Raish 2017). In general, this species has significant antioxidant activity, and can act as functional food aiding in the control of oxidative stress (Sin et al., 2013).

Anti-inflammatory activity

Numerous medicinal plants present scientific evidence of anti-inflammatory effects (Alhakmani et al., 2013; Sagnia et al., 2014; Dzoyem and Eloff, 2015). Among the plant species traditionally used for the control of inflammatory diseases, *M. charantia* can be highlighted. *M. charantia* was found to improve the biological responses against inflammation in rats with sepsis (Chao et al., 2014). Other authors also report the anti-inflammatory activity of this plant (Nagarani et al., 2014; and Liaw et al., 2015). Another report showed that *M. charantia* had anti-inflammatory activity on adipose tissue cells (Bao et al., 2013). Thus, there is great interest in new studies searching for active molecules with anti-inflammatory activity from this plant.

Antimicrobial activity

There is also evidence that the ethanolic extract of *M. charantia* presents low cytotoxicity, with antiepimastigotes and antifungal activities. 46.06 µg/mL was shown to effectively kill 50% of parasites. The extract showed effect similar to metronidazole, which may represent an alternative for the treatment of candidiasis (Santos et al., 2012). Extracts of *M. charantia* also had antimicrobial effects against the microorganisms: *Pasteurella multocida*, *Staphylococcus aureus* and *Salmonella typhi* (Mahmood et al., 2012). The effects of extracts of *M. charantia* on Gram-positive and negative bacteria and fungi are shown in Table 6.

The antimicrobial activity of *M. charantia* L. extract against *S. aureus*, *Bacillus subtilis*, *Escherichia coli* and *Pseudomonas aeruginosa* was evaluated. The extracts at concentration of 100 mg/ml were efficient to inhibit the growth of all bacteria, with different degrees of susceptibility (Mada et al., 2013). Other studies confirm that this medicinal plant has good antimicrobial activities (Ozusaglam and Karakoca, 2013; Shoba et al., 2014; Birla, 2016; Saengsai et al., 2015).

Malaria is one of the deadliest diseases in Africa (Murray et al., 2012). The infection is caused by *Plasmodium falciparum.* However, one of the major problems faced by health professionals is the resistance of parasites to antimalarial drugs. One way to avoid this resistance is by using bioactive compounds from medicinal plants such as *M. charantia*, which represents a potential new source of antimalarial drugs (Olasehinde et al., 2014). Pereira et al. (2016) demonstrated that *M. charantia* has antiprotozoal activity. The methanolic extract of *M. charantia* had an antimalarial effect at doses above 200 mg/kg (Akanji et al., 2016). Other works also reports the antimalarial activity of this plant (Adeyi et al., 2016; Syamsudin et al., 2017). These studies have great relevance for tropical countries, because they contribute to the diffusion of knowledge on alternative methods of controlling diseases caused by parasites such as *P. falciparum.* The antimalarial activity of *M. charantia* can be related to the synergistic and antagonistic effects of chemically active metabolites present in the extracts, such as alkaloid, flavonoid, saponin, tannin, quinone, steroid, triterpenoid and coumarine (Abdillah et al., 2015).

CONCLUSIONS

This review showed that *M. charantia* presents several

Table 6. The effects of different extracts of M. charantia on fungi and bacteria.

Fungi name	Bacteria name	Reference
Candida albicans, Candida neoformans, Candida glabrata, Candida epicola	*Staphylococcus aureus, Staphylococcus albus, Corynebacterium rubrum, Listeria monocytogenes, Micrococcus flavus, Pseudomonas aeruginosa, Pseudomonas stutzeri, Pseudomonas pictorum, Pseudomonas putida, Pseudomonas testosteroni, Pseudomonas syrigae*	Rakholiya et al. (2014)
Candida albicans	*Bacillus subtili, Staphylococcus aureus, Streptococcu pyogenes, Escherichia coli.*	Agyare et al. (2014)
Aspergillus niger subsp, Aspergillus flavus subsp. and *Penicillium* spp.	*Escherichia coli, Pseudomonas* spp., *Bacillus* spp., *Staphylococcus* spp.	Ajitha et al. (2015)
Not reviewed	*Pseudomonas aeruginosa, Staphylococcus aureus, Enterococcus faecalis, Salmonella typhimurium* and *Salmonella enteritidis*	Chang et al. (2017)
Not reviewed	*Escherichia coli, Pseudomonas* sp. and *Salmonella* sp.	Sathya et al. (2012)
Not reviewed	*Enterococcus faecalis* and *Aeromonas hydrophila.*	Malaikozhundan et al. (2016)
Candida albicans, Candida tropicalis and *Candida krusei.*	Not reviewed	Santos et al. (2012)

biological activities, indicating that this species can be a natural alternative to complement the treatment of many diseases and can also act as a bio-herbicide. In addition, its chemical composition is very diverse, and in recent years, new bioactive compounds have been identified, including 25ξ-isopropenylchole-5,(6)-ene-3-O-β-D-lucopyranoside and 28-O-β-D-xylopyranosyl. The use of alternative extraction techniques such as supercritical CO_2 extraction, which can also be modified with co-solvents (ethanol or water), may help in the discovery of new secondary metabolites present in this species.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

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