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Chemical composition and biological activities of *Momordica charantia* leaves: a review

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Abstract *Momordica charantia* is a climbing plant popularly known as melon-de-São-Caetano, erva-de-São-Vicente, fruit-de-snake, melonzinho and gourd-de-São-Caetano. Its traditional use in folk medicine, associated with a wide range of therapeutic effects—such as antioxidant, anthelmintic, anti-inflammatory, antifungal, gastroprotective, hepatoprotective and antihyperglycemic activities—has aroused scientific interest and motivated the performance of pharmacological analyses to investigate and prove such properties. Thus, the objective of the present study was to carry out a systematic review (SR) composed of studies to analyze the chemical composition and biological activities of *M. charantia* leaves. The systematic review followed the PRISMA protocol, with searches in the Lilacs, PubMed and SciElo databases, using descriptors related to *M. charantia* leaves. Original non-clinical articles, published between 2000 and March 2020, that evaluated the chemical composition and biological effects of the plant were considered. Initially, 542 publications were identified, resulting in 479 after removal of duplicates. After screening and exclusion based on specific criteria, 131 articles were fully evaluated, with 42 included in the final analysis. Brazil, Japan, and China accounted for the largest number of publications. Despite this, 92% of the studies demonstrated adequate statistical treatment and information on doses and routes of administration, while 54% mentioned submission to the animal ethics committee. Hypotheses and objectives were clearly described in 69% of the studies. Randomization and blinding were indicated as essential to reduce bias in nonclinical studies. The systematic review confirmed the significant pharmacological potential of *M. charantia* leaves, driven by triterpenoids, flavonoids, saponins, and tannins. Their activities point to promising clinical applications in three areas: combating resistant infections (antimicrobial effect), controlling metabolic diseases

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(antihyperglycemic potential), and acting as a chemopreventive agent (antitumor and antioxidant actions). The low reported toxicity supports their pharmaceutical viability. However, the analysis highlighted a critical need for rigorous methodological standardization in non-clinical studies (adherence to ethics, blinding, randomization) to reduce bias and guarantee data reliability. Comprehensive phytochemical, pharmacological, and toxicological studies are thus indispensable. Targeted investment in research and standardization is vital to transform this proven medicinal potential into a globally validated and safe therapeutic product.

Keywords *Momordica charantia* · Melon of São Caetano · Pharmacological effect

ABBREVIATIONS

AAI	Antioxidant activity index
ABTS	(2,2′-Azino-Bis (3-Ethylbenzothiazoline-6-Sulfonic Acid)
ALT	L-Alanine transaminase
AST	L-Aspartate transaminase
ATCC	American type culture collection
BHA	(2,3-Tert-Butyl-4-HydroxyAnisole)
BHT	Butylated hydroxytoluene
CD	Circular dichroism
CFU	Colony-forming units
CUPRAC	Cupric ions Cu^{2+} Reducing antioxidant power
DMBA	7,1 2-Dimethyl-benzo anthracene
DPPH	2,2-Diphenyl-1-picrylhydrazyl
DTA	Differential thermal analysis
DXR	Doxorubicin
ESI-EM	Electrospray ionization
Fe^{2+} – TPTZ	Ferrous tripyridyltriazine complex
Fe^{3+} – TPTZ	Ferric tripyridyltriazine complex
FRAP	Ferric reducing/antioxidant power
GPx	Glutathione peroxidases
HA	Hydrochloric acid
HB	High bioactivation cross
HPLC	High performance liquid chromatography
HPLC–DAD	High liquid chromatography performance coupled to diode array detector
IC_{50}	Median inhibition concentration
LC–MS	Liquid chromatography with mass spectrometry
MDA	Malon dialdehyde
MeOH	Methanol
MIC	Minimal inhibitory concentration
MS	Mass spectrometry
MTT	(3-(4,5-Dimethylthiazol-2yl)-2,5-diphenyl tetrazoline bromide)
n-BuOH	Butanol
NMR	Nuclear magnetic resonance
NO	Nitric oxide
ODS	Octadecyl silica gel
ORAC	Oxygen radical absorbance capacity
PYR-CG/MS	Pyrolysis coupled to gas chromatography and mass spectrometry
SMART	Somatic mutation and recombination test
SNP	Sodium nitroprusside
SOD	Superoxide dismutase
ST	Standard crossing
TEAC	Trolox equivalent antioxidant capacity
TEAC	Trolox equivalent antioxidant capacity
TGF-β1	Transforming growth factor
TLC	Thin layer chromatography
TRAP	Total radical -trapping antioxidant parameter
UV	Ultraviolet radiation
ZI	Zone of inhibition

Introduction

The leaves of *Momordica charantia*, popularly known as bitter melon, are widely used in traditional medicine to treat various diseases. Among the most common uses are the management of conditions such as diabetes, hypertension, inflammation, infections and gastrointestinal problems (Dah-Nouvlessounon et al. 2023).

Momordica charantia is widely used in folk medicine for its various biological and pharmacological properties, such as antioxidant (Kubola & Siriamornpun 2008), anthelmintic (Pereira et al. 2016), anti-inflammatory (Ganesan et al. 2008), antifungal

(Braga et al. 2007; Wang et al. 2016), gastroprotective (Polat et al. 2018), hepatoprotective (Pereira et al. 2010) and antihyperglycemic.

The species *M. charantia* is a vine native to Asia and Africa that has shown good adaptation to the tropical climate of Brazil, being popularly known as São Caetano melon, São Vicente herb, snake fruit, little melon, bitter gourd, among other denominations (Alzugaray & Alzugaray 1983; Xiong et al. 2009).

The Cucurbitaceae family is the largest in the order Cucurbitales, with about 95 genera and 965 species (Christenhusz & Byng 2016). It is considered one of the most important families of plants used for the production of food and fibers (Montes-Hernandez & Eguiarte 2002; Cardoso 2003). Many representatives of the Cucurbitaceae family have great economic importance, including several cultivated species, whose use of their edible fruits and seeds stands out in the food industry.

Chemical groups frequently found in this species include glycosides, saponins, alkaloids, triterpenes and steroids (Raman & Lau 1996). Several substances have already been identified in plant derivatives obtained from *Momordica charantia* such as momorcarins, momordenol, momordicillin, momordicins, momordicinin, momordina, momordolol, charantine, charina, cryptoxanthin, cucurbitines, cucurbitacins, cucurbitans, cycloarthenols, diosgenin, among others (Xie et al. 1998; Yuan et al. 1999; Murakami et al. 2001; Parkash et al. 2002), which makes this species relevant for the search for new bioactive compounds, however, most studies are related to plant derivatives of the fruit and seeds of *Momordica charantia*, which motivated us to study the leaves of this species.

The choice to focus exclusively on the leaves of *M. charantia* is justified by the lack of knowledge in studies that systematize information about this specific part of the plant, which is often overshadowed by research focused on fruits and seeds. In addition, the leaves are relevant in traditional use due to their potential therapeutic properties, and their production is more sustainable, reinforcing their value as a promising source for pharmacological exploration.

Therefore, the objective of this work was to carry out a bibliographic survey about the chemical composition and biological activities of the leaves of *Momordica charantia*.

Methodology

Search strategy

The systematic review (SR) was performed according to the preferred reporting items for SR and meta-analyses—PRISMA (Moher et al. 2009).

The search for articles was carried out from April 9 to 30, 2020, consulted in the electronic databases: Lilacs (Latin American and Caribbean Literature on Health Sciences), PubMed (US National Library of Medicine) and SciElo (Online Scientific Electronic Library) (Fig. 1) using the descriptors: "*Momordica charantia*" and the combination of the term "*Momordica charantia* and leaves", in order to track only articles that studied the leaves of *Momordica charantia*.

Advanced searches were performed in the electronic databases mentioned above using search filters as a specific search field [Title] and year of publication [2000—2020], with the following descriptor combinations: (*Momordica charantia*) or (*Momordica charantia* AND leaves). To perform the bibliographic search, filters were used in the [Title] field of the Lilacs, PubMed and SciElo databases, with the aim of identifying specific articles related to the species *M. charantia*.

Selection of studies

The inclusion criteria used for this systematic review include original articles with an experimental design (pre-clinical trials), considering all the works that carried out primary studies to evaluate the chemical composition and biological or pharmacological activities (in vivo and in vitro) of extracts, fractions, or compounds from the leaves of *M. charantia*, published between the years 2000 to March 2020, written in Portuguese, English and Spanish.

For the exclusion criteria, literature review articles, abstracts, book chapters, case reports, articles not available for download, articles that did not present phytochemical or biological activity data and articles that used other parts of the plant that were not either the leaves or that used leaves mixed with other parts to obtain a vegetable derivative.

The advanced search for articles by applying the filters of the electronic scientific databases was carried out independently by two researchers (TFR and

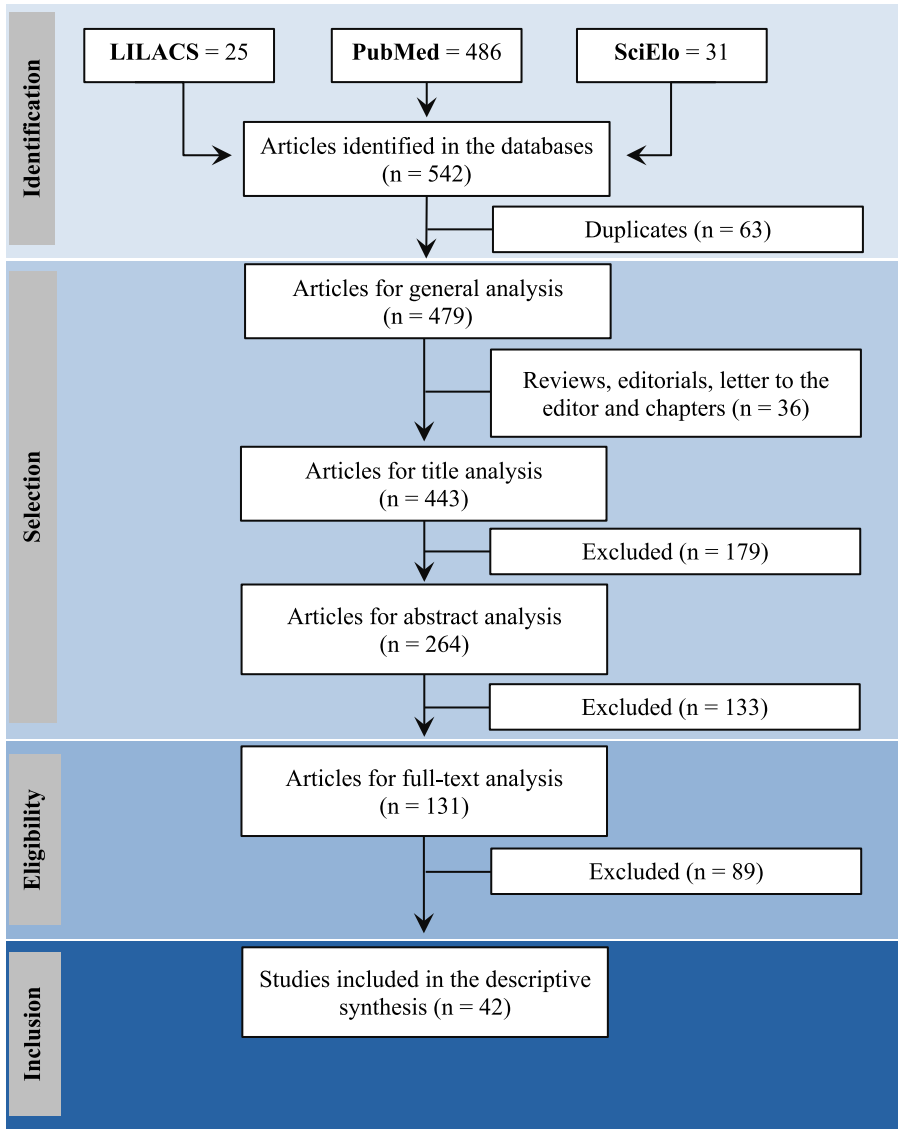


Fig. 1 Flowchart of the process of searching, sorting and selecting articles

CAFM), so that both could compare the results found. After identification, the screening of selected articles was performed by evaluating the title and abstract using the eligibility criteria. Subsequently, the selected publications underwent a complete reading, which is an essential step to confirm the inclusion criteria.

Data extraction and processing

The resulting articles were carefully reviewed in order to identify studies meeting the inclusion criteria and containing the necessary information for extracting phytochemical data and biological and pharmacological activities from the leaves of *M. charantia*.

Data were collected in pre-defined standardized forms containing article information (first author, year and place of study), methods (animal models, type of extraction, doses or concentrations and route of administration and techniques used to analyze chemical constituents) and results (main results and action mechanisms evaluated).

Methodological quality

In vivo studies ware assessed using a checklist adapted from previous reports (Hooijmans et al. 2014). The selected articles were examined for the randomization of treatment allocation, application of adequate statistical treatment, treatment of study groups, evaluation of blinded results, information on doses or concentrations and respective routes of administration of the tested substances and clarity in the objectives and results obtained by the respective works. Studies that reported randomization of animals, blinding and adequate statistical treatment were considered to be of higher methodological quality.

Results and discussion

General results

In the initial search, a total of 542 published works were identified, 25 in the LILACS database, 486 in PubMed and 31 records in SciElo. Of this total, 63 articles were indexed in more than one database and were considered only once, resulting in 479 studies. After a general analysis of the works, 36 works were removed because they were systematic reviews, editorials, letter to the editor, chapters and abstracts, leaving 443 articles, where they were submitted to the reading of the title and exclusion of 179 because they were works carried out with other plant parts or other study areas. The reading of abstracts was performed in 264 articles, 133 were eliminated, leaving 131 articles for full-text analysis, and 89 more articles were excluded for not meeting the inclusion criteria.

The articles included in this SR were categorically analyzed in relation to the study site, year of publication and the main biological activities of *M. charantia* leaves.

The species *M. charantia* is widely recognized for its traditional use in medicinal and culinary practices, which has driven a significant volume of scientific publications addressing its chemical composition, biological properties, and pharmacological activities. However, most studies focus on specific parts of the plant, such as stems, fruits, seeds, or the entire plant, with investigation of other structures being less frequent. In this review, the search strategy, which used only three databases, one descriptor, and a Boolean combination, may have limited the retrieval of potentially relevant studies, despite the high number of articles initially evaluated (n = 542). The main pharmacological activities reported include antimicrobial, antitumor, and antioxidant actions. Activities such as antiparasitic, antigenotoxic, antimutagenic, antifertility, cardioprotective, hepatoprotective, and inhibition of digestive enzymes, such as α-amylase and β-glucosidase, were also observed, although less frequently.

Among the main findings of the studies included in this systematic review, the pharmacological activities of antimicrobial, antitumor and antioxidant stand out, in addition to investigations on acute, subchronic and reproductive toxicity.

Ethnobotany uses

Momordica charantia leaves are widely used in traditional medicine to treat a variety of conditions, including ulcers, constipation, diarrhea, measles, malaria, hypertension, and diabetes. They are also used to treat wounds, inflammation, and pain, reflecting their therapeutic properties. These applications are based on folk practices that attribute antidiabetic, anti-inflammatory, analgesic, and antimicrobial properties to the leaves, which have led to scientific exploration of their bioactive composition to validate and expand their potential for medicinal use (Dah-Nouvlessounon et al. 2023; Wang et al. 2017).

The leaves and fruits of *M. charantia* are consumed as vegetables for cooking, the fruits are also used in tea preparations and eaten raw when they are green or yellow. All parts of the species have a bitter taste, especially the fruits, which are emerald green in the green phase and turn yellow-orange when ripe (Grover and Yadav, 2004).

Momordica charantia has traditionally been used as a medicinal herb in several developing countries such as Brazil, China, Colombia, Cuba, Ghana, Haiti, India, Mexico, Malaysia, New Zealand, Nicaragua, Panama and Peru. Several medicinal properties are attributed to *M. charantia* as antidiabetic, anthelmintic, antimalarial, antiviral, healing and for the treatment of dysmenorrhea, ulcers, eczema, emmenagogue, galactagogue, gout, jaundice, renal calculus, leprosy, leucorrhoea, hemorrhoids, pneumonia, psoriasis, rheumatism and scabies (Grover and Yadav, 2004).

These ethnomedicinal uses are supported by the scientific evidence gathered in this review, which reveals a rich phytochemical composition of the leaves, including phenolic compounds, flavonoids and triterpenes, known for their antioxidant, anti-inflammatory, antimicrobial and antidiabetic properties. The data demonstrate that the leaves of the plant have significant antioxidant activity, corroborating its traditional use in the relief of diseases associated with oxidative stress, such as hyperglycemia and inflammatory disorders (Oyedapo and Araba 2001).

Furthermore, the reviewed pharmacological studies indicate that leaf extracts exert antidiabetic effects through mechanisms such as inhibition of α-glucosidase, reduction of serum glucose and modulation of hepatic enzymes related to glucose metabolism, which reinforces the traditional practice of their use in the control of diabetes (Sallau et al. 2018). Likewise, the antimicrobial effects observed in laboratory tests are in line with the popular use of the leaves in the treatment of skin infections and gastrointestinal problems, suggesting that traditional knowledge has a solid empirical basis (Brandão et al. 2016). Thus, the correlation between popular uses and scientifically validated bioactivities points to the potential of *M. charantia* leaves as a natural therapeutic resource, justifying their in-depth study for the development of phytotherapeutic agents.

Assessment of methodological quality

The evaluation of the methodological quality of the articles that are part of this SR is an essential step to obtain reliable results, it is important for the designed research to be carried out efficiently, correctly analyzed and in which the data are interpreted and presented in a correct and understandable way (Festing and Altman, 2002). In this regard, we carefully investigated the methodological quality of all in vivo studies using a standard checklist (Fig. 2).

The main results, outcomes and allocation were adequately described in all articles, however, no study reported the sample size calculations used in the studies, nor did they report on blinding for knowledge of treatments between the evaluated groups, as well as they did not report on blinding the evaluator of the results. The random selection of animals was reported in only 15% of the studies evaluated. Randomization and blinding procedures are extremely important to reduce the risk of bias in non-clinical studies. The hypotheses and objectives were clearly described in 69% of the evaluated works. The studies showed a satisfactory rate (92%) of adequate statistical treatment and information on doses and routes of administration. The works that reported submission to the ethics committee in the use of animals were 54%.

In vitro biological activities

In vitro studies have robustly established the potential of *M. charantia* leaves (Table 1) as a source of antimicrobial agents, acting against a variety of pathogenic microorganisms, including Gram-positive and Gram-negative bacteria and fungi. Biological efficacy demonstrates a strong correlation between the extraction solvent, the phytochemical profile, and the observed pharmacological activity (Ceballos et al. 2017).

Extracts with higher polarity, such as ethanolic and methanolic extracts, consistently exhibit a broad spectrum of action against reference strains and clinical isolates, including *Escherichia coli*, *Staphylococcus aureus*, and Candida species (*C. albicans*, *C. krusei*, *C. tropicalis*), with remarkably low minimum inhibitory concentrations (MICs), reaching 75 µg/mL (Mwambete et al. 2009; Santos et al. 2012; Ceballos et al. 2017).

Phytochemical screening of these polar extracts reveals the prevalence of classes of secondary metabolites essential for activity, such as flavonoids, alkaloids, tannins, and saponins (Costa et al. 2011; Ceballos et al. 2017). On the other hand, fractionation of the crude extracts demonstrates a segregation of activity, as observed with the ethyl acetate fraction, of intermediate polarity, which proved to be particularly effective against *E. coli* and *Bacillus cereus*, suggesting the concentration of compounds of medium polarity with high bioactivity (Costa et al. 2011).

The antimicrobial action of *M. charantia* leaf extracts is a manifestation of the synergy between its various secondary metabolites, giving them the advantage of multiple cellular targets. This is an important factor in the fight against microbial resistance, as it makes it difficult for the pathogen to adapt to a single agent (Ceballos et al. 2017). The main mechanism involves the destabilization of the bacterial cell membrane and wall, mediated primarily by tannins and phenolic compounds (Costa et al. 2011).

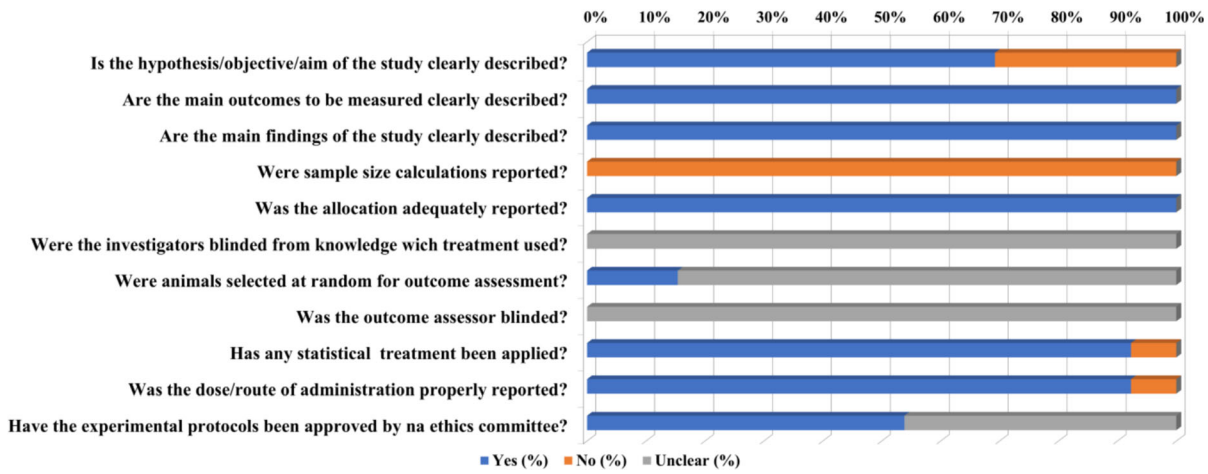


Fig. 2 Assessment of the methodological quality of included in vivo studies

Tannins are effective due to their ability to complex and precipitate vital proteins and enzymes on the surface and microbial cell wall, compromising structural integrity (Lomanowska et al. 2024). In addition, the chelation of essential metal ions deprives bacteria of crucial cofactors for their metabolism (Paterson et al. 2022).

In parallel, saponins contribute to the lytic effect (Desai et al. 2009). Their amphiphilic nature allows them to act as biological detergents, interacting with membrane lipids, causing the rupture of the lipid bilayer and osmotic collapse of the cell (Ceballos et al. 2017). Although alkaloids and flavonoids are also detected in bioactive extracts (Costa et al. 2011), their mechanisms of action contribute through potential intercalation into genetic material or interference in essential signaling pathways, reinforcing the polypharmacological nature of the crude extract (Mwambete et al. 2009). The combination of these effects ensures inhibition of bacterial and fungal growth, as demonstrated against strains of *E. coli* and *C. albicans* (Santos et al. 2012).

One of the most promising findings is the ability of the ethanolic extract of *M. charantia* (EEMC) to modify bacterial resistance when combined with conventional antibiotics. EEMC demonstrated a remarkable synergistic potentiating effect with aminoglycosides (such as amikacin, kanamycin, and gentamicin) against methicillin-resistant S. aureus (MRSA) strains (Coutinho et al. 2010).

This potentiating effect, comparable to that of chlorpromazine, a known inhibitor, suggests that the metabolites present in EEMC (probably alkaloids and/or flavonoids) act as efflux pump inhibitors (Coutinho et al., 2010). Efflux pumps are membrane proteins that actively eject the antibiotic out of the cell, constituting one of the main mechanisms of bacterial resistance (Poole 2007). By inhibiting these pumps, the extract allows the aminoglycoside to reach effective intracellular concentrations, restoring the bacteria's sensitivity to the drug. This mechanism represents a valuable therapeutic strategy to combat multidrug resistance (MDR) in hospital-acquired infections.

Anticancer effect in vitro

Analysis of in vitro data reveals that extracts from *M. charantia* leaves exert antineoplastic activity through pleiotropic mechanisms that converge towards the inviability and containment of cellular malignancy. Studies demonstrate direct cytotoxicity mediated by the induction of the intrinsic apoptosis pathway, characterized by DNA fragmentation, nuclear condensation, Caspase-3 activation, and cleavage of substrates such as DFF45 and PARP. These events are regulated by an increase in the pro-apoptotic protein Bax and a reduction in the anti-apoptotic protein Bcl-2 in various tumor cell lines (Li et al. 2012). Additionally, in androgen-dependent prostate cancer cells (LNCaP), it was observed that both the crude extract and the isolated triterpenoid Kuguacin J

Table 1 In vitro biological activities of *Momordica charantia* leaves

Extraction (extract or partition)	Dose/concentration (route of administration)	Kind of study (species, strain and/or cell line)	Biological activity	References
Ethanol extract	1.56, 3.12, 6.25, 12.5, 25, 50 mg	*Fasciola hepatic* (eggs)	Antiparasitic activity	Pereira et al. (2016)
Aqueous extract	25, 12.5, 6.25, 3.12, 1.56, 0.78, 0.39, 0.195 mg/mL	*E. coli* (ATCC 25922), *S. aureus* (ATCC 25923), *P. aeruginosa* (ATCC 27853) and *K. pneumoniae* (ATCC 4352)	Antimicrobian activity	Brandão et al. (2016)
Ethanol extract	1, 10, 100 µg/mL	*Trypanosoma cruzi* (Epimastigotes)	Antiparasitic, cytotoxic and antifungal activity	Santos et al. (2012)
	1, 10, 100 µg/mL	Macrophages (J774)		
	1024 a 8 µg/mL	*C. albicans* (ATCC 40227), *C. krusei* (ATCC 40147), *C. tropicalis* (ATCC 13803)		
Ethanol extract	32 µg/mL	*S. aureus* (SA358)	Modulating activity of antibiotic resistance	Coutinho et al. (2010)
Ethanol extract	10, 25, 50, 75, 100, 150, 200 µg/mL	(PLS10 cell line)	Anti-metastatic activity of prostate cancer	Pitchakarn et al. (2010)
Ethanol extract	8–512 µg/mL	*Staphylococcus aureus* (ATCC 12692), *Bacillus cereus* (ATCC 33018) Strains obtained at the clinic: *Staphylococcus aureus* (358), *Escherichia coli* (10,536) and *Escherichia coli* (27)	Antibacterial activity	Costa et al. (2011)
Ethanol extract	0–250 µg/mL	Androgen-dependent human prostate cancer cell (LNCaP)	Anticancer activity	Pitchakarn et al. (2011)
Ethanol extract	31.25, 62.5, 125, 250, 500, 1000 µg/mL	*S. aureus* (ATCC 25923), *S. epidermidis* (ATCC 12228), *K. pneumoniae* (ATCC 13883), *E. coli* (ATCC 25922), *P. aeruginosa* (ATCC 25922) and *P. aeruginosa* (ATCC 27853)	Antimicrobian activity	Ceballos et al. (2017)
Methanol extract	0.15 to 0.35 mg/mL	Human nasopharyngeal carcinoma cells (Hone-1), gastric adenocarcinoma cells (AGS), colorectal carcinoma cells (HCT-116) and lung adenocarcinoma cells (CL1-0)	Anticancer activity	Li et al. (2012)
Methanol extract	1000 mg/mL	Kidney bean leaf bioassay	Oviposition inhibition	Mekuria et al. (2005)
Methanol extract	10, 100 mg/mL	Melanoma cells (B16)	Melanogenesis inhibitory activity	Kikuchi et al. (2012)
Methanol extract	0.15, 0.3, 0.6, 1.25 mg/mL	Human lung adenocarcinoma cells (CL1-0, CL1-5 and A549) and Human embryonic cells (HEK293 and WI-38)	Antimetastasis activity	Hsu et al. (2012)
Methanol extract	0.2, 0.4, 0.6, 1.0 mg/µl	*Klebsiella pneumonia* (TK43/04), *Proteus vulgaris* (FN25/04), *Salmonella typhi* (LP06/04), *Cryptococcus neoformans* (MD81/04), *Pseudomonas aeruginosa* (ATCC27853), *Escherichia coli* (ATCC 25922), *Candida albicans* (ATCC 90028) and *Staphylococcus aureus* (ATCC25923)	Antimicrobian activity	Mwambete (2009)
Methanol extract	200 µg/mL	(B16-F10 cells)	Antioxidant activity, cellular protection and anti-melanogenic	Tsai et al., (2014)

Table 1 continued

Extraction (extract or partition)	Dose/concentration (route of administration)	Kind of study (species, strain and/or cell line)	Biological activity	References
Methanol extract	0.2, 0.4, 0.6, 0.8, 1.0 mg/mL	(α-glucosidase)	Inhibitor of alpha-glucosidase enzyme activity	Sallau et al. (2018)
Aqueous extract	1.25, 2.5, 5.0 mg/mL	*D. melanogaster* (somatic cells)	Genotoxic and antigenotoxic activity	Guterres et al. (2015)
Aqueous extract	0.25–10% (v/v)	Ovarian cancer cells (A2780cp, A2780s, C13, OV2008), immortalized ovarian epithelial cells (HOSE17-1 and HOSE 96–9-18)	Anticancer activity	Yung et al. (2016)
Aqueous extract	150 µL	Human blood cells	Reduction of blood viscosity	França et al., (2014)
Aqueous extract	0.1, 0.2, 0.4, 0.8, 1.6 mg/mL	DPPH, FRAP, hydroxyl radical scavenging activity, β-carotene-linoleate bleaching and total antioxidant capacity	Antioxidant activity	Kubola et al. (2008)
Aqueous extract Methanol extract	50–200 mg/mL	Antioxidant tests (ABTS)	Antioxidant Activity and ACE Inhibition	Shodehinde et al. (2016)
Aqueous extract and ethanol extract	5, 10, 15, 20, 25 mg/mL	α-amylase assay	Antioxidant and inhibitory activity of α-amylase and β-glucosidase enzymes	Chokki et al. (2020)
	1, 2, 3, 4, 5, 10 mg/mL	β-glucosidase assay		
	1000 µg/µL	β-carotene bleach		
	200 µg/mL	DPPH assay		
Hydroalcoholic extract	1, 2 e 5 mg/ml	Peripheral blood lymphocytes	Chromosome aberration assay	Lagarto et al. (2014)
Ethanol extract	3, 6, 12, 25, 50%	Nematodes (eggs and larvae)	Ovicidal and larvicidal activity	Cordeiro et al. (2010)
Ethanol extract	100, 500 mg/mL	*Leishmania braziliensis* (MHOM/BR/75/M2903)	Leishmanicidal Activity	Santos et al. (2013)
	200 mL	Cytotoxicity (fibroblasts NCTC929)		

promote cell cycle arrest in the G1 phase, an effect mechanistically associated with the reduction of cyclin (D1 and E) and cyclin-dependent kinase (Cdk2 and Cdk4) levels, concomitant with the upregulation of p21 and p27 inhibitors (Pitchakarn et al. 2011).

Regarding the ability to inhibit invasion and metastasis, cell assays indicate a significant suppression of cell motility and extracellular matrix degradation. The extract has been reported to inhibit the secretion of metalloproteinases (MMP-2 and MMP-9) and urokinase-type plasminogen activator (uPA), while increasing the expression of TIMP-2, an endogenous inhibitor of these enzymes (Pitchakarn et al. 2010). Delving deeper into molecular signaling in lung adenocarcinoma, it was shown that the extract blocks cell migration by inhibiting the phosphorylation of Src and FAK kinases, resulting in the downregulation of PI3K/Akt pathways and the stabilization of β-catenin, preventing epithelial-mesenchymal transition and the expression of MMPs. Notably, a phenotypic selectivity was observed where less invasive cells were more susceptible to direct cytotoxicity, while highly invasive cell lines were more sensitive to migration inhibition (Hsu et al. 2012).

From a metabolic and drug resistance standpoint, the extract demonstrated activation of AMP-activated protein kinase (AMPK) in ovarian cancer cells in a manner independent of AMP levels, with this activation being mediated by CaMKKβ. This metabolic modulation resulted in the suppression of the mTOR/p70S6K and AKT/ERK/FOXM1 pathways, with the inhibition of the FOXM1 transcription factor being crucial for sensitizing cisplatin-resistant cells, thus overcoming chemoresistance in vitro (Yung et al. 2016).

The correlation between chemical composition and biological effects suggests that cucurbit-type triterpenoids, such as Kuguacin J, are fundamental for inducing cell cycle arrest, apoptosis, and AMPK modulation (Pitchakarn et al. 2011), while phenolic compounds such as gallic acid and rutin, identified in the extracts, may act synergistically by conferring cytoprotection to normal cells against oxidative stress and inhibiting tyrosinase in melanocytes (Tsai et al. 2014). However, the extrapolation of these in vitro data faces significant methodological barriers. The lack of rigorous chemical standardization and the variability in the composition of extracts between different studies hinder the exact reproducibility of results, since the composition varies with the cultivar and geographical origin. In addition, the frequent use of supra-physiological concentrations in cell assays can trigger nonspecific effects that do not necessarily translate into achievable plasma levels in vivo (Pitchakarn et al. 2010).

Finally, the predominance of monolayer (2D) models limits the evaluation of the complex interaction with the tumor microenvironment, and the characterization of selectivity towards normal cells often lacks statistical robustness to accurately define the safe therapeutic window.

Other in vitro activities

Analysis of in vitro data from selected studies shows that extracts from *M. charantia* (MC) leaves possess a broad spectrum of biological activities, supported by a complex phytochemical matrix.

In the context of diabetes and hypertension, MC extracts have demonstrated the ability to inhibit key enzymes. The terpenoid-rich extract from MC leaves inhibited the α-glucosidase activity of Saccharomyces cerevisiae, presenting an IC_{50} of 1.60 mg/mL. Kinetic analysis via Lineweaver–Burk plot revealed that this extract acts as a partial mixed-type inhibitor, suggesting that the bioactive compounds can bind to both the free enzyme and the enzyme–substrate complex (Sallau et al. 2018). Corroborating this antidiabetic potential, dichloromethane and ethyl acetate extracts from MC leaves demonstrated α-amylase inhibition, while the methanolic extract exhibited potent β-glucosidase inhibition (76.74%) (Chokki et al. 2020).

In addition to glycemic control, the methanolic extract of MC leaves showed superior in vitro antihypertensive activity compared to the aqueous extract, evidenced by the inhibition of Angiotensin-Converting Enzyme (ACE), with an IC*50* of 109.63 µg/mL. This activity was attributed to the presence of phenolic compounds such as quercetin, catechin, and gallic, chlorogenic, and caffeic acids (Shodehinde et al. 2016).

The antioxidant capacity of MC leaves has been widely validated. Comparing different parts of the plant, the aqueous extract of the leaves showed the highest antioxidant activity in the DPPH radical scavenging and ferric reducing antioxidant power (FRAP) assays, surpassing the stem and fruit fractions. Antioxidant activity correlated positively with total phenolic content, with gallic acid and caffeic acid being the predominant compounds in the leaves (Kubola et al. 2008). Chloroform extracts of the leaves also effectively inhibited β-carotene bleaching, suggesting protection against lipid oxidation (Chokki et al. 2020).

Antiparasitic and ovicidal activity

In vitro studies have revealed significant antiparasitic properties. Extracts from MC leaves inhibited the embryonic development of *Fasciola hepatica* eggs, preventing the formation of miracidia. The n-butanol subfraction was the most potent, completely blocking embryogenesis at a concentration of 1000 µg/mL. Chemical analysis of this fraction confirmed the major presence of the flavonoid quercetin, which alone also demonstrated dose-dependent ovicidal activity (Pereira et al. 2016).

In addition, triterpenoid compounds isolated from the leaves, specifically momordicin II and the novel momordicin IV (cucurbitan glycosides), acted as oviposition deterrents for the leafminer fly *Liriomyza trifolii* in choice assays on bean leaves, confirming the

direct biological activity of these secondary metabolites (Mekuria et al. 2005).

Hemorheology and in vitro safety

In a biophysical approach, nanoparticles of MC extract, adsorbed or not on polyethylene glycol (PEG) microspheres, were able to reduce the blood viscosity of samples from diabetic patients to levels similar to those of normoglycemic individuals in ex vivo/in vitro assays (França et al. 2014).

Regarding toxicological safety at the cellular level, the hydroalcoholic extract of the leaves did not induce chromosomal aberrations in cultured human peripheral blood lymphocytes in vitro, neither in the presence nor in the absence of metabolic activation. Additionally, the extract fractions did not show relevant cytotoxicity against kidney (BGM) and liver (HEP2) cell lines, indicating a selective safety margin for the active compounds (França et al., 2014).

Strict analysis of in vitro data confirms that *M. charantia* leaves are a rich source of bioactive metabolites, including phenolics (gallic acid, caffeic acid, quercetin) and triterpenoids (momordicins). These compounds act synergistically to inhibit digestive enzymes and ACE, block renal oxidative damage, and interfere with the life cycle of parasites, without exhibiting significant genotoxicity or cytotoxicity in normal cell models (Chokki et al. 2020; Sallau et al. 2018; Pereira et al. 2016; França et al. 2014).

In vivo studies and metabolic correlation

M. charantia leaf is widely used in traditional medicine and has been the subject of several in vivo studies seeking to validate its pharmacological properties (Table 2). Analysis of assays in animal models reveals a spectrum of remarkable biological activities, which are intrinsically linked to its complex phytochemical profile, dominated by triterpenoids, flavonoids, and phenolic acids.

Antitumor and chemopreventive activity (triterpenoids)

The most robust findings demonstrate the potential of *M. charantia* leaves in combating cancer. The leaf extract demonstrated significant chemopreventive activity, reducing the incidence, yield, and tumor burden in DMBA-induced cutaneous carcinogenesis models in mice, in addition to reducing micronucleus formation and chromosomal aberrations (Agrawal et al. 2010).

The metabolic correlation for this effect was related to Kuguacin J, a cucurbit triterpene isolated from the leaf extract, which was identified as one of the main active agents (Pitchakarn et al. 2010). This metabolite was able to modulate the progression of prostate cancer (PC3 cells) in vivo (xenograft model), acting on the inhibition of cell invasion and the reduction of the activity of key enzymes in the metastatic process, such as matrix metalloproteinases (MMPs) (Pitchakarn et al. 2010).

Metabolic, hypolipidemic and antioxidant effects (flavonoids and phenolics)

In mouse models fed a high-fat diet, the ethanolic extract of the leaves exhibited marked hypolipidemic and antioxidant effects. Administration of the extract resulted in decreased serum levels of total cholesterol (TC), triglycerides (TG), and LDL-c, and increased HDL-c, in addition to reducing body fat index and weight (He et al. 2018).

This metabolic profile is correlated with the high concentration of phenolic compounds and flavonoids in the leaves (Shodehinde et al. 2016). These metabolites act as antioxidants, as demonstrated by the attenuation of MDA content (an indicator of lipid peroxidation) and the increase in SOD (superoxide dismutase) enzyme activity in liver tissue (He et al. 2018). This antioxidant capacity is also the basis for the hepatoprotective activity of the leaves, observed in models of acute liver injury induced by ethanol, where the hexane extract, rich in steroids and with antioxidant activity, protected liver tissue (Pereira et al. 2010).

Endocrine and antifertility effects (saponins and triterpenoids)

One finding with safety implications is the antifertility/endocrine activity. Oral administration of the aqueous leaf extract in female Wistar rats resulted in a dose-dependent reduction in plasma levels of the reproductive hormones estrogen and progesterone (Adewale et al. 2014).

Although the exact metabolites responsible are not detailed in the study, these effects are typically

Table 2 In vivo biological activities of *Momordica charantia* leaves

Extraction (extract or partition)	Dose/concentration (route of administration)	Kind of study (species, strain and/or cell line)	Biological activity	References
Ethanol extract	500, 1000 mg/kg	Melanoma model; Mice (*Mus musculus*) skin carcinogenesis	Antimutagenicity and anticarcinogenicity activity	Agrawal et al. (2010)
	500, 1000, 1500 mg/kg	Cytogenetic studies		
Ethanol extract	200, 400, 800 mg/kg (orally)	Mice (*Mus musculus*)	Antioxidant activity	He et al., (2018)
Ethanol extract	0.1 and 1%	Athymic mice (*Mus musculus*)	Anti-metastatic activity of prostate cancer	Pitchakarn et al. (2010)
Ethanol extract	1 and 5%	Athymic nude mice (*Mus musculus*) lineage KSN	Antitumor activity	Pitchakarn et al. (2011)
Methanol extract	250, 500, 1000 mg/kg	Mice (*Mus musculus*)	Antimicrobian activity	Mahamat et al. (2020)
Methanol extract	100 mg/kg	Rats (*Rattus norvegicus*) lineage Wistar	Vascular protection activity	Komolafe et al. (2013)
Aqueous extract	200, 400 mg/kg (orally)	Rats (*Rattus norvegicus*)	Cardioprotective activity	Saliu et al. (2022)
Aqueous extract	12.5, 25.0, 50.0 g/5000 mL (orally)	Rats (*Rattus norvegicus*)	Anti-fertility activity	Adewale et al. (2014)
Aqueous extract and ethanol extract	385 mg/kg (orally)	Rats (*Rattus norvegicus*) lineage Sprague–Dawley	Absence of toxicity	Oyedapo and Araba, (2001)
Aqueous and hydroalcoholic extract	112.5, 225, 450 mg/kg (oral)	Mice (*Mus musculus*), rats (*Rattus norvegicus*) lineage Wistar	Hypoglycemic activity and absence of toxicity	Lagarto et al. (2014)
	50, 150, 450 mg/kg (oral)	Hypoglycemic activity		
Hexanic and ethanol extracts	25, 50, 100 mg/kg	Mice (*Mus musculus*) Swiss lineage	Hepatoprotective activity	Pereira et al. (2010)
Aqueous and hydroethanol extract	2000 mg/Kg	*Rattus norvegicus* (lineage Wistar) and (albino rabbit) *Oryctolagus cuniculus*	Anti-toxic activity	Lagarto et al. (2008)

attributed to saponins and triterpenoids present in the leaves (Pitchakarn et al. 2011). These compounds can interfere with the synthesis or clearance of steroid hormones or modulate the hypothalamic-pituitary–gonadal axis, representing a pharmacological property of interest, but also a toxicological limitation (Kim et al. 2004).

The most critical methodological limitations in in vivo studies with *M. charantia* leaf extracts focus on the lack of standardization of the extracts, since variations in the extraction solvent result in different phytochemical profiles and biological activities, preventing comparison of results and reproducibility. Another central point is the risk of toxicology, since high animal doses make it difficult to safely extrapolate to humans and observe clinically relevant adverse effects, such as the suppression of reproductive hormones (estrogen and progesterone), requiring a more in-depth assessment of safety in chronic use. Finally, most studies evaluate the crude extract, which prevents the complete elucidation of molecular mechanisms of action and synergism between active metabolites (such as triterpenoids and flavonoids), limiting the development of optimized phytotherapeutic therapies (Table 3).

Phytochemical characterization of *Momordica charantia* leaves

M. charantia leaves are recognized in folk medicine for their therapeutic properties and are a rich and diverse source of phytochemicals (Brandão et al.

Table 3 Chemical composition of *Momordica charantia* leaves

Extract	Chemical composition		Technique used in identification	References
	Secondary metabolites	Identified substance		
Hydroethanol extract	Neophytadiene, palmitic acid, n-Hexatriacontane, farnesol, solanesol, myristic acid, pyrogallol, oleic acid, chloro-octadecanol, carvacrol, limonene and m- cresol	–	Pyrolysis coupled to gas chromatography and mass spectrometry (Pi—GC/MS); Proton NMR spectroscopy	Brandão et al. (2016)
Ethanol extract Petroleum ether fractions Ethyl and n-Butanolic acetate	–	Charantine A and Charantine B	Performance liquid chromatography (HPLC)	Zhang et al. (2014)
Methanol extract	–	Momordicine I	Performance liquid chromatography coupled with mass spectrometry (CL-EM) in electrospray ionization mode (ESI-EM)	Mekuria et al. (2005)
Methanol extract and butanol-soluble fraction		Hex-3-en-1-ol 1-Obd-glucopyranoside; benzyl alcohol 1-O-[al-arabinopyranosyl-(1 → 6)-bd-glucopyranoside]; (6S, 9R)-roseoside; 3-oxo-a-ionol 9-Obd-glucopyranoside; sacranoside A (myrthenol 10-O-[al-arabinopyranosyl-(1 → 6)-bd-glucopyra-noside] and myrtenol 10-Obd-glucopyranoside	Column chromatography with Diaion HP-20, SiO2 and octadecyl silica gel (ODS), and preparative High Performance Liquid Chromatography (HPLC)	Kikuchi et al. (2012)
Ethanol extract	Saponins, tannins and flavonoids	–	Uninformed	Oyedapo & Araba (2001)
Methanol extract	–	*(23E)-3b, 25-dihydroxy-7b-methoxycucurbite-5,23-dien- 19-al; (23S*)-3b-hydroxy-7b, 23-dimethoxycucurbite-5,24-dien-19- al; (23R*)-23-O-methylmomordicin IV; (25x)-26-hydroxymomordicoside L; 25-oxo-27-normomordicoside L; and 25-O-ethylkaravilagennin D; and eleven known compounds, (23E)-3b, 7b-dihydroxy-25-methoxycucurbita-5,23-dien-19-al; (23E)-3b-hydroxy-7b, 25-dimethoxycucurbite - 5,23-dien-19-al;*	Performance liquid chromatography (HPLC) and column chromatography	Zhang et al. (2012)

Table 3 continued

Extract	Chemical composition		Technique used in identification	References
	Secondary metabolites	Identified substance		
		momordicoside L; momordicoside K; kuguaglycoside C; karavilagenin D; karaviloside VI; (19R, 23E)—5b, 19-epoxy-19-methoxycucurbite-6,23-diene-3b, 25-diol; goyaglycoside-a; goyaglucoside-b; andmomordicoside G		
Ethanol extract and fractions of hexane, chloroform, ethyl acetate and methanol from fresh and dried leaves	Catechic tannins, flavones, flavonols, xanthones, flavonols, flavanones, alkaloids, steroids, triterpenes	–	Thin layer chromatography (TCD)	Costa et al. (2011)
Water methanol /1% HCl, ethanol, acetone, ethyl acetate, dichloromethane) and (chloroform and petroleum ether)	Tannic acid, gallic acid, p-coumaric acid, chlorogenic acid, daidzein, epicatechin, genistein, rutin, naringenin	–	Performance liquid chromatography coupled to a diode array detector (HPLC–DAD)	Chokki et al. (2020)
Methanol extract; hexane fraction Diethyl ether fraction; butanol fraction aqueous fraction	–	Momordicine V	Liquid chromatography coupled to mass spectrometry (LC–MS) in electrospray ionization (ESI) and nuclear magnetic resonance (NMR) mode	Kashiwagi et al. (2007)
Hexane fraction; Acetonitrile; Methanol	Vitamin C, beta carotene, lutein, rutin, narigenin, gentistic acid, benzoic acid, o-coumaric acid, t-cinnamic acid	–	Performance liquid chromatography (HPLC) and UV spectrometry	Zhang et al. (2009)
Ethanol extract	–	Kuguacina J	Performance Liquid Chromatography (HPLC)	Pitchakarn et al. (2011)
Methanol extract	–	Karavilagenin F, Karaviloside XII, Karaviloside XIII, Momordicina VI, Momordicina VII and Momordicina VIII	Circular dichroism (CD) spectroscopy, preparative high performance liquid chromatography (HPLC) and nuclear magnetic resonance (NMR)	Zhão et al. (2014)

2016). Phytochemical prospecting of these extracts reveals the presence of important classes of secondary metabolites, such as flavonoids, alkaloids, and tannins (Costa et al. 2011).

The most distinctive and extensively studied class of compounds in *M. charantia* leaves is that of cucurbitane-type triterpenoids (Zhao et al. 2014; Zhang et al. 2014). Among them, several compounds were isolated and identified, such as Kuguacin J (KuJ), and various derivatives of momordicins (including momordicins I, II, IV, V, VI, VII, and VIII) and karavilosides (Karavilagenin F, Karavillosides XII and XIII) (Pitchakarn et al. 2011; Kashiwagi et al. 2007; Zhao et al. 2014; Mekuria et al. 2005).

Another crucial category of metabolites are phenolic compounds, which include total polyphenols and flavonoids, such as rutin, gentisic acid, and o-coumaric acid, considered the main phenolic phytochemicals found (Zhang et al. 2009). The pharmacological importance of these compounds is closely linked to their strong antioxidant activity and antidiabetic potential (Chokki et al. 2020).

The efficiency of recovery and the profile of phytochemicals obtained from *M. charantia* leaves are directly dependent on the polarity of the solvents used for extraction (Chokki et al. 2020). Due to the diversity of chemical classes, solvents with different polarities are used to fractionate and isolate the compounds of interest (Mekuria et al. 2006; Kikuchi et al. 2012). More polar solvents, such as methanol (MeOH), are essential for the initial extraction and isolation of also polar compounds, such as glycosides (glycosylated triterpenoids and other glycosides) and most polyphenols/flavonoids (Chokki et al. 2020; Mekuria et al. 2006; Kikuchi et al. 2012).

The leaves of *M. charantia* represent a remarkable source of phytochemicals, with emphasis on the variety of cucurbit-type triterpenoids and the richness in phenolic compounds, which support a wide range of biological activities, including potential anticancer, antimicrobial, antioxidant, and antidiabetic properties (Pitchakarn et al. 2011; Costa et al. 2011; Chokki et al. 2020). The diversity of metabolites, from water-soluble compounds such as glycosides to fat-soluble constituents such as carotenoids and fats, demonstrates the chemical complexity of the plant (Zhang et al. 2009; Kikuchi et al. 2012).

However, research on the leaves faces methodological limitations. The first is the variability in the chemical composition of the plant material, which is influenced by the stage of maturity and the drying method used (Zhang et al. 2009). The second limitation lies in the extraction process itself, since the choice of solvent directly determines the yield and profile of isolated compounds, meaning that no simple extraction method is capable of isolating the chemical substances in their entirety (Chokki et al. 2020). Finally, the identification and structural quantification of these metabolites require the use of advanced and expensive analytical methods (such as High-Performance Liquid Chromatography—HPLC and Nuclear Magnetic Resonance—NMR), which can limit the standardization and quality control of the plant extract in resource-limited environments (Zhang et al. 2009; Kashiwagi et al. 2007).

Conclusion

This systematic review confirmed the significant pharmacological potential of *M. charantia* leaves, broadly validating their ethnomedicinal uses through preclinical evidence. The main biological activities identified, such as antimicrobial, antitumor, and antioxidant, are intrinsically linked to their complex phytochemical composition, highlighting the classes of triterpenoids, flavonoids, saponins, and tannins.

The broad biological activity observed in *M. charantia* leaves is a manifestation of the polypharmacology of the extracts, resulting from the synergistic action of various metabolites. However, the review identified crucial methodological limitations, including the lack of rigorous standardization of the extracts, high phytochemical variability, and weaknesses in experimental designs, which may increase the risk of bias. The use of high doses in animal models and supraphysiological concentrations in vitro makes safe extrapolation to the clinic and precise definition of the therapeutic window difficult, requiring an in-depth assessment of chronic toxicity.

With a view to the future development of validated and safe phytotherapeutic products, investments in isolation and structural characterization studies of bioactive compounds, such as triterpenoids and flavonoids, are essential. The use of more robust and standardized methodologies is imperative, including the validation of analytical methods and the conduct of assays investigating the synergism and interactions between different classes of metabolites in the extract. The complete elucidation of the molecular mechanisms of action and the establishment of a clear safety margin for chronic use will pave the way for the clinical application of *M. charantia* leaves in combating resistant infections, managing metabolic diseases, and as a chemopreventive agent.

In short, *M. charantia* leaves constitute a promising source for therapeutic innovation, but the advancement of knowledge requires a transition from studies of crude extracts to a more rigorous and integrated phytochemical and pharmacological approach.

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References

Adewale OO, Oduyemi OI, Ayokunle O (2014) Oral administration of leaf extracts of *Momordica charantia* affectreproductive hormones of adult female Wistar rats. Asian Pac J Trop Biomed 4:S521–S524

Agrawal RC, Beohar T (2010) Chemopreventive and anticarcinogenic effects of *Momordica charantia* extract. AsianPacific J Cancer Prev 11(2):371–375

Alzugaray D, Alzugaray C (1983) Plants that heal Ed. Three Sao Paulo

BragaTavares L et al (2007) Effect of levamisole and ethanol extract of *Momordica charantia* leaves on experimental dermatophytosis in rabbits. Brazilian Anim Sci 8(2):285–296

Brandão DO et al (2016) Model analytical development for physical, chemical, and biological characterization of *Momordica charantia* vegetable drug. J Anal Methods Chem. https://doi.org/10.1155/2016/7528297

Cardoso AII (2003) Seed yield and quality in response to pollen load of squash cv. piramoite. Bragantia 62:47–52

Ceballos LC, Sánchez Hoyos F, Gómez Estrada H (2017) Antibacterial activity of *Cordia dentata* Poir, *Heliotropium indicum* Linn and *Momordica charantia* Linn from the Northern Colombian Coast. Rev Colomb Cienc Quim Farm 46(2):143–159

Christenhusz MJM, Byng JW (2016) The number of known plant species in the world and its annual increase. Phytotaxa 261(3):201–217

Chokki M et al (2020) Exploring antioxidant and enzymes (A-amylase and B-glucosidase) inhibitory activity ofMorinda lucida and *Momordica charantia* leaves from Benin. Foods 9(4):434

Cordeiro LN et al (2010) Efeito in vitro do extrato etanólico das folhas do melão-de-São-Caetano (*Momordicacharantia* L.) sobre ovos e larvas de nematóides gastrintestinais de caprinos. Revista Brasileira De PlantasMedicinais 12:421–426

Coutinho HDC et al (2010) Effect of *Momordica charantia* L. in the resistance to aminoglycosides in methicilin-resistant Staphylococcus aureus. Comp Immunol, Microbial Infectious Dis 33(6):467–471

Dah-Nouvlessounon D et al (2023) Ethnopharmacological value and biological activities via antioxidant and anti-protein denaturation activity of *Morinda lucida* Benth and *Momordica charantia* L. leaves extracts from Benin. Plants Basel 12(6):1228

Desai SD, Desai DG, Kaur H (2009) Saponins and their biological activities. Pharma times 41(3):13–16

Festing MFW, Altman DG (2002) Guidelines for the design and statistical analysis of experiments using laboratory animals. ILAR J 43(4):244–258

França EL et al (2014) Effects of *Momordica charantia* L. on the blood rheological properties in diabetic patients. BioMed Res Int 1:840379

Ganesan, Arunachalam et al (2008) Anxiolytic, antidepressant and anti-Inflammatory activities of methanol extract of *Momordica charantia* Linn Leaves (*Cucurbitaceae*). Iran J Pharmacol Ther

Grover JK, Yadav SP (2004) Pharmacological actions and potential uses of *Momordica charantia*: a review. J Ethnopharmacol 93(1):123–132

Guterres ZR et al (2015) Genotoxic and antigenotoxic potential of *Momordica charantia* Linn (Cucurbitaceae) in thewing spot test of *Drosophila melanogaster*. J Med Food 18(10):1136–1142

He Q et al (2018) Hypolipidemic and antioxidant potential of bitter gourd (*Momordica charantia* L.) leaf in mice fedon a high-fat diet. Pakistan J Pharm Sci 31(5):1837–1844

Hooijmans CR et al (2014) SYRCLE's risk of bias tool for animal studies. BMC Med Res Methodol 14(1):1–9

Hsu HY et al (2012) Antimigratory effects of the methanol extract from *Momordica charantia* on human lungadenocarcinoma CL1 cells. Evi-based Complement Altern Med 2012(1):819632

José Galberto MC et al (2011) Antibacterial activity of *Momordica charantia* (Curcubitaceae) extracts and fractions. J Basic Clin Pharm 2(1):45

Kashiwagi T et al (2007) A new oviposition deterrent to the leafminer, *Liriomyza trifolii*: cucurbitane glucoside fromMomordica charantia. Zeitschrift Für Naturforschung C 62(7–8):603–607

Kikuchi T et al (2012) Glycosidic inhibitors of melanogenesis from leaves of *Momordica charantia*. Chem Biodivers 9(7):1221–1230

Kim K-A et al (2004) Inibição das atividades do citocromo P450 pelo ácido oleanólico e pelo ácido ursólico em microssomas hepáticos humanos. Ciências Da Vida 74(22):2769–2779

Komolafe AO et al (2013) Histological and histochemical studies of the aorta and pulmonary trunk in STZ-induced-diabetic Wistar rats treated with *Momordica charantia*. Int J Morphol 31(2):716–723

Kubola J, Siriamornpun S (2008) Phenolic contents and antioxidant activities of bitter gourd (*Momordica charantia* L.) leaf, stem and fruit fraction extracts in vitro. Food Chem 110(4):881–890

Lagarto A et al (2014) Evaluación preclínica y estudio de estabilidad de extractos a partir del follaje de Momordicacharantia Lin. Revista Brasileira De Plantas Medicinais 16(4):782–788

Li CJ et al (2012) *Momordica charantia* extract induces apoptosis in human cancer cells through caspase-andmitochondria-dependent pathways. Evid-based Complement Altern Med 2012(1):261971

Lomanowska M et al (2024) The molecular mechanisms of the antibacterial activity of sumac (*Rhus typhina* L.) tannin against *Pseudomonas aeruginosa*. Appl Sci 14(22):10728

Mahamat O et al (2020) Immunomodulatory activity of Momordica charantia L. (Cucurbitaceae) leaf diethyl ether and methanol extracts on Salmonella typhi-infected mice and LPS-induced phagocytic activities of macrophages and neutrophils. Evid-Based Complementary Altern Med 2020(1):5248346

Mekuria DB et al (2005) Cucurbitane triterpenoid oviposition deterrent from *Momordica charantia* to the leafminer, *Liriomyza trifolii*. Biosci Biotechnol Biochem 69(9):1706–1710

Moher D et al (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med 151(4):264–269

Montes-Hernandez S, Eguiarte LE (2002) Genetic structure and indirect estimatesof gene flow in three taxa of *Cucurbita* (Cucurbitaceae) in western Mexico. Love Jbotany 89(7):1156–1163

Murakami T et al (2001) Medicinal foods XXI Structures of new cucurbitan-type triterpene glycosides, goyaglycosides-a, -b, -c, -d, -e, -f, -g and h and of new oleanane-type triterpene saponins, gasasaponins I, II and III, from fresh fruits of the Japanese Momordica charantia L. Chem Pharm Bull 49(1):54–63

Mwambete KD (2009) The in vitro antimicrobial activity of fruit and leaf crude extracts of *Momordica charantia*: a Tanzania medicinal plant. Afr Health Sci 9(1):34–39

Oyedapo OO, Araba BG (2001) Stimulation of protein biosynthesis in rat hepatocytes by extracts of *Momordica charantia*. Phytother Res 15(2):95–98

Parkash A, Ng TB, Tso WW (2002) Purification and characterization of charantin, a napin - like ribosome - inactivating peptide from bitter gourd (*Momordica charantia*) seeds. J Pept Res 59(5):197–202

Paterson JR et al (2022) Insights into the antibacterial mechanism of action of chelating agents by selective deprivation of iron, manganese, and zinc. Appl Environ Microbiol 88(2):e01641-e1721

Pereira BS et al (2010) Hepatoprotective activity of ethanolic and hexane extracts from Momordica charantia leaves. Brazilian J Med Plants 12(3):311–316

Pereira CAJ et al (2016) Anti-helminthic activity of Momordica charantia L. against Fasciola hepatica eggs after twelve days of in vitro incubation. Veterinary Parasitol 228:160–166

Pitchakarn P et al (2010) *Momordica charantia* leaf extract suppresses rat prostate cancer progression in vitro and in vivo. Cancer Sci 101(10):2234–2240

Pitchakarn P et al (2011) Induction of G1 arrest and apoptosis in androgen-dependent human prostate cancer by Kuguacin J, a triterpenoid from *Momordica charantia* leaf. Cancer Lett 306(2):142–150

Polat AK et al (2018) Gastro protective effect of Momordica charantia in experimental corrosive gastric ulcer. Intern J Herb Med 6(1):26–29

Poole K (2007) Efflux pumps as antimicrobial resistance mechanisms. Ann Med 39(3):162–176

Raman A, Lau C (1996) Anti-diabetic properties and phytochemistry of *Momordica charantia* L. (Cucurbitaceae). Phytomedicine 2(4):349–362

Saliu JÁ et al (2022) Modulatory effects of stonebreaker (*Phyllanthus amarus*) and bitter gourd (*Momordica charantia*)on enzymes linked with cardiac function in heart tissue of doxorubicin-stressed rats. Drug Chem Toxicol 45(1):331–339

Sallau AB et al (2018) In vitro effect of terpenoid-rich extract of *Momordica charantia* on alpha glucosidase activity. Vitae 25(3):148–153

Santos KK et al (2012) Trypanocide, cytotoxic, and antifungal activities of *Momordica charantia*. PharmaceuticalBiology 50(2):162–166

Santos KKA et al (2013) Atividade leishmanicida in vitro de Eugenia uniflora e *Momordica charantia*. Revista deCiências Farmacêuticas Básica e Aplicada 34(1)

Shodehinde SA et al (2016) Phenolic composition and evaluation of methanol and aqueous extracts of bitter gourd(-*Momordica charantia* L) leaves on angiotensin-I-converting enzyme and some pro-oxidant-induced lipid peroxidationin vitro. J Evi-Based Complement Altern Med 21(4):NP67–NP76

Tsai T-H et al (2014) Antioxidant, cell-protective, and anti-melanogenic activities of leaf extracts from wild bitter melon (*Momordica charantia* Linn. var. *abbreviata* Ser.) cultivars. Bot Stud 55(1):1–11

Wang S et al (2017) *Momordica charantia*: the popular health-promoting vegetable with multifunctionality. Food Funct 8(5):1749–1762

Wang S et al (2016) Antifungal activity of Momordica charantia seed extracts toward the pathogenic fungus Fusarium solani L. J Food Drug Anal 24(4):881–887

Xie H et al (1998) Study on chemical components of Momordica charantia Zhong yao cai Zhongyaocai. J Chin Med Mater 21(9):458–459

Xiong SD et al (2009) Ribosome - inactivating proteins isolated from dietary bitter melon induce apoptosis and inhibit histone deacetylase-1 selectively in premalignant and malignant prostate cancer cells. Int J Cancer 125(4):774–782

Yuan Y-R et al (1999) Three-dimensional structure of β-momorcharin at 2.55 Å resolution. Acta Crystallogr D Biol Crystallogr 55(6):1144–1151

Yung MM et al (2016) RETRACTED: bitter melon (*Momordica charantia*) extract inhibits tumorigenicity andovercomes cisplatin-resistance in ovarian cancer cells through

targeting AMPK signaling cascade. Integr Cancer Ther 15(3):376–389

Zhang YB et al (2014) Cucurbitane-type triterpenoids from the leaves of *Momordica charantia*. J Asian Nat Prod Res 16(4):358–363

Zhao GT et al (2014) Cucurbitane-type triterpenoids from the stems and leaves of *Momordica charantia*. Fitoterapia 95:75–82

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