Review

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Biological activities of *Agave* by-products and their possible applications in food and pharmaceuticals

Julio Cesar López-Romero, Jesús Fernando Ayala-Zavala, Gustavo Adolfo González-Aguilar, Etna Aida Peña-Ramos and Humberto González-Ríos*

Abstract

***Agave* leaves are considered a by-product of alcoholic beverage production (tequila, mezcal and bacanora) because they are discarded during the production process, despite accounting for approximately 50% of the total plant weight. These by-products constitute a potential source of *Agave* extracts rich in bioactive compounds, such as saponins, phenolic compounds and terpenes, and possess different biological effects, as demonstrated by *in vitro* and *in vivo* tests (e.g. antimicrobial, antifungal, antioxidant, anti-inflammatory, antihypertensive, immunomodulatory, antiparasitic and anticancer activity). Despite their positive results in biological assays, *Agave* extracts have not been widely evaluated in food systems and pharmaceutical areas, and these fields represent a potential route to improve the usage of *Agave* plants as food additives and agents for treating medical diseases.**

Keywords: bioactive compounds; biological activities; *Agave* by-products; foods; pharmaceutical

INTRODUCTION

The genus *Agave* is distributed throughout the American continent, ranging from the USA to the tropical region of South America. This genus consists of approximately 200 species.[1] Mexico is considered an *Agave* diversity center because it contains approximately 75% of the species from this genus.[2,3]

In Mexican territory, these plants are mainly used for the production of alcoholic beverages, among which tequila, mezcal and bacanora are the most widely produced.[4,5] In the process of alcoholic beverage production, the head of the *Agave* plant is used when it is in an advanced stage of maturity (7–10 years), and more than 1 million tons per year are processed.[6,7] In this process, the *Agave* leaves, which can compose more than 50% of the total plant weight, are discarded, generating a large amount of agro-industrial waste annually.[8,9]

This natural by-product could be an extraction source for bioactive compounds, such as flavonoids, saponins and terpenes.[6,7,10,11] In this regard, several studies have been performed to analyze the antimicrobial and antioxidant effect of *Agave* extracts *in vitro*. The extracts have shown an antimicrobial effect against a broad range of Gram-positive (Gram +) and Gram-negative (Gram −) bacteria, as well as antioxidant potential from multiple assays (2,2-diphenyl-1-picrylhydrazyl (DPPH), Trolox equivalent antioxidant capacity (TEAC), oxygen radical absorbance capacity (ORAC), reducing power and β-carotene bleaching).[12–15] Moreover, other biological effects (*in vitro*) have been reported for *Agave* extracts, such as anticancer, anti-inflammatory, immunomodulatory, antihypertensive and antiparasitic activity.[16–18]

Additionally, the incorporation of bioactive compounds extracted from natural sources has been widely recognized to have a positive effect on foods by preserving their safety and quality.[19–24] The reported bioactive properties of *Agave* extracts suggest its potential use as an alternative additive to preserve nutritional quality and sensory attributes of food.

The current trend in the food industry and consumer preference towards natural alternatives opens the possibility of applying *Agave* extracts in different areas. Therefore, analyzing the effects of *Agave* extracts in different food matrices and human systems is necessary to determine their applications in the food and pharmaceutical industries. In this context, the goal of the present review is to describe the biological activities of *Agave* extracts and establish the possibility of their application in the food and pharmaceutical fields.

DISTRIBUTION, CHARACTERISTICS AND USE OF *AGAVE* GENUS

The genus *Agave* (*sensu stricto*) is endemic to America, with its distribution ranging from the USA to the tropical area of South America, and consists of approximately 200 species.[1] Mexico contains 75% [150] of these species and is thus considered an *Agave* diversity center.[2,3] In Mexico, this genus is abundant in the southern mountainous regions of central Mexico, Sierra Madre Occidental, Mexican Altiplano, Baja California and Sierra Madre

* *Correspondence to: H González-Ríos, Centro de Investigación en Alimentación y Desarrollo, AC, Carretera a La Victoria Km. 0.6, Hermosillo, Sonora 83304, México. E-mail: hugory@ciad.mx*

Centro de Investigación en Alimentación y Desarrollo, AC, Hermosillo, Sonora, Mexico

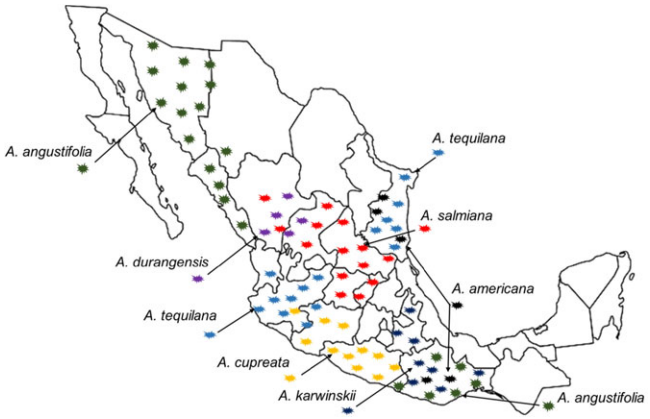

Figure 1. Distribution of the main types of *Agave* in Mexico.

Oriental (Fig. 1).[25] The states with the highest diversity are Oaxaca, Puebla, Sonora, Queretaro, Durango and Sinaloa, with 37, 31, 30, 26, 25 and 21 species, respectively.[3,14,26]

These plants have been used since pre-Hispanic times for their biological activity, especially for their use as medicinal auxiliary treatments against dysentery, urological disorder, gastrointestinal infections and inflammation.[7,27] Currently, *Agave* species are used as a feedstock for the production of alcoholic beverages, syrups and natural fibers.[2,6] These plants are also used as a food source, construction materials and ornamentals, and their cultivation has been exponentially expanded because of their minimal water and maintenance requirements.[28]

The main economic activity generated from *Agave* in Mexico is the production of alcoholic beverages, among which tequila, mezcal and bacanora are the most widely produced.[4,5] Tequila is yielded by fermenting *A. tequilana* Weber blue and is manufactured in Jalisco, Michoacán, Guanajuato, Nayarit and Tamaulipas, all of which possess denominations of origin for tequila. Similarly, mezcal has a denomination of origin and can be produced from only five *Agave* species (*A. angustifolia* Haw, *A. asperrima* Jacobi, *A. weberi* Cela., *A. salmiana* Otto and *A. potatorum* Zucc.) and processed in only seven states in Mexico (Guerrero, Zacatecas, San Luis Potosi, Durango, Oaxaca, Guanajuato and Tamaulipas). Similarly, bacanora is prepared from *A. angustifolia* Haw and is processed in the state of Sonora, which has a bacanora denomination of origin.[29–32]

In the production of alcoholic beverages, highly mature plants (7–10 years of development), which are pruned over time to prevent growth, are used. After being harvested, the plant is stored to allow biochemical changes in the sugars. Subsequently, the *Agave* leaves are removed, and the head is baked, fermented and distilled.[6,7] Mexico is the main worldwide producer in this traditional industry, with approximately 229 821 419 *Agave* plants inventoried, generating a total production in 2011 of 261.4 ML of tequila, 1 523 173 L of mezcal and 350 000 L of bacanora.[33,34]

BIOACTIVE COMPOUNDS IN *AGAVE* BY-PRODUCTS

The alcoholic beverage industry demands a high volume of *Agave* plants every year; however, more than 50% of the plant (leaves) is not used in the production process, generating almost the same volume of waste products as is used for production.[9,35] The removed leaves, which are considered by-products, could instead be used for beneficial purposes, thus representing a potential economical source of chemical constituents with diverse biological effects.[5,14,36–38] *Agave* by-products contain phytochemicals that are not essential nutrients for plant life but do provide protection against predators and environmental conditions. Among the primary phytochemicals found in *Agave* by-products, saponins, flavonoids and terpenes in particular influence the biological potential of obtained extracts, which may also represent a medical alternative as an auxiliary treatment against some diseases.

Saponins

Saponins comprise a sugar moiety (glucose, galactose, glucuronic acid, xylose, rhamnose or methylpentose) linked to a non-polar aglycone (sapogenin) and are classified as steroids (C_{27}) and triterpenoids (C_{30}). Normally, the oligosaccharide (or oligosaccharide chain) is attached at the C_3 position; these compounds are known as monodesmosidic saponins. By contrast, saponins with an additional sugar unit linked at C_{26} or C_{28} are called didesmosidic.[39,40]

Nasri and Salem[41] found that saponins are the main type of bioactive compounds present in *A. americana* extract, with a content of 80 g diosgenin equivalent kg^{-1} dry weight (d.w.). Conversely, various other studies have isolated and characterized different saponins from *Agave* extracts. For example, Zou *et al.*[42] and Macias *et al.*[43] identified spirostane saponins in *A. brittoniana* and *A. sisalana* extracts. Similarly, Eskander *et al.*[44] and Yokosuda and Mimaki[45] isolated spirostanol and furostanol saponins from *A. macroacantha* and *A. utahensis* extracts. Additionally, *A. sisalana* and *A. offoyana* were found to contain dongnoside E and magueyoside saponins, respectively.[15,46] Wilkomirski *et al.*[47] characterized two steroidal saponins (agavasaponin E and H) from *A. americana*. In a study performed by Abdel-Khalik *et al.*,[48] the authors determined the structure of two steroidal saponins (a monodesmosidic spirostanoside and a didesmosidic furostanol glycoside) isolated from *A. lophantha*.

Flavonoids

Flavonoids are phenolic compounds comprising 15 carbon atom structures (C6–C3–C6). Flavonoid compounds consist of two condensed rings (A and B) linked by a heterocyclic C ring (pyran). Flavonoids are classified according to their structure as flavones, flavonols, flavanones, flavanonols, flavanols, anthocyanidins, isoflavones, neoflavonoids and chalcones.[49] These compounds differ in the degree of hydroxylation or methoxylation of the condensed rings, and they naturally occur as aglycones and methylated and glycoside derivatives.[49,50] Moreover, different studies have identified the presence of phenolic compounds in *Agave* plants.

When considering flavonoid content in *Agave* extracts, some studies have examined the presence of these compounds via quantitative and qualitative testing. Accordingly, Fig. 2 summarizes the most representative flavonoids identified in Agave extracts. Hamissa *et al.*[51] reported that the flavonoid content in *A. americana* leaves ranged from 0.96 to 4.90 mg quercetin equivalents g^{-1} d.w.. In a study performed by Rizwan *et al.*[13] the authors observed a variation in the flavonoid content of *A. attenuate* leaf extracts (0.43–3.04 mg catechin equivalent g^{-1} d.w.), with methanol extracts exhibiting the highest content, followed by chloroform, ethyl acetate, *n*-butanol and *n*-hexane extracts. Similarly, Ahumada-Santos *et al.*[14] evaluated the phenolic content of six *Agave* species (*A. tequilana*, *A. ornithobroma*, *A. impressa*, *A. rzedowskiana*, *A. schidigera* and *A. angustifolia*), the phenolic content

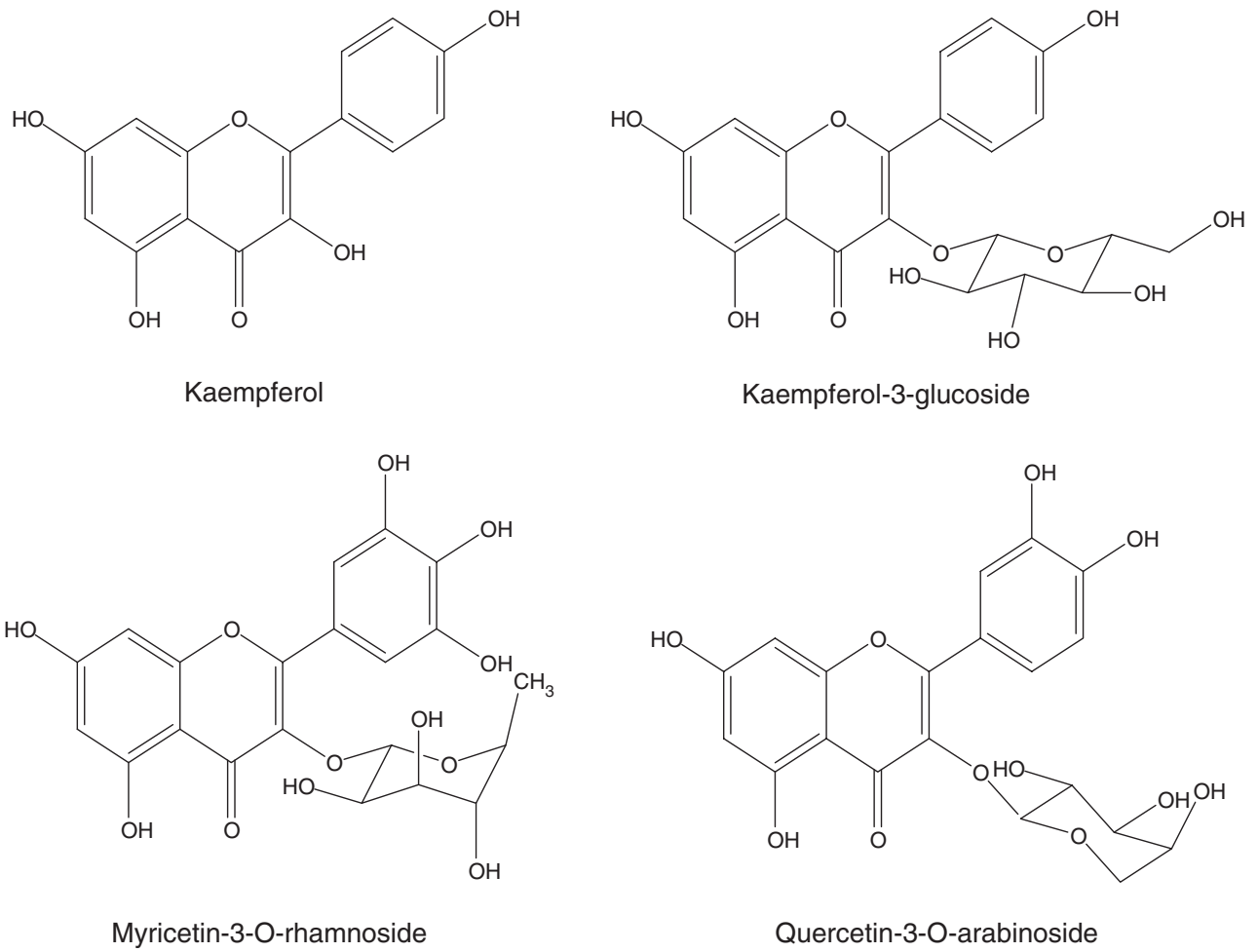

Figure 2. Flavonoids identified in *Agave*.

of which ranged from 2.06 to 12.37 mg gallic acid equivalents g^{-1} d.w. *A. ornithobroma* and *A. angustifolia* showed the highest and lowest content, respectively. Nasri and Salem[41] obtained 4.6 mg tannic acid equivalent g^{-1} d.w. (total phenols) from *A. Americana* leaf extract. Conversely, Ade-Ajayi *et al.*[52] reported the presence of flavonoids (qualitative test, yellow coloration) in *A. sisalana* Perrine juice obtained from the leaves.

Other studies have investigated the flavonoid profile of *Agave* extracts. For example, Almaraz-Abarca *et al.*[53] identified different flavonoids, such as kaempferol glycoside, quercetin glycoside, kaempferol-3,7-*O*-diglucoside, kaempferol-3-*O*-[6-acetylglucoside]-7-*O*-glucoside, kaempferol-3-*O*-[rhamnosyl(1-6)glucoside], quercetin-3-*O*-arabinoside and kaempferol-3-*O*-rhamnoside in *A. durangensis* extracts. Similarly, Almaraz-Abarca *et al.*[54] analyzed the phenolic profile of *A. striata* and *A. lechuguilla* extracts and identified the presence of quercetin-3-*O*-glycoside, kaempferol-3-*O*-glycoside, benzoic acid and cinnamic acid in the above-mentioned extracts. Additionally, Duke[55] identified kaempferol as the main flavonoid in *A. americana*.

In other studies, Chen *et al.*[37] and Morales-Serna *et al.*[56] analyzed the flavonoid composition of *A. sisalana* and *A. tequilana* Weber extracts, in which they identified three flavonoids (5,7-dihydroxyflavanone, kaempferol 3-rutinoside-4′-glucoside and kaempferol 3-(2-rhamnosylrutinoside)) and ten homoisoflavonoids (7-*O*-methyleucomol, 3′-deoxysappanona, 3,9-dihydroeucomin, dihydrobonducellin, 7-hydroxy-3-(4- hydroxybenzyl)chromane, 5,7-dihydroxy-3-(4′-hydroxybenzyl)-4-chromanone, 5,7- dihydroxy-3-(3′-hydroxy-4′-methoxybenzyl)-4-chromanone, 5,7-dihydroxy-3-(4-methoxybenzyl)chroman-4-one, 7-hydroxy-3-(4-hydroxybenzyl)chroman-4-one and 4′-demethyl-3,9-dihydropunctatin).

Terpenes

Terpenes are characterized by isoprene units (C_5) and are usually classified according to the number of isoprene units as hemiterpenes (C_5), monoterpenes (C_{10}), sesquiterpenes (C_{15}), diterpenes (C_{20}), triterpenes (C_{30}) and tetraterpenes (C_{40}). In plants, these compounds occur as hydrocarbons, alcohols, aldehydes, ketones, esters, ethers, peroxides and phenols.[57,58]

Terpenes have also been identified in *Agave* extracts. The most representative terpenes identified in *Agave* extracts are shown in Fig. 3. Peña-Alvarez *et al.*[10] analyzed different *Agave* extracts and reported diverse types of terpenes. For example, the terpenes found in *A. salmiana* included α-linalool, α-terpinene, *p*-cymene, limonene, β-*trans*-ocimene, linalool, 4-terpineol, geraniol and *trans*-nerolidol. In an *A. angustifolia* extract, the terpenes identified were *p*-cymene, limonene, β-*trans*-ocimene, linalool, α-terpineol, nerol, geraniol and *trans*-nerolidol. *A. tequilana* Weber blue contained α-linalool, α-terpinene, *p*-cymene, limonene, β-*trans*-ocimene, β-*cis*-ocimene, sabinene, linalool,

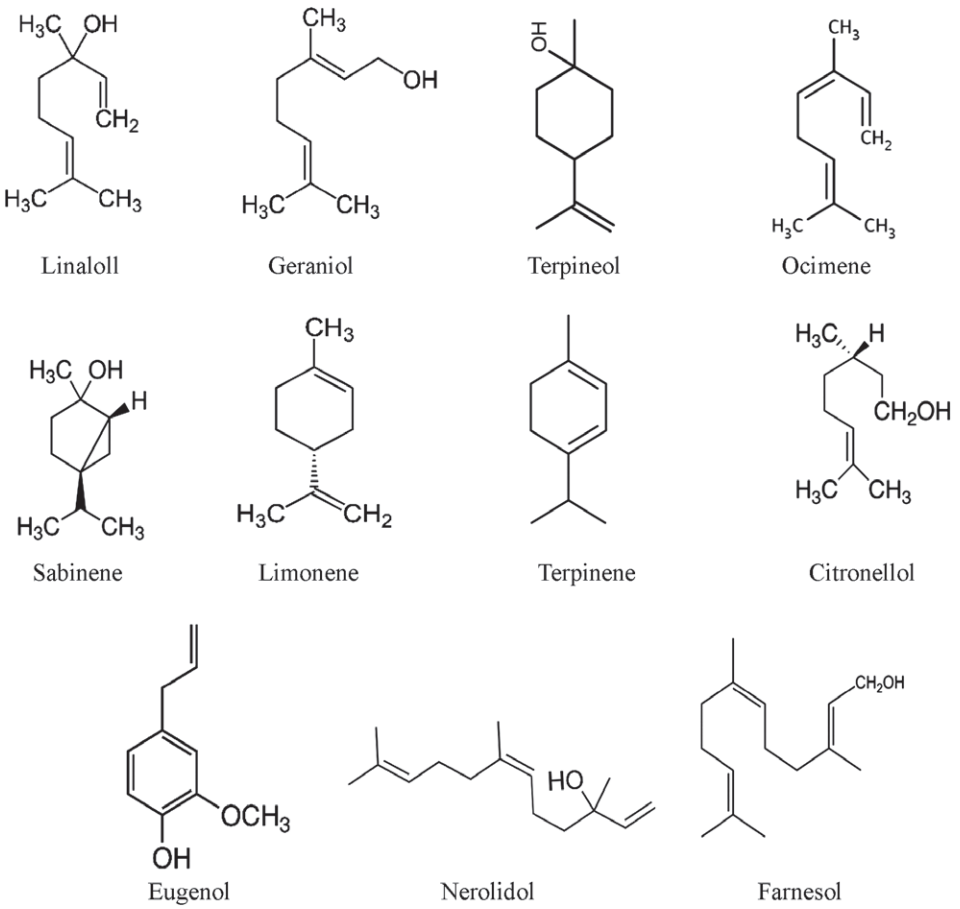

Figure 3. Identified terpenes in *Agave*.

2,4,6-octatriene, 4-terpineol, α-terpineol, nerol, bornyl formate, geraniol, α-cubebene, copaene, anastreptene, bergamotene, β-farnesene, 1,2,3,4-tetrahydronaphthalene, germacrene, α-curcumene, α-muurolene, α-bisabolene, cadinene, α-spirovetivene, cedrol, *trans*-nerolidol, cadalene, cadinol, patchouli alcohol and α-bisabolol.

In another study, De León-Rodríguez *et al.*[11] observed that beverages prepared from *A. salmiana* exhibited high quantities of limonene, α-terpinene and α-terpineol. Moreover, Peña-Alvarez *et al.*[59] principally detected linalool, terpinen-4-ol, α-terpineol, β-citronellol, eugenol, *cis*-nerolidol and *trans*-farnesol in *A. tequilana* beverages.

BIOLOGICAL ACTIVITIES OF *AGAVES*

Agave extracts have shown different biological effects, such as antimicrobial, antifungal, antioxidant, anti-inflammatory, antihypertensive, immunomodulatory, antiparasitic and anticancer activity (Table 1). These effects are attributed to the bioactive compounds present in their extracts, including saponins, flavonoids, terpenes, glycosides, steroids, tannins, fructans and policosanol.

Antimicrobial activity

One of the most remarkable effects of *Agave* extracts is their antimicrobial activity against Gram-positive and Gram-negative bacteria (Table 1). Several studies have demonstrated that *A. sisalana* extracts had an inhibitory effect on microorganisms such as *Escherichia coli*, *Salmonella typhi*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*.[12,15,52] This effect is attributed to the identified compounds in the extracts, including saponins, glycosides, terpenoids, steroids, flavonoids and tannins. Building on the studies described previously, Verástegui *et al.*,[60,61] Garcia *et al.*,[62] Vaghasiya and Chanda,[63], Ahumada-Santos *et al.*[14] and Rizwan *et al.*[13] discovered some of the above-mentioned compounds in different *Agave* extracts, such as those from *A. lechuguilla*, *A. picta*, *A. intermixta*, *A. impressa*, *A. ornithobroma*, *A. rzedowskiana*, *A. tequilana*, *A. schidigera*, *A. angustifolia* and *A. attenuata*. These extracts exerted an inhibitory effect on *Bacillus cereus*, *B. subtilis*, *E. coli*, *Serratia marcescens*, *Salmonella typhimurium*, *Listeria monocytogenes*, *Shigella dysenteriae* and *Clostridium perfringens*, among others. Generally, the antimicrobial activity of the active extracts ranged from 1.8 to 252 mg mL^{-1} (based on the minimum inhibitory concentration, MIC). The most active extracts were those from *A. picta*, *A. intermixta*, *A. sisalana*, *A. tequilana* and *A. schidigera*, which exhibited MIC values $\leq$10 mg mL^{-1} against Gram-negative and Gram-positive bacteria. These results showed the antimicrobial potential of *Agave* extracts against clinical pathogens and opened the possibility of using them against foodborne pathogens. Additionally, these findings suggested a positive correlation between antimicrobial effects and *Agave* extracts. Variations between different extracts originate from several factors, such as genetic, morphogenic, environmental, and extraction solvent and technique.[64,65] These factors determine the bioactive compound content and profile, which influence the antimicrobial potential of the natural extracts.

Table 1. Biological activities of different *Agave* extracts

Activity	*Agave* species	Extract type	Dose	Effect	Reference
Antimicrobial	*A. sisalana*	Methanol	0–>12 500 μg mL^{-1}	Inhibitory effect: *Ps. aeruginosa*, *E. coli*, *Staph. aureus*, *B. subtilis* and *Sal. choleraesuis* (MIC: >12 500 μg mL^{-1} for all tested bacteria)	15
	A. sisalana	Methanol Aqueous	0–40 mg mL^{-1}	Inhibitory and bactericidal effect: *Shigella dysenteriae* (MIC:10 mg mL^{-1}; MBC: 20 mg mL^{-1}), *B. atrophaeus* (MIC:20 mg mL^{-1}; MBC: 40 mg mL^{-1}) *Ps. aeruginosa* (MIC: 20 mg mL^{-1}; MBC: 20 mg mL^{-1}) and *Enterococcus faecalis* (MIC: 20 mg mL^{-1}; MBC: 40 mg mL^{-1})	52
	A. sisalana	Methanol Aqueous	0–40 mg mL^{-1}	Inhibitory and bactericidal effect: *Staph. aureus* (MIC: 10 mg mL^{-1}; MBC: 20 mg mL^{-1}), *Sal. typhi* (MIC: 20 mg mL^{-1}; MBC: 40 mg mL^{-1}) *E. coli* (MIC: 10–20 mg mL^{-1}; MBC: 20–40 mg mL^{-1}) and *Strep. pyogenes* (MIC: 10–20 mg mL^{-1}; MBC: 20–40 mg mL^{-1})	12
	A. lechuguilla *A. picta* *A. scabra* *A. lophantha*	Ethanol	0–12 mg mL^{-1}	Inhibitory and bactericidal effect: *Nippostrongylus brasiliensis* (MIC: 7.6 mg mL^{-1}), *Nocardia asteroides* (MIC: 7.3 mg mL^{-1}) *Shigella dysenteriae* (MIC: 12 mg mL^{-1}), *Clostridium perfringens* (MIC: 12 mg mL^{-1}) *E. coli* (MBC: 6 mg mL^{-1}), *L. monocytogenes* (MBC: 1.8 mg mL^{-1}) *V. cholerae* (MIC: mg mL^{-1}; MBC: 6 mg mL^{-1}) and *Staph. aureus* (MBC: 7 mg mL^{-1})	60,61
	A. impressa *A. ornithobroma* *A. rzedowskiana* *A. tequilana* *A. schidigera* *A. angustifolia*	Methanol *n*-Hexane	0–15 mg mL^{-1}	Inhibitory and bactericidal effect: *S. group A4* (MIC: 5–15 mg mL^{-1}), *S. typhi* (MIC: 5–10 mg mL^{-1}; MBC: 10 mg mL^{-1}) *Shigella dysenteriae* (MIC: 5–15 mg mL^{-1}), *E. coli* (MIC: 10 mg mL^{-1}) and *Ps. aeruginosa* (MIC: 5–10 mg mL^{-1}; MBC: 15 mg mL^{-1})	14
	A. attenuata	Methanol Chloroform Ethyl acetate *n*-Butanol *n*-Hexane	0–252 mg mL^{-1}	Inhibitory effect: *B. subtilis* (MIC: 158–250 mg mL^{-1}), *Pasteurella multocida* (MIC: 27.4–250 mg mL^{-1}) *Staph. aureus* (MIC: 89.3–252 mg mL^{-1}) and *E. coli* (MIC: 15.2–140 mg mL^{-1})	13
	A. vera	Methanol Acetone	20 μL disc	Inhibitory effect: *B. cereus* (13 mm), *B. subtilis* (15 mm) and *Klebsiella pneumoniae* (12 mm)	63
	A. intermixta	Aqueous	0–15 mg mL^{-1}	Inhibitory effect: *E. coli* (MIC: 10 mg mL^{-1}), *Serratia marcescens* (MIC: 15 mg mL^{-1}) *Sal. typhimurium* (MIC: 10 mg mL^{-1}), *Proteus vulgaris* (MIC: 15 mg mL^{-1}) *Moraxella lacunata* (MIC: 10 mg mL^{-1}), *B. subtilis* (MIC: 10 mg mL^{-1}) *B. cereus* (MIC: 10 mg mL^{-1}), *B. megaterium* (MIC: 10 mg mL^{-1}) *and Staph. aureus* (MIC: 12 mg mL^{-1})	62
Antifungal	*A. asperrima* *A. striata*	Methanol	0–60 mg mL^{-1}	Inhibitory effect: *Asp. flavus* (MIC: 0.5–>60 mg mL^{-1}) and *Asp. parasiticus* (MIC: 1–>60 mg mL^{-1}) % reduction of mycelial production: *Asp. flavus* (3–70%) and *Asp. parasiticus* (0–80%) % reduction of aflatoxin production: *Asp. flavus* (16–>99%) and *Asp. parasiticus* (0–>99%)	76
	A. lechuguilla *A. picta* *A. scabra* *A. lophantha*	Ethanol	0-6 mg mL^{-1}	Inhibitory and bactericidal effect: *Cryptococcus neoformans* (MIC: 6 mg mL^{-1}; MBC: 2–3 mg mL^{-1}), *Microsporum gypseum* (MIC: 6 mg mL^{-1}; MBC: 3–5.5 mg mL^{-1}), *Trichophyton tonsurans* (MIC: 4.5 mg mL^{-1}; MBC: 3.5–6 mg mL^{-1}), *Sporothrix schenckii* (MIC: 5 mg mL^{-1}; MBC: 4–6 mg mL^{-1}), *Candida albicans* (MIC: 4 mg mL^{-1}), *Candida rugosa* (MIC: 4 mg mL^{-1}), *Cryptococcus neoformans* (MIC: 6 mg mL^{-1}), *Chironius laurenti* (MIC: 5.3 mg mL^{-1}), *Cryptococcus albidus* (MIC: 4 mg mL^{-1}), *Microsporum canis* (MIC: 3.3 mg mL^{-1}), *Microsporum gypseum* (MIC: 6 mg mL^{-1}) and *Trichophyton tonsurans* (MIC: 4.5 mg mL^{-1})	60,61

Table 1. Continued

Activity	*Agave* species	Extract type	Dose	Effect	Reference
	A. lechuguilla	Ethanol *n*-Hexane	0–5000 μL L^{-1}	Inhibition of sporulation: *Rhizopus stolonifer* (9.4–77.1%), *Colletotrichum gloeosporioides* (100%) and *Penicillium digitatum* (6.5–52.6%) % of mycelial inhibition: *Rhizopus stolonifer* (43–100%), *Colletotrichum gloeosporioides* (44–100%) and *Penicillium digitatum* (20–84%)	75
	A. sisalana *A. sisalana*	Methanol	0–>12 500 μg mL^{-1}	Inhibitory effect: *Candida albicans, asp. Niger* (MIC: >12 500 μg mL^{-1} for the tested microorganism)	15
	A. attenuata	Methanol Chloroform Ethyl acetate *n*-Butanol *n*-Hexane	0–244 mg mL^{-1}	Inhibitory effect: *Asp. niger* (MIC: 115–244 mg mL^{-1}), *Asp. flavus* (MIC: 18.4–110 mg mL^{-1}) *Alternaria alternata* (MIC: 69.4–189 mg mL^{-1}) and *Rhizoctonia solani* (MIC: 20.4–140 mg mL^{-1})	13
	A. vera	Methanol Acetone	20 μL disc	Inhibitory effect: *Candida albicans* (14 mm), *Candida tropicalis* (14 mm) and *C. luteolus* (17 mm)	63
Antioxidant	*A. Americana*	Methanol	Not specified	DPPH assay *Cryptococcus luteolus* (3.7–23.9 μg_{DPPH} μL^{-1} extract)	51
	A. attenuata	Methanol Chloroform Ethyl acetate *n*-Butanol *n*-Hexane	0.1–5 mg mL^{-1}	DPPH assay (0.1 mg mL^{-1}; % inhibition 61.4–73.9), Inhibition of linoleic acid system (50.1-70.3 %), reducing power assay (1 mg mL^{-1}; abs. 0.21–0.66)	13
	A. impressa *A. ornithobrom* *A. rzedowskiana* *A. tequilana* *A. schidigera* *A. angustifolia*	Methanol	0–4 mg mL^{-1}	DPPH assay (6.4–27.4 μM TE g^{-1} d.w.), ABTS assay (9.7–212.2 μmol L^{-1} TE g^{-1} d.w.), ORAC assay (46.2–862.6 μmol L^{-1} TE g^{-1} d.w.) β-Carotene bleaching assay (−86.53–71.5%)	14
	A. sisalana	Methanol	0–<10 000 μg mL^{-1}	DPPH assay (EC50: 1452–<10 000 μg mL^{-1})	15
Anti-inflammatory	*A. americana* *A. americana*	Aqueous	0–13.1 mg kg^{-1} b.w.	Inhibitory effect: Inhibition of hind paw edema (50–100%)	101
	A. intermixta	Aqueous	0–500 mg kg^{-1} b.w. 0–5 mg ear	Inhibitory effect: Inhibition of hind paw edema (81.4%) Inhibition of ear edema (54.2–56.5%) Inhibition of myeloperoxidase (79.8–81.4%)	102
	A. attenuata	Pure compound	100 μg g^{-1} b.w.	Inhibitory effect: Inhibition of increase in vascular permeability (65 %)	103
	A. sisalana	Juice	500 mg kg^{-1} b.w.	Inhibitory effect: Inhibition of ear edema (37–48.1%) Inhibition of hind paw edema (17.3-67.3 %) Inhibition of abdominal writhing (30.7–88.7%)	104
Antiparasitic	*A. lophantha*	Ethanol	18.5–1120 μg mL^{-1}	Inhibitory effect: *Trichomonas vaginalis*, *Entamoeba histolytica* and *Giardia lamblia* (MIC: not specified)	117
	A. brittoniana *A. brittoniana* saponins	Ethanol	0–500 μg mL^{-1}	Cytocidal effect: *Trichomonas vaginalis* (0–100% reduction)	118
Anticancer	*A. schottii*	*n*-Butanol	37.5–75 mg kg^{-1}	Antitumor effect: Breast cancer (Walker carcinoma 256) (7–28%)	16
	A. lehmanni *A. atrovirens* *A. salmiana*	Methanol Acetone	Not specified	Colon cancer (Caco-2), breast cancer (MCF7) and liver cancer (HepG2) (inhibitory effect ranged from 67.9% to 84.8% for the tested cell lines)	17

Table 1. Continued

Activity	*Agave* species	Extract type	Dose	Effect	Reference
	A. americana	Methanol	0–826.1 μg mL^{-1}	Inhibitory effect: Breast cancer (MCF7) (IC_{50}: 545.9–826.1 μg mL^{-1})	131
	A. angustifolia	Juice	2 g d^{-1} (3 weeks)	Transepithelial electrical resistance assay: Colon cancer (Caco-2) (monolayer resistance 12.7%; paracellular permeability −19.3)	132
Antihypertensive	*A. americana*	Aqueous Methanol	25 μg	Inhibitory effect: ACE inhibition (72–82%)	139
Immunomodulatory	*A. sisalana* homoisoflavones and flavones	Pure compounds	0–100 μmol L^{-1}	Inhibitory effect: Inhibition of PBMC proliferation (IC_{50}: 19.4–73.8 μmol L^{-1}), inhibition of IL-2 production (~0–84%), inhibition of IFN-γ production (0–100%)	37

MIC, minimal inhibitory concentration; MBC, minimal bactericidal concentration; abs., absorbance; μmol L^{-1} TE g^{-1} d.w., μmol L^{-1} Trolox equivalents g^{-1} dry weight; b.w., body weight; ACE, angiotensin converting enzyme; PBMC, peripheral blood mononuclear cell; IL-2, Interleukin 2, IFN-γ, interferon gamma.

The antimicrobial effects of *Agave* extracts are attributed to their bioactive components. Several studies have demonstrated that phenolic compounds, terpenes and saponins alter the membrane properties of Gram-negative and Gram-positive bacteria, effecting changes in hydrophobicity, surface charge and membrane integrity, which are followed by leakage of intracellular constituents and subsequent cellular death.[66–68] In addition, other studies have reported that these bioactive compounds showed different modes of action, such as inhibition of cytoplasmic membrane functions, inhibition of energy metabolism, inhibition of nucleic acid synthesis and inhibition of vital enzymes, all of which can result in bacterial death.[69–72] The antimicrobial activity of the phenolic compounds, terpenes and saponins is associated with their structure, hydrophobicity and molecular size. These characteristics facilitate their interaction with membrane lipids and proteins and render the compounds stable and water soluble.[73] Furthermore, compared to higher-molecular-weight compounds, low-molecular-weight compounds can more easily penetrate the bacterial membrane, increasing their interactions with intracellular components and enhancing their antimicrobial effects.[74] Consequently, *Agave* extracts represent an important economical source of antimicrobial agents because of their diversity of bioactive compounds and range of mechanisms of action arising from the different characteristics of the active compounds, which further increases their antimicrobial potential.

Antifungal activity

The ability of *Agave* extracts to inhibit pathogenic spore germination has been reported in several studies (Table 1). De Rodríguez *et al.*[75] observed that a hexane extract of *A. lechuguilla* exhibited at least 50% mycelia and sporulation inhibition at ≤3000 μL L^{-1} against *Rhizopus stolonifer*, *Colletotrichum gloeosporioides* and *Penicillium digitatum*. Additionally, the ethanolic extract from the same plant at ≤5000 μL L^{-1} displayed mycelia (>38%) and sporulation (>50%) inhibition. Similarly, Sánchez *et al.*[76] found that *A. asperrima* and *A. striata* extracts had an inhibitory effect on *Aspergillus flavus* (0.5–30 mg mL^{-1}) and *Aspergillus parasiticus* (1–25 mg mL^{-1}). In addition, 75% of the MIC was observed to reduce mycelial production by 32–79%. The MIC also exhibited a 99% and 85% inhibition against aflatoxin and cyclopiazonic acid, respectively. Some studies[13,15,61,63] analyzed the antifungal activity of *Aloe vera*, *A. lechuguilla*, *A. picta*, *A. scabra*, *A. lophantha*, *A. attenuata* and *A. sisalana* extracts against *Candida albicans*, *Candida tropicalis*, *C. luteolus*, *Cryptococcus neoformans*, *Aspergillus niger*, *Aspergillus flavus*, *A. alternaria* and *Rhizoctonia solani*. The antifungal activity of the *Agave* extracts were determined using the MIC (2–244 mg mL^{-1}) and agar disc diffusion (14–17 mm) methods. These results highlight the inhibitory and fungicidal effects of *Agave* extracts on food and human fungus, indicating that these extracts can be used by the food and pharmaceutical industries.

The observed antifungal activity of the analyzed *Agave* extracts arises from the constituent phenolic compounds, terpenes and saponins. Phenolic compounds such as flavonoids, phenylpropanoids and polyphenols have demonstrated potent antifungal effects via inhibition of cell wall formation, disruption of cell membrane and inhibition of mitochondrial function.[77–81] Furthermore, these compounds can arrest cell cycle processes at the S-phase, inhibiting cell division and subsequently affecting fungal cell growth.[82] Similarly, at enzymatic level, phenolics can cause G_2/M cell cycle arrest, chromatin condensation, nuclear fragmentation and phosphatidylserine exposure, which induce apoptosis.[83] Conversely, the antifungal mechanisms of terpenes are mainly associated with disruption of membranes and cell walls, inhibition of proton motive force, electron flow, active transport and vital enzymes, and coagulation of cell contents, resulting in leakage of intracellular components.[73,84–87] The antifungal effect of terpenes is related to their polarity because less polar molecules easily interact with the lipid fractions of membranes, which affects their permeability and thus allows them to cause fungal death.[58] By contrast, saponins exert their antifungal effects by acting as a detergent, which arises from the lipophilic part of these compounds being anchored to the lipophilic membrane bilayer after complexing with cholesterol and the hydrophilic moiety being located outside the cell, thus causing a leakage of intracellular components and leading to cell death.[88,89] Therefore, the antifungal mechanism of saponins is associated with the close interaction between the non-polar components and the fungal membrane. In summary, *Agave* extracts could represent an alternative antifungal agent because of their bioactive components. Interactions between these compounds can result in a complementary effect, thus enhancing their antifungal potential.

Antioxidant activity

The antioxidant activities of *Agave* extracts have been observed using different assays (Table 1). Hamissa *et al.*[51] reported the presence of polyphenols and flavonoids in *A. americana* extracts, which exhibited antioxidant effects. The authors attributed the antioxidant effect of the extracts to these compounds because

they observed a positive correlation between the phenolic compounds ($R^2 = 0.94$) and antioxidant activity (determined using a reducing power assay). Similarly, Rizwan *et al.*[13] observed antioxidant activity in *A. attenuata* extracts. For example, the evaluated extract at 0.1 mg mL^{-1} was able to inhibit between 74% and 61% of the DPPH radical. Additionally, 5 mg of the extracts exhibited between 50% and 70% inhibition of peroxidation in a linoleic acid system. Furthermore, the analyzed extracts showed reducing power at 1 mg mL^{-1} (absorbance between 0.22 and 0.66). Similarly, Ahumada-Santos *et al.*[14] observed that *Agave* extracts (from *A. tequilana*, *A. ornithobroma*, *A. impressa*, *A. rzedowskiana*, *A. schidigera* and *A. angustifolia*) had antioxidant activity by the DPPH assay (6.4–27.4 μmol L^{-1} Trolox equivalent (TE) g^{-1} d.w.). In addition, the *A. rzedowskiana* hexane extract exhibited antioxidant effects, as determined using 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) (9.7–212.1 μM TE g^{-1} d.w.), ORAC (46.2–862.6 μmol L^{-1} TE g^{-1} d.w.) and β-carotene bleaching (71.5% inhibition) assays, whereas the methanol extract exerted a pro-oxidant effect. In a study performed by Ribeiro *et al.*,[15] the antioxidant activity of *A. sisalana* extracts and saponins was examined using the DPPH assay, and EC_{50} values of 1452 and >10 000 μg mL^{-1}, respectively, were observed.

The antioxidant capacity of natural extracts is mainly associated with the presence of phenolic compounds such as flavonoids. Accordingly, previous studies have evidenced the high antioxidant activity of these compounds, which arises from the catechol and chromane groups found in their structures.[90,91] This powerful activity is also related to the presence of hydroxyl groups at the 3′- and 4′-position of ring B, a hydroxyl group at the 3-position of ring C and a double bond between C2 and C3 of their structure.[92,93] Molecules with these structural characteristics are better able to donate electrons and protons to stabilized free radicals, to reduce and chelate metals and to impart stability via a resonance effect than compounds without these features. Terpenes have similar antioxidant potential as flavonoids, although their antioxidant activity depends on different structural characteristics, such as the presence of a phenolic structure, hydroxyl groups, conjugated systems and multiple bonds.[94–97] In contrast to flavonoids, terpenes are hydrophobic, which allows them to scavenge free radicals and reduce and/or chelate metals in systems with similar hydrophobicity.

Although saponins are known to exhibit less antioxidant activity than phenolic compounds and terpenes, these compounds still have important antioxidant activity. The antioxidant mechanism of these compounds is not completely clear. Hydroxyl groups and oligosaccharide moieties at C-3 play an important role in the antioxidant potential of these compounds and confer on them the ability to donate hydrogen atoms or electrons to terminate radical chain reactions.[98–100] Because of the above-mentioned characteristics of the bioactive components of *Agave* extracts, these compounds likely contributed to the antioxidant activity of the studied extracts.

Anti-inflammatory activity

Agave extracts have also shown anti-inflammatory effects (Table 1). An *A. Americana* extract (200 and 300 mg kg^{-1}) used to treat induced inflammation of the gastric mucous membrane caused an inflammation reduction (50%). Additionally, the analyzed dose displayed no harmful effects.[101] Similarly, Garcia *et al.*[102] observed a reduction in tissue inflammation when applying *A. intermixta* extracts (300 and 500 mg kg^{-1}), achieving 50% inflammation reduction compared with a control group. Moreover, Da Silva *et al.*[103] demonstrated that the application of *A. attenuata* saponin (100 μg kg^{-1}) to vascular permeability inflammation reduced inflammation by 60% compared to the control. Dunder *et al.*[104] induced inflammation in mouse ears and legs and found that *A. sisalana* extract at 500 mg kg^{-1} was able to decrease the inflammation. Compared to a control, ear inflammation was reduced by 50–60%, and leg inflammation was decreased by 10–60%.

The anti-inflammatory activities observed in these studies are attributed to the presence of saponins, phenolic compounds and terpenes. Different studies have demonstrated that the main mechanism of action of these compounds against inflammatory processes is inhibition of regulatory enzymes such as cyclooxygenases (COXs), phospholipases (PLs) and lipoxygenases (LOXs).[105–108] These enzymes play an important role in the release of arachidonic acid, which is a precursor in the biosynthesis of eicosanoids strongly associated with the inflammatory response, such as prostaglandins and prostacyclin.[109,110] Additionally, these bioactive compounds inhibited other regulatory enzymes involved in the inflammation and immune response, such as protein tyrosine kinases (PTKs), protein kinase C (PKC) and phosphodiesterase (PDE).[111] In addition, saponins, phenolic compounds and terpenes are associated with the inhibition of other important factors related to the inflammation process, including nitric oxide (NO), tumor necrosis factor-alpha (TNF-α), interleukin (IL) and transcriptional factors.[112–114] Generally, the anti-inflammatory effect of these compounds is based on inhibition of prostanoid biosynthesis, histamine release, PDEs, protein kinases (PKs) and transcription activation.[111,115,116]

Antiparasitic activity

The antiparasitic activity of *Agave* extracts has been analyzed by some authors (Table 1). Oranday *et al.*[117] observed that an *A. lophantha* extract exhibited an inhibitory effect on *Trichomonas vaginalis*, *Giardia lamblia* and *Entamoeba histolytica*. Similarly, Orestes Guerra *et al.*[118] reported the antiparasitic effect of *A. brittoniana* fractions, which could eliminate *T. vaginalis* when used at concentrations of 500, 100 and 10 μg mL^{-1}.

The antiparasitic activity of *Agave* extracts is enabled by the presence of phenolic compounds, terpenes and saponins, which exhibit different mechanism of actions. For example, saponins are mainly associated with membrane permeability alteration and pore formation, although the exact mechanism is unclear.[119] These effects are attributed to the lipophilicity of saponins, which allow them to interact with biomembranes, inducing a change in membrane protein fluidity and function.[120,121] The activity of these compounds depends on the type and number of sugar moieties, as these properties change the hydrophobicity of a molecule.[122] Similar to saponins, terpenes can also induce membrane disruption, and this effect was related to the hydrophobic nature of these compounds. Terpenes induced lipid oxidation in parasites, resulting in an overproduction of reactive oxygen species (ROS), which can cause mitochondrial damage.[123,124] In addition, these compounds inhibit vital enzymes such as topoisomerase reductase and effect irreparable damage to DNA.[125,126] Flavonoids are other type of compound present in *Agave* extracts that are associated with antiparasitic activity, which can induce membrane alterations because of their structure. Flavonoids with a double bond in the C ring and the B ring attached to C-2 have enhanced antiparasitic potential.[127] An important effect of flavonoids is the inhibition of enzymes involved in proliferation, differentiation and invasion,

such as PTKs and mitogen-activated PKs.[128] In addition, these compounds affect DNA replication via the inhibition of topoisomerase I and topoisomerase II, inducing apoptosis.[129,130]

Anticancer activity

The anticancer activity of *Agave* extracts (Table 1) was analyzed by Bianchi and Cole.[16] The authors observed antitumor activity of *A. schottii* extracts, which are abundant in saponins, against breast cancer, with concentrations of 75 and 37.5 mg kg^{-1} decreasing tumor incidence by 7% and 28 %, respectively. Similarly, another study found that an *A. americana* extract at 545.9 and 826.1 µg mL^{-1} (IC_{50} values) had a cytotoxic effect on MCP-7 and MCF-7 (human breast cancer) cells, respectively.[131] Similarly, the anticancer potential of *A. lehmanni* and *A. atrovirens* syrup was analyzed, with a concentration of 15 mg mL^{-1} causing 84.89%, 67.95% and 27% inhibition in human colon (Caco-2), liver (HepG2) and breast (MCF7) cancer cells, respectively.[17] The effect of *A. angustifolia* extracts on colon cancer (Caco-2) cells was also observed: specifically, the evaluated extract increased the bifidobacteria population, short-chain fatty acid levels and transepithelial electrical resistance, while decreasing the ammonia levels.[132]

Different studies have reported that the bioactive compounds present in *Agave* extracts (phenolic compounds, terpenes and saponins) have potent anticancer effects. The anticancer mechanism of these compounds is based on their ability to act as preventive agents by decreasing ROS generation, redox potential and chelating compound levels (as previously described). Additionally, these compounds showed activity against cancerous cell lines by inhibiting cancer propagation. The target of these compounds is the inhibition of the expression of important enzymes, such as TNF-α, nuclear factor kappa b (NF-κB), cytochrome P450 (CYP), PKs, heat shock proteins (Hsps) and COXs.[133–137] These enzymes play an essential role in immune response regulation, molecular signal mediator biosynthesis (e.g. cholesterol, fatty acids, bile acids, steroid hormones and compounds involved in exogenous substrate metabolism), cell division, proliferation, differentiation, invasion, metastasis, metabolism and apoptosis; as a result, these enzymes are targets for cancer therapy.[133,138] In summary, these compounds exhibited functional properties, such as carcinogen inactivation, cell cycle arrest, apoptosis induction, antiproliferation, differentiation and angiogenesis inhibition.[138] Consequently, the studied bioactive compounds could be considered promising anticancer agents.

Antihypertensive activity

The antihypertensive activity of *A. americana* extracts has been demonstrated using the angiotensin-converting enzyme (ACE) test (Table 1), with 25 µg achieving 72% (aqueous extract) and 82% (ethanol extract) ACE inhibition, suggesting their potential for treatment of high blood pressure.[139]

Most likely, the antihypertensive activity of *Agave* extracts is primarily related to the presence of phenolic compounds, terpenes and saponins. Antihypertensive effects result from antioxidant activity against ROS production, which is implicated in cardiovascular disease development. For example, different studies have demonstrated that these compounds inhibited or decreased the production of ROS such as O_2^- and $ONOO^-$, which are involved in hypertension.[140–142] These effects are attributed to inhibition of the enzyme nicotinamide adenine dinucleotide phosphate (NADPH) oxidase, which is the main source of O_2^- in endothelial cells.[143] Another important antihypertensive mechanism of these compounds is their renal effects, which are related to the downregulation of the epithelial sodium channel (ENaC) in the kidney, which is associated with decreased blood preasure.[144] Additionally, these compounds exhibited a vasodilator effect, which could be associated with ACE activity,[139,145,146] and could inhibit the expression of PKs, matrix metalloproteinases and inflammatory molecules associated with cell growth and apoptosis, which could interfere with blood pressure control.[97,147]

Immunomodulatory activity

The immunomodulatory effect of *A. sisalana* flavones and homoisoflavonoids on peripheral blood mononuclear cells (PBMC) was evaluated.[37] The *Agave* flavones and homoisoflavonoids at concentration of 0–100 µmol L^{-1} were observed to significantly inhibit the production of interleukin-2 (IL-2) (from 248 to 0 pg mL^{-1}) and interferon gamma (IFN-γ) (from 4800 to 0 pg mL^{-1}) (cytokines that induce the growth of PBMCs by antigens) in PBMCs in a concentration-dependent manner.

These results are in agreement with several other studies reporting that the immunomodulatory mechanism of flavonoids involved regulating the expression of proinflammatory cytokines.[148] Moreover, other bioactive compounds present in *Agave* extracts, such as saponins and terpenes, could be related to the observed immunomodulatory effect because of their immunomodulatory potential. In this regard, saponins and terpenes were also observed to interfere with the production of proinflammatory cytokines.[39,149] These results provide evidence that *Agave* extracts are a potential source of immunomodulatory compounds.

POSSIBLE APPLICATION OF *AGAVE* BY-PRODUCTS IN FOOD AND PHARMACEUTICALS

The application of *Agave* plants in foods has been insufficiently studied. In this regard, Zamora-Gasga *et al.*[150] tested the effect of adding *A. tequilana* syrup, fructans and dietary fiber to granola bars. The authors obtained bars with high fiber content (23.3%) and a balance between soluble (18.90%) and insoluble (3.21%) fiber fractions. Regarding hydrolysis (80.12% and 90.90%) and the glycemic (77.26% and 86.55%) index, the results showed that these *Agave* granola bars were statistically similar to the control (without *Agave* addition), suggesting that *Agave* granola bars could be an option as a supplement to the human diet.

Furthermore, Urias-Silvas *et al.*[151] evaluated the physiological effect of incorporating fructans of *A. tequilana* (10%) in mouse diets. After 5 weeks of feeding, mice fed with the fructans exhibited lower body weight and intake compared with the control group, and the same trend was observed for serum glucose and cholesterol levels. In addition, the *Agave* fructans diet increased the concentration of glucagon-like peptide 1 (GLP-1) and its precursor (proglucagon mRNA) in different colon segments. The obtained results suggest that *Agave* fructans could be fermentable and could stimulate satietogenic/incretin peptide production in the lower intestine, which in turn could induce beneficial effects on glucose metabolism, body weight and fat mass development.

Plant leaves are also commonly used in traditional foods as seasoning. Accordingly, *Agave* leaves have been traditionally used in the culinary practices of pre-Hispanic cultures due to their distinctive effect on the odor and flavor of foods.[152] Additionally, ancient cultures used *Agave* plants in folk medicine remedies

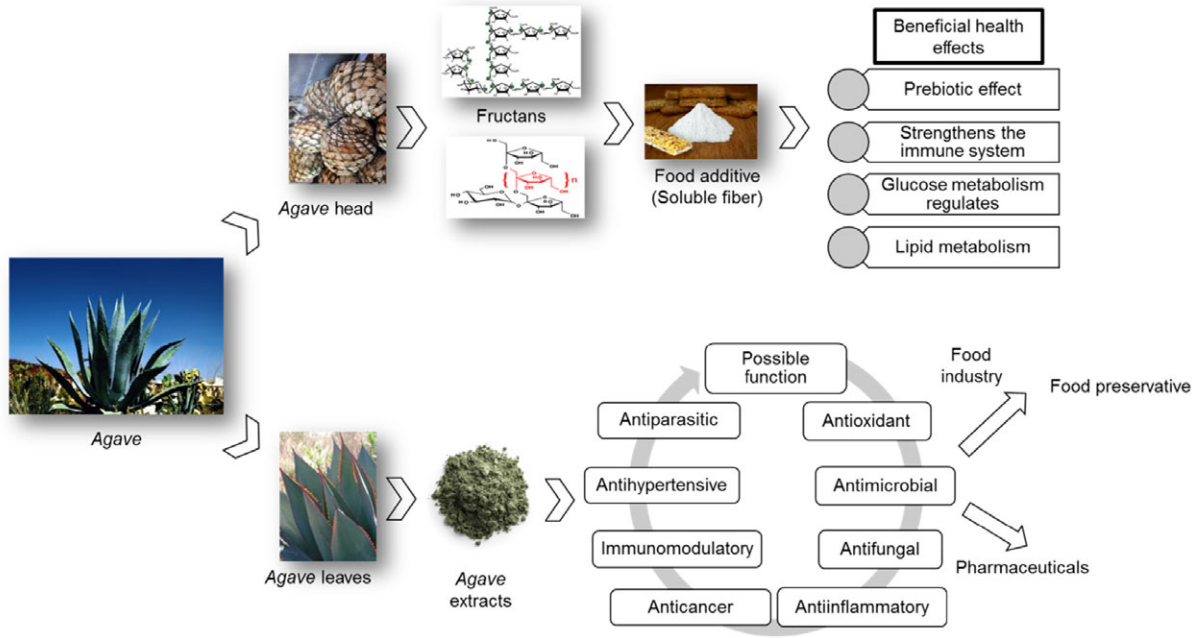

Figure 4. Possible application of *Agave* in food and pharmaceuticals.

against pain, bumps, inflammation, anemia and wounds, among others.[7]

Several studies have shown the potential of *Agave* extracts. As a result, *Agave* plants could be an alternative for use in the food industry as a safe food additive and then promote beneficial effects to the consumer (Fig. 4).

Food production is one of the largest economic activities globally. However, food production is affected by several factors. The principal factors affecting the food industry are microbiological and oxidative aspects.[153,154]

Regarding the microbiological aspect, foodborne diseases represent a serious public health problem.[155] This is evidenced by the 26 foodborne outbreaks occurring between 2012 and 2013 in the USA, where *Salmonella* sp., *E. coli* and *L. monocytogenes* were found to be highly prevalent in various foods.[156]

The oxidative aspect concerns autocatalytic reaction products resulting in rancidity development, which has become one of the main factors affecting food quality.[157] This process can occur at different stages, such as preparation, processing and storage, and can cause changes in appearance, taste, smell and shelf life.[158] These changes affect functional and nutritional compounds through, for example, fatty acid damage and oxidized polymer production, which can cause food security problems.[159]

Clearly, the food industry faces a serious problem. In this regard, natural additives are currently implemented, primarily because of consumer preferences shifting towards synthetic-free food additives. In this vein, due to their antimicrobial effects (as shown in *in vitro* testing) against pathogens and deteriorative microorganisms, *Agave* extracts could be an alternative agent for food applications, including as an additive for reducing microorganism incidence in food matrices and preventing food outbreaks. In addition, these extracts could be used to inhibit the food oxidative process, preserving the quality and prolonging the shelf life (Fig. 4). These proposals are based on previous research that evaluated natural extracts (thyme, oregano, mint, cinnamon, cloves, mustard, cranberry, pomegranate, grape, green and black tea) in different food matrices (meat, fish, dairy and vegetables), which revealed various antimicrobial and antioxidant effects.[19–24,94,95,160]

The extracts studied in the investigations mentioned above contained bioactive compounds that are also present in different *Agave* extracts: for example, linalool, eugenol, *p*-cymene, α-terpinene, nerolidol, *trans*-farnesol, β-*trans*-ocimene, sabinene, limonene, quercetin, kaempferol and myricetin. Consequently, *Agave* extracts could be an alternative additive for food products. Therefore, evaluating their incorporation into different food matrices is necessary in order to identify their effects and determine their feasibility for use in the food industry and for home consumption.

Another possible function of *Agave* extracts could be pharmaceutical, where they could be used as an auxiliary treatment for certain illnesses or diseases (Fig. 4). This option is based on their potential activity (antimicrobial, antifungal, antioxidant, anti-inflammatory, antihypertensive, immunomodulatory, antiparasitic and anticancer effects) shown in *in vitro* and *in vivo* tests (using animals as experimental models). In this sense, it is necessary to analyze the effects of *Agave* extracts on humans, and determine whether they would be a good auxiliary for the cited diseases.

CONCLUSIONS AND FUTURE TRENDS

Considering that plants of the genus *Agave* are abundant and generate a considerable amount of agro-industrial waste during alcoholic beverage production, *Agave* by-products are a potential source of extract elaboration and purified bioactive compounds, including molecules that have shown different biological effect in *in vitro* and *in vivo* tests. Based on the results, the food industry could use these extracts or pure compounds to decrease pathogen incidence and extend the shelf life of foods and food products. In addition, these by-products could be used by the pharmaceutical industry as auxiliaries in disease treatment. However, investigating their effects in different food matrices and human systems is necessary in order to determine whether these extracts or pure

compounds are safe alternatives for use in the food and pharmaceutical fields.

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