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An overview of phytomedicinal, ethnobotanical applications and phytochemical constituents of four major *Agave* species

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Agave plants are members of the Asparagaceae family and have a wide range of applications. They have been proven to be advantageous to mankind for centuries. The plant is an ideal crassulacean acid metabolism (CAM) crop model because of its succulent nature, ability to adapt to harsh climates, and capacity to thrive in water-limited environments. The genus *Agave* has many species and this review covers the most commonly found *Agave* species in India and also *Agave tequilana* that was recently introduced for cultivation at a few places in India due to its high commercial value. *Agave*, in general, is rich in carbohydrates and serves as a source of medicines, biofuels, and clothing. Selected species from this genus are used as a source of various commercially produced alcoholic beverages, like Tequila, Bacanora, and many others. *Agave* is rich in 'Inulin' type fructans that are indigestible carbohydrates, however, these are being explored as prebiotics for improving the growth of 'good' gut bacteria and for getting other health benefits, like enhanced nutrient absorption, reduced gut infections, better metabolism of fats and lipids. *Agave* is rich in steroidal saponins and produces diverse secondary metabolites (triterpenes, flavonoids, alkaloids, phenolics) that show utilizable biological activities including antimicrobial, anti-inflammatory, and anti-neoplastic potential. There are very few reviews available that are relatively constrained to a scope or obsolete. Research is being carried out on *Agave* to identify new metabolites having therapeutic potential for the treatment of diverse medical conditions. This review is an attempt to summarize the information on distribution, phytochemical constituents, ethnobotanical and phytomedicinal importance, and new research carried out on these aspects.

Keywords: *Agave americana*, *Agave cantala*, *Agave sisalana*, *Agave tequilana*, Ethnobotanical uses, Pharmacological activities

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Introduction

The genus *Agave* comprises around 300 species, out of which 210 have been recognised[1] while the remaining are yet to be categorised. They belong to the family Asparagaceae, previously known as Agavaceae[2]. *Agave* are considered, the natives of America, most commonly found in arid and semi-arid regions of North America (Utah)[3] extending towards Mexico, Northern-South America, and Caribbean Islands[4]. They are succulent monocots with leaves arranged in a manner forming rosettes extending from a few inches to several feet[5]. *Agave* has green to bluish colour striped or variegated leaves. The leaves are hard, thick and rigid, ranging from short and broad to long and narrow[2]. Tips and margins of leaves are lined with long and sharp spines (teeth). The interior of the leaves comprises longitudinal fibres representing the vascular system. *Agave* plants have a life span of 10-30 years[2]. Generally, they are monocarpic (flower once in their lifetime, die after flowering and fruiting) and propagate vegetatively by rhizomes, bulbils, stolons, suckers etc. *Agave* flowers on stalks (branched or unbranched) arising from the centre of the rosette[2,5]. The flowers may be red or yellow in colour, bearing an inferior ovary surrounded by six petals and producing an abundant amount of nectar. The nectar produced by the plant act as a major food source and attracts pollinators which are most commonly nectar-feeding bats, hummingbirds, insects, etc[6]. For centuries, *Agave* plants have been utilized by society for obtaining highly tensile and durable fibres, beverages (Mezcal, Tequila, *Agave*

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syrup) and food. *Agave* plants follow the crassulacean acid metabolism (CAM) photosynthetic pathway and serve as a model for CAM crops. In future, due to the effects of global warming (increasing temperature, loss of water resources), cultivating C_3 and C_4 crops would be a great challenge because these plants require huge amounts of water for cultivation, whereas *Agave* plants may serve as an alternative solution (due to their ability to grow in limited water resources) for foods, beverages, sweeteners (*Agave* granules) and even as an alternative of bio-fuels[7]. There are various *Agave* species with multiple ethnobotanical significances (Fig. 1). For instance, *Agave* stores abundant amount of carbohydrates (starch and sugar) in its leaves and core of the stem, which is fermented and used for the preparation of various beverages[2]. Traditionally, Mexican people used *Agave* (as the plant is abundant in the area) as a major source of liquor. A tribe named 'Mescalero Apache' in Southern Athabaskan and Northern America got their name due to their dependence on the Mescal *Agave* plant found in desert areas[8]. The females of this tribe used to collect the leaves of Mescal *Agave* and process them to produce Mescal, an alcoholic beverage. Tequila a well-known alcoholic drink is prepared from blue *Agave* found growing in the city of Tequila, Mexico. The plant is used for the preparation of *Agave* Inulin powder, *Agave* nectar syrup, *Agave* Tequila, and *Agave* granulated sweetener[9]. *Agave* fibres are used to produce ropes and fences. In Mexico and Brazil, *Agave sisalana* (commonly called sisal) plants are cultivated in large areas. The sisal leaves produce long fibres that are strong and durable and possess high mechanical strength. The ropes and cables made of these fibres are used for ship rigging[10]. Besides these uses, studies have shown the pharmacological potential of *Agave* against various diseases. The by-products generated after processing of *Agave* plants consist of important constituents like terpenes, saponins, alkaloids, and phenols showing both *in vitro* and *in vivo* anti-microbial, anti-cancer, immunomodulatory and anti-parasitic activities[11].

In view of the above-mentioned potentials of various *Agave sp.;* this review majorly includes the studies related to the three most common *Agave* species growing in India (*Agave americana, Agave sisalana*, and *Agave cantala*) and a crop species recently being cultivated in India for its high commercial value (*Agave tequilana*) with emphasis on their ethnobotanical and pharmacological potentials.

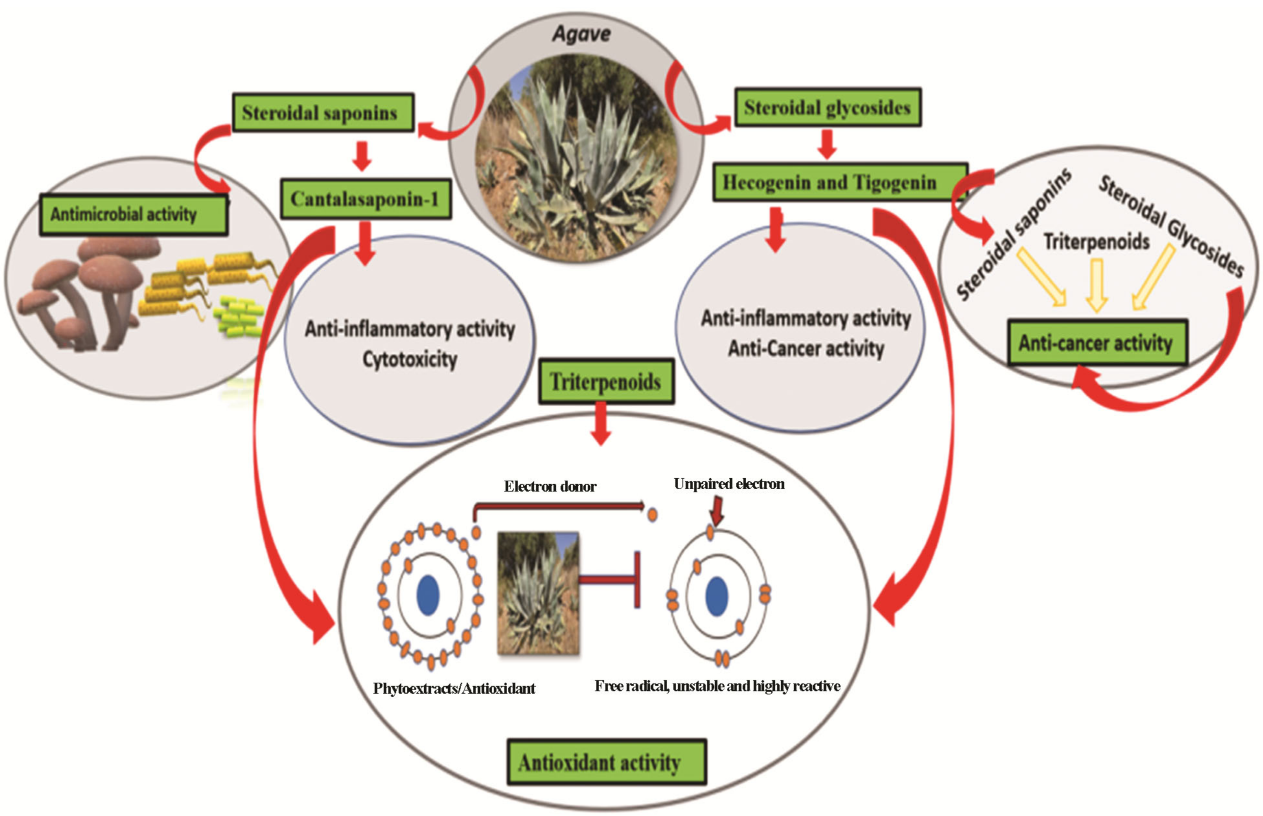

Fig. 1 — Biological activities of a few compounds isolated from *Agave*.

Methodology

Many biological, medical, and science documents were investigated to sort out major studies on *Agave* and obtain reasonable pertinent citations. The authors searched and investigated different web search engines including PubMed, Taylor and Francis, Web of Science, Wiley online library, Google Scholar, and Science Direct. The present review cites references including review articles, research articles, and information available on the webpage, book chapters, and book references.

Botanical classification

Agave belongs to Kingdom: Plantae, Division: Magnoliophyta, Class: Liliopsida, Order: Liliales, Family: Agavaceae, and Genus: *Agave.*

Status of *Agave* in India

Agave is a rosette plant with short stems having fleshy, pointed and erect leaves. The fibre of the plant is majorly used for making twines, rugs, ropes, brushes etc., also the waste residual generated after the processing of the leaves are used for making paper boards and craft papers. The genus *Agave* consists of about 200-300 species. Around the 15th century, the Portuguese introduced six species of *Agave* in India namely *Agave sisalana, Agave americana, Agave cantala, Agave angustifolia, Agave vera-cruz*, and *Agave lurida*, out of which three species are found beneficial namely *Agave sisalana*, *Agave americana* and *Agave cantala*[12]. Recently, *Agave tequilana* is being cultivated for commercial purposes in India. The plant yields hecogenin acetate, a type of steroid used by pharmaceutical industries in India. Hecogenin is used as an emmenagogue, laxative, and diuretic. It is also used for treating cancer, syphilis and scrofula. *Agave,* flower once and thereafter dies. The crop grows well on soil that are inappropriate for crop cultivation but cultivate vigorously on dry, and loam soils[10]. The plants are cultivated in the outer Himalayan regions, in different areas of Orissa, Tamil Nadu, Maharashtra, Karnataka and Andhra Pradesh[12]. The various *Agave* species examined in this review are described in the section below.

Agave americana

Agave americana, commonly known as Century plant or American aloe[13], is a native of North America, found from Texas and Arizona in the Northern USA to Central Mexico. It is used as an ornamental plant worldwide and now is grown in many countries like the Caribbean, Africa, South and North America, Europe, Oceania, and India. *A. americana* grows in different habitats and is resistant to drought, salinity, high temperature etc. It is a succulent plant and follows CAM photosynthetic pathway which helps it to tolerate extremely high temperatures by reducing the rate of transpiration. Basically, *Agave* fibres consist of numerous cells commonly known as ultimate cells which are highly lignified. These cells are organised such that they overlap with each other and are connected with a waxy film forming large continuous filamentous fibres. Each fibre is composed of one or more vascular bundles[14]. *A. americana* plants are harvested and processed for fibre extraction after the leaves get mature. The leaves and other bioactive compounds found in *A. americana* makes it a plant of benefit(s). The below section includes detailed ethnobotanical and pharmacological applications of *A. americana.*

Ethnobotanical uses of *A. americana*

A. americana is a plant of value, producing fibres, inulin, nectar, fructans, paper products, beverages etc. that are of great commercial importance. The leaves produce strong, tough, abrasive fibres which are lithe and superior compared to Manila hemp plant fibres[15]. The fibres have high moisture contents, high firmness, low density, and greater flexibility[16]. *A. americana* plants are rich in cellulose and require minimal maintenance for cultivation. During processing, they produce organic wastes that can be reused. Processing of the by-products is used for preparing organic-rich compost which is used as fuel for the production of biogas and manure for increasing soil fertility. Unlike synthetic fibre wastes, waste generated from the processing of *A. americana* is completely bio-degradable and can be recycled into low-grade papers. The plant is also used for making hedges for the protection of land and crops against predators[17]. The fibres are strong, having low density and high tensile strength and are used for producing wires, strings, and ropes that are used in agriculture and fishing. These fibres are also used for making doormats, nets, bags, carpets, drapes, saddle pads, headbands, furniture webbing, sandals, upholstery padding, decorative materials, bio-plastics, and geo-textiles. Low-grade fibres of *A. americana* are used for making papers[18]. The fibres are also used for leather embroidery using piteado technique[19].

Pharmacological activities of *A. americana*

Studies have shown the pharmacological importance of *A. americana*. The plant is rich in steroidal saponins, steroidal glycosides and triterpenoids, and possesses many phytomedicinal activities. The major phytochemicals reported from *A. americana* are enlisted in Fig. 2.

Traditionally, the plant is used for treating diarrhoea, dysentery, sciatica, rheumatoid arthritis, mucosal inflammation, and also as an antiseptic and antidiuretic. *A. americana* has been examined for their biological activities, such as antimicrobial, anti-neoplastic, anti-inflammatory etc. A study on *Agave americana,* showed the anti-inflammatory activity of lyophilized aqueous extract and two steroidal genins, namely, tigogenin and hecogenin isolated from the plant. Intraperitoneal administration of 200-300 mg/kg (doses) of lyophilized plant extract showed decent anti-inflammatory activity. Interestingly, the steroidal genins (both tigogenin and hecogenin) showed much greater anti-inflammatory activity in comparison to the standard corticosteroid drug dexamethasone[20].

Another study showed the anti-inflammatory activity of acetone extract of *A. americana* in TPA (12-O-tetra-decanoylphorbol-13-acetate) induced ear oedema in mice. Cantalasaponin-1, a bioactive compound isolated from acetone extract of *A. americana* showed 90% reduction in ear oedema with a maximum dose of

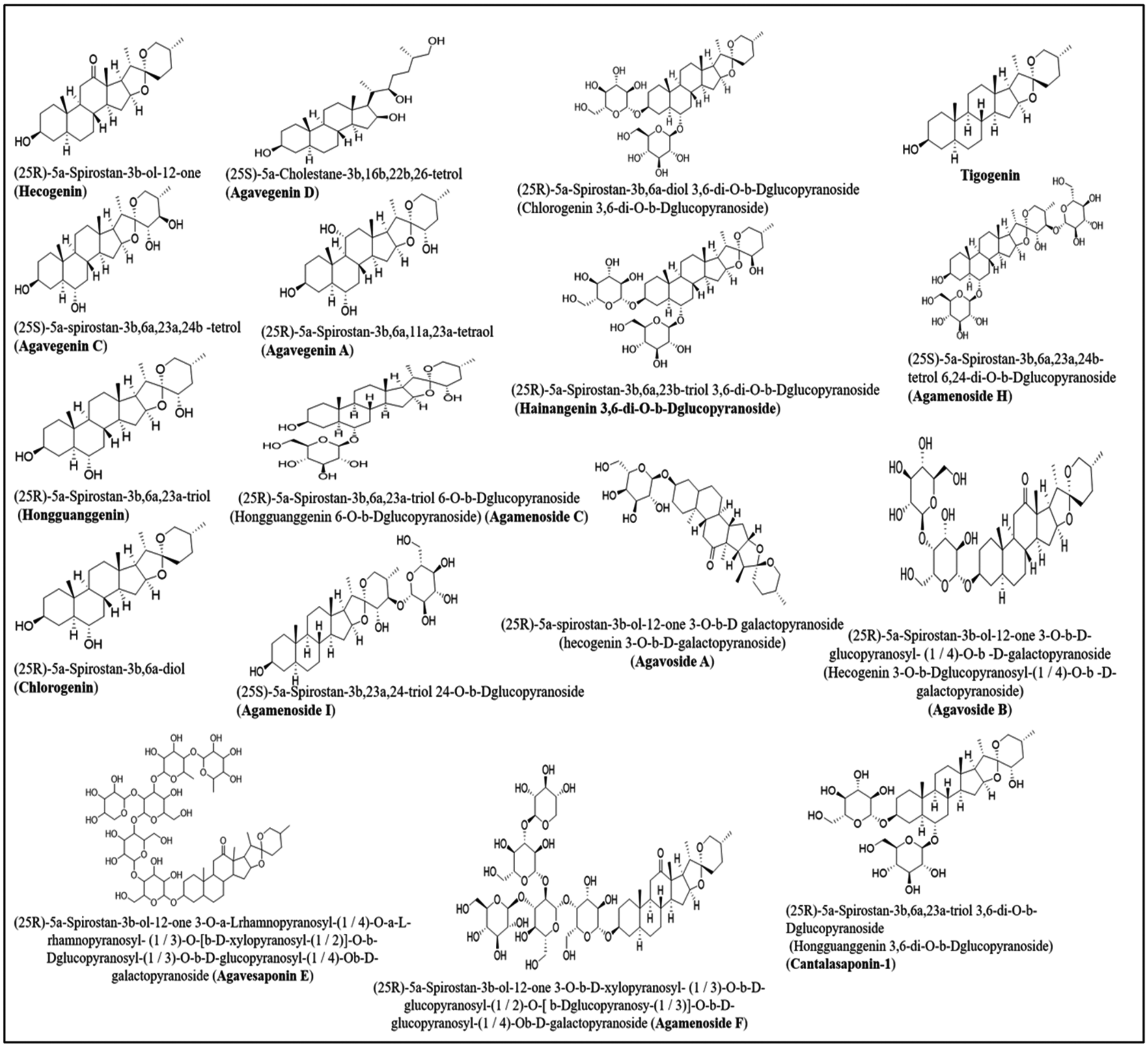

Fig. 2 — Important phytochemicals isolated from *Agave americana*.

1.5 mg/ear[21]. A study carried out by Misra and co-workers showed wound healing activity of *A. americana* hydroalcoholic extract (HEAA). In this experiment, a wound was incised in a mouse and HEAA was introduced, and the wound closure percentage was measured at regular intervals. The results showed that the wound closure was initiated on the 4th day and the rate of epithelialization was equivalent to the soframycin control, suggesting that *A. americana* extract possess marked wound healing activity[22]. In another study, the hydroalcoholic extract of *Agave americana* (HEAA) showed % inhibition in the paw oedema model induced by carrageenan and a reduction in the mass of granuloma in the cotton pellet-induced granuloma model. The results showed that 400 mg/kg of HEAA showed % inhibition of oedema equivalent to standard drug aspirin. Also, 400 mg/kg of HEAA showed a significant reduction in granuloma mass equivalent to Indomethacin[23]. Another study showed a reduction in acetic acid-induced colitis in rats. The *A. americana* extract (200 and 400 mg/kg) was administered in male Wistar rats having acetic acid-induced ulcerative colitis for 11 days daily. After 11 days of the treatment, the body weight, contraction of colonic muscles, reduction in ulcer score and antioxidant activity was measured. It was found that there was a significant reduction in ulcer scores, body weight was retained and the lipid peroxidase activity and myeloperoxidase activity was decreased significantly. Also, there was an improvement in the contraction of the colonic muscles. The results were equivalent to the positive control (a standard drug)[24]. A study was done to evaluate the cytotoxic potential of *A. americana* methanolic extract against MCF-7 and Vero cells. They used trypan blue dye exclusion assay, MTT and SRB assay to evaluate the cytotoxicity. After giving treatment, the viability was reduced to 85.50% and 81.13% in MCF-7 and Vero cell lines, respectively. While the IC_{50} was found to be 545.9µg/mL (SRB assay) and 775.1 pg/mL (MTT assay)[25]. *A. americana* also possesses potential antimicrobial activity against a broad range of microorganisms. According to a study, crude extract of *A. americana* showed potential antifungal activity against different plant pathogenic fungi namely *Fusarium solani, Macrophomina phaseolina, Aspergillus niger*, *Alternaria porii, Fusarium udum* and *Aspergillus awamori.* They measured the inhibition per cent of fungal hyphae growth and the maximum inhibition was observed against *Macrophomina phaseolina*[26]. In another study, methanolic extract of *A. americana* showed antifungal activity against *Alternaria brassicae* causing Alternaria blight of Indian mustard. The extract inhibited the germination of conidia of *Alternaria brassicae*[27]. Crude extract and different solvent fractions including methanol, petroleum ether, chloroform, and acetone fractions of *A. americana* showed significant antibacterial activity, equivalent to gentamycin standard drug. The extracts were effective with minimum inhibitory concentration (MIC) ranging from 2.5 mg/mL for *Staphylococcus aureus, Pseudomonas aeruginosa*, and 10 mg/mL for *Salmonella typhimurium* and *Escherichia coli* respectively[28]. The larvicidal activity of *A. americana* extract was observed against the larvae of various mosquitoes. In a study, the seed and leaf extracts of *A. americana* showed significant larvicidal activity against *Culex*, *Anopheles* and *Aedes* larvae. A 1:200 dilution of seed extract showed 100% larval mortality in 24 h against *Aedes* and *Anopheles* and 56% mortality against *Culex* larvae[29]. The ethyl acetate fraction of *A. americana* was also studied for its anti-leishmanial activity. The amastigote and promastigote parasitic forms of *Leishmania* were treated with ethyl acetate fraction of *A. americana* and the extract was able to inhibit both the pathogenic forms of *Leishmania* showing its potential to be used as an anti-leishmanial agent[30].

The only disadvantage associated with *A. americana* is that the weed is invasive. *A. americana* has been listed as an invasive species by the International Union for Conservation of Nature (IUCN) because of its ability to spread through seeds and colonize barren lands, roadside and desert[31]. The species has become invasive in many countries like New Zealand, China, Africa, Europe, Bermuda etc. Various management programs including physical and chemical methods have been initiated to control the growth of this weed worldwide and to some extents have been successful in controlling the growth of *A. americana.*

Agave sisalana

Agave sisalana is commonly known as sisal or sisal hemp. Sisal is widely known for its fibres and is classified amongst the important group of leaf fibres. It is a native of Mexico but has covered and spread to many parts of Asian and African countries like Kenya, Tanzania, India, China, Madagascar, Haiti, Brazil, etc[32]. The major producer of sisal is Brazil and exports approximately 100,000 tonnes of raw fibres to USA[33]. China, is the highest producer of sisal in terms of productivity, contributing 9 times of world's total sisal productivity[32]. In India, Central Research

Institute for Jute and Allied Fibres (CRIJAF) is the only place for sisal research.

Ethnobotanical uses of *A. sisalana*

Agave sisalana, *Agave cantala* and *Agave americana* are major fibre-producing *Agave* plants in India. Usually, sisal fibres are used to make carpets, rugs, brushes and mats. Sisal fibres because of their high durability and tensile strength, are widely used in shipping industries to anchorage small dexterity, and for handling heavy shipments[32]. Nowadays, decorticator machines are used for obtaining fibres from the plant. The procedure involves crushing the leaves by placing them in between the rollers of the decorticator and removing the pulp. The fibres are then washed and dried. The fibres produced by *A. sisalana* have high tensile strength, durability and stretch properties, which makes them useful for manufacturing ropes, twines and cables that are widely used in marine, shipping and agriculture[34]. The worldwide total contribution of *A. sisalana* in fibre production is nearly 85%[32]. Sisal is a "plant of benefit" having ample opportunity for the production of diverse value-added products such as sisal fibre-based thermostats, cement, thermoplastics, composites, gypsum, and geotextiles. The waste generated during the processing of sisal fibres could be used for enhancing the soil conditions such as moisture-retaining, nutrient enhancement etc. Sisal generates a large amount of fibre which can be utilized for producing tea bags, dielectric paper, filter paper, cigarette paper etc. The government has made initiatives for cultivating sisal in wastelands for providing employment to people from rural areas especially women for manufacturing sisal fibre-based handicrafts, on a cost-allocation basis consequently leading to a sustainable growth[32].

Pharmacological activities of *A. sisalana*

Apart from being known as the largest fibre producer in the world, *A. sisalana*, is also being researched for having any pharmacological properties. About 90% of *A. sisalana* biomass is wasted in the form of mucilage, pulp and sisal juice[35]. Sisal juice is rich in steroidal saponins, flavonoids, phenolics, glycosides, tannins and many other secondary metabolites that possess many medicinal activities[2]. Some of the phytochemicals isolated from *A. sisalana* have been presented in Fig. 3.

Many researchers have examined the antimicrobial, anti-inflammatory and antineoplastic potential of *A. sisalana* and have concluded that the species may

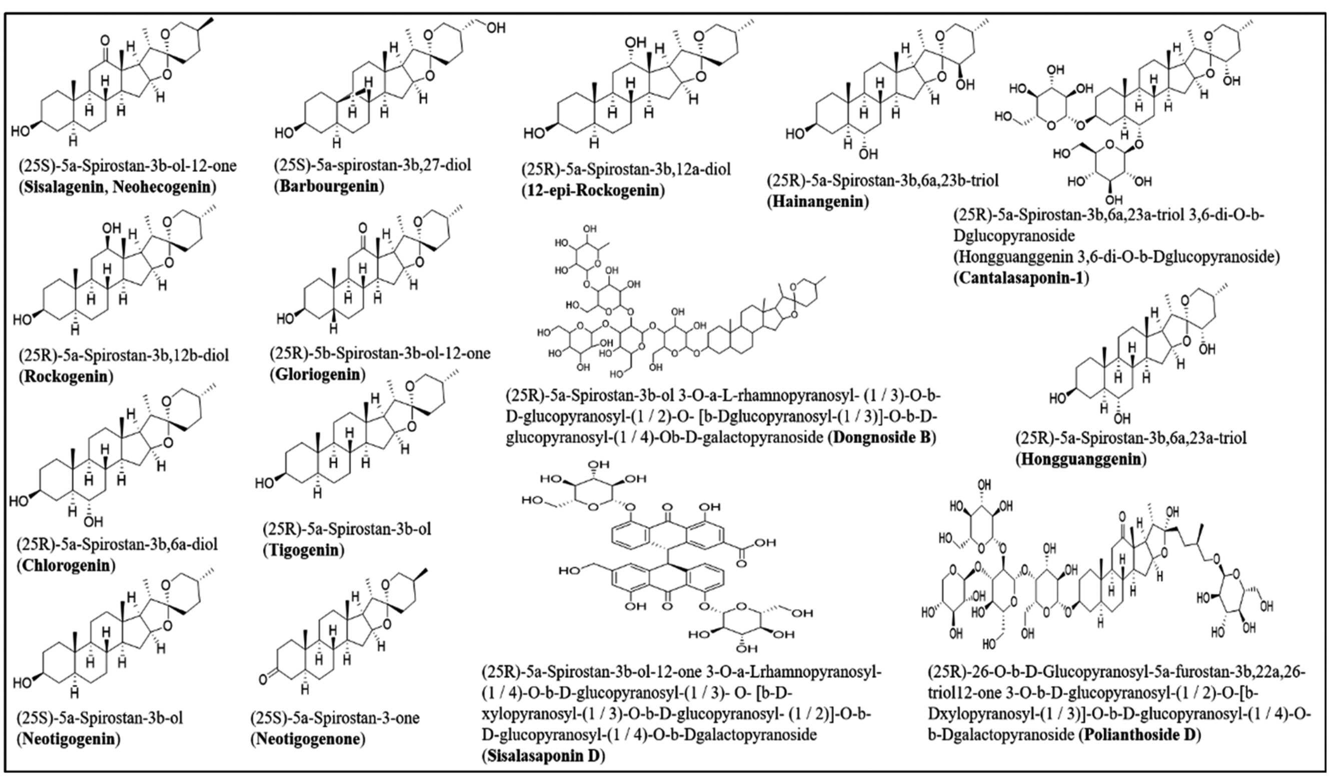

Fig. 3 — Important phytochemicals isolated from *Agave sisalana*.

be of pharmacological importance. A study showed the antimutagenic effect of three different sisal extracts *viz.* hexane (HAS), a dried precipitate of *A. sisalana* (DPAS) and extract obtained through acid hydrolysis (AHAS). The experiments were performed both *in vivo* (mice model) and *in vitro* (human lymphocytes and Vero cells). The results showed that different concentrations of the extracts had potential antioxidant activity. DPAS 250 µg/mL and AHAS50 µg/mL showed the highest cytotoxicity and antimutagenic effect in mice and Vero cells[36]. A study showed the anti-inflammatory activity of *A. sisalana* aqueous extract. They induced oedema in rats using formaldehyde, carrageenan and histamine. The *A. sisalana* extract, administered orally at doses of 400 mg/kg body weight, reduced histamine-induced oedema by 93.4% and carrageenan-induced oedema by 84.9%[37]. In another study, the anti-inflammatory and analgesic properties of the hexane fraction of *A. sisalana* (HFAS) in acute and chronic mouse models were studied. The experiments were performed on hind paw oedema, xylene-induced ear oedema, and on lung pleura with different concentrations of HFAS ranging from 5, 10, 25, and 50 mg/kg. In their study 10 and 25 mg/kg concentration of the extract showed more than 50% reduction in all the three acute mouse models. In the chronic mouse model (granuloma cotton pellet), the reduction was 58 and 46% in the 25 and 10 mg/kg treatment of extract, respectively[38]. A study showed the immunomodulatory function of various compounds (5,7, dihydroxy-3- (4'-hydroxy-benzyl)-4-chromanone; dihydrobonducellin and (+/-)-3,9-dihydroeucomine) isolated from *A. sisalana* leaves extract. The compounds showed inhibition of phytohemagglutinin (PHA) activated human peripheral blood mononuclear cells (PBMC). The compounds also inhibited the secretion of inflammatory cytokines IL-2 and IFN-Ƴ[39].

Several studies have been carried out to evaluate the antibacterial potential of *A. sisalana* leaves extract and it has been found that aqueous, hydroalcoholic and methanol extracts of sisal showed moderate to good antibacterial activity against *Escherichia coli*, *Salmonella typhi*, *Staphylococcus aureus*, *Streptococcus pyogenes*[35]. While the hydroalcoholic extract of sisal was effective against the fungus *Candida albicans*[40]. The *A. sisalana* aqueous extract showed inhibition of *Pyricularia oryzae* by inhibiting the spore formation and growth of mycelia. Thus, acting as a fungicide by preventing the growth of causative agent of rice blast[41]. Many studies have shown the cytotoxic effects of *A. sisalana* against mosquito larvae. According to a study carried out by Pizarro *et al.*, the liquid waste generated after the processing of *A. sisalana*, has larvicidal effects on both *Culex quinquefasciatus* and *Aedes ageypti*. They showed that the concentration of 322 ppm and 183 ppm of liquid waste was responsible for 50% larvicidal activity against *Aedes ageypti* and *Culex quinquefasciatus*[42]. The crude extract of *A. sisalana* was assessed for its larvicidal activity against *Aedes aegypti* fourth-stage larvae. The larvae were treated with *A. sisalana* crude extract for about 3 h, 6 h, 12 h, and 24 h. Thereafter, the LC_{50} was determined. An LC_{50} of 4.5±0.07 mg/mL of *A. sisalana* crude extract showed the insecticidal potential of *A. sisalana* in *Aedes aegypti* by promoting necrosis of hemocytes[43]. Studies have been conducted to evaluate the antioxidant activity of agro-industrial waste residues of *A. sisalana* (AsRE). In a study, the total antioxidant activity of AsRE was considerably high near about 91.75 mg of ascorbic acid equivalent per gram. Also, the reducing potential of AsRE evaluated using ferric ion reducing antioxidant assay (FRAP) showed 49.13%±2.03 activity. The antioxidant activity of AsRE was also evaluated *in vivo* using the model organism *Caenorhabditis elegans.* It was found that AsRE was efficient in reducing the levels of free radicals and reactive oxygen species and increasing the survival rates of *C. elegans*[44].

Agave cantala

Agave cantala, commonly known as Cantala, Cebu or Manila maguey, is a native of Mexico, also cultivated in Indonesia, Philippines, Bangladesh, Pakistan and South regions of India including Telangana[45].

Ethnobotanical uses of *Agave cantala*

A. cantala is a perennial plant having lanceolate-type leaves with narrow and pointed tips, arranged to form a rosette. Their height may reach up to 2 m in measurement[46]. They belong to the group of hard fibres producing plants along with *Agave sisalana* and *Musa textilis*. They are widely used for the production of commercial-grade cantala fibres. Traditionally, the fibres are used for preparing doormats, hammocks, cordage, carpets, baskets, rugs etc. Fibres of *A. cantala* are mixed with fibres of *Musa* for preparing binder twine, decorative items, ropes, fishing nets, bags, slippers etc. In Indonesia, *A. cantala* shoot buds are used as vegetables. It is cultivated for the production of a non-commercial alcoholic beverage called 'Pulque'[47].

Pharmacological activities of *Agave cantala*

A. cantala produces a variety of secondary metabolites (Fig. 4) chiefly steroidal saponins having many biological activities. Isolation of these steroidal saponins from rhizomes, leaves and fruits of *Agave cantala* has been reported. Two glycosides namely chlorogenin and diglucoside have been reported from the leaves of *A. cantala.* Cantalasaponin-1, a bisdesmoside has been isolated from the methanol fraction of *A. cantala* rhizomes. The cantalasaponin-1 possessed cytotoxicity against human cervical carcinoma cell lines (JCT-26 cell lines)[46]. Recent research carried out on *A. cantala,* showed the presence of pentaglycoside (a chlorogenin derivative) in the inflorescence (flower) having molluscicidal activity. Cantalasaponin-2 isolated from the rhizomes of *A. cantala* showed toxicity and lethality against *Biomphalaria glabrata*, the vector of diseases chistosomiasis at 7 ppm concentration[48]. The anti-inflammatory activity of the methanolic extract of *A. cantala* was examined by both acute (dextran and carrageenan-induced) and chronic models (granuloma-induced cotton pellet). It was found that there was 46.15% reduction with a 200 mg/kg dose and 61.53% with a 400 mg/kg dose of *A. cantala* methanol extract in carrageenan-induced model. In the dextran induced model, 20.56% (200 mg/kg) and 26.33% (400 mg/kg) reduction was measured[49]. The methanolic extract of *A. cantala* showed significant hydroxyl free radical scavenging activity and strong reducing potential. The ethanolic extract of *A. cantala* flower and an isolated purified compound pentaglycoside were tested for molluscicidal activity and it was found that 25 ppm of ethanolic extract of *A. cantala* and 10 ppm of isolated pentaglycoside were effective doses for the activity[48]. Another research showed the antimicrobial potential of *A. cantala* against *Plasmopara viticola*, a fungus responsible for powdery mildew disease in grapes. The extract of *A. cantala* was sprayed onto the leaves and an increase in polyphenol oxidase enzyme and polyphenolics was observed which reduced the fungal infection[50].

Agave tequilana

Agave tequilana is also known as blue *Agave (agave azul)*. It is a native of Tequila City, Mexico.

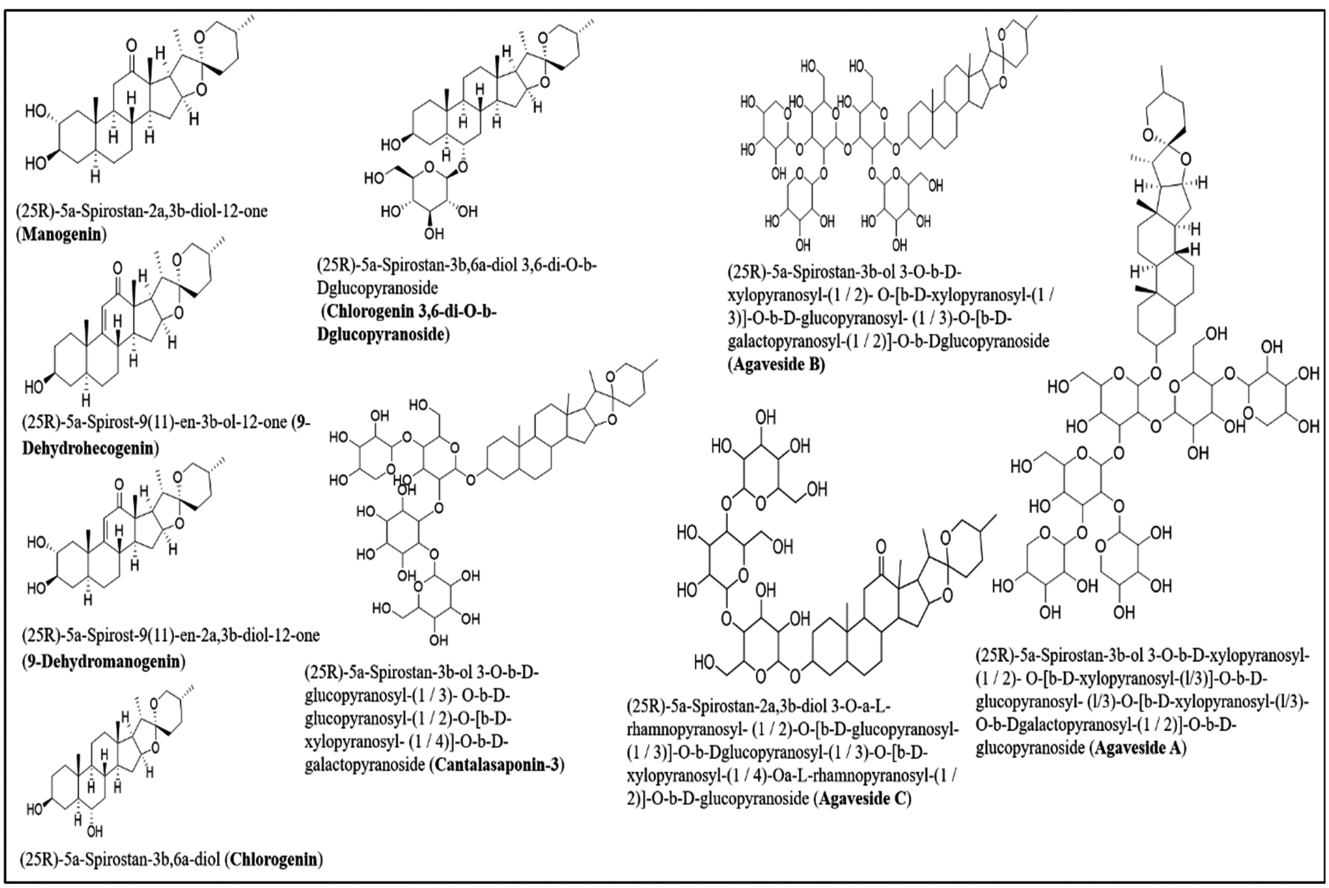

Fig. 4 — Important phytochemicals isolated from *Agave cantala*.

A. tequilana is cultivated in various parts of the world for the production of tequila, a famous distilled alcoholic beverage. The production and commercialization of tequila are certified by Mexican Tequila Regulatory Council (CRT)[51]. Amongst the highest producer of tequila, the US tops the list, followed by Germany, Spain, Japan and France. Around 1530s, the town currently known as Tequila was named Santiago de Tequila by a Spanish conqueror. It was the time when the Spanish consumed all their manufactured brandy. Thereafter, they began distilling *Agave* to produce the first original distilled spirit. This was the first event when the fusion of alcoholic beverages from Mexico and Spain arose, introducing Tequila. During 1600s, the Marquis of Altamira, Don Pedro Sanchez de Tagle started the mass production of Tequila in Jalisco[52]. The blue *Agave* was discovered by Dr. Frederic Albert Constantin Weber in the late 1800s. Dr. Weber was the one who encouraged the tequila makers to prepare tequila only by using blue *Agave* as it contained high natural sugars, perfect for making spirits. Any distilled spirit is considered tequila only if it is made from blue *Agave*. Therefore, to honour Dr. F.A.C. Weber blue *Agave* is known as "*Agave tequilana* Weber"[53]. According to Mexican laws only authorized manufacturer from specified territory or districts of Jalisco, Mexico is permitted to prepare the alcoholic beverage tequila from Blue *Agave*. The Declaration for the Protection of Appellation of Origin Tequila or Denomination of Origin Tequila (DOT) has specified that no other drink made from blue *Agave* could be sold under the name Tequila[54].

Status in India

Blue-green *Agave* is found in the Deccan plateau regions of India. The climatic conditions, temperature, average rainfall, and soil conditions all are appropriate for the cultivation of the blue-green *Agave* variety in the Deccan regions of India. Desmond Nazareth is the founder of Agave India, the first Indian company to intricate alcoholic brews directly from blue-green *Agave*. The micro-distillery is used for the preparation of global spirits meeting all international standards. The products produced are solely made in India, starting from raw materials to manpower involved in the extraction and preparation of beverages[55]. Due to the restrictions administered by Denomination of Origin Tequila (DOT), the tequila produced in India by Agave India is sold under the name of DesmondJi® as 51%, 100% Agave spirit and a 51% Agave Gold spirit. Agave India is the country's first fully integrated "field to bottle" alcohol beverage company focusing on global spirits made to international standards with Indian raw materials. Under the DesmondJi® label, the company produces a 100%, a 51% Agave spirit and a 51% Agave Gold spirit with an oak finish[54].

Tequila production

Tequila is prepared from 8-10-year-old *A. tequilana* plants. The inflorescence is removed to concentrate all the sugar into the stem. The presence of a few brown spots of bleeding exudates/sap on the surface of the pina (head) indicates that the pina is mature and ready for harvesting. Pina/heads are collected, cut into half and cooked (steam baked) in an oven to convert natural carbohydrates and starches into fermentable sugars. *Agave* is rich in 'inulin' which is converted into fructose and the carbohydrate is then fermented. The baked/cooked heads are crushed and the fermented *Agave* juice is converted into alcohol using yeast. The flavour and texture of tequila depend upon the nutrients and yeasts added. After fermentation, the juice must have 5%-7% alcohol content, after which it is subjected to distillation. The juice is distilled twice. The product obtained after the first distillation is called Ordinario. While the final product obtained after the second distillation process is known as Tequila. This is known as Blanco tequila. Thereafter, the tequila is stored in large Oak boxes/containers for cask maturation[53]. The production of tequila is classified in two ways. First, 100% *Agave,* in which the fermentation of *Agave juice* is not subjected to any kind of modifications or enrichment using different reducing sugars obtained from other *Agave* plants. Second is Tequila, in which about 51% of total sugar content must be purely obtained from blue *Agave* Weber variety, while 49% enrichment could be done with reducing sugars from other source prior to fermentation[55]. The waste generated after the processing of *A. tequilana* is used for the production of publication-grade papers. A recent study suggested that the pulping of *A. tequilana* waste through conventional and non-conventional pulping methods could be used for the production of valuable grade papers[56].

Pharmacological activities of *Agave tequilana*

A. tequilana juice produced as a by-product consists of steroidal saponins, triterpenes, alkaloids and tannins having biological activities. In a study, the insecticidal activity of *A. tequilana,* hexane and ethyl-acetate extracts and the juice obtained as a by-product during the production of tequila was evaluated. The insecticidal activity was examined against silverleaf whitefly and *P. redivivus* nematode, and it was found that undiluted juice of *A. tequilana* killed 31% of whitefly, while 12% diluted juice killed 100% *P. redivivus* nematodes. Similarly, hexane extract diluted to 4% and ethyl-acetate extract diluted to 0.4% killed 100% whitefly and *P. redivivus* nematodes, thereby suggesting the insecticidal potential of *A. tequilana*[57]. Fig. 5 shows the various phytochemicals that have been reported from *A. tequilana*.

Natural compounds from *Agave*

Agaves possess the ability to grow in desert and semi-arid areas. Therefore, they are known as “wild century plant”, “hardy century plant”, and “rough century plant”. Several studies have confirmed the use of various *Agave* species as natural sweeteners, nutraceuticals, biofuels and prebiotics. It has been studied that *Agave* is rich in saponins and sapogenins. Various saponins possess antimicrobial, anticancer, anti-inflammatory and antioxidant activities along

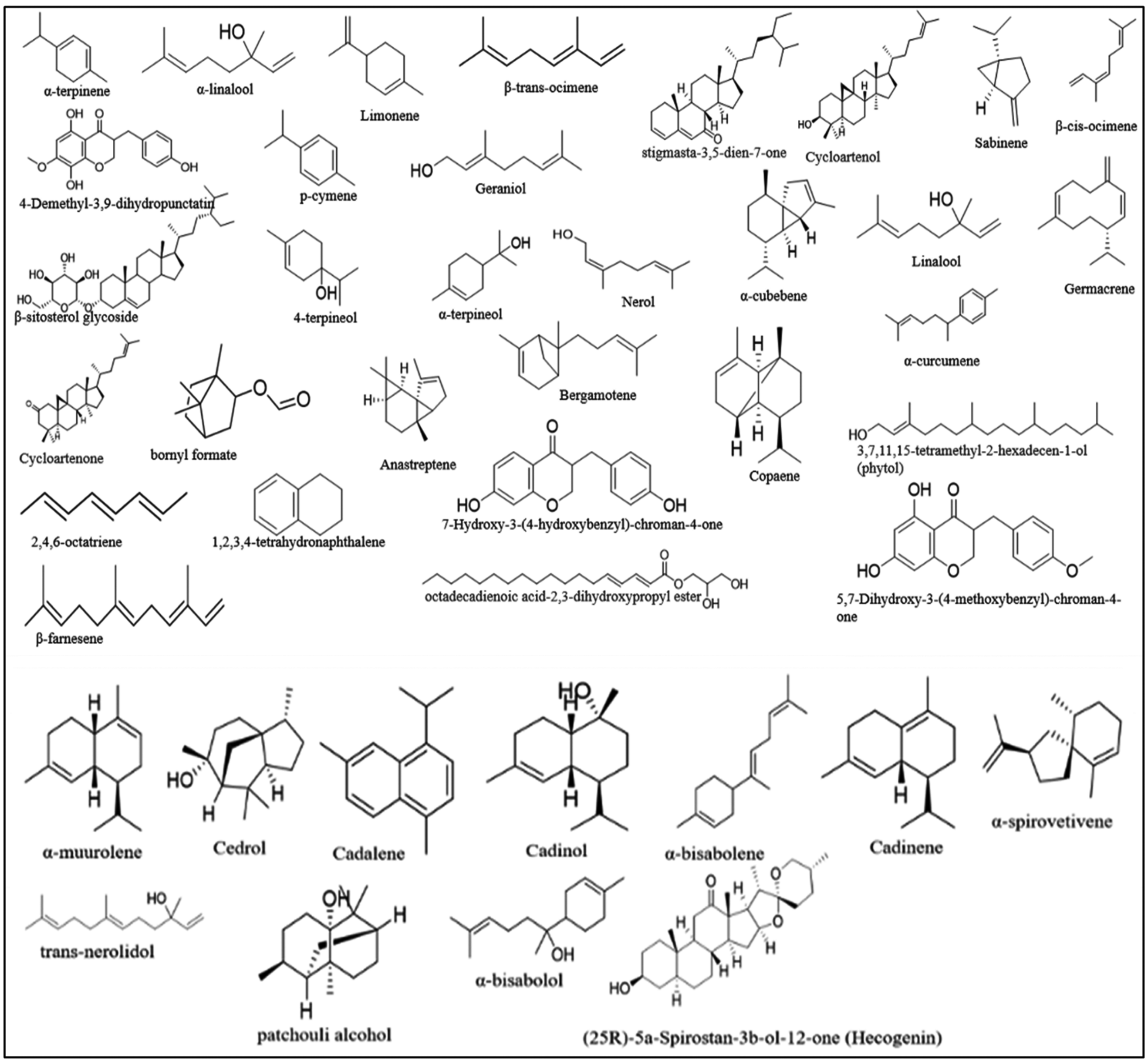

Fig. 5 — Important phytochemicals isolated from *Agave tequilana*.

with use as an immunostimulant, adjuvant and hypocholesterolaemic agent[58].

Sapogenins

Agave are rich in steroidal sapogenins. They contain cholestane-based and spirostanol-based steroidal sapogenins. The only cholestane-based steroidal sapogenin reported in *Agave* is Agavegenin D. Spirostanols are 16,22;22,26-bisepoxycholestanes derived from cholestane[59]. The spirostanol structural skeleton consists of a tetrahydropyran and tetra-hydrofuran ring joined in a spiral manner at C-22. Spirostanol-based steroidal sapogenins are isolated from the rhizomes, leaves, callus culture, and flowers of *Agave.*

Saponins

Saponins are compounds having a carbohydrate/sugar moiety and a non-carbohydrate moiety known as aglycone. The aglycone unit is hydrophobic while the sugar unit is hydrophilic. The sugars in saponins are usually β-D-galactopyranosyl, β-D-glucopyranosyl, α-L-rhamnopyranosyls and β-D-xylopyranosyl. Saponins commonly found in *Agave* are categorised into furostanol glycosides and spirostanol glycosides[60,61]. On the basis of the number of sugar moieties attached to aglycone, the compounds are classified as monoglycosides, diglycosides, triglycosides, tetraglycosides, pentaglycosides, and hexaglycosides. The major type of spirostanol saponins reported in *Agave* are monodesmosidic[60]. While, in the case of furostanol glycosides, bidesmosidic saponins are found in abundance in *Agave*.

Spirostanol glycosides

Spirostanol diglycosides (monodesmosidic) have two monosaccharide residues; one β-D-glucopyranoside, present at the terminal, and β-D-galactopyranoside present on the inner side. While, only β-D-glucopyranoside is present in spirostanol diglycosides (bidesmosidic). The spirostanol glycosides attain trans (B/C ring), trans (C/D ring), and cis (D/E ring) geometry[58].

Furostanol glycosides

Furostanol glycosides are pentacyclic having 16, 22-epoxycholestane derivative. In *Agave* bidesmosidic furostanol saponins are in abundance and are mostly 3- and 26-O-glycosides. The sugar at 26th position is always β-D-glucopyranoside. The furostanol glycosides are either 22-methoxy furostanols and 22-hydroxy furostanols[58].

***Agave* products**

Agave plants have many ethnobotanical applications. They are raw materials for the production of famous distilled and non-distilled alcoholic beverages. Their leaves are rich in fibres having high mechanical strength and durability, hence, are used in making cables, ropes etc. They are rich in carbohydrates and are used for making syrups, sweeteners, nectars etc[9]. Below are the following examples showing the uses of various *Agave* sp.

Commercial beverages

Tequila

Tequila is an alcoholic beverage prepared from *Agave tequilana* (Blue *Agave*) through fermentation and distillation process[62]. Tequilas are categorised into two types: (1) pure tequila and, (2) tequila mixto (51% tequila and 49% sugar). They are further classified as Tequila Silver - Blanco - Plata - White – Platinum, Tequila Gold - Joven – Oro, Tequila Reposado, Tequila Añejo (extra aged), Tequila Extra Añejo (ultra-aged)[63]. They are widely consumed almost all around the world.

Mezcal

Mezcal is a Mexican alcoholic beverage that is extracted from various species of *Agave* namely, *Agave angustifolia*, *Agave esperrimia Jacobi*, *Agave potatorum*, *Agave webericela*, *Agave cupreata*, *Agave durangensis* and *Agave salmiana*. Oaxaca region (Mexico) is the main producer of mezcal and is known as the 'Home of Mezcal'. In Mexico, *Agave* is known as maguey[64] and around 365 thousand tons of *Agave* are produced annually[65]. Mezcal is prepared by fermenting the carbohydrates stored in the stem of maguey. It has different textures, odours, and tastes and appears transparent. Mezcal is usually served both on a routine basis as well as on special occasions/rituals. Mezcal is considered a regional alcoholic beverage and an element of National Heritage. The procedure for the preparation of Mezcal is similar to that of tequila involving harvesting the stems and leaves, cooking/baking, fermenting, two rounds of distillation and cask maturation (oak containers). The only difference is that during fermentation, whole agave mash, including fibres is used. Organic acids such as acetic acid, ethanol, n-propanol, methanol and n-butanol are the main products obtained during fermentation of mezcal[66].

Bacanora

Bacanora is an alcoholic beverage prepared from *Agave angustifolia.* The brand or name is derived from the name of the town Bacanora in Sonora state (Mexico City). It is considered as a variety of mescal and a regional alcoholic beverage of Sonora[59].

Non-Commercial beverages

Pulque

Pulque is a very old, traditional alcoholic beverage (non-distilled and fermented) used in Mexico. Pulque is produced from the sap of different *Agave* species namely *A. americana, A. mapisaga, A. salmiana, A. ferox*, *A. atrovirens*. A major producer of Pulque is Hidalgo (Mexico). The state produced more than 206 litres of Pulque in 2010. During the processing of Pulque, many by-products are obtained that are of industrial interest such as inulin, fibre juice called Ixtle, *Agave* honey, gum, vinegar etc[67].

Agave nectar

Agave syrup/ *Agave* nectar is obtained from various *Agave* species namely *A. salmiana*, *A. americana, A. tequilana* etc. *Agave* syrup is prepared from 8-10-year *Agave* plants. The plants are harvested and pina/heads are collected because all the carbohydrate is accumulated in the head. Sap is extracted, filtered and heated at 48ºC. Heating causes the breakdown of carbohydrates into sugars (fructans). The colour of *Agave* nectar could be light to dark brown depending upon processing methods. *Agave* syrup is four times sweeter than sugar. It is used as a sweetening agent in cooking, drinks, garnishing etc[9].

Agave Granulated sugar

Granulated sugar is a powdered form of *Agave* nectar/syrup. The granulated sugar is caramel brown in colour. Once the syrup is prepared it is spray dried until all the moisture is evaporated. The final product obtained after drying is in the form of granules. Granulated *Agave* is used as a flavour enhancer having a low glycemic index[9].

Discussion

Agaves are considered as ‘zero-waste” plant and “plant of benefits”. They are succulent plants following CAM photosynthetic pathway, thus, easily colonising dry areas and withstanding harsh conditions and various environmental/climatic stresses. *Agave* has a rich fibrous system which is used for producing ropes, cables, carpets, matting and brushes. They are rich in carbohydrates. The processed carbohydrates are used for the production of inulin, granulated *Agave, Agave* nectar etc. Inulin improves the absorption of nutrients, provides dietary fibres and decreases appetite. *Agave* nectar has a low glycemic index and hence is considered a replacement for sugars. *Agaves* are used for the production of commercial alcoholic and non-alcoholic beverages like tequila, and mescal, by fermenting the carbohydrates stored in the stem of the plant. They are also rich in steroidal saponins and fructans which boost the immune system and possess anti-inflammatory, anti-microbial, and antioxidant potential. The plant has been used for the treatment of urine and gastrointestinal infections, hypertension, dysentery, wound infections and cancer. The phytochemicals isolated from *Agave* chiefly Cantalasaponin-1, Hecogenin (steroidal sapogenin), spirostanol, furostanol glycosides have shown significant anti-inflammatory activities. The presence of sapogenins and saponins is mainly responsible for the plant’s anti-fungal and anti-bacterial activities. About 141 steroidal saponins have been isolated from different species of *Agave.* Owing to the pharmacological advantages, long traditional use, and broad spectrum biological activities of these complex steroidal saponins and sapogenins, makes them potential therapeutic candidates in drug discovery.

Conclusion

From the review, it can be inferred that *Agave* is crucial for a variety of uses, including for pharmaceutical purposes. Research on *Agave* has focused on a variety of products, including biofuels, meals, beverages, textiles, and saponins. This is in addition to its importance for fibre. Despite the fact that the species is rich in economic and cultural beliefs, a therapeutic activity-based evaluation is however necessary. It is recommended that more research and pilot projects could be conducted for the establishment of *Agave* sp. as a new energy source and for its medicinal applications. Another interesting aspect of *Agave* is the production of biofuels. The economy places a high value on *Agave* plants. *Agave* is thought to have originated in Mexico, where scientists are currently searching for various industrial uses without compromising the plant's sustainability and environmental preservation. A thorough understanding of every component of the production process, agro-ecological management, plant biochemistry and physiology is necessary to make it practicable.

Conflict of interest

None of the authors have any conflict of interest regarding the present study.

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