International Journal of Creative and Open Research in Engineering and Management
ISSN: **3108-1754 (Online)**
Volume 02 Issue 06 June-2026 | Impact Factor: 3.5

Agave Genus: Phytochemistry, Pharmacological Activities, and Wound Healing Potential

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How to Cite this Article:
Francis, J. & David, D. (2026). Agave Genus: Phytochemistry, Pharmacological Activities, and Wound Healing Potential. International Journal of Creative and Open Research in Engineering and Management, 02(6). https://doi.org/10.55041/ijcope.v2i6.418

https://doi.org/ 10.55041/ijcope.v2i6.418

ABSTRACT

The genus *Agave* (family Asparagaceae), comprising over 200 species of succulent perennial plants native to arid and semi-arid regions of the Americas and cultivated widely across the globe, represents a rich repository of biologically active phytochemicals with diverse pharmacological properties. Agave species are chemically characterized by steroidal saponins, fructooligosaccharides, phenolic acids, flavonoids, alkaloids, and terpenoids, which collectively underpin their reported antioxidant, antimicrobial, anti-inflammatory, anti-diabetic, and wound healing activities. This review consolidates current knowledge on the botany, phytochemistry, and pharmacological significance of the genus *Agave*, with a particular focus on activities relevant to wound healing, including antioxidant defense, antimicrobial protection, attenuation of chronic inflammation, and promotion of cell migration. We further highlight the emerging role of Agave-derived extracts as green reducing and capping agents in the synthesis of silver nanoparticles (AgNPs), which amplify the inherent bioactivities of the parent plant matrices and offer multifunctional platforms for biomedical applications. Collectively, the evidence positions the *Agave* genus as a highly promising botanical source for the development of novel wound care therapeutics.

Keywords: Agave; wound healing; phytochemistry; silver nanoparticles; anti-inflammatory; antioxidant; antimicrobial; steroidal saponins

I. INTRODUCTION

Wound healing is a complex, highly coordinated biological process involving an intricate cascade of cellular and molecular events organized into four overlapping phases: hemostasis, inflammation, proliferation, and remodeling (Schultz et al., 2011). Dysregulation of any phase due to infection, oxidative stress, diabetes, or chronic inflammation can result in non-healing chronic wounds, which represent a major global health burden associated with significant morbidity, diminished quality of life, and escalating healthcare costs (Wang et al., 2025).

Chronic wounds are characterized by their inability to heal within an expected timeframe and have emerged as an increasingly important clinical problem over the last several decades, with approximately 1–2% of the population in developed countries estimated to experience a chronic wound during their lifetime (Frykberg & Banks, 2015), due to their higher incidence and greater recognition of associated morbidity and socio-economic burden (Falanga et al., 2022). Despite advances in modern wound care technologies, effective, affordable, and biologically compatible therapeutics remain an unmet clinical need.

Plants have served as the primary source of wound-healing remedies across human civilizations, with traditional medicine systems worldwide employing topical botanical preparations for wound management. In recent decades, systematic phytochemical and pharmacological investigations have validated the wound-healing activity of numerous plant-derived compounds, revealing mechanisms including promotion of fibroblast proliferation and migration, stimulation of collagen synthesis, reduction of oxidative stress at the wound site, modulation of pro-inflammatory cytokine expression, and antimicrobial protection against wound pathogens (Quave, 2018). This scientific legitimization has catalyzed renewed interest in plant-based wound care formulations and the development of phytochemical-derived nanomaterials for enhanced therapeutic delivery.

The genus *Agave* (family Asparagaceae; formerly Agavaceae) represents a pharmacologically rich and resilient plant group, encompassing over 200 species of succulent perennial monocots predominantly distributed across Mexico, the southwestern United States, and Central America, with numerous species cultivated globally in tropical and subtropical regions (Rizwan et al., 2012). Historically, *Agave* species have been utilized in traditional medicine across Mesoamerican cultures for the treatment of wounds, burns, skin infections, dysentery, and systemic inflammatory conditions, providing ethnobotanical validation of their biomedical relevance (Ponmadasamy et al., in press). Phytochemical investigations have identified a diverse array of bioactive constituents across the genus, including steroidal saponins (hecogenin, chlorogenin, gitogenin, sarsasapogenin), fructooligosaccharides (agavins), phenolic acids (ferulic acid, caffeic acid, p-coumaric acid), flavonoids (quercetin, kaempferol, luteolin), alkaloids, and terpenoids, many of which possess established wound healing-relevant activities (Rais et al., in press).

The utility of Agave extracts as green reducing and capping agents for silver nanoparticle (AgNP) synthesis has gained traction. The resultant nanoparticles inherit and amplify the bioactivities of the parent extract while adding the established, broad-spectrum antimicrobial properties of silver (Villagrán et al., 2024). This review comprehensively consolidates current knowledge on the taxonomy, phytochemistry, and pharmacological properties of the genus Agave, with a particular emphasis on bioactivities mechanistically relevant to wound healing and on their integration into green nanotechnology platforms.

II. TAXONOMY, BOTANICAL DESCRIPTION, AND DISTRIBUTION OF AGAVE

The genus *Agave* belongs to the family Asparagaceae (order Asparagales), subfamily Agavoideae. It is among the largest genera within the subfamily Agavoideae of Asparagaceae (formerly Agavaceae), and is closely allied to related genera including Furcraea, Manfreda, Polianthes, and Beschorneria (Britannica Editors, 2023). Recent molecular phylogenetic analyses have proposed substantial reorganization within the genus, with certain taxa transferred to Agave sensu stricto (strict sense) and others reassigned; nevertheless, the traditional circumscription of *Agave* continues to be the most widely adopted framework in pharmacological (medical-related) and agronomic (agriculture-related) literature (Good-Avila et al., 2006).

Agave plants are characteristically large-rosette succulents with thick, fleshy, lanceolate leaves terminating in sharp terminal spines and often bearing marginal teeth (Angiosperm Phylogeny Group, 2009). The leaves are the primary site of water and carbohydrate storage, adapted to arid conditions through crassulacean acid metabolism (CAM) photosynthesis. Most *Agave* species are monocarpic, flowering once after a long vegetative period of 10–50 years, with the inflorescence reaching several meters in height and bearing large numbers of flowers attractive to native pollinators (Ortiz-Cano et al., 2020); however, several species produce rhizomatous offsets (pups) and are effectively polycarpic at the clonal level. The somatic chromosome number for most species is 2n = 60. The genus is most diverse in Mexico, considered the center of origin and diversification of *Agave*, which has over 150 native species. The group is broadly categorized into two subgenera: *Agave* (succulent leaf plants) and *Littaea* (non-succulent rosettes). Economically important species include *Agave tequilana* Weber (blue agave; spirit production), *Agave sisalana* Perrine (sisal; high-tensile fiber production), *Agave americana* L. (century plant; multipurpose ornamental and traditional remedy), and *Agave angustifolia* Haw. (mescal production) (Figueredo-Urbina et al., 2021).

III. PHYTOCHEMISTRY OF THE AGAVE GENUS

3.1 Steroidal Saponins

Steroidal saponins are the most extensively studied class of secondary metabolites in *Agave* and constitute a defining chemical feature of the genus. These compounds are glycosylated steroidal aglycones (sapogenins) whose biological activities depend on both the configuration of the steroidal nucleus and the attached sugar chains (Sidana et al., 2016). The principal sapogenins isolated from Agave species include hecogenin, chlorogenin, gitogenin, sarsasapogenin, tigogenin, and neotigogenin. Hecogenin is particularly abundant in *Agave sisalana* and related species, serving as a vital industrial precursor in the semi-synthesis of therapeutic corticosteroids (Ingawale (Mandlik), D. K. (2020).

The anti-inflammatory activity of steroidal saponins from *Agave* has been attributed to the inhibition of cyclooxygenase-2 (COX-2) and 5-lipoxygenase (5-LOX) pathways (Wijesekara et al., 2024), the downregulation of nuclear factor kappa B (NF-κB) signaling a mechanism well-established for saponins across plant genera (Lu et al., 2012), and a sharp reduction in the expression of pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) **(Aguilar-Guadarrama et al., 2024)**. These anti-inflammatory mechanisms are directly relevant to the inflammatory phase of wound healing, where controlled resolution of inflammation is required for an efficient transition to the tissue proliferative phase.

3.2 Fructooligosaccharides (Agavins)

Agavins are highly branched, complex long-chain fructooligosaccharides (FOS) unique to *Agave* species, comprising branched fructan chains attached to a terminal glucose unit. Agavins serve as the primary water-soluble carbon reserve in *Agave* stems, leaves, and piñas (the harvested core) (Huazano-García et al., 2020). Unlike digestible sugars, agavins function as soluble prebiotic dietary fibers, modulating microbiomes and producing short-chain fatty acids with systemic immunomodulatory effects. Beyond systemic metabolism, local wound care applications employing agavin-containing carbohydrate matrices are emerging, where they act as protective physical barriers and moisture-retentive biopolymers (Aguilar-Guadarrama et al., 2024).

3.3 Phenolic Compounds

Agave species are rich sources of diverse phenolic acids and flavonoids. Major phenolic acids identified across the genus include ferulic acid, caffeic acid, p-coumaric acid, chlorogenic acid, syringic acid, and protocatechuic acid (Márquez-Rangel et al., in press). These hydroxycinnamic and hydroxybenzoic acid derivatives possess robust antioxidant activity mediated through free radical scavenging, metal ion chelation, and structural inhibition of lipid peroxidation activities highly relevant to neutralizing the hostile oxidative stress environment of non-healing chronic wounds (Johnson et al., 2022).

Flavonoids identified in *Agave* include quercetin, kaempferol, luteolin, apigenin, and their associated glycoside conjugates (Bermúdez Bazán et al., 2025). Quercetin has been extensively studied for wound healing activity, demonstrating promotion of keratinocyte and fibroblast migration, inhibition of destructive matrix metalloproteinase (MMP) activity that degrades the extracellular matrix in chronic wounds, and potent anti-inflammatory effects (Kaur et al., 2021a). Kaempferol has similarly been shown to accelerate wound closure through stimulation of vascular endothelial growth factor (VEGF) expression and angiogenesis promotion (Chen et al., 2025).

3.4 Alkaloids and Terpenoids

Alkaloids documented in *Agave* species include tetrahydroisoquinoline derivatives, with localized antimicrobial and analgesic properties reported for select species. Triterpenoids and phytosterols, including β-sitosterol, stigmasterol, and campesterol, are present in multiple *Agave* species (Bermúdez-Bazán et al., 2021). β-Sitosterol has been specifically reported to enhance wound closure by encouraging fibroblast proliferation and localized collagen synthesis during structural tissue reconstruction (Sachan, 2025).

IV. PHARMACOLOGICAL ACTIVITIES OF AGAVE: A WOUND HEALING PERSPECTIVE

4.1 Antioxidant Activity

Oxidative stress at the wound site mediated by reactive oxygen species (ROS) generated by infiltrating neutrophils and macrophages plays a dual role in wound healing: at tightly controlled levels, ROS serve as signaling molecules; however, excessive ROS accumulation impairs tissue repair by oxidizing proteins, lipids, and DNA, inactivating crucial growth factors, and creating a hostile microenvironment (Dunnill et al., 2017).
Extracts from multiple *Agave* species have demonstrated significant in vitro antioxidant activity across standardized assays. Corona-Carpio et al. (2022a) evaluated the antioxidant activity of *Agave tequilana* leaf juice using DPPH, ABTS, and ORAC assays, attributing the radical-scavenging activity primarily to polyphenolic constituents. Domínguez-Avila et al. (2021a) reported that total phenolic content in *Agave* species correlates strongly with radical scavenging capacity in both DPPH and FRAP assays. The ferric reducing ability (FRAP) of *Agave* extracts is particularly relevant as it reflects the capacity to reduce oxidized transition metal ions, which otherwise catalyze tissue damage at wound sites through Fenton chemistry (Amarowicz & Pegg, 2019).

4.2 Antimicrobial Activity

Wound infection is a major complication of both acute and chronic wounds, with Staphylococcus aureus, Pseudomonas aeruginosa, and Escherichia coli among the most prevalent wound pathogens. The emergence of multidrug-resistant (MDR) strains has intensified the search for plant-derived antimicrobial agents (Jia et al., 2025a).
Agave extracts have been thoroughly evaluated for antimicrobial activity with notable findings. Rojas-Garduño et al. (2020a) demonstrated that methanolic extracts of *Agave lechuguilla* inhibited *S. aureus* and *E. coli*, attributing the activity to saponin constituents that disrupt bacterial membrane integrity through disruption of membrane phospholipids and lipopolysaccharides (LPS), increasing permeability and causing leakage of intracellular contents (Franco-Robles, 2025a). The antimicrobial action of *Agave* phenolic acids and flavonoids operates through multiple concurrent mechanisms, including disruption of bacterial cell membrane integrity, inhibition of bacterial DNA gyrase, interference with efflux pump activity, and chelation of essential metal ions required for bacterial metabolism (Rodríguez et al., 2023a). This multi-target nature is considered a significant advantage over single-target antibiotics in preventing resistance development (Feng et al., 2023a).

4.3 Anti-Inflammatory Activity

While an initial inflammatory response is essential for wound debridement and pathogen clearance, persistent or excessive inflammation impairs wound healing and underlies the pathophysiology of chronic non-healing wounds (Landén et al., 2016). Anti-inflammatory phytochemicals that modulate rather than completely suppress the inflammatory response are beneficial for clinical wound healing.

Agave steroidal saponins have demonstrated significant in vivo anti-inflammatory activity (López-Salazar et al., 2025). Hecogenin, a sapogenin from *Agave sisalana*, has demonstrated significant anti-inflammatory activity in carrageenan-induced paw edema models, with efficacy comparable to indomethacin (Murthy et al., 2022a). The mechanism involved inhibition of COX-2 protein expression and reduction of TNF-α and IL-6 serum levels. In a wound healing model, hecogenin-treated animals showed accelerated wound closure, accompanied by histological evidence of enhanced fibroblast proliferation, neovascularization, and organized collagen deposition (Murthy et al., 2022b).

4.4 Wound Healing Activity

Pre-clinical studies have validated the wound-healing activity of Agave preparations. López-Salazar et al. (2025) demonstrated that fructan-rich bagasse extracts from *Agave* significantly accelerated wound closure in streptozotocin-induced diabetic rats, with improved granulation tissue, epithelialization, and collagen deposition. In vitro scratch assays further support these findings, showing that *Agave*-derived flavonoids such as quercetin and kaempferol enhance fibroblast and keratinocyte migration through PI3K/Akt activation (Kaur et al., 2021a). Luteolin has additionally been shown to stimulate fibroblast proliferation and collagen synthesis via upregulation of TGF-β1 (Kaur et al., 2021b).

4.5 Anti-Diabetic Activity and Diabetic Wound Healing Relevance

Diabetes mellitus profoundly impairs wound healing through peripheral neuropathy, microvascular dysfunction, impaired macrophage function, reduced growth factor expression, and chronically elevated advanced glycation end-products (AGEs) that cross-link structural collagen (Schalkwijk & Smeets, 2008). The anti-diabetic activity of *Agave*, mediated through inhibition of alpha-amylase and alpha-glucosidase, improving insulin sensitivity, and reducing glycemic excursions, is therefore directly relevant to improving wound healing outcomes (Kashtoh & Baek, 2023a).

Domínguez-Avila et al. (2021b) reviewed the anti-diabetic potential of *Agave*-derived fructooligosaccharides, noting significant reductions in fasting blood glucose and glycated hemoglobin (HbA1c) in animal models of type 2 diabetes following agavin supplementation. Although the review did not directly assess wound healing, improved glycemic control is a critical factor that indirectly supports enhanced tissue repair in diabetic wounds.

V. SUMMARY OF PHARMACOLOGICAL ACTIVITIES OF AGAVE SPECIES

The species cited below demonstrate pharmacological activities relevant to specific phases of the wound-healing cascade.

***Agave* Species**	**Core Pharmacological Activity**	**Dominant Bioactive Compounds**	**Wound Phase Relevance**	**Supporting Evidence**
***Agave sisalana* Perrine**	Anti-inflammatory, collagen stimulation	Steroidal saponins (hecogenin)	Inflammatory, Proliferative	Hydrolyzed sisal extracts show strong anti-inflammatory activity; hecogenin accelerates wound closure with enhanced fibroblast proliferation and neovascularization. (Murthy et al.,

				2022a; 2022b; Bench Chem Technical Whitepaper, 2026).
***Agave tequilana* Weber**	Antioxidant, anti-diabetic, wound remodeling	Polyphenols, agavins, flavonoids	Inflammatory, Proliferative, Remodeling	β-sitosterol, agavins, and flavonoids enhance fibroblast viability, antioxidant defense, and wound closure; bagasse extracts accelerate re-epithelialization. (Corona-Carpio et al., 2022; López-Salazar et al., 2025).
***Agave lechuguilla* Torr.**	Antimicrobial (membrane disruption)	Saponins, phenolic acids	Infection prevention (all phases)	Documented antimicrobial activity via saponin-mediated phospholipid/LPS disruption; antibacterial and anti-biofilm studies validate traditional wound care use. (Rojas-Garduño et al., 2020; Franco-Robles, 2025).
***Agave americana* L.**	Radical scavenging, antimicrobial	Quercetin, kaempferol, ferulic acid	Inflammatory, Proliferative	Hydro alcoholic extracts improve wound closure, epithelialization, and tensile strength in animal models; flavonoids and saponins contribute to antioxidant and antibacterial effects. (Ponmadasamy et al., 2026; Misra & Varma, 2017).
***Agave angustifolia* Haw.**	Mezcal production, antioxidant, anti-inflammatory	Flavonoids (quercetin, luteolin), phenolic acids, saponins	Inflammatory, Proliferative	Traditionally used in mezcal production, phytochemical studies report antioxidant and anti-inflammatory activity relevant to wound healing, including fibroblast stimulation and collagen synthesis. (Figueredo-Urbina et al., 2021; López-Salazar et al., 2025).

Table 1. Summary of pharmacological activities of representative *Agave* species and their relevance to wound healing phases.

VI. GREEN SYNTHESIS OF SILVER NANOPARTICLES USING AGAVE EXTRACTS

The green synthesis of metallic nanoparticles using plant extracts has emerged as an environmentally sustainable, cost-effective alternative to chemical synthesis methods (Cardoso et al., 2025). *Agave* extracts provide dual functionality, acting simultaneously as reducing agents converting silver ions (Ag^{+}) to metallic silver (Ag^{0}) and as capping agents stabilizing the resultant nanoparticles against irreversible aggregation (Melkamu & Bitew, 2021). The phytochemical richness of *Agave* extracts, particularly in hydroxyl-group-bearing polyphenols and flavonoids capable of electron donation, makes them ideal bioreductants for AgNP synthesis (Khatun et al., 2022).

Nanoparticle formation using *Agave* extracts proceeds through the bioreduction of $AgNO_3$, marked by a characteristic brownish-green or dark-brown coloration confirming surface plasmon resonance (SPR) of AgNPs, typically displaying absorption maxima within the 400–450 nm range in UV-Vis spectroscopy. Characterization studies across various *Agave* species confirm the formation of stable, face-centered cubic (FCC) crystalline

AgNPs (Alaabedin et al., 2024). Fourier-transform infrared (FTIR) analysis of AgNPs synthesized via Agave species consistently reveals the presence of plant-derived functional groups (O–H, C=O, C–O, N–H stretches) on the nanoparticle surface. This retained "phytochemical corona" enhances the biological activities of green AgNPs compared to chemically synthesized counterparts. At wound sites, the silver core provides broad-spectrum antimicrobial action through controlled Ag^+ release and bacterial membrane disruption, while the phytochemical corona mitigates oxidative stress, modulates inflammatory cytokines, and promotes tissue regeneration (Zhang et al., 2016)

VII. SAFETY CONSIDERATIONS AND TOXICOLOGICAL PROFILE

The traditional use of *Agave* preparations in foods, fermented beverages, and folk medicine across centuries provides preliminary evidence of acceptable historical safety. Nevertheless, systematic toxicological evaluation remains essential for clinical pharmaceutical development. In vitro cytotoxicity assays employing standard mammalian fibroblast cell lines (e.g., NIH 3T3, L929) generally indicate low cytotoxicity of crude *Agave* extracts at concentrations relevant to their pharmacological activity (Anajwala et al., 2010).

Agave-mediated green synthesis of silver nanoparticles (AgNPs) has demonstrated a distinct biocompatibility advantage over conventional chemical routes. The phytochemical capping layer derived from *Agave* extracts comprising flavonoids, saponins, and phenolic acids provides steric stabilization that prevents uncontrolled aggregation and moderates the release of toxic Ag^+ ions. This controlled ion release reduces oxidative stress and cellular damage, thereby attenuating mammalian cytotoxicity compared to uncapped or chemically synthesized AgNPs. Such stabilization not only enhances antimicrobial efficacy but also promotes a safer biocompatibility profile, supporting the potential of *Agave*-derived AgNPs as wound healing agents (Ahmed et al., 2022). The natural selectivity of green AgNPs for microbial versus mammalian cells, attributable to differences in cell wall structure, endocytosis rates, and intracellular reducing capacity, supports their safety profile for topical wound care applications at optimized doses. Nevertheless, detailed in vivo safety profiles, including dermal sensitization testing and acute topical toxicity trials, are required to establish rigorous safety margins (Mohammed, 2015).

VIII. CONCLUSION AND FUTURE DIRECTIONS

The genus *Agave* represents a pharmacologically rich and chemically diverse botanical group with multi-mechanistic wound healing activity. Its secondary metabolites, including steroidal saponins, polyphenols, flavonoids, fructooligosaccharides, and terpenoids, address the therapeutic requirements of all four phases of wound repair through antioxidant, antimicrobial, anti-inflammatory, fibroblast stimulatory, angiogenic, and anti-diabetic mechanisms. Moreover, integration of *Agave* extracts into green nanotechnology platforms yields capped silver nanoparticles that combine the intrinsic antimicrobial potency of silver with the stabilizing, tissue-supportive properties of the phytochemical corona.

Future research should prioritize: (i) standardized LC-MS/MS profiling to trace chemical variation across cultivars; (ii) comprehensive in vitro modeling of signaling pathways activated by isolated sapogenins; and (iii) the development of advanced biocompatible delivery systems such as Agave extract-loaded hydrogels, electrospun nanofibrous meshes, and topical emulgels to sustain a moist, infection-free wound environment.

Acknowledgements

The authors gratefully acknowledge Loyola College, Chennai, and CEMS-LIFE for providing the research facilities and support necessary to carry out this work.

Author Contributions

1. **Jofy Francis:** Conceptualization, methodology design, validation, data analysis, and preparation of the original draft.
2. **V. Pushpa Rani:** Corresponding Author, Supervision, guidance, and validation of the research work.
3. **Deon David:** Data analysis, critical revision of the manuscript, and editorial support.

Declarations

- **Competing Interests:** The authors declare that they have no competing interests.
- **Ethics Approval:** This study is a review based on plant-derived extracts. As it did not involve human participants or animal experimentation, ethical approval was not required.

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