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Aloe vera Gel-Loaded Alginate Hydrogel Beads for Controlled Wound Healing: A Comprehensive Review of Formulation, Ionic Gelation and In-Vitro Evaluation

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Abstract- ***Chronic and infected wounds remain a major clinical and economic burden, and conventional topical formulations such as creams, ointments and gels often fail to provide sustained therapeutic action because of poor retention, uncontrolled release and short residence time at the wound site. Aloe vera (Aloe barbadensis Miller) is among the most extensively studied medicinal plants for wound healing, owing to the acemannan-rich polysaccharide fraction of its inner-leaf gel, which stimulates fibroblast proliferation, collagen synthesis, angiogenesis and epithelialisation while also exerting antioxidant and antimicrobial effects. Direct application of the raw gel is nevertheless limited by physicochemical instability, rapid degradation of bioactives, microbial contamination and brief contact time. This review examines the rational encapsulation of Aloe vera gel within sodium alginate hydrogel beads prepared by ionic (ionotropic) gelation, in which divalent calcium ions cross-link alginate guluronate blocks through the well-known "egg-box" mechanism to form a biocompatible, biodegradable, moisture-retaining matrix. The pathophysiology of wound healing, the role of medicinal plants, the phytochemistry and pharmacology of Aloe vera, the properties of alginate and the principles of ionic gelation are reviewed in turn, followed by the complete battery of physicochemical and biopharmaceutical evaluation parameters—percentage yield, particle size, swelling index, entrapment efficiency, surface morphology, in-vitro release and kinetics, DPPH antioxidant activity and antimicrobial testing against common wound pathogens. Illustrative analytical data and current market trends are presented graphically. Encapsulation is shown to enhance stability, convert burst release into sustained release and preserve antioxidant and antimicrobial efficacy, establishing Aloe vera-loaded alginate hydrogel beads as a scientifically validated, herbal-based platform for wound care.***

Keywords: Aloe Vera, Acemannan, Sodium Alginate, Hydrogel Beads, Ionic Gelation, Wound Healing, Controlled Release, DPPH Antioxidant, Antimicrobial.

I. INTRODUCTION

Wound healing is one of the most intricate biological processes in the human body, requiring the precise spatial and temporal coordination of numerous cell types, signalling molecules and extracellular-matrix components to restore the structural and functional integrity of injured tissue. When this orchestration is disrupted—by diabetes mellitus, vascular insufficiency, pressure, burns or persistent infection—the result is a chronic, non-healing wound characterised by prolonged inflammation, excessive oxidative stress, impaired angiogenesis and a heavy microbial burden. Chronic wounds represent a substantial and growing global health problem, consuming a disproportionate share of healthcare resources and severely diminishing patient quality of life.

Despite a broad armamentarium of wound-care products, the management of chronic wounds remains clinically challenging. Conventional topical dosage forms such as creams, ointments and simple gels are convenient but frequently inadequate: they are poorly retained at the wound surface, release their active agents in an uncontrolled manner, require frequent reapplication and penetrate tissue only superficially. Moreover, the prolonged use of synthetic antimicrobial and anti-inflammatory agents carries the risk of adverse effects and the emergence of antimicrobial resistance. These limitations have driven a search for safer, more effective and more sustainable therapeutic strategies, in which natural products and modern novel drug delivery systems converge.

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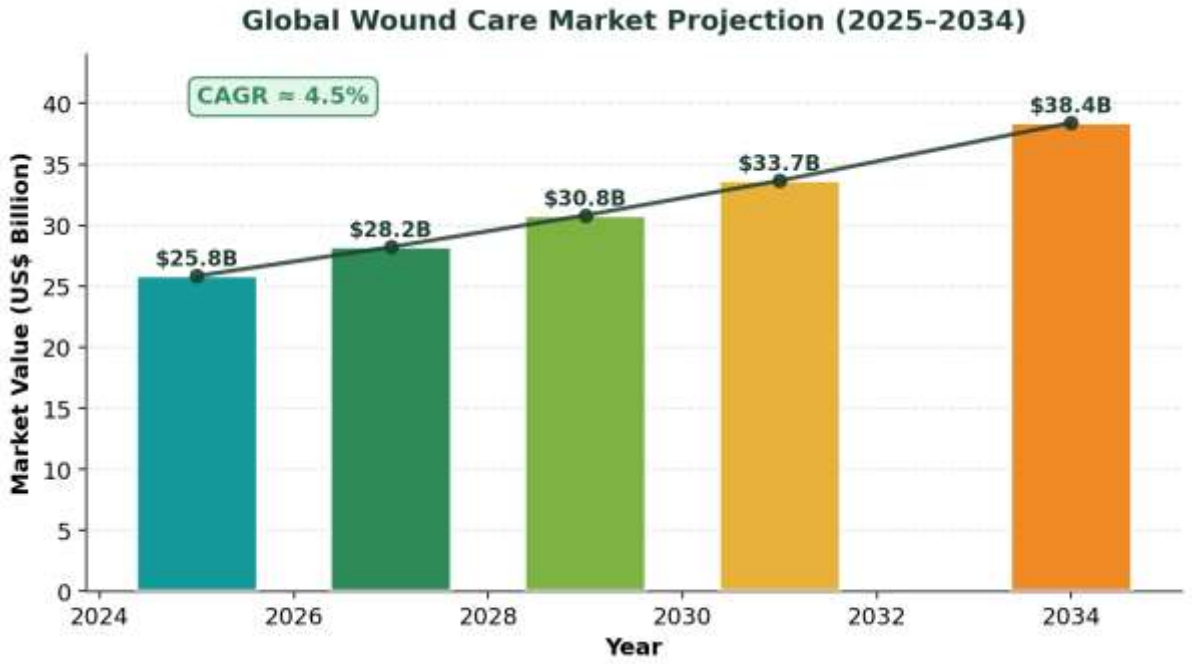

Figure 1. Projected growth of the global wound care market, 2025–2034. Advanced wound dressings, including hydrogels and alginates, constitute the fastest-growing and largest product segment, underlining the commercial relevance of hydrogel-based delivery systems.

The commercial dimension of wound care reflects this clinical need. The global wound care market was valued at roughly US$25.84 billion in 2025 and is projected to reach approximately US$38.39 billion by 2034, expanding at a compound annual growth rate of about 4.5%, with chronic wounds accounting for the largest application share and advanced wound dressings dominating the product segment (Figure 1) [1, 2]. Within this landscape, moist-wound-care dressings—hydrogels, hydrocolloids, alginates and foams—form the single largest product category, and hydrogel and alginate systems in particular are valued for their ability to maintain a moist healing environment, absorb exudate and deliver therapeutic agents in a controlled fashion [2].

Among medicinal plants, Aloe vera (Aloe barbadensis Miller) occupies a pre-eminent position in wound care, with a documented history of use across Ayurvedic, Unani and other traditional systems and a substantial body of modern scientific evidence. The inner-leaf gel contains a complex mixture of bioactive constituents—chiefly the acetylated polysaccharide acemannan, together with glucomannan, vitamins, enzymes, phenolics, sterols and amino acids—that act synergistically to accelerate tissue regeneration [5, 8]. However, the therapeutic promise of the raw gel is undermined by its physicochemical fragility: the bioactives degrade rapidly, the gel is prone to microbial spoilage, and its residence time on a wound is short. To realise the plant's full potential, a delivery system is required that protects the bioactives, prolongs contact and controls release.

Encapsulation of Aloe vera gel within sodium alginate hydrogel beads, prepared by the mild and solvent-free technique of ionic gelation, offers an elegant solution. This review integrates the pathophysiology of wound healing, the pharmacology and phytochemistry of Aloe vera, the materials science of alginate and the principles of ionotropic gelation, and sets out the comprehensive in-vitro framework by which such beads are characterised and evaluated. Illustrative analytical data are presented throughout to frame the scientific rationale of this herbal-based novel drug delivery system.

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II. WOUND HEALING: PATHOPHYSIOLOGY AND THERAPEUTIC CHALLENGES

Wound healing proceeds through four overlapping and tightly regulated phases—haemostasis, inflammation, proliferation and remodelling—each defined by characteristic cellular and molecular events (Figure 2). Haemostasis begins immediately upon injury: vasoconstriction and platelet aggregation produce a fibrin clot that arrests bleeding and provides a provisional matrix. The inflammatory phase, spanning roughly the first one to three days, sees the recruitment of neutrophils and macrophages that clear debris and pathogens and release cytokines and growth factors orchestrating the subsequent repair.

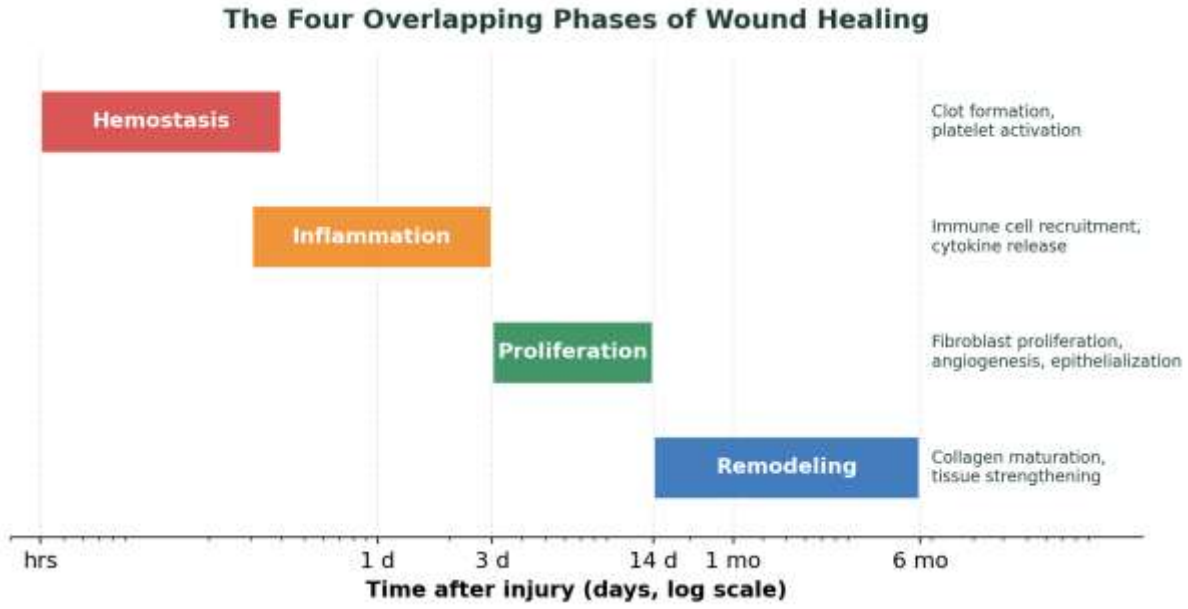

Figure 2. The four overlapping phases of wound healing, with their approximate time course (logarithmic scale) and principal biological events. Disruption of this sequence underlies chronic, non-healing wounds.

The proliferative phase, extending from about day three to day fourteen, is the constructive heart of repair. Fibroblasts migrate into the wound and synthesise collagen and other extracellular-matrix components; new blood vessels form through angiogenesis; and keratinocytes re-epithelialise the wound surface. Finally, during the remodelling phase, which may last weeks to months, type III collagen is gradually replaced by stronger type I collagen, the matrix is reorganised, and tissue tensile strength is progressively restored. Any disturbance of this carefully choreographed sequence may convert an acute wound into a chronic one.

Chronic wounds are typically arrested in a state of persistent inflammation. They exhibit elevated levels of reactive oxygen species and pro-inflammatory cytokines, reduced collagen synthesis, impaired angiogenesis and, frequently, a high microbial load that may organise into resistant biofilms. Oxidative stress and infection are therefore two of the most important and therapeutically tractable obstacles to healing, and an effective wound-care agent should ideally combine antioxidant, anti-inflammatory and antimicrobial actions with the capacity to stimulate fibroblast proliferation and angiogenesis. The principal pharmacological activities required for effective wound healing are summarised in Table 1.

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Table 1. Pharmacological activities required for effective wound healing.

Pharmacological activity	Role in wound healing
Antioxidant	Neutralises reactive oxygen species and reduces oxidative damage
Anti-inflammatory	Modulates excessive inflammation and cytokine release
Antimicrobial	Prevents and controls wound infection
Fibroblast stimulation	Enhances collagen synthesis and matrix deposition
Angiogenic activity	Improves blood supply and oxygenation of the wound bed

III. ROLE OF MEDICINAL PLANTS IN WOUND MANAGEMENT

Herbal medicines have been employed for the treatment of wounds and skin disorders for millennia within traditional systems such as Ayurveda, Unani and Siddha. Their continuing appeal in modern pharmaceutics rests on several genuine advantages over single-target synthetic drugs: generally superior biocompatibility, lower systemic toxicity, cost-effectiveness and, importantly, a multiplicity of complementary therapeutic actions arising from their complex phytochemical composition. Plant extracts characteristically contain flavonoids, phenolics, polysaccharides, terpenoids, tannins and alkaloids that act synergistically rather than through a single mechanism.

In the specific context of wound healing, medicinal plants contribute antioxidant activity that neutralises the reactive oxygen species responsible for oxidative tissue damage and delayed repair; anti-inflammatory activity that tempers the excessive and prolonged inflammation typical of chronic wounds; antimicrobial activity that suppresses wound-infecting organisms; and direct stimulation of fibroblast proliferation and collagen deposition. The convergence of these actions within a single natural material is difficult to replicate with individual synthetic agents and is precisely what makes botanicals such as Aloe vera so attractive for wound care. The contemporary research challenge is not to rediscover their efficacy, which is well established, but to formulate them into stable, standardised and controlled-release delivery systems that meet modern pharmaceutical standards—an aim that motivates the present review.

IV. ALOE VERA: PHYTOCHEMISTRY AND WOUND-HEALING PHARMACOLOGY

A. Botanical Profile and Composition

Aloe vera (Aloe barbadensis Miller) is a perennial, xerophytic succulent of the family Asphodelaceae, native to the Arabian Peninsula and now cultivated widely across tropical and subtropical regions, including the Indian states of Rajasthan, Gujarat, Maharashtra, Tamil Nadu and Andhra Pradesh. Its drought resistance and ease of cultivation make it economically attractive for large-scale medicinal use. The plant bears thick, fleshy, lance-shaped leaves arranged in a rosette; the pharmaceutically valuable material is the clear, mucilaginous parenchymatous gel of the inner leaf, which must be carefully separated from the bitter, aloin-containing yellow latex beneath the rind that is pharmacologically and toxicologically distinct.

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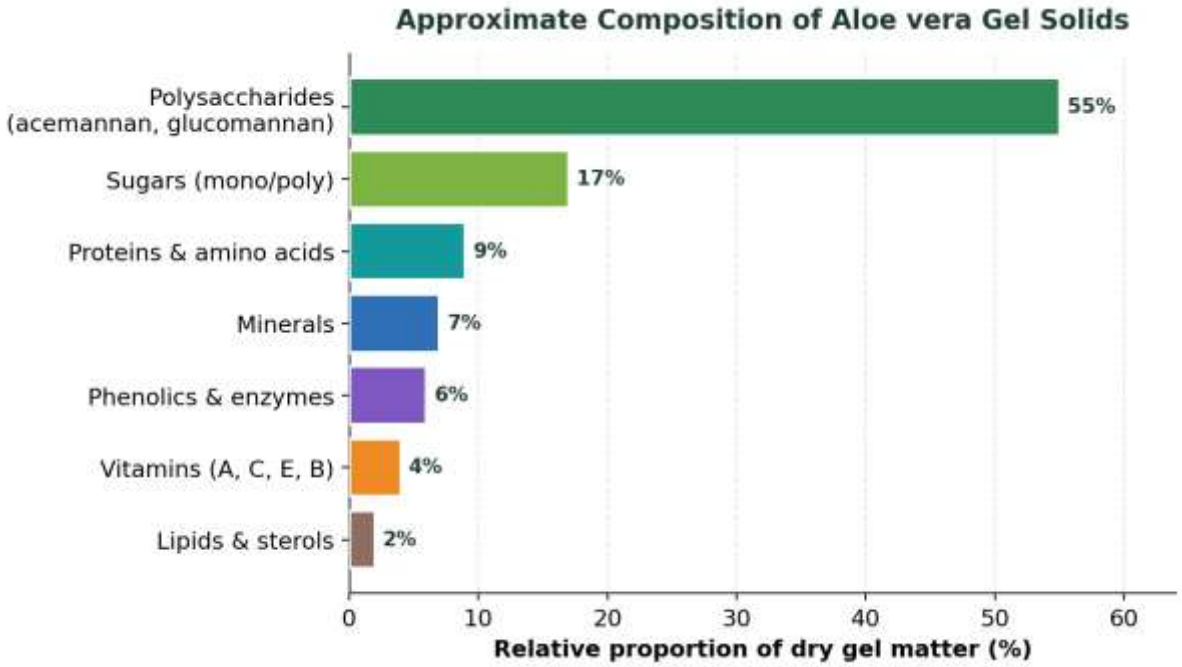

Figure 3. Approximate composition of Aloe vera gel solids. Polysaccharides—chiefly acemannan and glucomannan—dominate the dry matter and are the principal mediators of the gel's wound-healing activity.

The inner gel is more than 98% water, but its dry matter comprises a remarkably diverse array of bioactive compounds (Figure 3). The polysaccharide fraction predominates and is led by acemannan, a long-chain acetylated polymannose (a β-(1,4)-linked acetylated polymannose bearing mannose-6-phosphate residues), accompanied by glucomannan. Also present are vitamins A, C, E and the B-complex; enzymes such as bradykinase and catalase; phenolic compounds and chromones including aloesin; sterols such as lupeol and campesterol; and a full complement of essential and non-essential amino acids. This compositional richness underlies the gel's multifaceted pharmacology [8, 9].

B. Mechanisms of Wound Healing

The wound-healing activity of Aloe vera is mediated principally by its polysaccharides, and acemannan in particular has attracted intensive mechanistic study. Acemannan stimulates the proliferation of fibroblasts and up-regulates the expression of keratinocyte growth factor-1 (KGF-1), vascular endothelial growth factor (VEGF) and type I collagen, thereby simultaneously driving epithelialisation, angiogenesis and matrix deposition [16, 20]. Aloe polysaccharides have been shown to promote fibroblast generation of hyaluronic acid and hydroxyproline and to regulate the expression of matrix metalloproteinases and their tissue inhibitors during extracellular-matrix remodelling [5]. At the molecular level, acemannan is reported to act as a mitogenic stimulator that activates the AKT/mTOR signalling pathway and cyclin expression to promote cell-cycle progression, providing a molecular explanation for its pro-proliferative effect [17].

Beyond direct tissue regeneration, Aloe vera contributes the two complementary actions most relevant to chronic wounds. Its vitamins, phenolics and other antioxidants scavenge free radicals and reduce the oxidative stress that impairs healing, while its phenolic and other constituents exert antimicrobial activity against the Gram-positive and Gram-negative organisms that commonly colonise wounds. The plant also displays anti-inflammatory and immunomodulatory effects, inhibiting inflammatory mediators and enzymes and modulating the immune response. Acting in concert, these activities address multiple obstacles to healing simultaneously, which is the central pharmacological argument for selecting Aloe vera as the active agent in a wound-care formulation [5, 8].

C. Traditional Use and Rationale for Selection

The modern pharmacological evidence for Aloe vera rests on a deep foundation of traditional use. In Ayurveda the plant is known as Kumari and is classified as a rejuvenative (rasayana) herb, traditionally indicated for wound healing, burns, skin infections, ulcers and a range of internal disorders; comparable applications appear in Unani and other ethnomedical systems, and the topical application of fresh gel to burns, cuts and abrasions for its cooling and soothing action is a near-universal folk practice. This long ethnomedicinal record, now substantially corroborated by preclinical and clinical research, provides strong justification for selecting Aloe vera as the active agent in a wound-healing formulation. The convergence of proven efficacy, a well-characterised regenerative polysaccharide in acemannan, complementary antioxidant and antimicrobial activity, an excellent safety profile and clear formulation limitations together make the plant an ideal candidate for incorporation into a polymeric controlled-release system.

D. Limitations of the Raw Gel

Notwithstanding this compelling pharmacological profile, the direct clinical application of Aloe vera gel is constrained by several practical limitations. The bioactive polysaccharides are thermolabile and oxidation-sensitive, degrading rapidly once the gel is harvested; the high water content renders the gel susceptible to microbial contamination; and, when applied to a wound, the gel is poorly retained and has a short residence time, necessitating frequent reapplication. The structural integrity of acemannan is essential to its bioactivity, so any processing or storage that degrades the polysaccharide diminishes therapeutic value [13, 19]. These shortcomings establish a clear formulation imperative: to encapsulate the gel within a protective matrix that stabilises its constituents, prolongs contact with the wound and governs their release.

V. NOVEL DRUG DELIVERY SYSTEMS AND HYDROGELS FOR WOUND HEALING

Novel drug delivery systems (NDDS) are engineered to improve the safety, efficacy and patient acceptability of therapeutic agents by controlling the rate, duration and location of their release. In wound care, an ideal delivery system must do more than carry a drug: it should maintain a moist wound environment, absorb excess exudate, provide a barrier against microbial invasion, conform to the wound surface and deliver its therapeutic payload in a sustained manner. These requirements have made several NDDS platforms—nanoparticles, films, foams, fibres, sponges and hydrogels—the focus of intense wound-healing research, and they explain the dominance of advanced, interactive dressings in the contemporary market.

Hydrogels are particularly well suited to this role. They are three-dimensional, hydrophilic polymer networks capable of absorbing and retaining very large volumes of water while remaining insoluble owing to physical or chemical cross-linking. Their high water content, soft and pliable texture and intrinsic biocompatibility allow them to be applied directly and comfortably to a wound, where they cool and soothe the tissue, donate moisture to dry wounds and absorb exudate from exuding ones. Crucially, hydrogels mimic the natural extracellular matrix, creating a microenvironment that favours cell migration, proliferation and tissue regeneration. These attributes have positioned hydrogels and hydrogel-forming polymers among the fastest-growing categories of advanced wound dressing [4, 7].

Hydrogel beads represent a discrete, particulate form of this technology that offers additional advantages for herbal delivery. By compartmentalising the active within individual cross-linked microspheres, beads provide a high surface area for controlled release, protect sensitive bioactives within a defined matrix, and permit straightforward modulation of release through formulation variables. Among the natural polymers available for bead fabrication, sodium alginate stands out for its biocompatibility, biodegradability and uniquely mild gelation chemistry, which together make it the polymer of choice for encapsulating thermolabile herbal extracts such as Aloe vera gel. The advantages of alginate-based hydrogel beads for wound healing are summarised in Table 2.

Table 2. Advantages of alginate-based hydrogel beads in wound healing.

Property	Benefit in wound healing
High swelling capacity	Absorbs exudate and maintains a moist healing environment
Biocompatibility	Safe, non-irritant and well tolerated on skin and wounds
Controlled drug release	Provides prolonged, sustained therapeutic action
Mild gel-forming ability	Enables encapsulation of sensitive bioactives via ionic gelation
Biodegradability	Avoids the need for removal and reduces tissue trauma

VI. SODIUM ALGINATE AND THE IONIC GELATION TECHNIQUE

A. Alginate as a Biomaterial

Sodium alginate is a naturally occurring anionic polysaccharide extracted chiefly from brown seaweed. It is a linear copolymer of (1→4)-linked β-D-mannuronic acid (M) and α-L-guluronic acid (G) residues, arranged in homopolymeric M-blocks, homopolymeric G-blocks and alternating MG-blocks. It is widely employed in pharmaceutical, food and biotechnological applications because of its biocompatibility, biodegradability, low toxicity, low cost and, above all, its capacity to form hydrogels under exceptionally mild conditions [6, 19]. For wound care specifically, alginate hydrogels maintain a moist healing environment, absorb wound exudate, provide a degree of microbial barrier and support cell migration and tissue regeneration—properties that have made alginate a polymer of choice in modern dressings [4, 12].

The functional behaviour of an alginate is strongly determined by its monomer composition and sequence, in particular the ratio of guluronic to mannuronic acid (the M/G ratio) and the length of the G-blocks, since it is the guluronate residues that participate in calcium cross-linking. Alginates rich in G-blocks form stronger, more rigid and more porous gels, whereas mannuronate-rich alginates yield softer, more elastic gels. Molecular weight and concentration further influence solution viscosity, bead sphericity and mechanical strength. An appreciation of these structure–property relationships allows the formulator to select an alginate grade matched to the desired bead characteristics, and explains why the same encapsulation method can yield beads of markedly different swelling and release behaviour depending on the raw material employed [19, 29].

B. The Egg-Box Mechanism of Ionic Gelation

The defining feature of alginate is its ability to gel in the presence of divalent cations through ionotropic (ionic) gelation. When a sodium alginate solution contacts calcium ions, the calcium preferentially binds the guluronate G-blocks of adjacent polymer chains, which align and co-operatively cradle the cations in a structure classically described as the “egg-box” model, in which the calcium ions sit like eggs within the buckled chains (Figure 4). The result is a three-dimensional, cross-linked hydrogel network formed without heat, organic solvents or harsh chemistry [54, 56].

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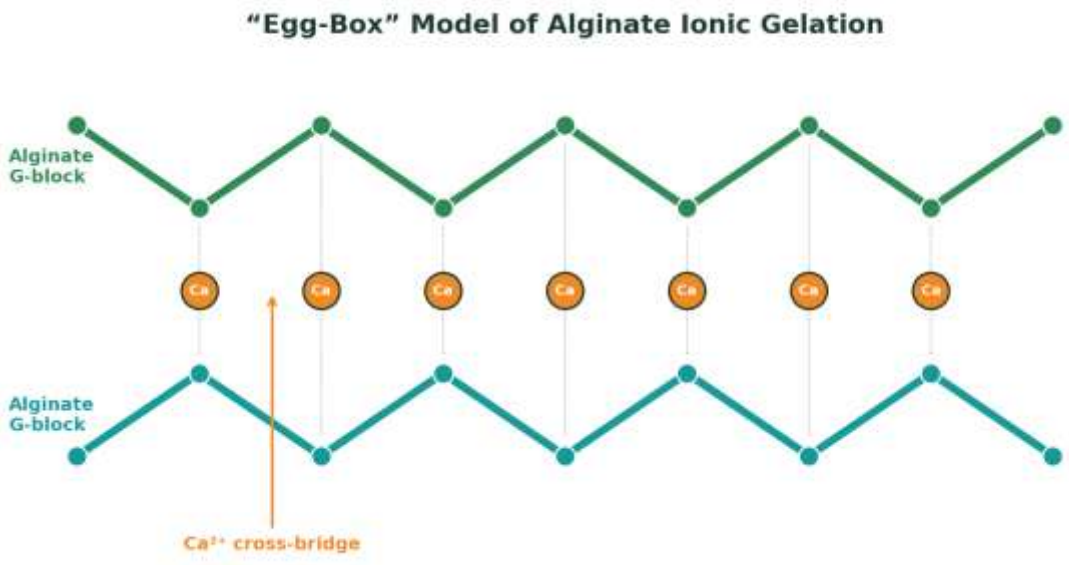

Figure 4. The "egg-box" model of alginate ionic gelation. Divalent calcium ions co-operatively bridge the guluronate (G) blocks of adjacent alginate chains, forming the cross-linked three-dimensional hydrogel network that constitutes the bead matrix.

This mildness is precisely what makes ionic gelation ideal for encapsulating sensitive herbal bioactives such as the polysaccharides of Aloe vera, which would be damaged by the elevated temperatures or reactive reagents of alternative cross-linking routes. In practice, beads are most commonly produced by external gelation: droplets of the alginate–Aloe vera blend are extruded into a calcium chloride bath, where each droplet gels instantaneously on contact to form a discrete spherical bead. The degree of cross-linking—and hence the mechanical strength, swelling behaviour and release rate of the beads—can be tuned by adjusting the concentrations of alginate and calcium chloride and the curing time, giving the formulator direct control over performance [55, 58]. Where a denser matrix and slower release are required, a chemical cross-linker may be added, although ionic cross-linking alone is generally preferred for biocompatibility.

Figure 5. Workflow for the preparation of Aloe vera gel-loaded alginate hydrogel beads by ionic gelation, from gel extraction through extrusion into a calcium chloride bath to curing, drying and evaluation.

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The complete preparation workflow (Figure 5) begins with the extraction and homogenisation of fresh, authenticated Aloe vera gel under hygienic conditions, followed by dispersion of sodium alginate, blending of the two, dropwise extrusion of the blend into a calcium chloride solution, and the curing, washing and drying of the resulting beads prior to evaluation. The simplicity, reproducibility and scalability of this process are major advantages for pharmaceutical development [15].

VII. RATIONALE FOR ALOE VERA GEL-LOADED HYDROGEL BEADS

Encapsulating Aloe vera gel within alginate hydrogel beads is a rational response to the limitations of the raw gel, and the advantages are best appreciated by comparing the two systems directly (Figure 6). The hydrogel matrix shields the thermolabile, oxidation-sensitive bioactives from environmental degradation and microbial spoilage, markedly improving physicochemical stability. By adhering to and absorbing exudate at the wound surface, the beads prolong residence time and maintain the moist environment that favours epithelialisation. Crucially, the cross-linked network converts the rapid, uncontrolled "burst" release characteristic of the plain gel into a sustained, controlled release, ensuring a prolonged therapeutic presence of the active constituents and reducing the frequency of application.

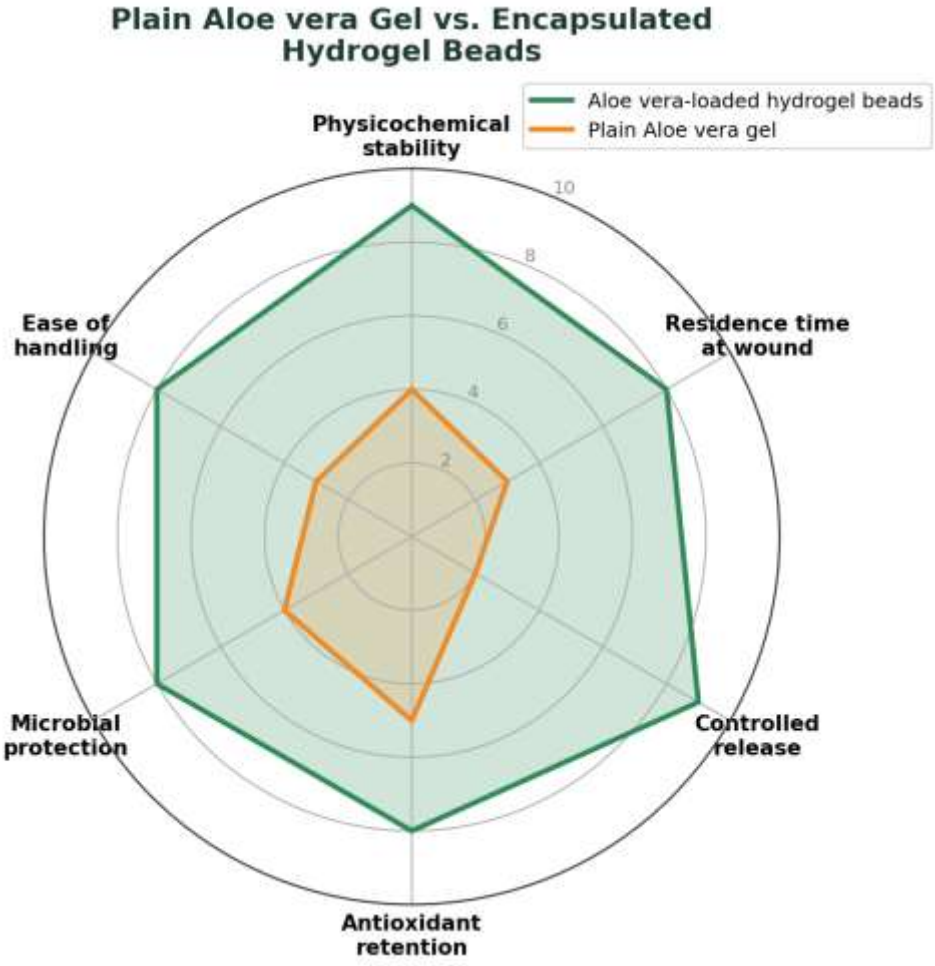

Figure 6. Comparative profile of plain Aloe vera gel versus encapsulated alginate hydrogel beads across six performance attributes. Encapsulation improves stability, residence time, release control and the retention of antioxidant and antimicrobial activity.

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Encapsulation additionally preserves biological activity. Studies on alginate-encapsulated plant extracts have repeatedly shown that the matrix protects polyphenolic and polysaccharide constituents, so that encapsulated forms retain higher antioxidant activity over time than their non-encapsulated counterparts [3, 11]. The same protective effect maintains antimicrobial potency. Taken together, these benefits convert a pharmacologically potent but pharmaceutically fragile natural material into a stable, standardised, controlled-release dosage form—uniting traditional herbal medicine with modern pharmaceutics. The remaining sections set out the in-vitro framework by which the success of this strategy is judged.

VIII. PHYSICOCHEMICAL EVALUATION OF HYDROGEL BEADS

A systematic programme of physicochemical characterisation is essential both to optimise the formulation and to confirm that the beads meet the required quality attributes. The principal parameters are percentage yield, particle size, swelling index, entrapment efficiency and surface morphology.

A. Percentage Yield and Particle Size

Percentage yield, calculated as the ratio of the dried bead mass to the total mass of solids used, provides a simple index of process efficiency and reproducibility. Particle size, an important determinant of surface area, release rate and handling, is measured by optical or scanning electron microscopy with image analysis, or by sieving, and is governed largely by the alginate concentration, the diameter of the extrusion orifice and the height of the drop into the gelation bath. Higher alginate concentrations increase solution viscosity and tend to produce larger beads, whereas excessively dilute solutions yield beads that lose their spherical morphology [55].

B. Swelling Index

The swelling index quantifies the capacity of the beads to absorb water, a property of direct relevance to wound care because it determines exudate uptake and the maintenance of a moist environment, and it strongly influences drug release. It is measured by immersing weighed dried beads in a defined medium and recording the increase in mass over time. Swelling behaviour is governed by the balance between polymer content and cross-link density: increasing the alginate concentration generally raises the swelling capacity by providing more hydrophilic polymer, whereas increasing the calcium chloride concentration produces a denser, more highly cross-linked matrix that swells less and releases its payload more slowly (Figure 7) [11, 58]. This reciprocal relationship gives the formulator two independent levers with which to tune performance.

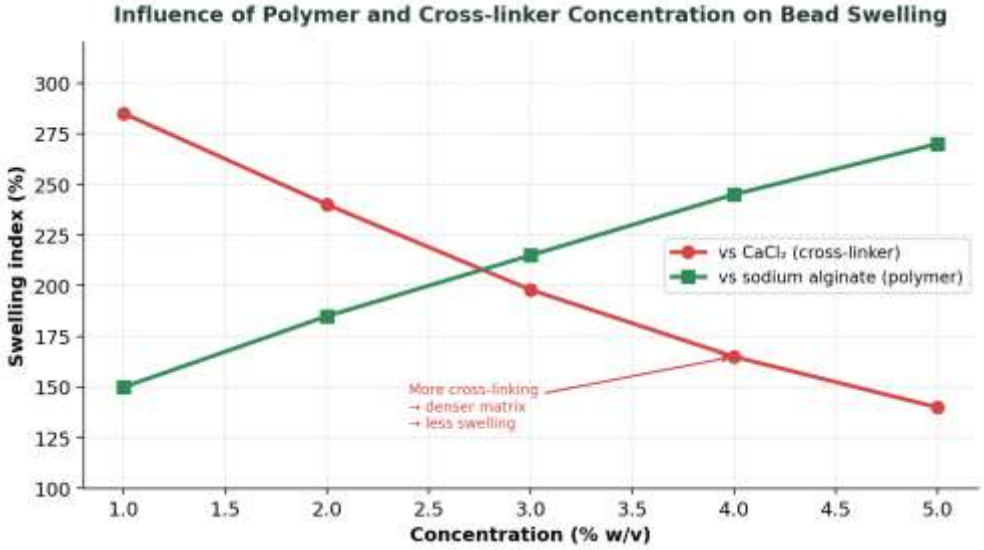

Figure 7. Illustrative effect of sodium alginate (polymer) and calcium chloride (cross-linker) concentration on the swelling index of hydrogel beads. Higher polymer content increases swelling; higher cross-linker content reduces it.

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C. Entrapment Efficiency and Surface Morphology

Entrapment (encapsulation) efficiency expresses the proportion of the Aloe vera bioactives successfully incorporated into the beads relative to the amount added, and is determined by assaying either the entrapped content or the residual free drug in the gelation medium. High entrapment efficiency is desirable for dose economy and reproducibility; reported alginate systems frequently achieve values in excess of 80% [3, 11]. Entrapment is influenced by polymer and cross-linker concentration, the molecular size of the encapsulated species and the curing conditions, with the large polysaccharide molecules of Aloe vera generally being well retained within the matrix. Surface morphology, examined by scanning electron microscopy, confirms the sphericity, surface texture and porosity of the beads; a smooth, uniform surface with appropriate porosity indicates a well-formed matrix and correlates with predictable swelling and release behaviour.

IX. IN-VITRO RELEASE AND KINETIC ANALYSIS

In-vitro release testing is the central biopharmaceutical evaluation of the beads, providing the evidence that encapsulation achieves the intended controlled-release behaviour. Release studies are typically conducted in phosphate buffer (commonly pH 7.4 to approximate the wound environment), with the beads immersed in the medium under gentle agitation and samples withdrawn at intervals and assayed spectrophotometrically for the released Aloe vera constituents. The plain gel characteristically exhibits a rapid burst release, whereas the encapsulated beads release their payload gradually over many hours, the rate being modulated by alginate and cross-linker concentration (Figure 8) [55, 73].

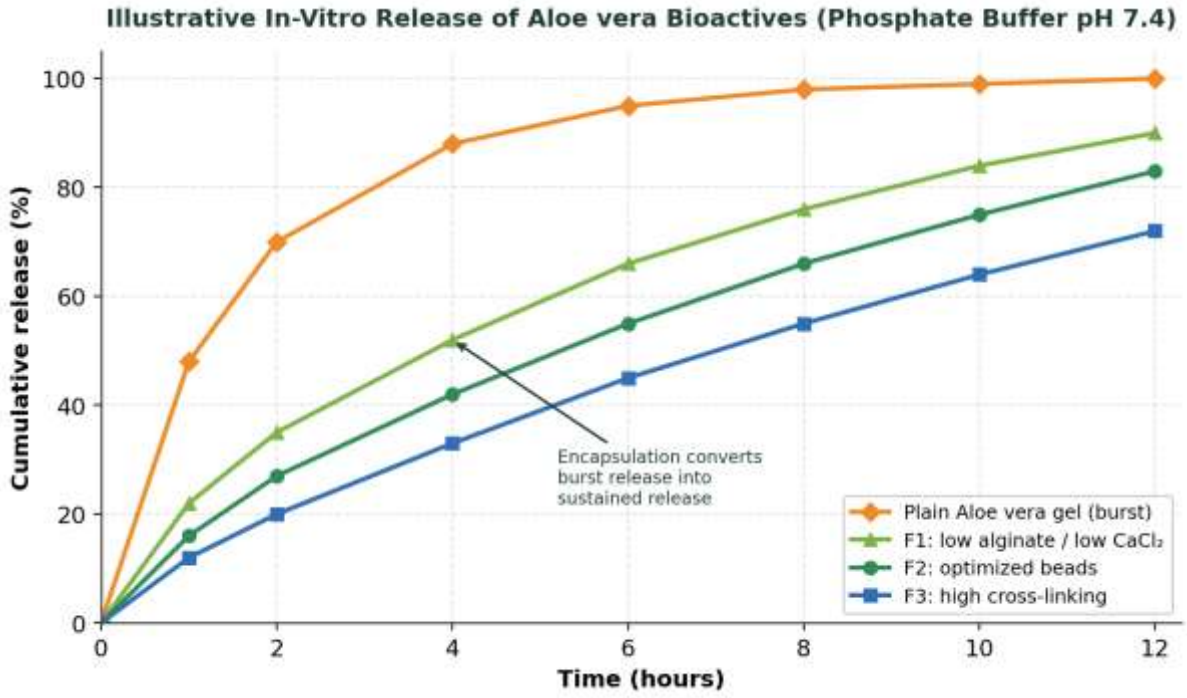

Figure 8. Illustrative in-vitro release profiles in phosphate buffer (pH 7.4). Plain Aloe vera gel shows a rapid burst, whereas the hydrogel beads provide sustained release; higher cross-linking (F3) further retards release.

The mechanism of release from alginate beads combines diffusion of the dissolved bioactives through the swollen, porous hydrogel network with progressive swelling and, eventually, erosion of the matrix. The relative contribution of these processes is commonly elucidated by fitting the release data to established kinetic models: the zero-order model (constant release rate), the first-order model (release

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proportional to residual content), the Higuchi model (diffusion-controlled release from a matrix) and the Korsmeyer–Peppas power-law model. The release exponent of the Korsmeyer–Peppas model distinguishes Fickian (diffusion-dominated) transport from anomalous and erosion-controlled mechanisms; for many alginate bead systems the data fit the Korsmeyer–Peppas model best, with release governed predominantly by Fickian diffusion [73, 76]. Kinetic modelling thus provides a rigorous, comparative description of release behaviour and supports the rational optimisation of polymer and cross-linker levels to achieve a target profile.

X. IN-VITRO PHARMACOLOGICAL EVALUATION

A. Antioxidant Activity (DPPH Assay)

Because oxidative stress is a major impediment to wound healing, the antioxidant activity of the formulation is a directly relevant biological endpoint. The 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay is the most widely used method for this purpose: DPPH is a stable, deep-violet free radical that absorbs strongly at 517 nm, and when an antioxidant donates a hydrogen atom or electron, the radical is reduced to the pale-yellow DPPH-H, with the decrease in absorbance being proportional to the antioxidant capacity of the sample [71, 80]. Results are expressed as percentage radical scavenging across a concentration range and summarised by the IC_{50}, the concentration required to scavenge half of the initial radical; a lower IC_{50} denotes greater antioxidant potency.

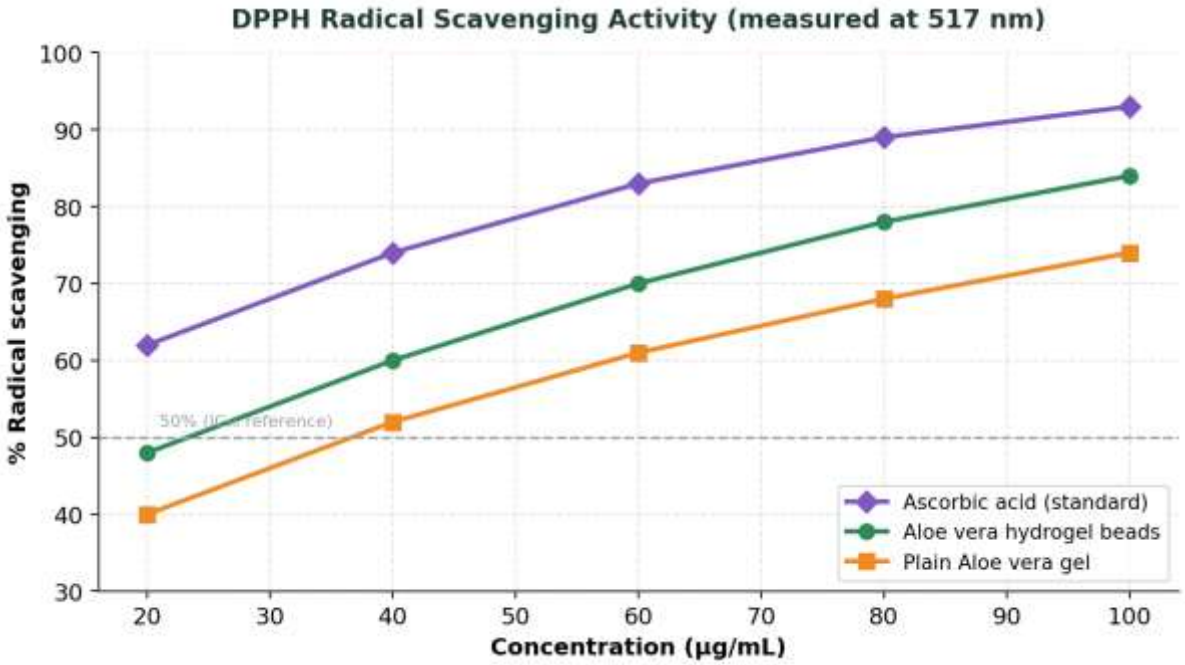

Figure 9. Illustrative DPPH radical scavenging activity (measured at 517 nm) as a function of concentration. The encapsulated beads retain strong, concentration-dependent antioxidant activity approaching that of the ascorbic-acid standard.

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In the context of Aloe vera beads, the assay serves two purposes: it confirms that the gel's intrinsic antioxidant constituents—vitamins, phenolics and polysaccharides—remain active after processing, and it demonstrates that encapsulation preserves, rather than diminishes, this activity. Encapsulated plant extracts characteristically retain antioxidant capacity better than free extracts because the matrix protects the labile phenolic and polysaccharide constituents from oxidation, with activity rising in a concentration-dependent manner toward that of a standard antioxidant such as ascorbic acid (Figure 9) [3, 11]. A favourable DPPH profile therefore provides direct in-vitro evidence of wound-relevant antioxidant efficacy.

B. Antimicrobial Activity

Infection is the other principal cause of delayed healing, so the antimicrobial activity of the beads is evaluated against organisms that commonly colonise and infect wounds, typically the Gram-positive Staphylococcus aureus and the Gram-negative Escherichia coli and Pseudomonas aeruginosa. Activity is most often assessed by the agar diffusion (zone of inhibition) method, in which the diameter of the clear zone surrounding the test material reflects the degree of microbial growth inhibition, and may be quantified further by minimum inhibitory concentration determination. Aloe vera's antimicrobial action arises from its phenolic compounds and other constituents, and the alginate matrix itself contributes a degree of barrier protection (Figure 10).

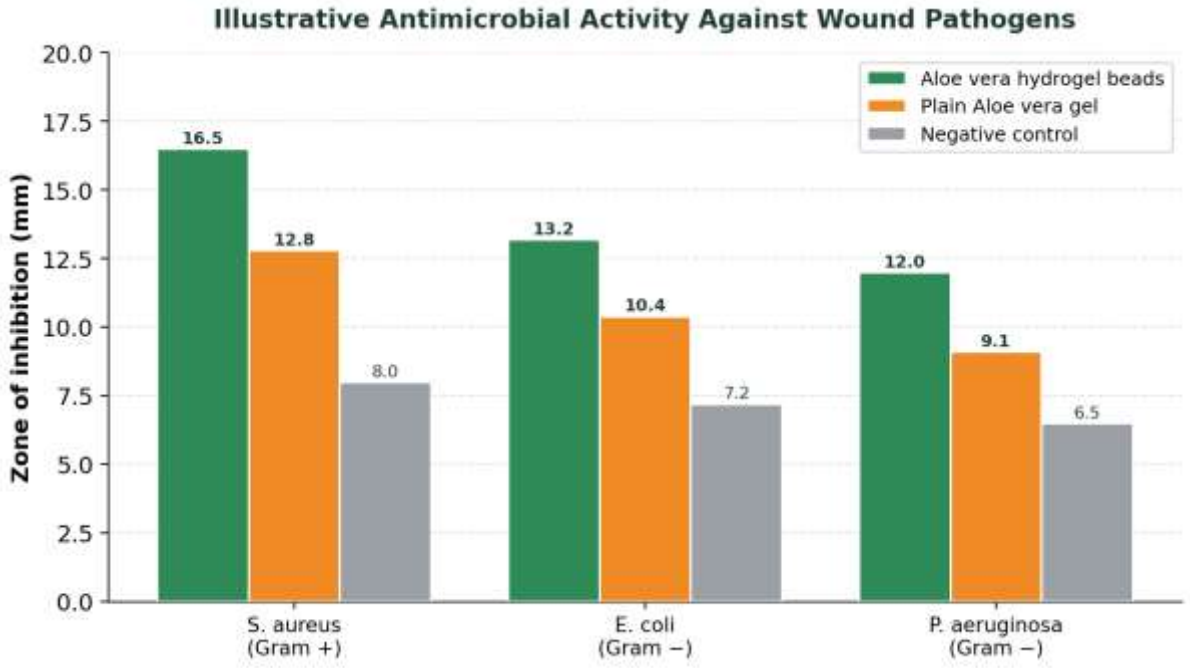

Figure 10. Illustrative antimicrobial activity (zone of inhibition) of Aloe vera hydrogel beads, plain gel and control against common wound pathogens. Activity is generally greatest against the Gram-positive S. aureus.

In comparative testing, Aloe vera-loaded beads typically produce larger zones of inhibition than the plain gel, reflecting both the preservation of antimicrobial constituents within the matrix and their sustained local release, with activity generally most pronounced against Gram-positive organisms such as S. aureus owing to differences in cell-wall architecture. Demonstrable antimicrobial efficacy against these representative pathogens provides important preliminary evidence that the formulation can help control the microbial burden of a wound, complementing its antioxidant and regenerative actions [5, 8].

C. Stability Studies

Finally, the optimised formulation is subjected to accelerated stability testing under International Council for Harmonisation (ICH) conditions—

commonly 40 ± 2 °C and 75 ± 5% relative humidity over a defined period—with periodic assessment of physical appearance, swelling, entrapment efficiency, drug content and antioxidant and antimicrobial activity. Such studies establish the shelf life of the product and confirm that the protective benefit of encapsulation is maintained over time, an essential requirement for any practical pharmaceutical dosage form.

XI. CHALLENGES AND FUTURE PERSPECTIVES

Despite their evident promise, Aloe vera-loaded alginate hydrogel beads face challenges that shape ongoing research. The natural variability of plant material—differences in Aloe vera composition with cultivar, geography, season and processing—complicates standardisation, underscoring the need for authenticated raw material and validated, marker-based quality control of acemannan content. Ionically cross-linked alginate matrices are sensitive to the ionic environment and can destabilise or release their payload prematurely in the presence of chelating or monovalent ions, which may necessitate composite or dual cross-linking strategies to achieve robust, predictable release. Achieving simultaneously high entrapment efficiency, appropriate swelling and a target release profile requires careful, often statistically guided, optimisation of polymer and cross-linker levels.

The trajectory of the field is nonetheless encouraging. The incorporation of secondary polymers such as chitosan, of nanocarriers, and of additional bioactive agents into alginate matrices is extending control over release and broadening the therapeutic spectrum, while design-of-experiments methodologies such as the Box–Behnken and factorial designs are bringing rigour and predictability to formulation development. Composite alginate systems, alginate–Aloe vera films and 3D-printed alginate scaffolds represent natural extensions of the bead concept toward tailored wound dressings [4, 24]. Most importantly, the in-vitro evidence reviewed here provides the foundation for the ex-vivo and in-vivo investigations—permeation, animal wound models and ultimately clinical evaluation—that will be required to translate this herbal-based delivery system into practice. Continued work in this direction sits squarely within the broader movement toward evidence-based herbal formulations and sustainable, biocompatible novel drug delivery systems.

XII. CONCLUSION

Chronic and infected wounds demand therapeutic strategies that combine biological efficacy with controlled, sustained delivery, and the encapsulation of Aloe vera gel within sodium alginate hydrogel beads addresses this need with notable elegance. Aloe vera offers a uniquely multifaceted wound-healing pharmacology—acemannan-driven stimulation of fibroblast proliferation, collagen synthesis, angiogenesis and epithelialisation, together with antioxidant, anti-inflammatory and antimicrobial activity—but its raw gel is pharmaceutically fragile, unstable, prone to contamination and poorly retained at the wound. Ionic gelation of alginate, proceeding through the mild, solvent-free egg-box cross-linking of guluronate blocks by calcium ions, provides a biocompatible and biodegradable matrix that protects the bioactives, prolongs residence time, maintains a moist healing environment and converts burst release into sustained release. The comprehensive in-vitro framework reviewed here—percentage yield, particle size, swelling index, entrapment efficiency, surface morphology, release kinetics, DPPH antioxidant activity and antimicrobial testing against representative wound pathogens—enables rational optimisation and provides preliminary evidence of performance. Drawing together the pathophysiology of wound healing, the pharmacology of Aloe vera, the materials science of alginate and the principles of ionic gelation, this review establishes Aloe vera gel-loaded hydrogel beads as a scientifically validated, herbal-based novel drug delivery system with strong potential for wound care, and as a sound foundation for the ex-vivo and in-vivo studies that should follow.

REFERENCES

[1] Precedence Research. Wound care market size, growth, share and trends analysis, 2025–2034; 2025.

[2] Fact.MR. Advanced wound care market: forecast 2024–2034. Market Research Report; 2024.

[3] Tomé AC, et al. Alginate based encapsulation as a protective carrier for plant-derived bioactive compounds: a review. 2022.

[4] Abourehab MAS, et al. Recent advances of chitosan and alginate-based drug delivery systems in wound healing applications. 2022.

[5] Liang J, et al. Aloe vera: a medicinal plant used in skin wound healing – molecular and cellular mechanisms. Tissue Eng Part B Rev. 2021.

[6] Hariyadi DM, Islam N. Current status of alginate in drug delivery. Adv Pharmacol Pharm Sci. 2020.

[7] Zhang M, et al. Alginate hydrogel dressings for advanced wound management. Int J Biol Macromol. 2020.

[8] Sánchez M, et al. Pharmacological update properties of Aloe vera and its major active constituents. Molecules. 2020;25(6):1324.

[9] Liu C, et al. Extraction, characterisation and biological activity of Aloe vera polysaccharides (acemannan). 2019.

[10] Hęś M, et al. Aloe vera (L.) Webb: natural source of antioxidants – a review. Plant Foods Hum Nutr. 2019.

[11] Wongverawattanakul C, et al. Alginate beads loaded with plant extract: physicochemical properties and antioxidant activity. 2022.

[12] Aderibigbe BA, Buyana B. Alginate in wound dressings. Pharmaceutics. 2018;10(2):42.

[13] Quezada MP, et al. Acemannan and fructans from Aloe vera: structural characterisation and biological activity. Carbohydr Polym. 2017.

[14] Moriyama M, et al. Beneficial effects of Aloe vera on keratinocyte and fibroblast function in wound healing. PLoS One. 2016.

[15] Szekalska M, et al. Alginate: current use and future perspectives in pharmaceutical and biomedical applications. Int J Polym Sci. 2016.

[16] Xing W, et al. Acemannan accelerates cell proliferation and skin wound healing through AKT/mTOR signalling. J Dermatol Sci. 2015.

[17] Sierra-García GD, et al. Acemannan, an extracted polysaccharide from Aloe vera: a review. Nat Prod Commun. 2014.

[18] Andersen T, et al. 3D cell culture in alginate hydrogels. Microarrays. 2015.

[19] Lee KY, Mooney DJ. Alginate: properties and biomedical applications. Prog Polym Sci. 2012;37(1):106–26.

[20] Jettanacheawchankit S, et al. Acemannan stimulates gingival fibroblast proliferation and KGF-1, VEGF and type I collagen expression. J Pharmacol Sci. 2009;109(4):525–31.

[21] Somboonwong J, et al. Therapeutic effects of Aloe vera on cutaneous microcirculation and wound healing. J Med Assoc Thai. 2000.

[22] Bialik-Wąs K, et al. Sodium alginate–Aloe vera hydrogel composites: physicochemical, structural and thermal properties. 2022.

[23] Liu P, et al. Acemannan from Aloe vera: extraction, structure, biological activity and pharmacological applications – a review. Int J Biol Macromol. 2019. PMC6515206.

[24] Hu Q, et al. A new biomaterial derived from Aloe vera – acemannan from basic studies to clinical application. Pharmaceutics. 2023. PMC10385217.

[25] Pharmacological efficacy of Aloe vera in wound healing: a narrative review. 2023.

[26] In vitro wound-healing potential of phenolic and polysaccharide extracts of Aloe vera gel. J Funct Biomater. 2024;15(9):266.

[27] Mei J, et al. Preparation of alginate hydrogel microparticles by ionic cross-linking: a review of methods. Biomater Res. 2021;25:1.

[28] Agulhon P, et al. Encapsulation in alginate hydrogels and controlled release: an overview. 2024. PMC11173704.

[29] Ionotropic gelation: a promising cross-linking technique for hydrogels. Res Rev J Pharm Pharm Sci. 2014.

[30] Preparation of alginate hydrogel beads on a superhydrophobic surface to enhance mechanical strength and encapsulation efficiency. 2024. PMC11676131.

[31] Munarin F, et al. Advances in biomedical applications of pectin and alginate gels (egg-box model). Int J Biol Macromol. 2012.

[32] Highly flexible thermoresponsive alginate-containing hydrogels: encapsulation, release

kinetics and mechanism. Int J Biol Macromol. 2025.

[33] Gulrez SKH, et al. Hydrogels: methods of preparation, characterisation and applications. 2011.

[34] Gülçin İ, Alwasel SH. DPPH radical scavenging assay. Processes. 2023;11(8):2248.

[35] Blois MS. Antioxidant determinations by the use of a stable free radical. Nature. 1958;181:1199–200.

[36] Brand-Williams W, Cuvelier ME, Berset C. Use of a free radical method to evaluate antioxidant activity. LWT Food Sci Technol. 1995;28:25–30.

[37] Korsmeyer RW, et al. Mechanisms of solute release from porous hydrophilic polymers. Int J Pharm. 1983;15:25–35.

[38] Determination of antioxidants by DPPH radical scavenging activity and phytochemical analysis. Sci World J. 2022. PMC8878429.

[39] Design-of-experiment-assisted fabrication of biodegradable alginate–chitosan nanoparticles: in vitro characterisation and biological activity. ACS Omega. 2023.