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Nano Aloe Vera Based Chitosan Delivery Systems in Dentistry: Therapeutic Potentials and Biomedical Advancements

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Abstract

Aloe vera is a well-documented medicinal plant known for its potent anti-inflammatory, antimicrobial, antioxidant, and wound-healing properties. However, its direct application in dental therapeutics is limited due to poor stability and bioavailability. The advancement of nanotechnology has enabled the development of Aloe vera-loaded chitosan nanoparticles, which offer enhanced mucoadhesion, controlled drug release, and targeted delivery to oral tissues. This review explores the therapeutic potential of nano Aloe vera chitosan systems in the context of dental applications, including periodontitis, oral ulcers, caries prevention, and post-surgical healing. The mechanisms of action, such as mucoadhesion, antimicrobial synergy, sustained release, and immune modulation, are critically discussed. Furthermore, the review highlights relevant preclinical and clinical findings, challenges in standardization and regulatory pathways, and emerging directions like stimuli responsive delivery and integration with regenerative materials. The convergence of phytotherapy and nanotechnology presents a promising frontier for biocompatible and effective oral healthcare interventions.

Keywords: Aloe vera; Chitosan nanoparticles; Nanotechnology; Oral drug delivery; Periodontitis; Dental caries; Oral ulcers; Remineralization; Mucoadhesion; Phytotherapy; Biomedical applications in dentistry

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1. Introduction

Oral health is an essential component of general well-being, yet it remains a significant global health burden due to the high prevalence of conditions such as dental caries, periodontal disease, oral ulcers, and mucositis. The limitations of conventional treatment strategies ranging from adverse effects to limited bioavailability have directed research interest toward naturally derived bioactive agents and their integration into advanced drug delivery platforms. One such bioactive agent, Aloe vera, has garnered widespread attention for its therapeutic properties, including anti-inflammatory, antimicrobial, antioxidant, and wound-healing effects [1-2]. Despite these promising attributes, the clinical utility of Aloe vera is hindered by instability, rapid degradation, and limited permeability when used in its raw or gel form. Recent advances in nanotechnology have provided innovative strategies to overcome these challenges. Nanocarrier systems not only improve the solubility and bioavailability of therapeutic compounds but also facilitate controlled and targeted delivery, especially in the complex microenvironment of the oral cavity [3]. Among the various nanomaterials explored, chitosan-based nanoparticles stand out due to their muco adhesiveness, biodegradability, and intrinsic antimicrobial properties. Chitosan which is a deacetylated derivative of chitin forms stable complexes with a variety of bio actives and is particularly effective in mucosal drug delivery, making it a suitable candidate for oral therapeutic applications [4-5]. Combination of Aloe vera and chitosan in a nanoscale delivery system represents a novel and synergistic approach to managing oral diseases. When Aloe vera is incorporated into chitosan nanoparticles, the nano delivery system facilitates sustained release and enhanced tissue penetration, while amplifying its anti-inflammatory, antioxidant, and antimicrobial actions [1-6]. This review aims to provide a comprehensive overview of current knowledge regarding use of nano Aloe vera formulations specifically those utilizing chitosan nanocarriers in the field of dentistry. The article will explore their therapeutic mechanisms, formulation strategies, biomedical applications, and future prospects for clinical translation. By addressing the intersection of phytomedicine and nanotechnology, this review contributes to the growing body of research advocating for integrative, biomaterial-based solutions in modern dental therapy.

2. Phytochemistry and Medical Potential of Aloe vera

Aloe vera has been extensively utilized in traditional medicine systems due to its broad spectrum of biological activities. Modern research has identified over 75 active compounds within Aloe vera, including vitamins A, C, E,

B12, amylase enzyme, lipase enzyme, calcium, magnesium, zinc, acemannan which is polysaccharides, anthraquinones (aloin, emodin), lignins, saponins, and amino acids [7]. These constituents contribute synergistically to the plant's anti-inflammatory, antioxidant, immunomodulatory, and wound healing properties [8] Table (1). The most bioactive component of Aloe vera is the acemannan which is a β (1→4)-linked acetylated mannan that stimulates macrophage activity, promotes fibroblast proliferation, and enhances collagen synthesis which are critical for tissue repair and regeneration [9]. Additionally, the anthraquinones such as aloin and emodin have been shown to exert antimicrobial effects against both Gram positive and Gram-negative bacteria, making Aloe vera particularly valuable in the treatment of oral infections and biofilm related conditions [10]. Moreover, Aloe vera's antioxidant compounds, including vitamins C and E, play a crucial role in neutralizing reactive oxygen species (ROS), which are elevated in inflammatory oral diseases such as periodontitis. This antioxidant mechanism helps in stabilizing tissue damage and promoting faster healing [11]. Despite Aloe vera's therapeutic potential, the direct application of the gel often presents limitations such as instability, short shelf life and poor mucosal retention. That's why need for more effective delivery platforms such as nano formulations to harness its full therapeutic efficacy in oral healthcare applications [12].

3. The Role of Nanotechnology in Healthcare

Nanotechnology has transformed biomedical sciences by allowing development of materials and devices at molecular and atomic scale. Application of nanomaterials in medicine commonly referred to as nanomedicine which has gained significant attention for its ability to enhance drug solubility, control its release, improve pharmacokinetics, and enable targeted delivery to diseased tissues [13]. Oral environment which is constantly exposed to saliva, mechanical forces, and microbial biofilms, the nanocarrier systems offer distinct advantages for stability and localized delivery [14]. Nanoparticles, typically ranging from 1 to 100 nm in size, can be engineered from organic or inorganic materials. organic materials e.g., liposomes, chitosan, PLGA or inorganic materials e.g., silica, gold, silver. These systems protect active compounds from enzymatic degradation, enhance permeation across mucosal barriers, and sustain release over extended periods [6]. Additionally, surface modifications with binding agents or functional groups allow nanoparticles to exhibit site specific targeting, reducing systemic toxicity and enhancing efficacy of the delivering drug [15]. In dentistry, nanotechnology has been employed in various domains, including drug delivery, restorative materials, antimicrobial coatings, & diagnostics. Nano formulations enhance the therapeutic index of bioactive agents such as antimicrobials, anti-inflammatory, and growth factors by improving their retention at the target site and modulating their interaction with host tissues and pathogens [16]. The incorporation of Aloe vera into nanocarrier systems has garnered considerable attention due to its potential to enhance therapeutic outcomes. Encapsulation within nanoparticles significantly improves Aloe vera's absorption, stability, and mucosal adhesion, thereby augmenting its pharmacological efficacy [17]. Emerging evidence demonstrates that nanostructured *Aloe vera* exhibits superior antibacterial and wound-healing activities compared to its conventional formulations, particularly in the management of oral infections and soft tissue injuries [3-6-18]. A synergistic enhancement is achieved when *Aloe vera* is combined with chitosan-based nanoparticles. Chitosan not only serves as a stabilizing matrix that shields bioactive components from enzymatic degradation and oxidative damage but also enables sustained release, thereby prolonging therapeutic effects [19]. Furthermore, nanoparticle encapsulation significantly improves the bioavailability of key active constituents such as acemannan and aloin, which are otherwise susceptible to rapid degradation within the gastrointestinal tract and oral cavity [20]. Thus, nanotechnology serves as a critical platform for transforming Phyto therapeutic agents like Aloe vera into clinically viable, targeted therapies suitable for complex oral health challenges.

4. Chitosan as a Nanocarrier

Chitosan, a naturally derived polysaccharide obtained through the deacetylation of chitin, has emerged as a highly effective nanocarrier in drug delivery systems due to its exceptional biocompatibility, biodegradability, non-toxicity, and mucoadhesive properties making it particularly suitable as a nanocarrier for drug delivery in mucosal environments [21]. Structurally composed of β-(1→4)-linked D-glucosamine and Nacetyl-Dglucosamine units, chitosan offers the ability to form stable nanoparticles via ionic gelation, emulsification, and polyelectrolyte complexation methods [22]. It also has the most distinctive advantages of positive surface charge, which promotes strong adhesion to negatively charged mucosal surfaces such as those in the oral cavity Figure (1). This characteristic enhances drug retention, permeability, and cellular uptake, making it an ideal candidate for mucosal delivery [23]. Furthermore, it also has an intrinsic antimicrobial activity, which is beneficial when used to deliver bioactive aimed at managing microbial infections in the oral cavity [24]. In conclusion, chitosan stands as a multifunctional nanocarrier that not only enables efficient delivery of Aloe vera but also contributes additional therapeutic benefits, particularly in the challenging environment of the oral cavity. Synergistic Antimicrobial and Healing Effects of Aloe Vera Loaded Chitosan.

5. Nanoparticles in Oral Medicine

The combination of Aloe vera with chitosan in nanoparticle form provides a synergistic therapeutic strategy that leverages the healing power of natural compounds and the targeted delivery capabilities of nanotechnology owing to their antimicrobial, anti-inflammatory, and wound healing properties, these nanocomposites have demonstrated efficacy in treating multiple oral diseases including periodontitis, ulcers, caries, and tissue injuries [3]. Furthermore, the combination has shown potential in accelerating wound healing, reducing oxidative stress, and modulating inflammatory cytokines in oral ulcers and surgical wounds [25]. Consequently, due to the small particle size of the nanoparticles it facilitates better penetration into oral mucosal tissues, ensuring that Aloe vera reaches the target site efficiently and exerts a prolonged biological effect [26] and also having a chitosan as a carrier due to its mucoadhesive nature and ability to form protective colloidal systems, provide an ideal environment for encapsulating Aloe vera gel. The nano encapsulation shields the bioactive from enzymatic degradation and photochemical instability, thereby

improving their shelf life and therapeutic effectiveness [5]. The Formulation methods such as ionic gelation and polyelectrolyte complexation allow for the efficient loading of Aloe vera into chitosan nanoparticles without requiring harsh solvents or high temperatures, preserving the integrity of the bioactive [27]. These nanoparticles can also be incorporated into various delivery platforms, including hydrogels, mouth rinses, films, and periodontal inserts, further expanding their clinical utility [9]. Multiple studies have demonstrated that Aloe vera loaded chitosan nanoparticles exhibit enhanced antimicrobial and anti-inflammatory properties compared to their non nano counterparts. These systems can effectively inhibit the growth of Streptococcus mutans, Porphyromonas gingivalis, and Candida albicans, which are key pathogens in dental caries, periodontitis, and oral candidiasis respectively [28]. Furthermore, the combination has shown potential in accelerating wound healing, reducing oxidative stress, and modulating inflammatory cytokines in oral ulcers and surgical wounds [29].

6. Periodontal Disease

Periodontitis is a chronic inflammatory disease initiated by pathogenic bacteria such as Porphyromonas gingivalis and Aggregatibacter actinomycetemcomitans. Nano Aloe vera with chitosan formulations have shown remarkable antibacterial activity against these pathogens and modulate host immune responses by reducing proinflammatory cytokines like IL-1β and TNF-α [10]. Their mucoadhesive nature ensures prolonged retention in the periodontal pocket, promoting sustained drug release and enhanced healing [5]. Clinical and preclinical studies indicate that use of Aloe vera loaded chitosan nanoparticles as an adjunct to scaling and root planning significantly reduces pocket depth and improves gingival health [19].

7. Oral Ulcers, Mucositis

Oral ulcers, particularly recurrent aphthous stomatitis and chemo therapy induced mucositis, represent painful lesions affecting quality of life. Nano Aloe vera formulations provide rapid pain relief, promote epithelial regeneration, and minimize microbial colonization due to their antimicrobial and anti-inflammatory properties [30]. Chitosan enhances mucoadhesion and forms a protective film over the ulcer, reducing irritation and accelerating healing [31-32].

8. Dental Caries and Remineralization

Aloe vera contains bioactive polysaccharides and flavonoids that inhibit Streptococcus mutans and support remineralization [33]. Arnaud et al. (2010) demonstrated that chitosan reduces enamel demineralization and enhances surface hardness by acting as a protective barrier and penetrating the enamel to limit acid diffusion [20]. When delivered via chitosan nanoparticles, the anticariogenic potential of Aloe vera is significantly enhanced due to better delivery and retention in enamel defects [32]. Figure (2).

9. Surgical Healing and Implantology

In post operative care, such as after tooth extraction or implant placement, Aloe vera chitosan hydrogels can be applied topically to reduce inflammation, prevent infection, and accelerate wound closure. Their controlled release profile ensures consistent therapeutic activity over several days [29]. Upon reaching the site of infection or inflammation, Aloe vera compounds exert antimicrobial effects by disrupting microbial membranes, inhibiting biofilm formation, and interfering with bacterial metabolism [32]. Chitosan, independently, also disrupts bacterial cell walls by binding to phospholipids, creating a dual action against oral pathogens [1]. Simultaneously, anti-inflammatory phytochemicals in Aloe vera such as acemannan and C-glucosyl chromone modulate the inflammatory cascade by suppressing prostaglandins and cytokines (e.g., IL-6, TNF-α), thereby accelerating healing and reducing discomfort [19].

10. Synergistic, antimicrobial and healing effects

Chitosan's cationic nature allows for strong electrostatic interactions with the negatively charged mucosal surfaces of oral cavity, leading to improved muco adhesion and prolonged retention time [1]. This adhesion increases the residence time of the Aloe vera payload at site of action, improving therapeutic efficiency. Furthermore, the small size of these nanoparticles facilitates their movement between epithelial cells and enables deep infiltration into inflamed or compromised tissues, which are typically present in conditions such as ulcers, periodontal disease, and post-surgical wounds. [16]. Chitosan nanoparticles also allow for controlled release of Aloe vera compounds via diffusion mechanisms. The release profile is influenced by particle size, cross-linking density, pH sensitivity, and solubility of encapsulated phytochemicals [19]. At neutral to slightly acidic pH, commonly found in inflamed tissues, chitosan swells and promotes a sustained diffusion of active ingredients such as acemannan, aloin, and flavonoids from Aloe vera [22]. This prolonged release ensures constant therapeutic levels of drug at site, reducing need for frequent administration and improving patient compliance. Figure (3).

11. Clinical Trials and Preclinical Studies

The biomedical application of nano Aloe vera–chitosan formulations has been explored in a growing number of preclinical and clinical studies, particularly within dental and oral healthcare settings. These investigations have evaluated efficacy in inflammation reduction, wound healing, antimicrobial effects, and patient reported outcomes.

12. Preclinical Studies

In animal models, Aloe vera-loaded chitosan nanoparticles have shown significant potential in enhancing periodontal regeneration and reducing inflammatory markers. Rat models with induced periodontitis treated with these nanoparticles demonstrated a reduction in alveolar bone loss and lower levels of TNF-α and IL-1β compared to controls [34]. Histological assessments revealed improved fibroblast activity and collagen fiber organization, indicating active tissue repair [35]. Other preclinical models have confirmed the superior bioavailability and retention of Aloe vera when encapsulated in chitosan nanoparticles, particularly at mucosal sites. These formulations showed minimal systemic absorption and localized action, which is ideal for oral diseases where targeted therapy is required [6]. While clinical trials remain limited, early-phase investigations have provided encouraging data. A randomized controlled study involving patients with chronic gingivitis compared Aloe vera–chitosan gel as an adjunct to scaling and root planning versus chlorhexidine gel.

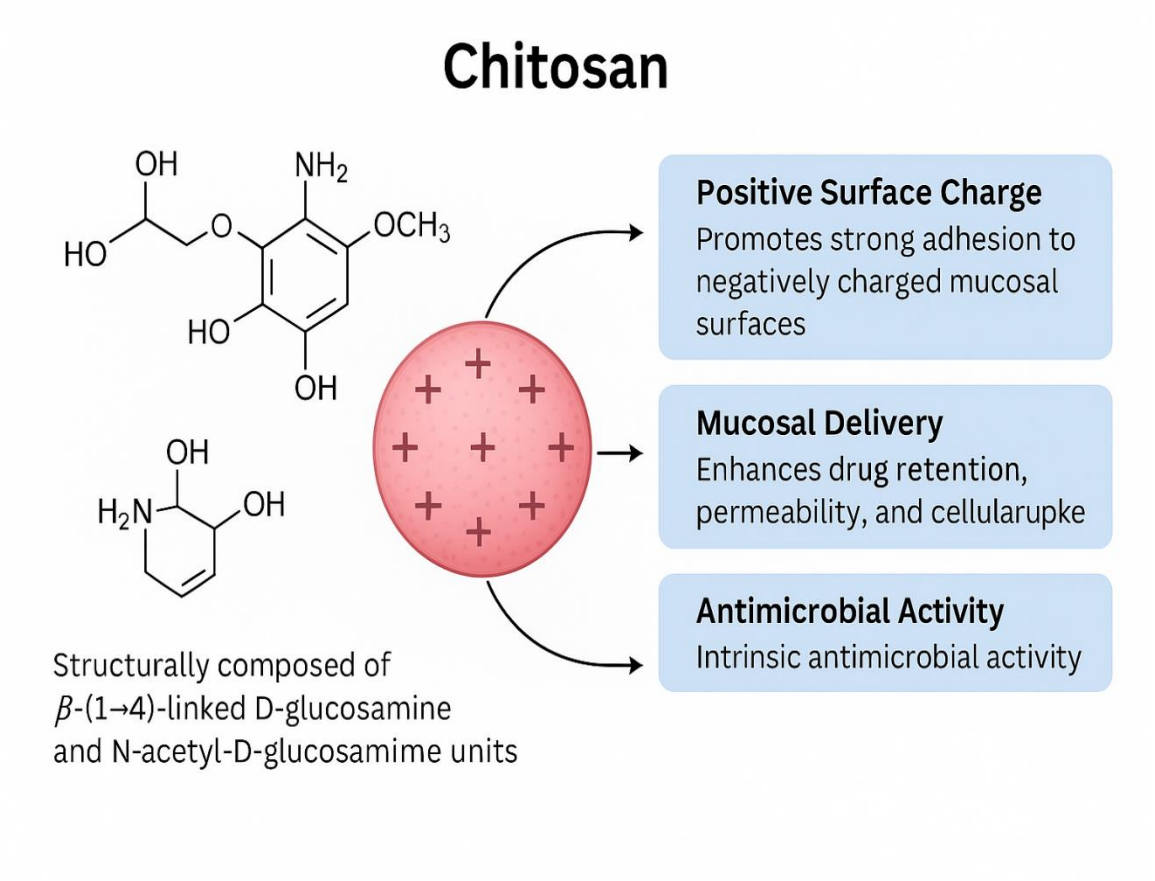

Figure 1: Chitosan properties

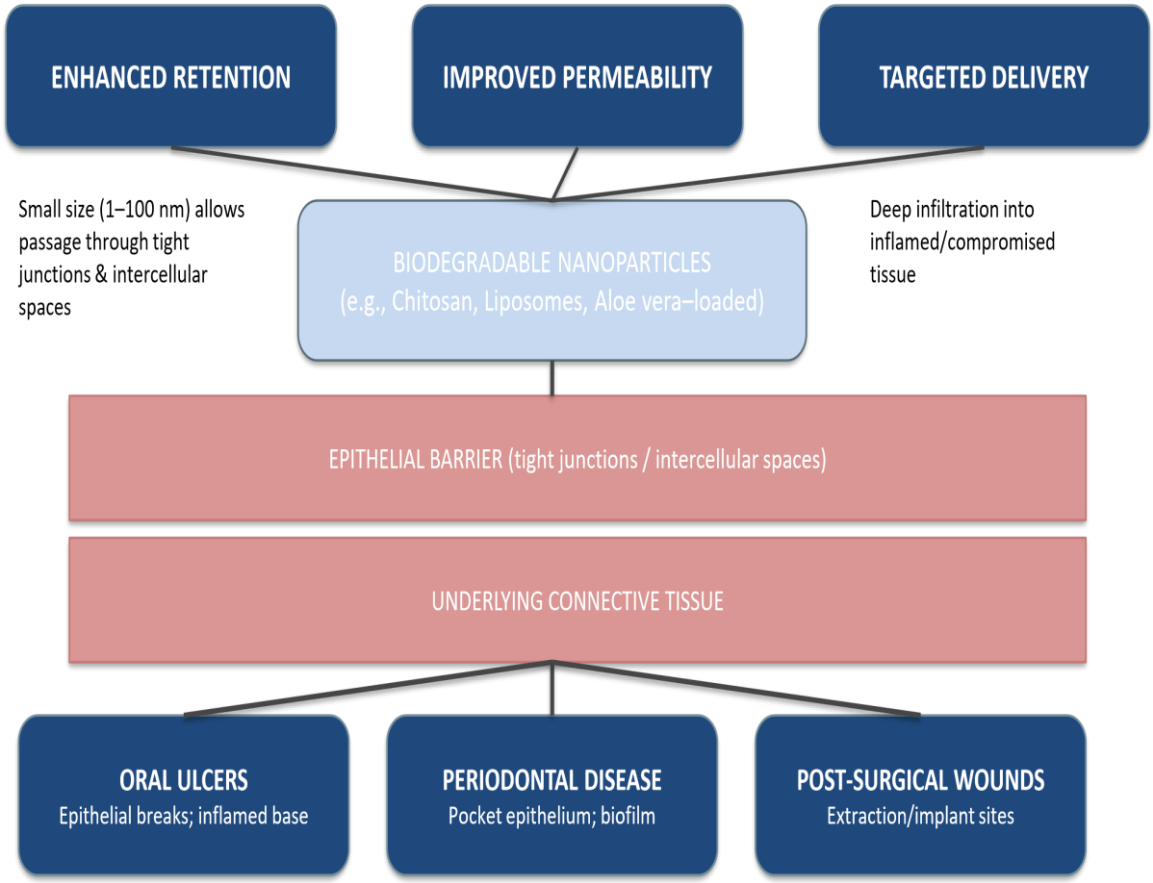

Figure 2: Nanocarriers may be chitosan, liposomes, PLGA, or inorganic (silica, gold); surface functionalization enables site-specific targeting and reduced systemic toxicity.

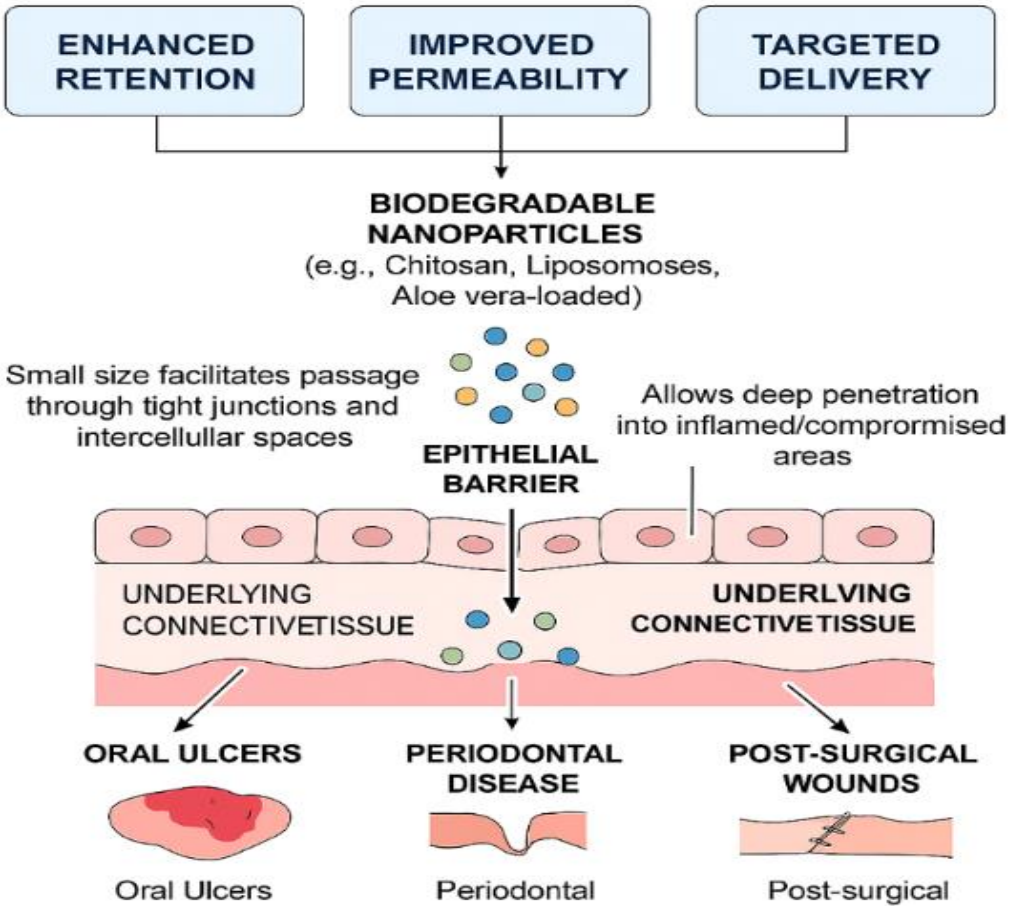

Figure 3: Biodegradable nanoparticles

Table 1: Roles of Essential Minerals

Name of the Mineral	Role of Each Mineral
Calcium	Structural role in bones and teeth Essential for cellular structure and nerve transmission Requires a balance of phosphorus and magnesium to work effectively Needs Vitamin D for its absorption
Manganese	Forms part of complex proteins that act as biochemical catalysts Speeds up clinical/biochemical reactions in plants and the body
Sodium	Prevents body fluids from becoming too acidic or too alkaline Involved in electrical conductivity in muscles and nerves Facilitates uptake of nutrients by individual cells
Potassium	Helps maintain acid–base balance in the body Involved in electrical conductivity in nerves and muscles
Copper	Component of several enzymes Facilitates iron's role as an oxygen carrier in red blood cells
Magnesium	Closely involved in calcium metabolism during bone formation Needed by nerve and muscle membranes to conduct electrical impulses
Zinc	Contributes to metabolism of proteins, carbohydrates, and fats Deficiency affects rapidly renewing tissues (skin, gut lining, immune system) Deficiency linked to schizophrenia in some studies Important for men's reproductive health and function
Chromium	Essential for proper insulin function Regulates blood sugar levels Vital for diabetics to maintain adequate levels
Iron	Enables oxygen transport around the body as oxyhemoglobin

Table 2: List of studies in which the effect of Aloe vera formulations has been investigated

Author/ year	*In vivo*/*in vitro*/ human	Herbal / others	Effect/mechanism
Bhat et al. 2011	Human	*Aloe vera* gel	Decrease of plaque, pocket depth, and gingival indices
Ashouri Moghaddam et al. 2017	Human	*Aloe vera* gel	Decrease of plaque index
Abdelmonem et al. 2014	Human	*Aloe vera* gel	Decrease of the activity of *P. intermedia* and *P. gingivalis* bacteria
Mokhtar et al. 2016	*In vivo*	*Aloe vera* gel	Reduction of inflammatory reactions and caspase-3 area
Deepu et al. 2018	Human	*Aloe vera* gel	Decrease of pocket depth index and gingival inflammation
Hudwekar et al. 2019	Human	*Aloe vera* extract	Wound healing effects following periodontal flap surgery
Shamim et al. 2016	Human	*Aloe vera* extract	Wound healing effects following periodontal flap surgery
Vangipuram et al. 2016	Human	*Aloe vera* extract	Reduction of plaque and gingival indices
Pradeep et al. 2016	Human	*Aloe vera* gel	Reduction of plaque, bleeding, and pocket depth indices
Kurian et al. 2017	Human	*Aloe vera* gel	Decrease of pocket depth, gingival, and bleeding indices
Penmetsa et al. 2019	Human	*Aloe vera* gel	Decrease of plaque, gingival, bleeding, and pocket depth indices
Susanto et al. 2021	*In vivo*	*Aloe vera* hydrogel	Reduction of the number of neutrophil.

The Aloe vera group showed comparable improvement in gingival index and bleeding scores, with fewer side effects such as staining or taste alteration [8]. In another small-scale human trial, chitosan-based Aloe vera mouthwash significantly reduced microbial counts of Streptococcus mutans and improved patient comfort in subjects with early-stage caries [9]. A clinical application of Aloe vera loaded chitosan hydrogel was also explored for post-extraction wound healing, where subjects reported faster epithelialization and less discomfort during the first week post-surgery [14]. Although large scale and long-term randomized trials are lacking, these preliminary results provide a strong rationale for expanded clinical investigation. The data support the biocompatibility, safety, and effectiveness of the Aloe vera chitosan Nano formulation in oral disease management.

13. Future Directions

As research in nano Aloe vera chitosan systems advances, several promising avenues can be pursued to further enhance their application in dentistry and oral therapeutics. These directions encompass multifunctional delivery systems, smart drug release platforms, broader clinical validation, and integration with advanced dental biomaterials. Recent researchers are increasingly exploring multifunctional nanoparticles that combine Aloe vera and chitosan with inorganic additives like silver or zinc oxide to boost antimicrobial, remineralizing, and healing effects in oral cavity. For example, a chitosan Aloe vera silver

nanoparticle hydrogel has shown enhanced wound healing and antimicrobial performance compared to formulations without metal additives [36]. Similarly, chitosan alginate films infused with Aloe vera and silver nanoparticles demonstrated strong antibacterial activity against S. aureus and P. aeruginosa, alongside controlled release and suitable structural properties for wound dressings [37].

Also, Membranes blending chitosan and Aloe vera showed promising antimicrobial outcomes across various bacterial strains, highlighting their broad therapeutic potential [38]. Looking ahead, smart delivery platforms are gaining attention especially those that respond to environmental triggers like pH, temperature, or enzymes allowing Aloe vera release specifically in inflamed oral areas e.g., ulcers or periodontitis. Thermo sensitive chitosan hydrogels are already being tested in models of periodontitis, showing sustained release, antioxidant action, and nearly complete eradication of pathogens like P. gingivalis [39]. These systems can be incorporated into scaffolds, films, or 3D-printed devices to personalize regenerative dental treatments. Nonetheless, moving these technologies into clinical practice requires rigorous trials, long term outcome tracking, and updated regulations to ensure safety, standardization, and patient effectiveness.

14. Conclusions

The incorporation of Aloe vera into chitosan-based nanoparticle systems represents a significant achievement in the field of dental therapy. These nano formulations combine Aloe vera's bioactivity, which includes antibacterial, anti-inflammatory, antioxidant, & wound-healing characteristics, with chitosan's biocompatibility and mucoadhesive strength, resulting in more effective and targeted treatments for a variety of oral ailments. Nano Aloe vera chitosan systems can treat oral ulcers, periodontitis, dental caries, and help with the post-surgical recovery. Preclinical and clinical research suggest their efficacy and safety, but standardized, large scale clinical trials are needed to validate and contribute regulatory approval. Formulation repeatability, long term safety, and regulatory clarity remain an issue, but smart delivery methods, composite nanoparticles, and tailored therapies are building a future where herbal nanomedicine is a dental mainstay. In conclusion, Aloe vera chitosan nanoparticle carriers are a promising, natural, and scientifically confirmed method for improving oral health and nano dentistry. Interdisciplinary research and innovation could lead to clinical translation and commercial use of these formulations.

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