

REVIEW

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A comprehensive review on *Ziziphus spina-christi* gum–alginate composite beads: from physicochemical properties to advanced sustained-release applications

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Abstract

Background The gradual release of a drug over a longer period of time is an important area of modern pharmaceutical research which includes sustained release drug delivery systems. This controlled release maintains therapeutic concentrations of the drug in plasma and reduces the dosage frequency and patient non-compliance for chronic diseases. Natural polymers have recently grown in their interest as pharmaceutical excipients. This is as they are biodegradable, biocompatible, and low toxic and cheaper than synthetic polymers.

Objective The review focuses on the feasibility of sodium alginate-*Ziziphus spina-christi* gum (ZSC gum) system as natural polymeric system for the preparation of hydrogel beads for sustained delivery.

Methodology / approach Sodium alginate is utilized in the formulations of drugs because it easily forms hydrogel beads by ionotropic gelation upon contact with divalent cations, such as calcium ions. These beads can encapsulate drug well and swell to pH. However, the use of alginate alone might create beads with low mechanical strength as well as an undesired burst release of the encapsulated drug. ZSC gum has been introduced as a natural polymer to overcome these challenges and composite hydrogel bead system development.

Key findings Through the incorporation of ZSC gum, the viscosity and mucoadhesive properties of alginate matrices can potentially be improved to ensure the formation of a stable IPN. These changes in structure helps to improve bead integrity, reduce instant release of drug, improve drug entrapment efficiency and provide a better sustained release pattern.

Implications Through the incorporation of ZSC gum, the viscosity and mucoadhesive properties of alginate matrices can potentially be improved to ensure the formation of a stable IPN. This change in structure helps to improve bead integrity, reduce instant release of drug, improve drug entrapment efficiency and provide a better sustained release pattern.

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Conclusion The addition of ZSC gum to sodium alginate may help improve the performance of alginate systems. The use of natural polymer composites can be an effective and sustainable way to create drug delivery systems that can have sustained release and improve efficacy.

Keywords ZSC gum, Sodium alginate, Sustained release, Multiparticulate drug delivery, Natural polymer, Ionotropic gelation

Introduction

Oral administration remains the most common mode of administering drugs due to its non-invasive nature, cheap and non-invasive nature and mostly acceptable by patients. Nonetheless, most of the traditional oral dosage preparations cannot ensure a steady concentration of the drug in the blood. It frequently leads to the oscillation of the plasma concentration that might necessitate re-dosing and elevate the risk of side effects or toxicity [1, 2].

To address these shortcomings, there has been an emergence of sustained-release multiparticulate systems which include hydrogel beads, microspheres, and pellets to offer a slow and controlled release of the active pharmaceutical ingredient during a long duration. Unlike monolithic dosage delivery modes such as tablets, multiparticulate systems are better distributed in the gastrointestinal tract. The distribution can minimize the variability in drug absorption among people and can reduce chances of unintended drug release also known as dose dumping. By maintaining drug concentrations within the therapeutic range and reducing gastric irritation, these advanced drug delivery systems offer a more effective and patient friendly strategy for the long-term management of chronic inflammatory diseases [3].

Since natural polymers are biocompatible, biodegradable, non-toxic, and inexpensive; they have significant interest in the formulation of controlled and sustained release system. The excellent capability of alginates to form hydrogels and its interaction with ionic complexes and encapsulation of hydrophilic and hydrophobic drugs makes them suitable for controlled release applications [4, 5].

Natural polysaccharides including sodium alginate, Xanthan gum, guar gum and gums from medicine plants are being demonstrated to be especially good as matrix-forming agents in pharmaceutical formulations [6].

Sodium alginate is a naturally occurring anionic polysaccharide (polyanion) that is isolated from brown seaweeds. It is made up of the different order of β -D-mannuronic (M) and α -L-guluronic (G) acid residues. It has two types of residue arrangement that means homopolymeric blocks or heteropolymeric blocks [7]. It forms hydrogels by ionotropic gelation under the influence of multivalent cation, like calcium ion (Ca^{2+}) following the well-established “egg-box” model [8]. Alginate-based beads are extensively used for drug, enzyme, and Probiotic encapsulation because of their mild processing

and biocompatibility and then high encapsulation efficiency [9]. Nonetheless, mechanical fragility, great swelling tendency, and initial burst release have limited their applications for long-term delivery of the drugs causing uncontrolled diffusion of drugs [10]. To surmount these issues, a strategy that is touted as effective involves blending alginate with that of the secondary natural polymer for gel stability, integrity, and controlled release behaviour.

The ZSC, or Christ's thorn Jujube, is a medicinal plant that is found in arid and tropical regions of Asia and Africa. Resin obtained from its stem and branches is a complex polysaccharide mainly composed of arabinose, galactose, rhamnose and uronic acid residues [11, 12]. The gum possesses positive pharmaceutical characteristics like emulsifying, binding, thickening and mucoadhesive properties which make it a valuable natural excipient [13]. Recent studies have found ZSCgum suitable for matrix systems, solid dispersions and film forming formulations improving mechanical strength, sustained release behaviour of formulation and ZSC gum's overall stability [14, 15].

Blending sodium alginate with ZSC gum yields a polymeric matrix capable of forming an interpenetrating polymer network (IPN) due to the electrostatic and hydrogen bonding interactions occurring between the different biopolymers. This hybrid system has the potential to enhance structural strength, reduce burst release, and provide prolonged and controlled release of the drug from the gel matrix through hydration [16]. As a result, alginate-ZSC-ZSCgum composite beads are a sustainable, green, and biocompatible choice for next-generation multiparticulate sustained release formulations.

This article summarizes the formulation strategies, characterization methods, and applications of ZSC-gum-alginate composite beads as a natural matrix for the sustained-release multiparticulate drug delivery system. The combination of alginate and Ziziphus gum works together to improve mechanical strength. In addition, it improves encapsulation efficiency and regulates release. There is a major stress on understanding their interpenetrating polymeric structure, swelling behaviour, and diffusion mechanisms along with their biocompatibility, biodegradability, and mucoadhesive property to application in safe and ecofriendly oral sustained release formulations [1, 5].

Ziziphus spina-christi Gum

Source and extraction method of *Ziziphus spina-christi* Gum

Ziziphus spina-christi (L.) Desf., commonly referred to as the **Christ’s thorn jujube** or **Sidr tree**, belongs to the Rhamnaceae family and is widely found in arid and semi-arid regions of Africa, the Middle East, and South Asia [17, 18]. This plant is well adapted to dry climates and produces edible fruits that contain significant amounts of mucilage and gum-like polysaccharides, which have recently gained attention for pharmaceutical applications [19].

The natural gum derived from *Z. spina-christi* can be obtained from different parts of the plant, including the fruit pulp, seeds, and sometimes from exudates released on the plant surface. Chemically, this gum mainly consists of polysaccharide components such as **arabinose, galactose, rhamnose, and galacturonic acid**. These components help in its functional characteristics such as emulsifying, binding, thickening and stabilizing properties and as a result it can be used in different formulation systems, Shown in Table 1 [20, 21].

To extract *Z. spina-christi* gum, fresh fruits are normally washed and crushed. The broken product is then immersed in distilled water 24–72 h whereby the mucilage is dissolved in the liquid medium. The mixture is filtered after soaking to take out plant material that could not be dissolved. The mucilage that has been dissolved in the filtrate is then precipitated with a solvent that removes the gum i.e. ethanol or acetone. The gum is then dried to recover it to between 40 and 50 °C and milled into fine powder to be used further [22].

Chemical composition and pharmaceutical properties of ZSC gum

Several conditions of processing such as the ratio of solvents, the extraction temperature and the type of precipitation solvent would change the yield and quality of the extracted gum. Such factors may have a potent effect on the viscosity and the total extraction effectiveness [23]. It has been found that the optimum conditions that produce gum with desirable functional properties are a ratio of 1: 7 of sample to water, 60 °C of extraction temperature and 1: 3 of ethanol to extract. In such a scenario, the gum exhibits great water-holding capacity, good oil absorption, and high viscosity just like other popular hydrocolloids like Xanthan gum and guar gum [24, 25].

Ionic cross-linking

Ionic cross-linking for plant gums like *Ziziphus spina-christi* involves multivalent cations (e.g., Ca²⁺, Zn²⁺) interacting with carboxyl or hydroxyl groups to form gels or beads via ionotropic gelation. While no specific protocols exist for ZSC gum, analogous processes in carboxymethyl guar gum or sesbania gum use metal ion baths to create gastric-resistant microbeads for drug delivery, enhancing mechanical properties and stability. This mild method promotes chain associations without covalent bonds, ideal for ZSC’s potential in controlled release systems [26].

Molecular weight

No exact molecular weight for native *Ziziphus spina-christi* gum is reported in available literature. Comparable plant gums range from 500,000 Da (sesbania gum) to over 1,000,000 Da (gellan gum), with cross-linking affecting effective chain dynamics rather than intrinsic MW. Characterization techniques like gel permeation

Table 1 Key application of ziziphus spina christi (ZSC) gum in drug formulation

S. No.	Authors (Year)	Formulation / Application	Key Pharmaceutical Findings
1	Zayed et al. (2015)	Silver nanoparticles synthesized using ZSC	The biopolymer in ZSC acts as a reducing and capping agent, helping to control nanoparticle size [28].
2	Mostafa et al. (2020)	Silver nanoparticles derived from ZSC fruit extract	Components of ZSC gum contribute to antimicrobial activity and stabilize the nanoparticles effectively [29].
3	Yagoub et al. (2021)	Methanolic root extract-stabilized silver nanoparticles	Enhanced antimicrobial and anti-inflammatory activity; the extract also stabilizes the nanoparticles [30].
4	Gong et al. (2022)	Plant polysaccharide-based drug delivery systems	Highlights the use of natural polysaccharides, including ZSC, as carriers for sustained drug delivery [31].
5	Wang et al. (2022)	Polysaccharides from traditional medicinal plants	Supports biocompatibility and use in drug delivery applications [32].
6	Alwossabi et al. (2022)	Solid dispersion formulations for poorly soluble drugs	ZSC gum improves the solubility and dissolution rate of BCS class II drugs, enhancing bioavailability [33].
7	Abdul rahman et al. (2022)	ZSC leaf extract	Demonstrates antioxidant, anticancer, and ethno pharmacological activities, supporting use in natural polymer-based formulations [34].
8	Alharbi (2024)	Methanolic leaf extract	Exhibits anticancer and antioxidant effects against human gastric carcinoma cells [35].
9	Abdellatif et al. (2024)	Eco-friendly silver nanoparticles for wound healing	Shows strong antibacterial activity and promotes wound healing; polymeric properties help stabilize nanoparticles [36].

chromatography (GPC) would be required for precise measurement [27].

Key applications of *Ziziphus spina-christi* (ZSC) gum in drug formulations

Some Key Applications of *Ziziphus spina-christi* (ZSC) Gum in Drug Formulations are shown in Table 1.

Pharmaceutical applications of *Ziziphus spina-christi* gum and it's potential in alginate beads

Ziziphus spina-christi (ZSC) gum is an excellent natural excipient that is promising to offer with its good physicochemical and functional properties in recent years. It has been investigated in several pharmaceutical applications including a binding agent, emulsifier, stabilizer and matrix forming agent in various formulations like tablets, gels and suspensions. The gum has good viscosity, hydrophilic properties, and mucoadhesive properties and is thus of great use in the development of sustained and controlled drug delivery systems. It has been reported that it can successfully be used as a binder and disintegrant in the tablets, providing the best hardness and disintegration characteristics [37]. Compared to other studies, its emulsifying capacity was also comparable to gum acacia, which has been known to be most efficient as a natural emulsifier [38]. Furthermore, the use of polysaccharide composition and high swelling index have allowed it to be used as a thickening and stabilising agent in a gel-based system [39]. The direct studies on the introduction of ZS gum into the system of the agar beads are not conducted yet, however, its hydrocolloid nature and mucoadhesive properties demonstrate that it can be

successfully combined with ionic gelation methods. Thus, the addition of ZS gum and polymers: alginate or Chitosan might improve the structural integrity of beads, drug encapsulation and release kinetics. All these properties make ZS gum a sustainable and versatile biopolymer with a great potential in the development of advanced oral, topical and mucoadhesive drug delivery system [40–42].

Alginate as a matrix polymer and its synergistic potential with ZSC gum

A polymer produced from brown seaweeds, alginate, is an anionic polysaccharide which finds application as matrix-forming polymer in the pharmaceutical and biomedical field. Alginic acid is specified by a linear copolymer of β - D - mannuronic acid (M) and α - L - guluronic acid (G) mono units in homopolymeric (M - M or G - G) and heteropolymeric (M - G) sequences respectively [43]. The presence of carboxyl functional groups along the alginate chain allows ionic cross linking with calcium ion (Ca^{2+}) to form a three-dimensional hydrogel network. According to the egg-box model, calcium ions preferentially bind to the G-block regions, forming a hydrogel under mild aqueous conditions [44]. Calcium alginate is a polysaccharide which is produced from algae. Due to its gentle gelation, non-toxic and highly biocompatible, alginate is an excellent carrier for encapsulating fragile bioactive like drugs, proteins and enzymes [45]. Alginate beads are also useful in controlled and targeted delivery of drugs, which provide a protection of encapsulated compounds against enzymatic degradation and acidic conditions, shown in Table 2 [46]. However, the disadvantages of pure alginate matrices include low mechanical strength, excessive

Table 2 Literature review of alginate-based and composite polymer systems in drug encapsulation and controlled release

S. No	Author Name	Polymer / Gum	Method	Conclusion	Reference
1	Hari et al., (1996)	Alginate Chitosan	Ionic gelation	Composite beads enhanced encapsulation efficiency and reduced burst drug release.	[50]
2	Anal et al., (2005)	Alginate– Chitosan	Polyelectrolyte complex bead formation	Alginate–Chitosan beads improved stability and controlled drug release properties.	[51]
3	George et al., (2006)	Alginate, Chitosan	Review of polyionic hydrocolloids for intestinal protein drug Delivery	Alginate and Chitosan are promising carriers due to their biocompatibility, gel-forming ability, and controlled release potential.	[52]
4	Sriamornsak et al., (2007)	Sodium alginate	Ionotropic gelation technique	Alginate beads provide effective encapsulation and sustained drug release due to Ca^{2+} cross linking.	[53]
5	Sipos et al., (2023)	Sodium alginate	Optimization of alginate hydrogel beads	Alginate beads exhibited high drug loading and extended drug release behaviour.	[54]
6	Cao et al., (2024)	Alginate hydrogel beads	Ionotropic gelation for oral delivery	Alginate beads protected bioactive compounds in gastric conditions and enabled intestinal release.	[55]
7	Kučuk et al., (2024)	Sodium alginate	Ionotropic gelation	Protected bioactive in gastric medium and enabled sustained intestinal release.	[56]
8	Jing et al. (2025)	Alginate – a natural anionic polysaccharide	Ionotropic gelation technique	Composite sodium alginate gum beads improved encapsulation efficiency, Probiotic protection, and release control, with low methoxyl pectin + alginate showing the best performance.	[57]

porosity, and burst release mode during the initial stages due to ion exchange and rapid swelling in the physiological media [47].

To overcome these limitations, other natural polymers are blended with the alginate. Adding ZSCgum polysaccharide improves the rheological and structural characteristics of alginate gels by taking advantage of its mucoadhesive and viscous properties. The alginate and ZSCgum act in a synergistic way which increase the mechanical stability of the vesicular system enhance the drug loading of the vesicular system and exhibit more controlled and sustained release behaviour from the composite matrix making it suitable for multiparticulate delivery systems [48, 49].

Formulation of alginate–ZSC beads

The ionotropic gelation technique is usually adopted to formulate alginate–ZSCgum beads (shown in Table 3) either via external or internal gelation technique. In the procedure of external gelation, a homogeneous mixture of drug and polymer is extruded drop wise in a calcium chloride (CaCl₂) solution. Calcium ions diffuse from the solution into the alginate droplets where they interact with guluronic acid blocks forming stable calcium alginate beads [58]. This egg-box cross linking mechanism allows for the quick creation of gelled spheres under mild and aqueous conditions (shown in Fig. 1). In contrast, internal gelation entails adding an insoluble calcium source to a polymeric dispersion, such as calcium carbonate or calcium sulphate. The ions Ca gradually dispersed when the medium was made acidic which lead to a more uniform cross linking throughout the bead matrix and increase the encapsulation efficiency and structural homogeneity [59, 60].

The properties of the beads are dependent on the parameters used during the formulation like the type of polymer used. Mechanical strength of the beads and polymer solution viscosity are determined by the concentration of the alginate. In general, increased concentration will result in increased density and reduced porosity of beads accompanied by longer drug release [67].

The ratio of ZSC gum has an important influence on the swelling characteristics and the diffusion behaviour of the drug owing to the hydrophilic polysaccharides to enhance mucoadhesion and change the porosity of the matrix (shown in Fig. 2) [68, 69]. The concentration of calcium chloride correlates to cross linking density and stiffness. A suitable range for compactness must be maintained, so as not to hinder drug diffusion [70]. The process parameters stirring speed and curing time affect the bead size distribution, surface morphology and entrapment efficiency. When parameters are properly optimized, it results in the design of the alginate–ZSC Gum beads with controlled-release characteristic and good physicochemical stability [71].

Evaluation

Comprehensive evaluation is essential to conduct a detailed analysis of drug release and sustained drug delivery. Characterization of beads helps to evaluate its physicochemical properties, mechanical strength and release profile. They are follows:

Particle size and distribution

The size of the particles has strong effect on drug release kinetics, swelling behaviour and uniformity of dosage form. The measurement of thickness is usually done by optical microscopy, laser diffraction, and the use of

Table 3 Summary of Recent Alginate-Based Bead Formulations: Preparation Methods and Drug Delivery Outcomes

No.	Authors (Year)	Formulation System	Method Used	Key Findings / Application	Reference
1	Park et al. (2022)	Chitosan–Alginate–Gentamicin beads	Ionotropic gelation with CaCl ₂ and Chitosan	Multi-component beads showed controlled antibiotic release and strong antimicrobial activity. Drug release could be modulated by cross linking density and Chitosan concentration.	[61]
2	Saad et al. (2023)	Valsartan-loaded alginate beads	Calcium chloride cross-linking	Entrapment efficiency around 80% with sustained drug release for 24 h, following Korsmeyer-Peppas kinetics.	[62]
3	Lee et al. (2024)	Calcium alginate beads containing xylitol and gelatin	Ionic gelation with CaCl or Ca-lactate	Polymer concentration and cross-linking salt affected bead size, diffusion rate, and mechanical strength, showing suitability for controlled drug delivery systems.	[63]
4	Egbeyemi et al. (2024)	Modified calcium alginate beads with polyphosphate	Gel-confined coacervation	Modification improved encapsulation stability and reduced permeability of alginate beads, enabling better sustained drug release.	[64]
5	Parvez et al. (2024)	Green tea extract-loaded alginate hydrogel beads	Ionotropic gelation followed by freeze-drying or oven drying	Freeze-dried beads showed higher encapsulation efficiency (~ 75%) and enhanced release and antioxidant activity compared to oven-dried beads.	[65]
6	Alallam et al. (2025)	Curcumin-loaded calcium alginate microbeads	Ionotropic gelation optimized by Box-Behnken design	Optimized beads showed particle size ≈ 708 μm and entrapment efficiency of 88.4%, with controlled colon-targeted release.	[66]

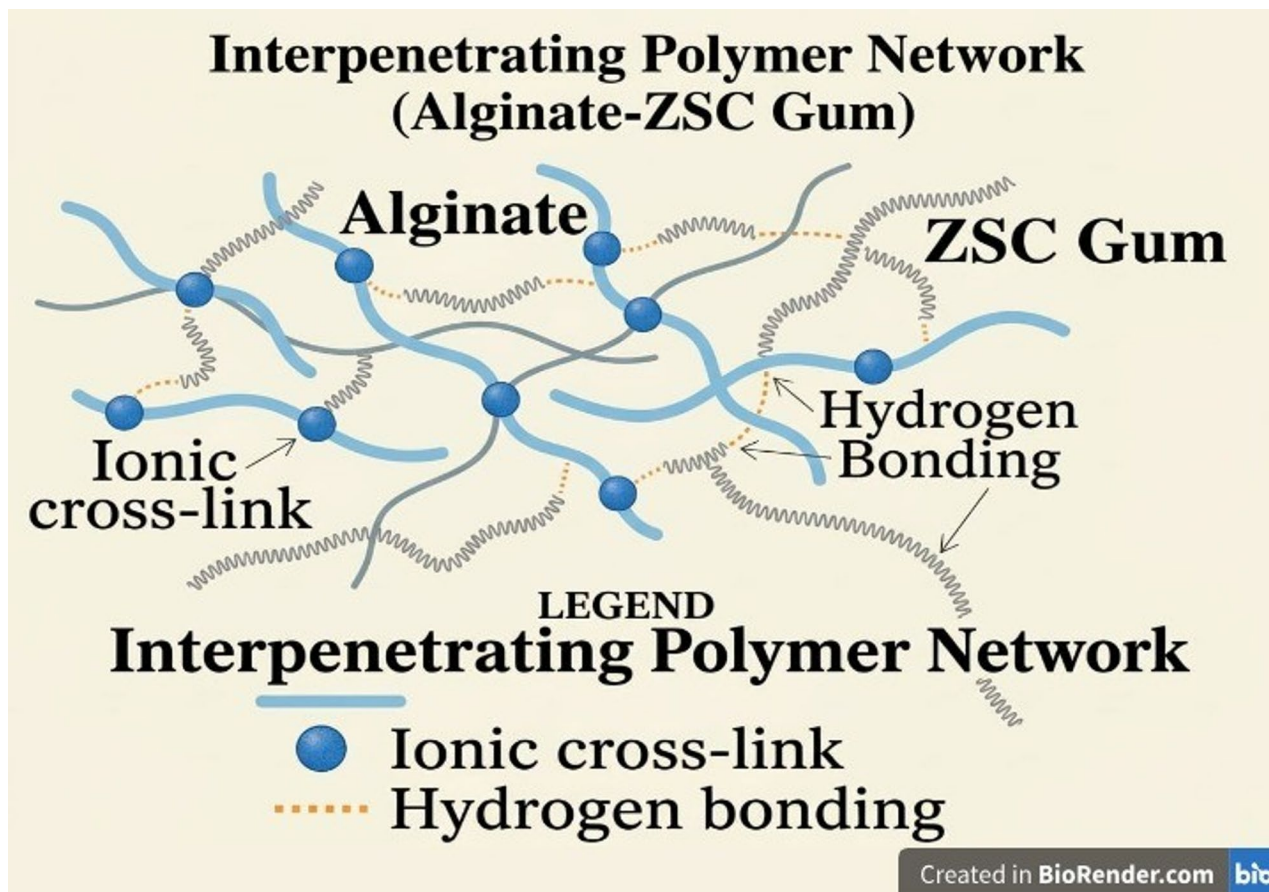


Fig. 1 Illustrates the interpenetrating network of alginate–ZSC gum, showing how the combination of ionic and hydrogen-bonded interactions enhances matrix integrity and drug entrapment. <https://app.biorender.com/illustrations/674fc7bbf4f1b51106b97f2b?slideId=567607f438e2-4643-81df-5507c5136a62>

dynamic light scattering (DLS). Uniformity of particle size can lead to similar drug release profiles and better reproducibility. With an increase in the concentration of polymer, particularly alginate or ZSC gum, the viscosity would increment, causing lesser breakage of the droplets during gelation and eventually resulting in larger diameter beads [72, 73].

Drug entrapment efficiency (EE %)

Entrapment efficiency (EE %) is the percentage of drug that is retained in the polymeric network. It is usually determined using UV–Visible spectrophotometry or HPLC after dissolving the beads in sodium citrate or phosphate buffer. A high EE% indicates cross linking effectiveness and good polymer–drug interaction so that the drug does not leak during bead formation and curing [74, 75].

Morphological characterization

Surface and internal structure characterization is mostly done using Scanning Electron Microscopy. Spherical and smooth beads are densely packed and possess reduced

porosity that will diffuse slowly. While rough or porous surface will lead to quick drug release. The findings from SEM imaging further confirm the uniform distribution of calcium cross links and the effect of ZSCgum addition on beads texture and surface integrity [76, 77].

Swelling behaviour

In order to model gastrointestinal conditions, the swelling experiments were conducted by placing the beads in buffer solutions (pH 1.2, 6.8 and 7.4). The swelling index is used to show water uptake ability and gel relaxation. The hydrophilic properties of ZSC gum and the presence of polysaccharides improve water absorption because of its hydrophilic properties and the capacity to control release by the expansion of the matrix and diffusion mechanisms [78].

In vitro drug release studies

The in vitro drug release tests are usually carried out in a USP Type II (paddle) dissolution apparatus in conditions that represent the gastrointestinal environment. The received cumulative data of drug release is then

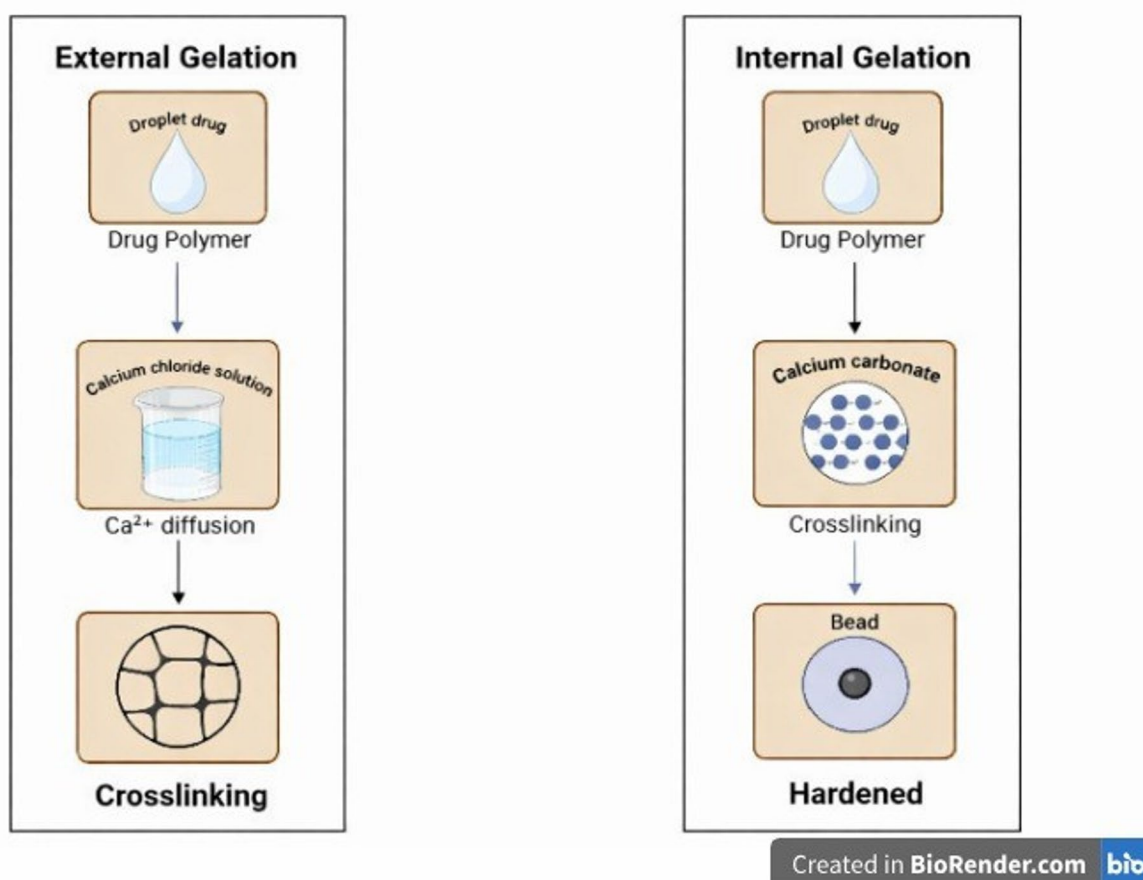


Fig. 2 Schematic of external and internal gelation mechanisms. In external gelation, Ca^{2+} diffuses from CaCl_2 solution to crosslink alginate droplets. In internal gelation, Ca^{2+} is released from CaCO_3 within the droplet, forming uniformly cross linked beads. <https://app.biorender.com/illustrations/670769f11422ba2f6b95cf89?slideId=41131fff-defa-46d5-89a9-6f6c9a059b76>

examined with the help of various kinetic models, including zero order, Higuchi, and Korsmeyer-Peppas to have a better insight into the mechanism that controls the drug release. The inclusion of *Ziziphus spina-christi* (ZS) gum in the alginate matrix increases the complexity and density of the polymer network. This enhanced matrix structure slows down the diffusion of the drug, thereby promoting a more controlled and sustained release profile [79, 80].

Additional analytical evaluations

Drugs and polymers compatibility is confirmed using complementary techniques like Fourier Transform Infrared Spectroscopy (FTIR), Differential Scanning Calorimetry (DSC) and X-Ray Diffraction (XRD). These analyses demonstrate the presence of molecular interactions between alginate and ZS gum. This supports the improved physicochemical stability and structural stability of the composite beads [81].

Sustained release mechanism

ZS gum beads sustained release behaviour mainly governed by a combination of diffusion and polymer relaxation mechanism of alginate. As the beads come in contact with the dissolution medium, it leads to water incorporation and swelling of the alginate – ZS gum network. The channels become supported by the formation of hydrated channels in the gel that allow drug molecules to diffuse through the matrix gradually [82, 83].

The release behaviour, of a formulation containing an interpenetrating polymer network (IPN) of alginate and ZS gum, is studied. Alginate interacts with divalent calcium ions (Ca^{2+}) through ionic cross linking, while ZS gum forms hydrogen bonds and entangles the chains with the matrix. The interaction between the polymer-polymer and the polymer-drug result in gel densification, increase tortuosity of the diffusion path, and reduce burst release which is common in single polymer systems [84, 85].

Furthermore, as the dissolution process advances, it becomes increasingly affected by polymer relaxation and surface erosion during the release phase. The gradual

breakdown of the hydrated matrix ensures that the drug release occurs predictably and at a constant rate. The cross linked gel structure of alginate and the mucoadhesive and viscoelastic property of ZSC gum allow for dual controlled release where the first phase is diffusion controlled and later phase is polymer erosion controlled resulting in prolonged release [86, 87].

Applications and future perspective

Alginate -ZSC gum composite beads is a potential bio polymeric vehicle to controlled and site-specific drug delivery. Due to the natural origin and tunable gelation property and biocompatibility of these systems, such systems are flexible in encapsulating the hydrophilic or hydrophobic therapeutic agent. Combination of alginate and ZSCgum results in formation of a highly robust matrix useful in the improvement of entrapment efficiency and control of the diffusion of the drug consequently endowing sustained and predictable release behaviour [88, 89]. At the intended destinations oral and colon delivery can be used where retention and localized drug release can enhance drug effects and reduce systemic exposure. The especial feature of ZSCgum is that it is mucoadhesive, which prolongs the residence time of the drug in the GIT (gastrointestinal tract) that may enhance the localised absorption. Also, the two mentioned polymers are biodegradable, renewable, and non-toxic, thus, keeping in line with the creation of environmentally friendly pharmaceutical carriers [90, 91].

Later research has shown that through Design of Experiments (DOE) and response surface methodology (RSM), we are able to maximise the ratio of polymers, cross linking density and the curing time to obtain the required particle size, encapsulation efficiency and release kinetics [92, 93]. In addition, computer modelling and artificial intelligence have been used in the research of formulating drugs, and this practice is progressing continuously. These methods are under development to come up with simulation tools that can be used to predict the release mechanisms of drugs and drug formulation performance and stability behaviour so as to enable more efficient formulation design [94].

The future research should aim at assessing the *in vivo* pharmacokinetic behaviour of alginate -ZSC gum systems and also test its stability over long period and the viability of large scale production of the systems so as to ascertain its applicability in practice. Besides these, polymers derived in medicinal plants could be used further to develop wound dressings, transdermal delivery systems, and tissue engineering scaffolds and especially to incorporate therapeutic bio molecules, antioxidants, or antimicrobial agents [95].

Alginate based-ZSC gum composite systems have a significant future as bio polymeric carriers of

pharmaceutical and biomedical use due to their biocompatibility and natural gel-forming ability [96]. Ionic cross linked and hydrogen bonded polymers can be used to create stable hydrogel networks, which effectively entrap a large variety of therapeutic molecules. Moreover, the polymeric matrices are important due to their swelling behaviour, mucoadhesion, and drug diffusion to the body that can be regulated, which can be helpful to design the desired drug delivery systems. Due to these favourable characteristics, alginate -ZSC gum composites are examined more and more in terms of pharmaceutical and biomedical uses [97].

Alginate -ZSC gum composites systems have been explored for various pharmaceutical and biomedical applications, as described below in Table 4:

Conclusion

The effect of ZSC gum with sodium alginate polymeric composition was studied for controlled release and sustained release drug delivery. Two said polymers are naturally derived, biodegradable, non-toxic, and able to replace synthetics. The interactions of ionic gelation, hydrogen bonding and inter-polymer entanglement among the composites result in the formation of stable and cohesive IPN. The enhanced matrix can minimize burst release, prolong drug diffusion and maintain the structure of the drug in a physiological environment. ZSCgum is hydrophilic in nature and hence controls the swelling and diffusion, while alginate imparts density to the system to ensure repeated performance of the therapeutic effect with controlled release.

The alginate-ZSCgum composite will have effective encapsulation efficiency, particle size and release profiles if the device fabrication parameters such as polymer ratio cross linker concentration and curing conditions are optimized. Due to its swelling and mucoadhesive character, it is a good candidate for delivery systems aimed at gastrointestinal and oral site-specific delivery to increase bioavailability. Besides taken orally, its natural compatibility with the bioactive compound allows applications in topical gels, wound dressings, and other formulations as well. The natural polymer blend shows the utilization of sustainable materials for biomaterial design in pharmaceuticals is an increasingly important trend and demonstrates a multifunctional platform for sustained-release and targeted drug delivery of the next generation.

Table 4 Summary of pharmaceutical and biomedical applications of Alginate–ZSC gum composites systems

S. No.	Application	Description	Reference
1	Oral sustained release drug delivery systems	Gum matrices from Alginate-ZSC alter drug diffusion and regulate release kinetics for sustained drug release, maintaining therapeutic plasma levels, improving patient compliance, and reducing dosing frequency.	[98, 99]
2	Delivery of drugs to colon	Alginate systems show pH-responsive swelling to protect drugs from stomach acid and enable selective colon release, effective for colonic diseases like IBD and colorectal cancer.	[100]
3	Gastro retentive drug delivery systems (GRDDS)	ZSC gum's high swelling potential increases gastric residence time, enhancing drug absorption and bioavailability.	[101]
4	Mucoadhesive drug delivery systems	ZSC gum's natural mucoadhesive properties bind carriers to GIT mucosal surfaces, prolonging contact and improving drug uptake.	[102]
5	Protein and peptide encapsulations	Alginate beads via ionic gelation protect proteins/peptides from GI enzymes, preserving biological activity.	[103]
6	Probiotic encapsulation	Alginate-ZSC protects probiotics from gastric conditions, enabling controlled release in the small intestine for improved viability.	[104]
7	Delivery of antioxidant compounds	Encapsulation in alginate-ZSC stabilizes antioxidants, preventing oxidative degradation and enhancing activity.	[105]
8	Controlled delivery of anti-inflammatory drugs	Polymeric beads with alginate-ZSC sustain anti-inflammatory drug release, minimizing systemic side effects.	[106]
9	Antimicrobial drug delivery systems	Alginate-ZSC composites deliver antimicrobials directly to infection sites, maintaining effective concentrations.	[107]
10	Wound dressing materials	Alginate-natural gum hydrogels retain moisture, offer biocompatibility, promote regeneration, and accelerate healing.	[108]
11	Topical drug delivery systems	Gels, films, or hydrogels from these polymers enable prolonged local drug release for dermatological use.	[109]
12	Transdermal drug delivery systems	Polymeric films act as controlled-release carriers in patches for skin permeation.	[110]
13	Tissue engineering scaffolds	Alginate hydrogels form 3D porous structures supporting cell adhesion, proliferation, and differentiation.	[111]
14	Micro- and nanoparticle drug carriers	Alginate-ZSC systems form micro/nanoparticles for targeted, controlled delivery with reduced side effects.	[112]
15	Drug delivery for chronic diseases	Sustained-release formulations maintain stable drug levels for managing diabetes, hypertension, and arthritis.	[113]
16	Encapsulation of herbal extracts	Matrices improve stability, mask taste, and enhance bioavailability of plant extracts.	[114]
17	Systems for delivering vaccines	Alginate carriers protect antigens and enable controlled release to boost immune response.	[115]
18	Bioactive compound stabilization	Encapsulation shields bioactive from pH, oxidation, and light.	[116]
19	pH-responsive drug delivery systems	Composites swell pH-dependently for site-specific GI release.	[117]
20	Eco-friendly pharmaceutical excipients	Alginate-ZSC are biodegradable, renewable polymers for sustainable delivery systems.	[118]

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Author contributions

The authors confirm contribution to the paper as follows: study conception and design: Shashi Verma; Writing – Original Draft: Ritesh Kumar Tiwari; Data curation – Abhay Pratap Singh. All authors reviewed the results and approved the final version of the manuscript.

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Data availability

The data that support the fundings of this study are available from the corresponding author upon reasonable request.

Declarations**Ethical approval**

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Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used ChatGPT in order to improve readability and grammar. After using ChatGPT, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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