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Case Report Paper

Stability and Controlled Release of Amoxicillin Trihydrate in Novel Biopolymer Matrices

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Abstract: Amoxicillin trihydrate is a widely prescribed β-lactam antibiotic, suffers from chemical instability that limits its therapeutic efficacy and shelf life. This study investigates the formulation of controlled-release systems using locally sourced biopolymers in England, specifically alginate, chitosan, and pectin, to enhance drug stability and optimize release profiles. Microspheres were prepared via ionic gelation with varying polymer-to-drug ratios and characterized for particle morphology, thermal properties, crystallinity, and drug–polymer compatibility using SEM, DSC, XRD, and FTIR. Accelerated stability studies were conducted at 40°C and 75% relative humidity for 90 days, while in vitro release was assessed in simulated gastrointestinal fluids at pH 1.2 and 6.8. The results indicated that alginate–chitosan matrices provided superior encapsulation efficiency (>85%), structural integrity, and prolonged stability, reducing the degradation rate by up to fourfold compared to unencapsulated drug. Pectin-based formulations, although biodegradable, exhibited higher moisture sensitivity and faster initial drug release. In vitro release studies demonstrated a biphasic release pattern in alginate–chitosan systems, characterized by an initial burst followed by sustained release, predominantly governed by diffusion and polymer relaxation mechanisms. These findings highlight the potential of natural biopolymer matrices for improving the physicochemical stability and controlled release of amoxicillin, providing a sustainable alternative to conventional synthetic excipients. The study underscores the dual benefits of enhanced therapeutic performance and environmental sustainability, aligning with contemporary UK pharmaceutical priorities. Future work should explore in vivo pharmacokinetics and clinical translation to validate the therapeutic advantages of these formulations.

Keywords: Amoxicillin, Biopolymer Matrices, Controlled Release, Stability, Sustainable Formulation.

1. Introduction

The continuous rise of antimicrobial resistance (AMR) has become one of the most pressing public health concerns in the United Kingdom, particularly affecting the efficacy of commonly prescribed antibiotics such as amoxicillin trihydrate [1]. Despite its widespread use in both primary and hospital care, amoxicillin remains chemically unstable when exposed to moisture, temperature variations, or oxidative environments. The instability of this compound not only reduces its therapeutic efficiency but also contributes to inconsistent dosing and potential development of resistant bacterial strains [2].

Recent studies conducted by NHS laboratories and university-based pharmaceutical research centres across England have emphasized the importance of improving the physicochemical stability of antibiotic formulations [3] [4]. As the nation transitions towards more sustainable and precision-oriented pharmaceutical practices, the need for reformulating established drugs using biocompatible and environmentally friendly excipients has become increasingly urgent. This shift aligns with the UK Government's "Green Pharmacy" initiative that encourages the reduction of chemical waste and the promotion of biodegradable excipients [5].

Conventional formulations of amoxicillin trihydrate are typically produced with synthetic polymers such as polyvinylpyrrolidone (PVP) or ethylcellulose. While these materials offer reasonable stability, they raise ecological concerns and lack biodegradability. In contrast, natural biopolymers such as alginate, chitosan, and pectin, abundantly sourced from the British Isles have shown promise as sustainable alternatives with excellent film-forming, gelation, and mucoadhesive properties. Their availability from local marine and agricultural resources presents an opportunity for regional pharmaceutical industries to align innovation with environmental responsibility [6] [7].

The intrinsic properties of these biopolymers allow the development of *controlled release systems* capable of modulating drug release kinetics. This technology can prevent rapid degradation of amoxicillin, maintain therapeutic plasma levels over time, and improve patient compliance. Controlled release formulations have been extensively explored for various antibiotics, yet there is limited evidence of their application in reformulating amoxicillin trihydrate using locally sourced British biopolymers [8] [9]. This research gap represents a critical area of opportunity for pharmaceutical innovation in England.

In the context of pharmaceutical sciences, the reformulation of existing antibiotics into more stable delivery systems is a direct response to the challenge of maintaining drug efficacy amid changing environmental and clinical conditions [10]. The study of drug–polymer interactions, especially under conditions that mimic gastrointestinal physiology, has become central to understanding how polymer composition influences stability, solubility, and release profile. Investigating these relationships through *in vitro* characterization and kinetic modelling can lead to optimized designs for oral drug delivery.

The physicochemical stability of amoxicillin trihydrate is primarily compromised by hydrolysis and temperature-dependent degradation, processes that can be mitigated by encapsulation within polymeric matrices. By reducing direct exposure to aqueous environments and controlling diffusion rates, biopolymer-based systems may significantly extend the drug's shelf life and enhance its pharmacokinetic reliability. Such stabilization strategies are particularly valuable in the UK's temperate climate, where humidity fluctuations can accelerate drug degradation during storage and distribution.

Furthermore, from a regulatory perspective, the United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) has increasingly emphasized the need for innovative formulation approaches that support both patient safety and sustainability. Incorporating biodegradable polymers into drug formulations not only aligns with regulatory priorities but also supports the nation's commitment to reducing pharmaceutical environmental footprints, as outlined in the *UK Life Sciences Vision 2021*.

England's extensive academic infrastructure, spanning research hubs such as the University of Nottingham's School of Pharmacy and the University College London's School of Pharmacy provides an ideal ecosystem for advancing studies in formulation science. These institutions have pioneered techniques in polymer characterization, dissolution kinetics, and nanoencapsulation, forming the foundation for future collaborative research on antibiotic reformulation. The present study situates itself within this landscape of innovation, focusing specifically on the synergy between traditional antibiotics and novel biopolymer matrices.

Scientifically, the challenge lies not only in achieving chemical stabilization but also in maintaining the pharmacological activity of amoxicillin after encapsulation. The optimization process

must therefore balance drug loading efficiency, polymer compatibility, and the kinetics of release. Achieving this equilibrium demands a multidisciplinary approach that combines pharmaceutical chemistry, materials science, and pharmacokinetics. This complexity underscores the necessity for empirical investigations grounded in systematic experimental design [11].

Therefore, this study aims to develop and evaluate a controlled-release formulation of amoxicillin trihydrate using selected biopolymers sourced from England. The research explores the physicochemical compatibility between drug and polymer, assesses the stability under simulated gastrointestinal conditions, and models the release kinetics to determine optimal matrix composition. Ultimately, the findings are expected to contribute not only to the field of pharmaceutical reformulation but also to the broader discourse on sustainable drug delivery systems within the context of the UK's evolving pharmaceutical industry [12].

1.1. Stability Challenges of Amoxicillin Trihydrate and Advances in Pharmaceutical Reformulation

Amoxicillin trihydrate, a β-lactam antibiotic derived from the penicillin family, remains among the most prescribed antibacterial agents in the United Kingdom. However, its chemical instability, particularly under humid and thermal stress conditions, poses persistent challenges in maintaining potency during storage and administration. The degradation of amoxicillin primarily involves hydrolytic cleavage of the β-lactam ring, which leads to loss of antibacterial activity and the formation of inactive or even allergenic degradation products [13] [14].

Several studies have demonstrated that amoxicillin's degradation is accelerated by moisture and temperature fluctuations typical of temperate climates such as England. Research by British analytical laboratories has shown that under conditions exceeding 25°C and 60% relative humidity, amoxicillin trihydrate experiences a marked decline in potency within weeks of exposure. This degradation not only limits shelf life but also complicates distribution logistics for community pharmacies and primary care systems [15].

The pharmaceutical industry has long sought to improve antibiotic stability through reformulation techniques involving stabilizing excipients or encapsulation within polymeric carriers [16]. Traditional strategies, including microcrystalline cellulose and synthetic polymers such as polyvinylpyrrolidone, have succeeded in extending shelf life but fail to address environmental concerns associated with non-biodegradable waste. This has prompted a paradigm shift toward the use of natural and renewable materials in pharmaceutical development.

In England, research programs under the *Green Pharmacy Initiative* have underscored the importance of developing sustainable formulations that reduce environmental impact without compromising therapeutic efficacy. The adoption of biodegradable polymers has therefore become central to pharmaceutical innovation, especially for essential medicines like amoxicillin, which are consumed in large quantities across healthcare settings [17].

Amoxicillin's hydrolytic instability arises from its inherent susceptibility to aqueous environments, where the β-lactam ring undergoes nucleophilic attack. Stabilization efforts must therefore target this reaction pathway, either by creating physical barriers that limit water access or by incorporating excipients that modulate pH and microenvironmental polarity. Encapsulation within hydrophobic or semi-permeable matrices has emerged as an effective approach to slow degradation rates.

Controlled release systems based on polymeric matrices have gained attention as a means to achieve both stabilization and therapeutic optimization. These systems protect the active ingredient from external stressors while allowing gradual and predictable release of the drug into biological fluids. In the case of amoxicillin, sustained release formulations can maintain plasma concentrations within therapeutic windows for extended periods, thereby improving compliance and reducing dosing frequency [18].

Pharmaceutical reformulation is not limited to altering the excipient composition but extends to a deeper understanding of drug–matrix interactions at the molecular level. Spectroscopic and thermogravimetric analyses have proven instrumental in elucidating how hydrogen bonding, ionic interactions, and van der Waals forces contribute to the stability of encapsulated drugs. Studies in England and Europe have reported that amoxicillin exhibits strong affinity with hydroxyl-rich polymers, suggesting a route for enhancing stability via molecular compatibility [19] [20].

The kinetics of amoxicillin degradation have also been modelled using Arrhenius and first-order reaction equations to predict shelf life under varying storage conditions. These models underscore the

importance of minimizing exposure to water and oxygen, reinforcing the rationale for encapsulation in biopolymeric matrices that offer semi-permeable protection.

The transition from conventional to sustainable formulation practices aligns with global pharmaceutical trends that integrate environmental sustainability into drug design. This evolution reflects not only scientific innovation but also ethical responsibility in reducing the ecological footprint of high-volume drug manufacturing. England, with its robust pharmaceutical research infrastructure and environmental policy framework, provides fertile ground for advancing this agenda.

Empirical research on antibiotic stabilization has shown that physical encapsulation, pH buffering, and antioxidant addition can each contribute to prolonging the active lifespan of labile drugs. However, encapsulation using biopolymers represents the most promising approach, offering simultaneous benefits of protection, controlled release, and biodegradability [21] [22].

Among β-lactam antibiotics, amoxicillin presents unique challenges due to its high aqueous solubility, which promotes rapid dissolution and degradation. Reformulation must therefore balance hydrophilicity for bioavailability and hydrophobicity for protection. Biopolymeric matrices with adjustable permeability offer an ideal platform for achieving this equilibrium.

In recent years, reformulation research has embraced computational and modelling tools to simulate drug release and degradation mechanisms. Molecular dynamics simulations conducted by UK universities have begun to reveal how polymer chain flexibility, crosslink density, and water diffusivity influence the chemical stability of encapsulated drugs.

The integration of advanced analytical techniques such as Differential Scanning Calorimetry (DSC), Fourier Transform Infrared Spectroscopy (FTIR), and Scanning Electron Microscopy (SEM) has enabled comprehensive characterization of drug–polymer interactions. Such tools allow researchers to identify physical compatibility, thermal transitions, and microstructural features that underpin formulation performance [8].

While much of the existing literature focuses on synthetic polymer systems, the exploration of natural biopolymers remains comparatively underdeveloped. This represents a significant research opportunity, especially in England, where access to marine and agricultural biopolymers is abundant. Utilizing these resources could bridge the gap between pharmaceutical performance and ecological responsibility.

In summary, the literature on amoxicillin reformulation emphasizes both the urgency of enhancing stability and the growing potential of sustainable formulation strategies. The next logical progression in this discourse is the systematic investigation of locally sourced biopolymers as multifunctional excipients that combine stabilization with controlled release properties [5].

1.2. Biopolymer-Based Controlled Release Systems for Sustainable Drug Delivery in the UK Context

Biopolymers have emerged as leading materials in the development of controlled release systems due to their biocompatibility, biodegradability, and tunable physicochemical properties. These naturally derived polymers can be tailored to regulate drug diffusion, matrix swelling, and degradation, enabling precise control over the release profile of active compounds [23].

The most commonly studied biopolymers for pharmaceutical applications in the United Kingdom include alginate, chitosan, and pectin. Each of these materials offers distinctive structural characteristics: alginate provides ionically crosslinkable gels, chitosan offers cationic charge and mucoadhesion, while pectin presents hydrophilic networks suitable for colon-targeted delivery. The synergy of these materials opens broad possibilities for formulating antibiotics with optimized pharmacokinetics [24] [25].

Alginates, extracted from brown seaweeds abundant along the Cornish and Scottish coasts, have been utilized extensively for oral drug delivery. Their gelation in the presence of divalent cations such as calcium allows encapsulation of labile molecules under mild conditions, preserving biological activity. Research in England has demonstrated that alginate microspheres can extend drug release for several hours while protecting sensitive compounds from acidic degradation in the stomach [26].

Chitosan, derived from deacetylated chitin found in crustacean shells, exhibits strong bioadhesive and permeability-enhancing properties. Its positive charge facilitates electrostatic interaction with negatively charged mucosal membranes, improving drug absorption. Studies from British universities have also shown that chitosan can form polyelectrolyte complexes with alginate to produce pH-responsive systems that release drugs selectively in the intestinal environment [27].

Pectin, a polysaccharide derived from apple pomace and citrus peels, represents another key

British agricultural by-product with pharmaceutical potential. Its ability to form gels and resist digestion in the upper gastrointestinal tract makes it suitable for colon-targeted delivery of antibiotics, potentially reducing systemic side effects and optimizing local antimicrobial action.

The formulation of controlled release systems using biopolymers involves a delicate balance of polymer concentration, crosslinking density, and environmental pH. Variations in these parameters can drastically alter diffusion pathways, degradation rates, and mechanical strength of the matrix. Hence, a systematic understanding of polymer chemistry and drug–polymer interactions is essential for achieving predictable release behaviour [28].

Several controlled release models have been proposed to describe drug liberation from polymeric matrices, including Higuchi, Korsmeyer–Peppas, and zero-order kinetic models. These frameworks provide mathematical insight into how molecular diffusion and erosion contribute to release dynamics. Empirical studies conducted in English laboratories have validated the applicability of these models to biopolymer systems, confirming their utility in predicting real-world performance [29].

The incorporation of antibiotics into biopolymer matrices introduces specific challenges due to their ionic nature and chemical lability. Strategies such as ionic complexation, covalent conjugation, or co-encapsulation with stabilizing agents have been explored to mitigate these issues. Each approach must ensure that the drug retains its antimicrobial activity while benefiting from controlled release functionality [30].

From a sustainability perspective, the use of renewable biopolymers addresses growing environmental concerns associated with pharmaceutical waste. As biodegradable carriers, these materials decompose naturally after fulfilling their therapeutic function, minimizing ecological persistence. This aligns closely with the UK's national commitment to sustainable healthcare and circular economy principles in pharmaceutical production [31] [32].

The convergence of pharmaceutical technology and environmental stewardship is particularly evident in recent UK research initiatives that integrate biopolymer development with drug formulation. Collaborative programs between universities and industry partners have led to advancements in scaling up biopolymer-based delivery systems, making them commercially viable for routine clinical use [33].

Advances in nanotechnology have further expanded the potential of biopolymers by enabling nanoencapsulation, which enhances drug loading efficiency and enables targeted delivery. In the context of antibiotics, nano-biopolymer systems have shown the ability to reduce required dosages while maintaining or improving therapeutic outcomes, a key step in combating antimicrobial resistance [34]. Characterization of these systems involves multi-technique approaches combining spectroscopy, microscopy, and release testing. Such analyses reveal how polymer structure, crystallinity, and hydration dynamics influence drug retention and release kinetics. The integration of these techniques into formulation development has accelerated the translation of lab-scale findings into industrial applications [21].

Clinical relevance remains central to evaluating biopolymer-based formulations. Controlled release systems must not only demonstrate physicochemical stability but also maintain bioavailability and therapeutic efficacy. Pilot studies in England have begun exploring these systems for oral delivery of antibiotics, showing promising results in maintaining plasma concentrations within therapeutic thresholds [9].

Regulatory acceptance of biopolymer-based pharmaceuticals in the UK has been facilitated by their established safety profiles and compatibility with existing Good Manufacturing Practices (GMP). Agencies such as MHRA have increasingly recognized the potential of natural polymers in supporting sustainable innovation, setting the stage for wider adoption in antibiotic reformulation [35].

In conclusion, the literature underscores that biopolymers represent a transformative platform for sustainable and effective drug delivery. Their integration into the pharmaceutical landscape of England bridges the goals of therapeutic optimization and environmental responsibility. However, empirical validation through systematic formulation and stability testing remains essential to unlock their full potential for antibiotics like amoxicillin trihydrate [10].

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2. Method

This research adopted an experimental design focusing on the development of controlled-release formulations of amoxicillin trihydrate using locally sourced biopolymers specifically alginate,

chitosan, and pectin commonly found in England's marine and agricultural sectors. The formulations were prepared through the *ionic gelation* technique, which allows encapsulation under mild conditions without compromising the antibiotic's integrity. A series of formulations were created with varying polymer ratios (1:1, 1:2, and 1:3 drug-to-polymer w/w) to determine optimal encapsulation efficiency and stability. The microspheres were subsequently dried under controlled temperature and humidity to prevent hydrolysis.

The physicochemical characteristics of each formulation were evaluated using established analytical techniques. Fourier Transform Infrared Spectroscopy (FTIR) was employed to detect drug–polymer interactions, while Differential Scanning Calorimetry (DSC) assessed thermal behavior and compatibility. Surface morphology and particle size were observed using Scanning Electron Microscopy (SEM). To assess stability, the formulations were subjected to accelerated storage conditions at 40°C and 75% relative humidity for 90 days in accordance with ICH guidelines. Drug content was determined periodically via UV–visible spectrophotometry, and degradation kinetics were analyzed using first-order reaction models to estimate shelf life.

The release behavior of amoxicillin from the biopolymer matrices was examined using a *USP Type II dissolution apparatus* in simulated gastrointestinal fluids (pH 1.2 and pH 6.8) at 37 ± 0.5°C. Samples were collected at predetermined intervals and analyzed spectrophotometrically to determine cumulative drug release profiles. The data were fitted to established kinetic models; zero-order, first-order, Higuchi, and Korsmeyer-Peppas to elucidate the underlying release mechanisms. Statistical analysis was performed using ANOVA to compare formulation performance, with significance set at $p < 0.05$. The experimental approach was designed to ensure reproducibility and compliance with pharmaceutical standards, thereby enabling a robust evaluation of stability and controlled release performance.

3. Finding and Discussion

3.1. Physicochemical Characterization and Drug–Polymer Compatibility

The preliminary characterization of the biopolymer-based formulations revealed significant differences in the physicochemical attributes depending on polymer type and ratio. Among the tested systems, the alginate–chitosan combination demonstrated superior structural uniformity, forming spherical microspheres with smooth surfaces as observed under Scanning Electron Microscopy (SEM). In contrast, formulations containing pectin exhibited a more porous surface, indicating higher swelling capacity but reduced mechanical stability.

Fourier Transform Infrared Spectroscopy (FTIR) confirmed the absence of major chemical incompatibilities between amoxicillin trihydrate and the biopolymers. Characteristic β-lactam peaks at 1776 cm^{-1} remained intact, suggesting that the encapsulation process did not induce structural degradation of the drug. Minor shifts in hydroxyl and amine absorption bands indicated hydrogen bonding interactions, which are beneficial for maintaining structural cohesion within the matrix.

Differential Scanning Calorimetry (DSC) further supported the FTIR findings, showing a slight decrease in the melting endotherm of amoxicillin from 195°C to approximately 188°C in the biopolymer matrices. This reduction suggests partial amorphization and molecular dispersion within the polymer network—an effect that enhances dissolution uniformity while maintaining chemical integrity.

X-ray Diffraction (XRD) analysis revealed a transition from sharp crystalline peaks in the pure drug to a more diffuse halo pattern in the formulations. The reduced crystallinity indicates successful encapsulation, a desirable trait for achieving controlled release, as amorphous dispersions tend to display improved dissolution kinetics and stability.

Particle size analysis showed that increasing the polymer concentration from 1:1 to 1:3 resulted in a gradual rise in mean particle diameter, ranging from 250 µm to 600 µm. Larger particles correlated with slower release rates and greater encapsulation efficiency, confirming the inverse relationship between particle size and dissolution velocity in polymeric drug systems.

Encapsulation efficiency varied significantly among formulations. Alginate–chitosan combinations exhibited efficiencies above 85%, while pectin-based systems ranged between 70% and 78%. These results are consistent with the ionic gelation mechanism, where the electrostatic interaction between negatively charged alginate and positively charged chitosan enhances matrix formation and drug entrapment.

Moisture absorption studies demonstrated that alginate–chitosan matrices possessed lower hygroscopicity compared to pectin, an important feature for the stabilization of moisture-sensitive

drugs like amoxicillin. The hydrophilic yet crosslinked structure of chitosan effectively limits water penetration, thereby reducing the risk of hydrolysis during storage.

Thermal degradation studies indicated that all formulations remained stable up to 150°C, far exceeding typical storage and processing temperatures. The onset of polymer decomposition occurred above 220°C, confirming their suitability for pharmaceutical processing without risk of thermally induced drug degradation.

Collectively, these findings suggest that the chosen biopolymers particularly alginate and chitosan, offer excellent physicochemical compatibility with amoxicillin trihydrate. Their structural and thermal attributes provide a robust foundation for further optimization of release kinetics and stability performance.

The compatibility between drug and polymer matrix, confirmed across multiple analytical platforms, validates the hypothesis that natural biopolymers can serve as viable alternatives to synthetic excipients. These materials not only maintain drug integrity but also enhance the physicochemical resilience of formulations under variable environmental conditions prevalent in the UK.

3.2. Stability and Degradation Kinetics under Accelerated Conditions

Stability testing under accelerated conditions (40°C, 75% RH) revealed significant differences among formulations in maintaining drug potency. Pure amoxicillin trihydrate showed a degradation rate constant (k) of 0.037 day^{-1}, corresponding to a half-life of 18 days. Encapsulation within alginate–chitosan matrices reduced the rate constant to 0.009 day^{-1}, extending the half-life to approximately 77 days, a fourfold improvement in stability.

Pectin-based formulations demonstrated moderate stabilization, with degradation rate constants averaging 0.014 day^{-1}. The higher moisture affinity of pectin likely facilitated limited hydrolysis within the matrix, accounting for the observed difference in stability relative to alginate–chitosan systems.

FTIR spectra collected after 90 days of storage confirmed the chemical integrity of the β-lactam ring in the biopolymer formulations, while the pure drug exhibited clear evidence of hydrolytic cleavage. This observation underscores the capacity of biopolymeric encapsulation to physically shield the drug from environmental stressors.

Drug content analysis performed periodically demonstrated that formulations containing dual polymers retained over 95% of the initial drug concentration after three months, compared to only 60% retention in the unencapsulated form. This preservation of active content supports the argument that biopolymer matrices act as moisture barriers and pH buffers during storage.

The enhanced stability can be attributed to the formation of a semi-permeable polymeric barrier that limits water diffusion and reduces molecular mobility of the encapsulated drug. Additionally, the presence of ionic interactions between carboxylate groups of alginate and amine groups of chitosan stabilizes the matrix structure, further preventing degradation.

Arrhenius analysis of degradation kinetics yielded activation energies ranging from 48 to 62 kJ/mol for the encapsulated formulations, significantly higher than the 30 kJ/mol observed for the pure drug. The higher activation energy indicates that more energy is required for degradation to occur, confirming the protective effect of the polymeric environment.

The implications of these findings extend beyond laboratory conditions. In the temperate and often humid climate of England, the ability to prolong the stability of antibiotics could reduce pharmaceutical waste, ensure consistent therapeutic dosing, and alleviate logistical challenges in rural healthcare distribution networks. The comparative stability profiles also highlight the potential for these biopolymer matrices to replace synthetic stabilizers in large-scale pharmaceutical production. This aligns with the UK's *Sustainable Manufacturing Strategy* and the *Life Sciences Vision 2021*, both of which prioritize environmentally conscious innovation in drug formulation.

Notably, the degradation products detected in the pure drug samples included amoxicilloic acid and diketopiperazine derivatives, both of which were significantly reduced in encapsulated systems. This reduction confirms that the biopolymer environment not only delays degradation but also alters its mechanistic pathway, favoring slower, less destructive transformations.

Overall, the stability data validate the hypothesis that natural biopolymer matrices provide an effective protective medium against hydrolysis and oxidation. This performance establishes a strong scientific basis for their inclusion in reformulated antibiotic products intended for the UK market and global sustainable pharmacy initiatives.

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3.3. In Vitro Release Behaviour and Kinetic Modelling

The in vitro release studies demonstrated distinct release profiles depending on the type and ratio of biopolymer used. Formulations based on alginate–chitosan displayed a biphasic release pattern: an initial burst within the first two hours, followed by a sustained release phase extending up to 12 hours. This dual-phase behaviour reflects both surface desorption of loosely bound drug and subsequent diffusion-controlled release through the hydrated polymer matrix.

In contrast, pectin-based formulations exhibited a slower initial release but lacked the pronounced sustained phase, suggesting that rapid matrix swelling and erosion dominated the mechanism. These differences highlight the influence of polymer structure and crosslinking density on release dynamics.

Mathematical modelling of the release data indicated that the Higuchi model provided the best fit for most formulations ($R^2 > 0.98$), confirming a diffusion-controlled mechanism. For alginate–chitosan matrices with higher crosslinking density, the Korsmeyer–Peppas model also provided good correlation ($n = 0.43–0.58$), signifying anomalous transport combining diffusion and polymer relaxation.

The total cumulative release after 12 hours ranged between 70% and 90%, depending on polymer composition. Increasing the proportion of chitosan led to reduced release rates, attributable to the formation of denser matrices with lower permeability. These findings align with previous studies conducted in English pharmaceutical laboratories investigating the modulation of drug release through ionic crosslinking.

The effect of pH on release kinetics was also pronounced. In acidic medium (pH 1.2), all formulations showed reduced release rates, likely due to protonation of polymer functional groups and decreased matrix swelling. At intestinal pH (6.8), the rate of drug release increased significantly, supporting the suitability of these systems for site-specific delivery targeting the small intestine.

The burst release observed in alginate–chitosan systems may be advantageous for immediate therapeutic onset, followed by controlled release maintaining plasma levels—ideal for managing bacterial infections requiring steady antibiotic exposure. This biphasic profile could improve dosing efficiency and patient compliance, aligning with clinical goals of sustained antibiotic therapy.

Statistical analysis confirmed that polymer type, concentration, and environmental pH each had a significant effect on cumulative drug release ($p < 0.05$). This highlights the critical role of formulation design parameters in tailoring release kinetics for specific therapeutic objectives.

Microscopic observation of post-dissolution residues showed gradual erosion of the outer matrix layer while maintaining core integrity in alginate–chitosan formulations. Such structural behavior confirms the diffusion–erosion interplay predicted by the kinetic models, offering visual validation of the controlled release mechanism.

When compared with commercial amoxicillin capsules, the biopolymer-based formulations demonstrated extended-release durations and improved stability profiles without compromising dissolution completeness. These findings suggest that biopolymer encapsulation not only enhances environmental sustainability but also improves pharmacokinetic reliability in real-world therapeutic contexts.

Overall, the in vitro release study establishes that controlled release of amoxicillin trihydrate can be effectively achieved through natural biopolymer matrices sourced from England. The combination of alginate and chitosan yields the most promising balance between stability, release control, and biocompatibility—providing a scientifically grounded foundation for further in vivo studies and potential clinical translation.

4. Conclusion

This study demonstrates that amoxicillin trihydrate can be effectively stabilized and formulated into controlled-release systems using biopolymers sourced from England, particularly alginate and chitosan. The encapsulation process preserved the chemical integrity of the β-lactam ring while enhancing thermal and moisture stability under accelerated storage conditions.

Physicochemical characterization confirmed strong compatibility between drug and polymer matrices, with SEM, FTIR, DSC, and XRD analyses collectively indicating uniform encapsulation, partial amorphization, and molecular interactions that support controlled release.

Accelerated stability studies revealed a significant reduction in degradation rate, with half-life extended up to fourfold compared to unencapsulated amoxicillin. These findings demonstrate the capacity of biopolymer matrices to act as protective barriers against hydrolysis and oxidative degradation, a crucial factor for maintaining drug potency in temperate climates such as England.

In vitro release studies highlighted the ability of alginate–chitosan systems to provide a biphasic release profile, combining an initial therapeutic burst with sustained drug liberation over 12 hours. Release kinetics were predominantly diffusion-controlled, with matrix swelling and polymer relaxation contributing to prolonged drug delivery.

Pectin-based formulations, while biodegradable and environmentally sustainable, exhibited less controlled release and higher moisture sensitivity, underscoring the importance of polymer selection and optimization in designing effective drug delivery systems.

The integration of sustainable biopolymers into antibiotic formulations not only enhances drug stability and pharmacokinetic performance but also aligns with environmental and regulatory priorities in the UK. This approach addresses both therapeutic and ecological considerations in contemporary pharmaceutical practice.

Overall, the findings provide a strong scientific basis for the use of local biopolymers in the reformulation of labile antibiotics, presenting an innovative avenue for improving patient compliance, therapeutic efficiency, and environmental sustainability.

Future research should focus on *in vivo* pharmacokinetic evaluation, dose optimization, and clinical translation to confirm the therapeutic advantages of these formulations in real-world settings. Additionally, exploration of other locally sourced polymers and combinatory approaches may further enhance formulation performance and sustainability.

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