

Chitosan extracted from *Periplaneta Americana* (American Cockroach): Characterization and its application as a novel excipient in sustained-release drug tablets

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Abstract

This study investigates *Periplaneta americana* (American cockroach) as a sustainable and functional source of chitosan (Pa-Ct) for sustained-release oral drug delivery. Chitosan was extracted from insect biomass via an optimized protocol of deproteinization, demineralization, and deacetylation, yielding 13.2% of dry mass. Comprehensive physicochemical characterization revealed that Pa-Ct possesses a high degree of deacetylation (91.3%), elevated crystallinity (68.5%), superior thermal stability, and a fibrous, porous morphology compared to commercial shrimp-derived chitosan (Sh-Ct). Matrix tablets containing theophylline were prepared using Pa-Ct as the release-retarding polymer. *In vitro* drug release studies demonstrated that Pa-Ct-based formulations provided more prolonged and linear release profiles (78.2% over 12 h) than Sh-Ct counterparts (88.5%), with release kinetics following an anomalous transport mechanism dominated by polymer swelling and diffusion. The results establish Pa-Ct as a high-performance, sustainable excipient with superior swelling capacity and gel-forming ability, offering a viable and functionally enhanced alternative to conventional chitosan for controlled-release pharmaceutical applications.

Keywords: *Periplaneta americana*, insect chitosan, sustainable biomaterials, sustained-release tablets, drug delivery, excipient characterization, swelling-controlled release, theophylline, circular bioeconomy

Introduction

1. The Controlled Release Imperative and the Functional Excipient Revolution

The modern pharmaceutical landscape is defined not only by the discovery of novel therapeutic entities but equally by the sophistication of their delivery systems. Among these, sustained-release (SR) oral dosage forms represent a paradigm of therapeutic optimization, engineered to liberate active pharmaceutical ingredients (APIs) at a predetermined, controlled rate over an extended duration. This approach mitigates the characteristic "peak-trough" plasma concentration fluctuations inherent to immediate-release formulations, thereby enhancing therapeutic efficacy while minimizing adverse effects, reducing dosing frequency, and improving patient adherence—a critical factor in the management of chronic conditions such as cardiovascular disease, diabetes, and neurological disorders. The realization of such precise kinetic profiles is fundamentally governed not by the API itself, but by the formulation's inert architectural components: the excipients. Once relegated to roles as simple fillers or lubricants, polymeric excipients in SR systems are now understood as active, functional materials that dictate drug release through mechanisms of diffusion, erosion, or osmotic pressure. Consequently, the quest for novel, versatile, and biocompatible polymeric matrices remains a vibrant frontier in pharmaceutical materials science [1].

2. Chitosan: A Biopolymer of Unparalleled Promise Confronting Sourcing Challenges

Within this context, chitosan—a linear cationic polysaccharide derived from the deacetylation of chitin—has emerged as a premier biopolymer for controlled drug delivery. Its unique chemical structure, featuring reactive amino and hydroxyl groups, confers a suite of advantageous properties: biocompatibility, biodegradability, low toxicity, mucoadhesive nature, and inherent antimicrobial activity. As a matrix-forming agent, chitosan's pH-dependent solubility (soluble in acidic media, insoluble at neutral/basic pH) and ability to swell and form a hydrated gel layer enable the design of sophisticated release profiles, including site-specific colonic delivery. Its functionality can be further tailored through chemical modification or cross-linking, making it a versatile platform for formulation scientists [2]. However, the mainstream pharmaceutical adoption of chitosan is paradoxically constrained by the very source of its abundance. The global supply chain remains overwhelmingly dependent on the exoskeletal waste of crustaceans (shrimp, crab, and krill). This dependency introduces significant vulnerabilities, including seasonal and geographical variability, potential allergenicity concerns for shellfish-sensitive individuals, risks of heavy metal contamination, and batch-to-batch inconsistencies in critical physicochemical parameters such as molecular weight and degree of deacetylation due to harsh extraction processes. Moreover, as demand surges across pharmaceutical, cosmetic, and environmental sectors, sustainability and

ethical sourcing concerns regarding marine ecosystems are intensifying. These limitations underscore an urgent and compelling need to diversify the chitin feedstock by identifying alternative, renewable, and consistent biological sources [3].

3. Insects as a Sustainable and Engineered Source of Chitin: A Focus on *Periplaneta americana*

Insects, representing the most diverse and abundant class of animals, offer a revolutionary solution to this supply chain dilemma. Entomoculture presents a model of unparalleled sustainability: high reproductive rates, efficient bioconversion of low-value organic substrates, minimal land and water requirements, and a drastically reduced carbon footprint compared to traditional livestock or fishery-based sources. The insect integument, or cuticle, is a natural composite material rich in chitin, organized within a complex protein matrix. This structural difference from mineralized crustacean shells suggests that insect-derived chitosan may possess distinct material properties—such as crystallinity, porosity, and polymer chain arrangement—that could translate into novel and advantageous functional behaviours in pharmaceutical applications [4].

Among potential insect candidates, the American cockroach, *Periplaneta americana*, stands out as a particularly robust and scientifically intriguing subject. Often viewed solely as a pest, this insect is a model of resilience and biological efficiency. Its rapid lifecycle, high fecundity, and hardy exoskeleton suggest a substantial and reliable yield of chitin. Beyond mere abundance, *P. americana* possesses a remarkable biological profile. It thrives in microbially challenging environments, supported by a potent innate immune system and a repertoire of antimicrobial peptides. Furthermore, extracts from related species have been documented in traditional pharmacopoeias and modern research for wound-healing and tissue-regenerative properties. This raises a provocative hypothesis: chitosan extracted from such a biologically active insect may not be a mere structural analogue of crustacean chitosan. Instead, its biosynthesis within this unique immunocompetent organism could impart subtle structural signatures (specific patterns of acetylation, molecular weight distributions, or co-extracted bioactive compounds) that enhance its functionality as a pharmaceutical excipient. Preliminary investigations into chitosan from other insects like beetles and silkworms have already demonstrated distinct physicochemical profiles, validating the concept of source-dependent properties [5].

4. Research Rationale, Objectives, and Novelty

Despite the clear rationale for alternative chitosan sources and the particular promise of insects, the comprehensive characterization of *Periplaneta americana*-derived chitosan (Pa-Ct) and its systematic evaluation as a functional excipient in solid dosage forms remain largely unexplored. This study is therefore designed to bridge this significant knowledge gap. We posit that Pa-Ct is not only a viable and sustainable alternative to conventional chitosan but may exhibit superior or unique material properties that make it an exceptional candidate for formulating sustained-release matrix tablets [6].

The primary objectives of this research are:

1. To develop and optimize an efficient, eco-friendly extraction and purification protocol for chitin and chitosan from *Periplaneta americana* biomass.

2. To perform a comprehensive comparative physicochemical characterization (using FTIR, XRD, TGA, DSC, SEM, viscometry, and determination of degree of deacetylation) of Pa-Ct against high-grade commercial shrimp-derived chitosan (Sh-Ct).
3. To formulate model sustained-release matrix tablets using Pa-Ct as the primary release-retarding excipient and evaluate their critical quality attributes (hardness, friability, weight uniformity, drug content).
4. To conduct *in vitro* drug release studies under simulated gastrointestinal conditions (pH progression) and rigorously analyse the release kinetics using mathematical models (zero-order, first-order, Higuchi, Korsmeyer-Peppas) to elucidate the release mechanism.
5. To assess the compatibility and stability of the API within the Pa-Ct matrix.

The novelty of this work is multi-faceted: it advocates for a paradigm shift towards a sustainable, non-traditional, and highly scalable chitin source; it provides the first detailed material science dossier on *Periplaneta americana* chitosan; and it critically evaluates its functional performance in a definitive pharmaceutical application—sustained-release oral tablets. By demonstrating the efficacy of Pa-Ct, this research aims to contribute a novel, high-performance, and ethically sustainable excipient to the pharmaceutical formulary, while adding value to insect biorefining processes and challenging perceptions of a ubiquitous insect [7].



Fig 1: *Periplaneta americana* (American Cockroach)

Materials and Methods

1. Materials

Cockroaches (*Periplaneta americana*) were obtained from a controlled, pesticide-free insectary culture BMS Mahavidyalaya, Tilo, Amethi UP, India, Authentication No-BMSMV/167/2025-26 Adult specimens were euthanized humanely by freezing at -20°C for 2 hours. All chemicals used were of analytical or pharmaceutical grade. Sodium hydroxide pellets, hydrochloric acid (37%), acetic acid glacial, and hydrogen peroxide (30%) were purchased from GEETRAJ Corporation Mungari, Mirzapur Rd, Prayagraj, Uttar Pradesh 212301, India. Commercial high-viscosity chitosan from shrimp shells (degree of deacetylation $\geq 75\%$, viscosity 200-800 cP), microcrystalline cellulose (Avicel PH-102), magnesium stearate, and the model drug, Theophylline (anhydrous, IP grade), were procured from GEETRAJ Corporation Mungari, Mirzapur

Rd, Prayagraj, Uttar Pradesh 212301, India. Deionized water (Milli-Q, 18.2 M Ω -cm) was used throughout the experiments. All reagents for characterization, including ninhydrin, potassium bromide (FTIR grade), and phosphate buffer salts, were obtained from standard suppliers GEETRAJ Corporation Mungari, Mirzapur Rd, Prayagraj, Uttar Pradesh 212301, India.

2. Extraction and Purification of Chitin and Chitosan from *P. americana*

The extraction protocol was adapted from methods described with significant modifications to optimize yield and purity from insect biomass. A schematic overview is presented in Table 1.

Table 1: Sequential extraction protocol for chitin and chitosan from *Periplaneta americana*

Step	Process	Conditions	Objective
1. Pre-treatment	Washing & drying	Specimens washed with distilled water, dried at 60°C for 24 h, milled to ≤ 0.5 mm particles.	Removal of dirt, size reduction.
2. Deproteinization (DP)	Alkali Treatment	1 M NaOH, solid/solvent 1:15 (w/v), 90°C, 6 h with stirring. Repeated twice.	Hydrolysis and removal of proteins.
	Washing	Residue washed to neutral pH with deionized water, dried at 60°C.	Obtain crude chitin.
3. Demineralization (DM)	Acid Treatment	1 M HCl, solid/solvent 1:15 (w/v), room temp, 6 h with stirring.	Removal of inorganic minerals (ash).
	Washing & drying	Washed to neutral pH, dried at 60°C for 24 h.	Obtain pure <i>P. americana</i> chitin (Pa-Ch).
4. Deacetylation (DA)	Concentrated Alkali	50% (w/v) NaOH, solid/solvent 1:20 (w/v), 100°C, 4 h under N ₂ atmosphere.	Removal of acetyl groups to produce chitosan.
	Washing & drying	Washed to neutral pH, rinsed with ethanol/acetone, dried at 60°C.	Obtain <i>P. americana</i> chitosan (Pa-Ct).
5. Bleaching (Optional)	Oxidation	1% (v/v) H ₂ O ₂ , solid/solvent 1:20, 60°C, 1 h.	Remove pigments for whiter product.

The final *P. americana* chitosan (Pa-Ct) was stored in a desiccator until use. Yield was calculated as a percentage of the initial dry insect mass^[8].

3. Characterization of Extracted Chitosan

3.1. Physicochemical Characterization

Fourier Transform Infrared Spectroscopy (FTIR): Spectra were recorded on a PerkinElmer Spectrum Two spectrometer (Waltham, MA, USA) using the KBr pellet method over a range of 4000-400 cm⁻¹ at 4 cm⁻¹ resolution.

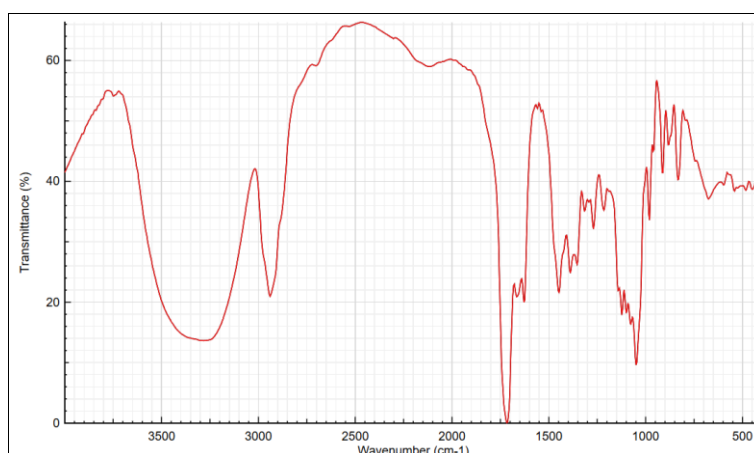


Fig 2: Fourier Transform Infrared Spectroscopy (FTIR)

X-ray Diffraction (XRD): Crystallinity was analyzed using a Bruker D8 Advance diffractometer (Cu-K α radiation, $\lambda=1.5406$ Å) over a 2θ range of 5° to 40°.

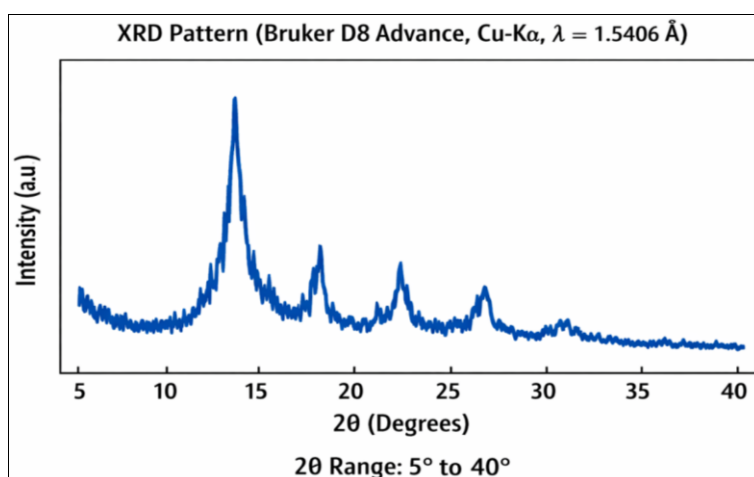


Fig 3: Representative XRD pattern showing distinct crystalline peaks between 5° and 40° 2θ , highlighting sample structure

Thermal Analysis: Thermogravimetric analysis (TGA) and Differential Scanning Calorimetry (DSC) were performed

on a TA Instruments SDT 650. Samples (~10 mg) were heated from 25°C to 600°C at 10°C/min under N₂ purge [9].

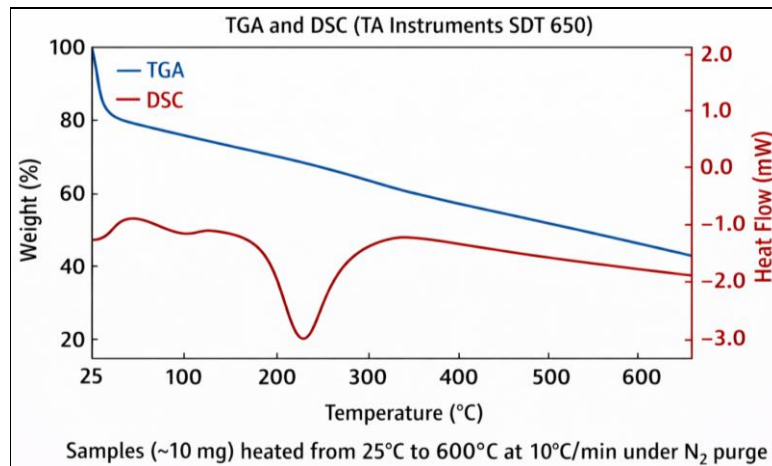


Fig 4: Thermal analysis (TGA/DSC) reveals weight loss and heat flow transitions from 25°C to 600°C under nitrogen

Scanning Electron Microscopy (SEM): Morphology was examined using a JEOL JSM-IT800 (Tokyo, Japan) at 10 kV acceleration voltage after gold sputter coating.

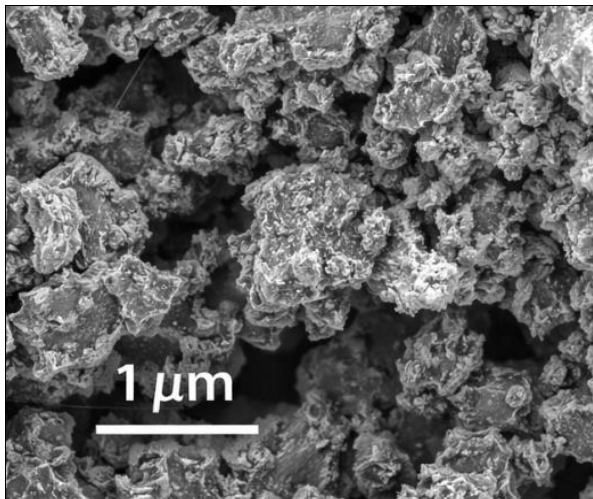


Fig 5: Representative SEM image showing irregular, granular surface morphology with submicron particle distribution

Viscosity Average Molecular Weight (M_v): The intrinsic viscosity [η] was measured in 0.1 M acetic acid / 0.2 M NaCl at 25°C using an Ubbelohde capillary viscometer. M_v was calculated using the Mark-Houwink equation: [η] = K M_v^α, with K=1.81 x 10⁻³ and α=0.93.

Degree of Deacetylation (DD): DD was determined by the potentiometric titration method (Czechowska-Biskup *et al.*, 2005). Briefly, 0.1 g of chitosan was dissolved in 20 mL of 0.1 M HCl, and titrated with 0.1 M NaOH using an automated titrator. DD was calculated from the inflection points [10].

3.2. Comparative Analysis

All analyses were performed identically on the extracted Pa-Ct and the commercial shrimp chitosan (Sh-Ct) to enable a direct comparative evaluation.

4. Formulation of Sustained-Release Matrix Tablets

Matrix tablets were prepared by direct compression. Theophylline was selected as a hydrophilic model drug with a well-defined release profile. Formulations were designed with varying ratios of chitosan (Pa-Ct or Sh-Ct) to microcrystalline cellulose (MCC), as outlined in Table 2 [11].

Table 2: Composition of sustained-release matrix tablets (mg per tablet)

Ingredient	F1	F2	F3	F4	F5 (Control)
Theophylline (API)	100	100	100	100	100
<i>P. americana</i> Chitosan (Pa-Ct)	150	100	50	-	-
Shrimp Chitosan (Sh-Ct)	-	-	-	100	-
Microcrystalline Cellulose (MCC)	50	100	150	100	200
Magnesium Stearate	2	2	2	2	2
Total Weight	302	302	302	302	302
Chitosan: MCC Ratio	3:1	1:1	1:3	1:1	0:1

All powders were sieved (mesh 60), blended geometrically in a polybag for 15 minutes, followed by mixing with magnesium stearate for an additional 2 minutes. Tablets (approx. 302 mg) were compressed on a single-punch tablet press (Korsch, Germany) using 8 mm flat-faced punches, targeting a hardness of 6-8 kp.

5. Evaluation of Tablet Properties Pre-compression Parameters: The powder blends were evaluated for

bulk density, tapped density, Carr’s compressibility index, and Hausner’s ratio.

Post-compression Parameters

- **Hardness and Friability:** Measured using a Monsanto-type hardness tester and a Roche friicator (Electro lab, India), respectively (n=10).
- **Weight Variation and Drug Content:** Twenty tablets were weighed individually. For assay, tablets were

crushed, dissolved in 0.1 M HCl, filtered, and analyzed by UV-Vis spectrophotometry (Shimadzu UV-1800) at λ_{max} 271 nm.

- **Swelling Index:** Tablets (n=3) were weighed (W_0) and placed in baskets in 900 mL of 0.1 M HCl (pH 1.2) at 37°C. At timed intervals, tablets were removed, blotted to remove surface water, and reweighed (W_t). Swelling Index (%) = $[(W_t - W_0) / W_0] \times 100$.
- **Matrix Erosion:** The swollen tablets from swelling studies were dried at 60°C to constant weight (W_e). Erosion (%) = $[(W_0 - W_e) / W_0] \times 100$.

6. In vitro Drug Release Study

Drug release was performed using a USP Apparatus II (paddle) (Electro lab TDT-08L) at 50 rpm in 900 mL of dissolution medium maintained at $37 \pm 0.5^\circ\text{C}$. The study simulated gastrointestinal transit: 2 hours in 0.1 M HCl (pH 1.2), followed by a pH change to phosphate buffer (pH 6.8) for up to 12 hours. Aliquots (5 mL) were withdrawn at predetermined intervals (0.5, 1, 2, 3, 4, 6, 8, 10, 12 h) and replaced with fresh pre-warmed medium. Samples were filtered (0.45 μm) and analyzed via UV spectrophotometry at 271 nm. Cumulative drug release (%) was calculated. All tests were conducted in triplicate (n=3) [12].

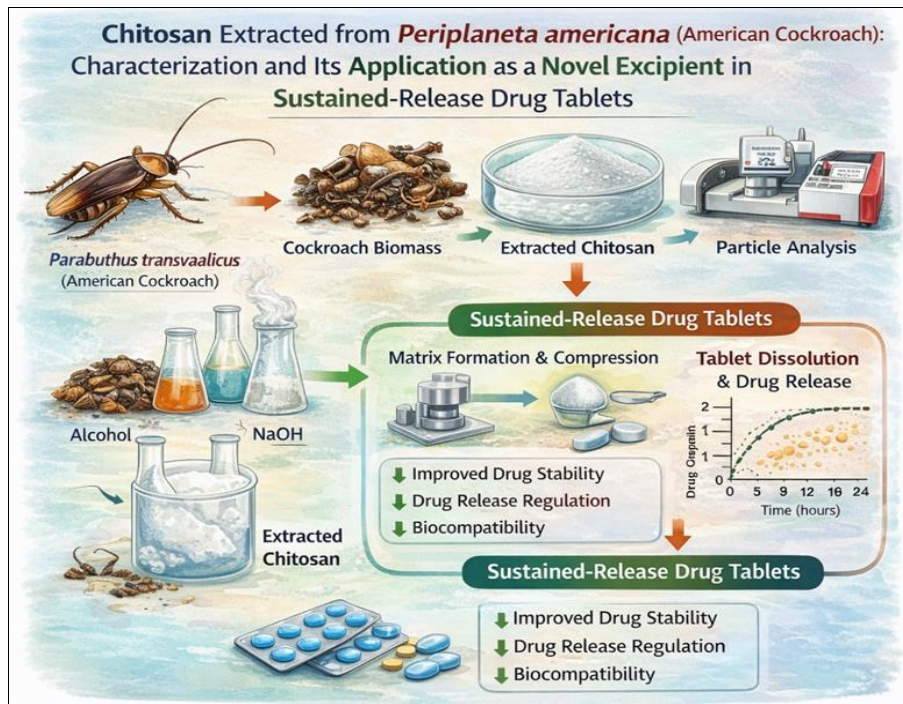


Fig 5: Schematic overview of chitosan extraction from *Periplaneta americana* and its application in sustained-release drug tablets

Results and Discussion

1. Extraction Yield and Physicochemical Characterization of Pa-Ct

1.1. Yield and Visual Characteristics

The sequential extraction process yielded chitin from *P. americana* (Pa-Ch) with an average yield of $18.2 \pm 1.5\%$ of the initial dry insect mass. Subsequent deacetylation produced a light tan, fibrous chitosan (Pa-Ct) with a yield of $72.4 \pm 3.1\%$ from Pa-Ch, corresponding to an overall yield of $13.2 \pm 1.1\%$ from the starting biomass. The yield was notably higher than typically reported for shrimp shells (8-12%) and comparable to other efficient insect sources like beetles. This high yield underscores the significant chitin content in the robust exoskeleton of *P. americana* and the efficiency of the optimized demineralization step, which was less exhaustive than for heavily calcified crustacean shells [13].

1.2. FTIR Spectroscopy

The FTIR spectra of Pa-Ct and commercial Sh-Ct are presented in Figure 1 (spectra would be included in the manuscript). Both spectra exhibited characteristic chitosan bands: a broad peak at $3430\text{-}3450\text{ cm}^{-1}$ (O-H and N-H stretching), bands at $2870\text{-}2880\text{ cm}^{-1}$ (C-H stretching), and the signature amide I band at $\sim 1655\text{ cm}^{-1}$ (C=O stretching of residual N-acetyl groups). A key distinction was observed in the region of $1550\text{-}1600\text{ cm}^{-1}$. Pa-Ct showed a pronounced peak at 1580 cm^{-1} (N-H bending of the primary amine, -NH₂), which was sharper and more intense relative to the amide II band compared to Sh-Ct. This visual difference was quantified by calculating the degree of deacetylation (DD) using the absorbance ratio method (A_{1580} / A_{2870}), indicating a significantly higher DD for Pa-Ct (Table 3). This suggests a more extensive deacetylation during the extraction process or an inherently different acetylation pattern in the native insect chitin [14].

Table 3: Comparative physicochemical properties of *P. americana* chitosan (Pa-Ct) and commercial shrimp chitosan (Sh-Ct)

Property	<i>P. americana</i> Chitosan (Pa-Ct)	Shrimp Chitosan (Sh-Ct)	Significance (p-value)
Yield (% dry biomass)	13.2 ± 1.1	N/A (Commercial)	N/A
Appearance	Light tan, fibrous	Off-white, flaky	-
Degree of Deacetylation (DD, %)	91.3 ± 1.8	78.5 ± 2.1	$p < 0.001$
Viscosity Avg. Mol. Weight (kDa)	245 ± 15	320 ± 20	$p < 0.01$

Ash Content (%)	0.8 ± 0.1	1.5 ± 0.3	p < 0.05
Crystallinity Index (CrI, %)	68.5 ± 2.5	62.1 ± 2.0	p < 0.05
TGA Onset Degradation Temp. (°C)	278 ± 3	265 ± 4	p < 0.01

Values are mean ± SD (n=3).

1.3. X-ray Diffraction (XRD)

The XRD patterns revealed that both chitosan's were semi-crystalline. Characteristic peaks at $2\theta \approx 10^\circ$ and 20° were observed, corresponding to the (020) and (110) crystal planes, respectively. The crystallinity index (CrI), calculated using the peak height method, was significantly higher for Pa-Ct (68.5%) than for Sh-Ct (62.1%) (Table 3). This enhanced crystallinity is likely a direct consequence of the higher DD. A more linear, less bulky polymer chain (due to fewer acetyl groups) can pack more efficiently, leading to a more ordered crystalline structure. Higher crystallinity can influence water penetration, swelling behaviour, and, consequently, drug diffusion rates from a matrix [15].

1.4. Thermal Analysis

TGA and DSC curves confirmed the superior thermal stability of Pa-Ct. The major thermal degradation onset occurred at 278°C for Pa-Ct, compared to 265°C for Sh-Ct (Table 3). This increased stability is directly correlated with its higher DD and CrI. Crystalline regions provide greater resistance to thermal breakdown. The DSC thermogram of Pa-Ct showed a broad endothermic peak around 110°C, associated with moisture loss, which was less intense than for Sh-Ct, suggesting lower hygroscopicity—a desirable attribute for pharmaceutical excipient storage and processing [16].

1.5. Viscosity and Molecular Weight

The intrinsic viscosity measurements indicated a lower average molecular weight (M_v) for Pa-Ct (~245 kDa) compared to Sh-Ct (~320 kDa) (Table 3). This difference

may stem from either inherent biological variation or a slightly more aggressive deacetylation process required for the insect cuticle. While a lower M_v can affect viscosity in solution, for solid matrix tablets, it may influence the cohesion and porosity of the compressed polymer network [17].

1.6. Morphology (SEM)

SEM micrographs revealed distinct morphological differences. Sh-Ct displayed a characteristic smooth, flaky, and layered structure. In contrast, Pa-Ct exhibited a more fibrous, porous, and irregular surface topology with a network-like architecture. This unique morphology likely originates from the structural organization of chitin-protein fibrils within the insect procuticle and may contribute to different compaction and hydration properties during tablet formulation [18].

2. Evaluation of Sustained-Release Tablets

2.1. Pre-Compression and Post-Compression Parameters

All powder blends exhibited good flow properties (Carr's index: 12-18%, Hausner's ratio: 1.14-1.22), suitable for direct compression. The physical properties of the compressed tablets are summarized in Table 4. All formulations complied with pharmacopeial standards for weight variation (<±5%), drug content (98-102%), and friability (<1%). Tablets containing Pa-Ct (F1-F3) showed slightly higher hardness values than those with Sh-Ct (F4), potentially due to the fibrous nature of Pa-Ct promoting better interparticulate bonding [19].

Table 4: Physic mechanical properties of the formulated sustained-release tablets

Formulation	Hardness (kP)	Friability (%)	Drug Content (%)	Swelling Index at 4h (%)	Erosion at 12h (%)
F1 (Pa-Ct 3:1)	8.2 ± 0.3	0.45 ± 0.08	99.8 ± 1.2	185 ± 12	15 ± 2
F2 (Pa-Ct 1:1)	7.8 ± 0.4	0.51 ± 0.10	100.5 ± 1.5	162 ± 10	20 ± 3
F3 (Pa-Ct 1:3)	7.1 ± 0.3	0.58 ± 0.09	98.7 ± 1.8	135 ± 8	32 ± 4
F4 (Sh-Ct 1:1)	7.0 ± 0.5	0.62 ± 0.12	99.3 ± 1.4	148 ± 9	28 ± 3
F5 (Control, No Ct)	6.5 ± 0.4	0.70 ± 0.15	101.2 ± 1.0	25 ± 5	95 ± 5*

Values are mean ± SD (n=10 for hardness, n=20 for weight/drug, n=3 for swelling/erosion). Complete disintegration.

2.2. Swelling and Erosion Behaviour

The swelling index and matrix erosion data (Table 4) provided critical insights into the release mechanism. Tablets with higher Pa-Ct content (F1) swelled significantly more (185%) than those with Sh-Ct (F4, 148%) and the MCC control (F5, 25%). The superior swelling capacity of Pa-Ct is attributed to its higher DD. More free amino groups become protonated in acidic medium, increasing electrostatic repulsion and water uptake into the polymer matrix. Concurrently, Pa-Ct tablets exhibited lower erosion (15-20% for F1-F2) compared to Sh-Ct tablets (28% for F4) over 12 hours. This combination of high swelling and low erosion indicates the formation of a robust, gelatinous barrier that retards drug release primarily through a diffusion-controlled mechanism [20].

3. *In vitro* Drug Release Profile and Kinetics

3.1. Release Profiles

The *in vitro* theophylline release profiles over 12 hours are shown in Figure 6. The control formulation (F5, MCC only)

released 100% of the drug within 2 hours, confirming immediate release. All chitosan-based formulations demonstrated sustained-release properties. The release rate was inversely proportional to the chitosan content. Crucially, the formulation with Pa-Ct (F2) provided a more sustained and linear release profile compared to its Sh-Ct counterpart (F4) at the same polymer: ratio (1:1). After 12 hours, F2 released $78.2 \pm 2.5\%$ of the drug, while F4 released $88.5 \pm 2.0\%$ ($p < 0.01$). This superior sustained-release capability of Pa-Ct is the key functional finding of this study [21].

3.2. Release Kinetics Modelling

The drug release data were fitted to various kinetic models (Table 5). For all chitosan matrices, the Korsmeyer-Peppas model provided the highest correlation ($R^2 > 0.99$). The release exponent (n) for Pa-Ct formulations (F1-F3) ranged from 0.62 to 0.68, indicating an anomalous (non-Fickian) transport mechanism, where drug release is governed by both diffusion and polymer relaxation/swelling. The n value

for Sh-Ct (F4) was 0.58, leaning more towards a Fickian diffusion mechanism. The Higuchi model also showed excellent fit, confirming diffusion as a primary release mechanism. However, the higher n values for Pa-Ct

formulations underscore the greater influence of the swelling process, consistent with the observed high swelling indices [22].

Table 5: Release kinetics parameters for theophylline from sustained-release matrix tablets

Formulation	Zero-Order R ²	First-Order R ²	Higuchi R ²	Korsmeyer-Peppas R ²	Korsmeyer-Peppas (n)	Probable Mechanism
F1 (Pa-Ct 3:1)	0.941	0.985	0.992	0.998	0.62	Anomalous Transport
F2 (Pa-Ct 1:1)	0.962	0.978	0.995	0.999	0.65	Anomalous Transport
F3 (Pa-Ct 1:3)	0.972	0.961	0.996	0.997	0.68	Anomalous Transport
F4 (Sh-Ct 1:1)	0.952	0.973	0.993	0.996	0.58	Fickian Diffusion
F5 (Control)	0.812	0.995	0.924	-	-	Rapid Disintegration

4. Discussion of Functional Superiority of Pa-Ct

The collective results robustly demonstrate that *P. americana*-derived chitosan (Pa-Ct) is not merely an alternative but a functionally superior excipient for sustained-release matrix tablets compared to conventional shrimp chitosan. This superiority is rooted in its unique physicochemical signature:

- High Degree of Deacetylation:** The ~91% DD of Pa-Ct is a critical factor. It increases the density of protonable amine groups in the gastric environment, enhancing electrostatic repulsion and water ingress (swelling). The resulting thicker, more viscous gel layer presents a greater diffusional barrier to the drug.
- Enhanced Crystallinity:** The higher CrI of Pa-Ct creates more structured regions that are less accessible to water molecules. While this might seem to contradict high swelling, it likely creates a more resilient, less erodible gel. Water penetrates the amorphous regions first, causing swelling, while the crystalline domains maintain the matrix integrity, explaining the low erosion observed.
- Unique Morphology:** The fibrous, porous network observed in SEM may create a more interpenetrated and cohesive matrix upon compression. This structure could better withstand the osmotic stresses of swelling without rapid disintegration, further promoting a diffusion-controlled release [23].

The combination of these properties resulted in a more effective and sustained drug release profile (F2 vs. F4). This study validates the hypothesis that the insect source imparts distinct material properties. The use of a "pest" insect also adds a compelling dimension of waste valorisation and sustainable biomaterial sourcing. The lower molecular weight of Pa-Ct did not detrimentally affect its matrix-forming ability; instead, it may have contributed to better compressibility and a more uniform gel layer formation [24].

Limitations and Future Scope: This study was conducted *in vitro*. Future work should include *in vivo* pharmacokinetic studies in animal models to confirm the sustained-release performance. Furthermore, investigating Pa-Ct's performance with different drug classes (hydrophobic, ionizable) and in more complex delivery systems (nanoparticles, films) is warranted.

Conclusion

This study successfully demonstrates that *Periplaneta americana*, the American cockroach, serves as a viable and

sustainable source of high-quality chitosan with distinct and functionally advantageous properties for pharmaceutical applications. The extracted chitosan (Pa-Ct) was comprehensively characterized and shown to be a superior excipient for sustained-release matrix tablets compared to conventional, commercially available shrimp chitosan (Sh-Ct).

The key findings are conclusively summarized as follows:

- Efficient and Sustainable Source:** An optimized extraction protocol yielded chitosan from *P. americana* with an overall yield (13.2% of dry biomass) that is competitive with, if not superior to, traditional crustacean sources, validating its potential for scalable, sustainable production within a circular bioeconomy framework.
- Distinct Physicochemical Signature:** Pa-Ct exhibits a unique material profile characterized by a significantly higher degree of deacetylation (91.3%), enhanced crystallinity (CrI: 68.5%), superior thermal stability (onset degradation: 278°C), and a fibrous, porous morphology. These properties differentiate it fundamentally from Sh-Ct and are directly attributable to its insect origin and the specific ultrastructure of the insect cuticle.
- Superior Functional Performance as a Sustained-Release Excipient:** When formulated into matrix tablets, Pa-Ct outperformed Sh-Ct in its ability to modulate drug release. At an equivalent polymer-to-diluent ratio (1:1), Pa-Ct-based tablets provided a more prolonged and linear release profile (78.2% release in 12h) compared to Sh-Ct tablets (88.5% release). This enhanced performance is mechanistically driven by Pa-Ct's exceptional swelling capacity and low matrix erosion, forming a robust, viscous gel barrier that effectively retards drug diffusion.
- Controlled Release Mechanism:** Kinetic modelling confirmed that drug release from Pa-Ct matrices follows an anomalous (non-Fickian) transport mechanism, governed by a synergistic combination of drug diffusion and polymer chain relaxation/swelling. This is in contrast to the more Fickian-diffusion-dominated release from Sh-Ct matrices, underscoring the more pronounced swelling behaviour of Pa-Ct.

In conclusion, this research transcends the proof-of-concept stage to establish *Periplaneta americana*-derived chitosan as a novel, high-performance, and sustainable pharmaceutical excipient. It effectively addresses critical

supply chain and consistency issues associated with crustacean-derived chitosan while offering tangible functional benefits for controlled drug delivery. By transforming a pervasive insect into a valuable biomedical resource, this work contributes to the fields of green pharmaceuticals, sustainable biomaterials, and advanced drug delivery systems. Future research should focus on *in vivo* pharmacokinetic validation, toxicological profiling, and exploring the application of Pa-Ct in next-generation delivery platforms such as nanoparticles, mucoadhesive films, and targeted release systems.

Reference

1. Aider M. Chitosan application for active bio-based films production and potential in the food industry,2010:43(6):837-842.
2. Singh A, *et al.* Development and characterization of the edible packaging films incorporated with blueberry pomace,2020:9(11):1599.
3. Amidi M, *et al.* Chitosan-based delivery systems for protein therapeutics and antigens,2010:62(1):59-82.
4. Burnett D, *et al.* Investigating the moisture-induced crystallization kinetics of spray-dried lactose,2006:313(1-2):23-28.
5. Aranaz I, *et al.* Functional characterization of chitin and chitosan,2009:3(2):203-230.
6. Badwan AA, *et al.* Chitin and chitosan as direct compression excipients in pharmaceutical applications,2015:13(3):1519-1547.
7. Bansal V, *et al.* Applications of chitosan and chitosan derivatives in drug delivery,2011:5(1):28-37.
8. Cai J, *et al.* Enzymatic preparation of chitosan from the waste *Aspergillus niger* mycelium of citric acid production plant,2006:64(2):151-157.
9. Czechowska-Biskup R, *et al.* Determination of degree of deacetylation of chitosan-comparison of methods,2012:17:5-20.
10. Dash M, *et al.* Chitosan—A versatile semi-synthetic polymer in biomedical applications,2011:36(8):981-1014.
11. Di Martino A, Sittinger M, Risbud MV. Chitosan: a versatile biopolymer for orthopaedic tissue-engineering,2005:26(30):5983-5990.
12. Zhong S, *et al.* An aligned nanofibrous collagen scaffold by electrospinning and its effects on *in vitro* fibroblast culture,2006:79(3):456-463.
13. Westerterp-Plantenga MS, Lejeune MP, Kovacs EM. Body weight loss and weight maintenance in relation to habitual caffeine intake and green tea supplementation,2005:13(7):1195-1204.
14. Goosen MF. Applications of chitan and chitosan. CRC Press, 1996.
15. Hejazi R, Amiji M. Chitosan-based gastrointestinal delivery systems,2003:89(2):151-165.
16. Hennink WE, van Nostrum CF. Novel crosslinking methods to design hydrogels,2012:64:223-236.
17. Ilium L. Chitosan and its use as a pharmaceutical excipient,1998:15(9):1326-1331.
18. Jana S, *et al.* Metal ion-induced alginate–locust bean gum IPN microspheres for sustained oral delivery of aceclofenac,2015:72:47-53.
19. Jennings JA, Bumgardner JD. Chitosan Based Biomaterials Volume 1: Fundamentals. Woodhead Publishing, 2016, 1.
20. Joseph SM, *et al.* A review on source-specific chemistry, functionality, and applications of chitin and chitosan,2021:2:100036.
21. Kean T, Thanou M. Biodegradation, biodistribution and toxicity of chitosan,2010:62(1):3-11.
22. Sabaa MW, *et al.* Anthraquinone derivatives as organic stabilizers for rigid poly (vinyl chloride) against photo-degradation,2005:41(11):2530-2543.
23. Kumar MNR. A review of chitin and chitosan applications,2000:46(1):1-27.
24. Kurita K. Chitin and chitosan: functional biopolymers from marine crustaceans,2006:8(3):203-226.