International Journal of Entomology Research
www.entomologyjournals.com
ISSN: 2455-4758
Received: 03-08-2024, Accepted: 02-09-2024, Published: 17-09-2024
Volume 9, Issue 9, 2024, Page No. 71-77

Review on pharmaceutical excipients derived from insects

Shivraj Popat Jadhav[1*], Sushant Mothabhau Ahire[2], Nilesh Ramkrushna Chitte[3], Parag Ashok Pathade[4], Chandrashekhar Dinkar Patil[5]

[1] Department of Pharmaceutics, Divine College of Pharmacy, Satana, Maharashtra, India
[2] Department of Quality Assurance, Divine College of Pharmacy, Satana, Maharashtra, India
[3] Department of Pharmaceutics, RG Sapkal College of Pharmacy, Nashik, Maharashtra, India
[4] Department of Pharmaceutical Chemistry, KBHSS Trust's Institute of Pharmacy, Malegaon, Maharashtra, India
[5] Department of Pharmacology, Divine College of Pharmacy, Satana, Maharashtra, India

Abstract

Insect-derived excipients offer sustainable alternatives to traditional materials in pharmaceutical formulations, thanks to their biocompatibility, biodegradability, and unique properties. This review explores a range of insect-derived materials, including chitosan, silk fibroin, and beeswax, highlighting their applications in drug delivery systems, controlled-release formulations, wound healing, and tissue engineering. Benefits include enhanced drug bioavailability, antimicrobial properties, and regenerative potential. However, challenges such as variability in raw materials, allergenicity, and regulatory hurdles need to be addressed. Advances in biotechnology, nanotechnology, and sustainable insect farming are crucial to unlocking the full potential of these materials. Overcoming these challenges will be essential for their successful integration into pharmaceutical formulations.

Keywords: Insect-derived excipients, biocompatible materials, chitosan, Silk fibroin, insect

Introduction

Excipients are crucial components of pharmaceutical formulations, serving a range of functions that enhance drug delivery, stability, and patient compliance. These substances, which include binders, disintegrants, fillers, lubricants, and preservatives, play a pivotal role in transforming an active pharmaceutical ingredient (API) into an effective and stable drug product. Binders help form tablets and granules, while disintegrants ensure that these tablets break down appropriately in the gastrointestinal tract. Fillers increase the volume of the formulation, making dosing accurate, and lubricants reduce friction during manufacturing. Preservatives extend the product's shelf life by preventing microbial growth. [1] Recent advancements in excipient technology, such as the development of nanomaterials and biodegradable polymers, have further enhanced drug delivery systems and targeted therapies. Additionally, natural excipients derived from plant and animal sources are gaining interest for their biocompatibility and environmental benefits. The selection of excipients must align with regulatory standards to ensure safety and efficacy, underscoring their integral role in pharmaceutical development.

Excipients are critical components in pharmaceutical formulations, serving a variety of roles beyond mere drug delivery. They enhance the drug's stability, solubility, and bioavailability, ensuring that the active pharmaceutical ingredients (APIs) are delivered effectively to their intended site of action. For instance, excipients can improve the solubility of poorly water-soluble drugs, enabling them to be more readily absorbed in the gastrointestinal tract. [2] Additionally, excipients can modify the release profile of drugs, allowing for controlled or sustained release, which can optimize therapeutic outcomes and minimize side effects. They also contribute to the physical properties of dosage forms, such as tablet hardness, disintegration, and dissolution rates, which are crucial for the consistency and reliability of drug performance. Furthermore, excipients can influence the taste, odour, and appearance of oral medications, enhancing patient compliance. The selection and formulation of excipients thus play a pivotal role in achieving the desired efficacy and safety of pharmaceutical products, making them indispensable in the development of effective and patient-friendly medications.

Insect-derived excipients are an emerging area of interest in the field of pharmaceutical sciences, reflecting a novel approach to leveraging natural resources for drug formulation. Insects, being rich in various biomolecules, offer a unique source of excipients with potential advantages in drug delivery and formulation. These excipients are derived from various insect parts, such as their chitinous exoskeletons or body fluids, and can be processed to extract valuable compounds. [3]

One of the primary components extracted from insects is chitin, which can be deacetylated to produce chitosan. Chitosan is notable for its biocompatibility, biodegradability, and its ability to form gels and nanoparticles, making it an excellent candidate for drug delivery systems. Additionally, insect-derived waxes and oils are used for their emollient and stabilizing properties, beneficial in topical formulations and controlled-release systems. [4]

The utilization of insect-derived excipients offers several potential benefits. They are often biodegradable and biocompatible, which aligns with the growing emphasis on sustainable and environmentally friendly pharmaceutical practices. Moreover, insects are abundant and have a rapid reproduction rate, providing a renewable resource that could alleviate some of the resource constraints faced by conventional excipient sources.

As research progresses, insect-derived excipients hold promise for expanding the range of available materials in drug formulation, potentially leading to innovative drug delivery systems with enhanced performance and reduced environmental impact.

This review aims to explore the role of insect-derived excipients in pharmaceutical formulations, focusing on their properties, applications, and benefits.

Types of insect-derived excipients

1. Chitin and Chitosan

Chitin and chitosan are primarily sourced from the exoskeletons of insects, such as beetles and cockroaches, as well as from crustaceans like shrimp and crabs. These biopolymers are extracted from the hard outer shells of these organisms. [5]

Chitin is a natural polymer consisting of N-acetylglucosamine units linked by β(1→4) glycosidic bonds. When chitin is deacetylated, it forms chitosan, which is soluble in acidic conditions due to its amino groups. Both chitin and chitosan are characterized by their high molecular weight, crystallinity, and the presence of functional groups that confer biocompatibility and biodegradability. [6]

Chitin and chitosan are utilized in various pharmaceutical applications due to their unique properties. They are used in drug delivery systems as carriers for controlled-release formulations, enhancing the stability and bioavailability of drugs. Additionally, chitosan is employed in wound dressings due to its antimicrobial properties and ability to promote wound healing. These applications leverage the biocompatibility and versatility of chitin and chitosan to improve therapeutic outcomes.

2. Insect Proteins and Peptides

Insect proteins include silk proteins and haemolymph proteins. Silk proteins, produced by insects like silkworms, are known for their strength and elasticity, while haemolymph proteins, found in the circulatory fluid of insects, are involved in immune responses and nutrient transport. [7] Insect silk proteins possess exceptional tensile strength and biocompatibility, making them valuable in biomedical applications such as tissue engineering and sutures. Haemolymph proteins, with their antimicrobial and immunomodulatory properties, are used in drug formulations to enhance immune responses and as carriers in drug delivery systems. Both types of insect-derived proteins offer unique functionalities that are leveraged to improve pharmaceutical and medical products. [8]

Fig 1: Silkworm

3. Natural dyes obtained from insects-Cochineal and lac

Natural dyes derived from insects have been used for centuries in textiles, food, cosmetics, and art. Two prominent examples of such dyes are cochineal and lac, which are extracted from different insect species and have been highly valued for their vibrant colours and unique properties. [9] Cochineal dye is derived from the *Dactylopius coccus*, a scale insect native to Latin America, primarily found on prickly pear cacti (*Opuntia* species). The main pigment in the cochineal is carmine or carminic acid, producing a rich red or crimson hue. Cochineal insects are harvested, dried, and then crushed to extract the carminic acid. This substance can be used to create various shades of red depending on the mordant used. Cochineal dye has been widely used in dyeing wool, silk, and cotton, producing shades ranging from bright red to deep purple as well as a natural colourant (E120) in food, beverages, and cosmetic products such as lipsticks and blushes. Cochineal is considered more environmentally friendly than synthetic dyes due to its biodegradability and natural origin. [10]

Lac dye is obtained from the secretions of *Kerria lacca*, a species of scale insect found in India and Southeast Asia. This insect produces a resin (lac), which is processed to obtain the dye. Lac dye yields a red to reddish-brown colour, although it is less vibrant than cochineal. The lac resin, which is harvested from trees where the insects live, is processed to extract the dye. The extracted resin is dissolved in water, and the dye is separated from the solid components. Lac dye has been historically used as a food additive and in cosmetics but is now less commonly used in these applications compared to cochineal. Lac resin is also the primary source for shellac, a natural varnish. The lac insect secretes a resinous substance to protect itself as it forms cocoons. This resin hardens on the branches of host trees, which is then harvested by humans to produce shellac. Shellac is FDA-approved as a food glaze (E904) and is used in candies, fruits, and pills to provide a glossy sheen and to protect the product. It serves as a coating for pills to mask unpleasant tastes and odours and to provide moisture resistance. Shellac is used in nail polish and hair sprays, contributing to gloss and hardness. [11]

Fig 2: Cochineal insect and Lac insect

4. Insect Oils

Insects are not only valuable for their proteins and peptides but also for their oils and waxes, which have diverse applications across industries such as cosmetics, pharmaceuticals, food, and even biotechnological processes. Insect oils and waxes are unique in their composition, offering sustainable and eco-friendly alternatives to traditional sources of oils and waxes.

Insect oils are rich in essential fatty acids, including omega-3 and omega-6, and have nutritional and industrial uses. They are extracted from various insect species, typically by mechanical pressing or solvent extraction. Insect oils typically contain SFAs such as palmitic acid. Oleic acid is commonly found in insect oils, contributing to their health benefits. Insect oils are also a source of omega-3 (α-linolenic acid) and omega-6 (linoleic acid) fatty acids, which are essential for human nutrition. [12] Common insect oils include Black Soldier Fly Oil **(**BSF**)** (*Hermetia illucens*). BSF larvae oil is rich in lauric acid, making it useful for antimicrobial applications in cosmetics and pharmaceuticals. It is also used in animal feed. [13] Another insect oil is Mealworm Oil (*Tenebrio molitor*), known for its high content of unsaturated fatty acids, mealworm oil has potential applications in the food and cosmetic industries. [14] Cricket Oil (*Acheta domesticus*) contains both MUFAs and PUFAs, making it beneficial for heart health. It can be used in nutritional supplements and food products. [15] Insect oils are used in moisturizers, soaps, and creams due to their hydrating and skin-soothing properties. The high content of fatty acids makes them suitable for skincare products. With a favourable fatty acid profile, insect oils can be incorporated into functional foods and dietary supplements to promote cardiovascular health. Insect oils, particularly from BSF, are increasingly used in animal feed due to their antimicrobial properties and high nutrient content.

Fig 3: Black Soldier Fly, Mealworm, and Cricket

5. Insect Waxes

Insect waxes are natural, biodegradable substances secreted by certain insect species. They have a wide range of applications in industries such as cosmetics, pharmaceuticals, and food due to their unique chemical properties. Beeswax (*Apis mellifera*) is the most well-known insect wax, beeswax is secreted by honeybees and is composed primarily of esters, fatty acids, and hydrocarbons. [16] Shellac Wax (*Kerria lacca*) is resinous secretion from the lac bug, shellac wax is used in coatings and polishes. It has hydrophobic properties, making it useful in water-resistant applications. [17] Cochineal Wax (*Dactylopius coccus*), derived from the cochineal insect, this wax is used in cosmetics, particularly as a colouring agent. Insect waxes are rich in hydrocarbons, making them highly stable and resistant to degradation. The ester content gives insect waxes their characteristic texture and emollient properties, making them ideal for cosmetics and topical applications. Waxes may also contain long-chain alcohols, which contribute to their water-resistant and protective qualities.

Insect waxes, particularly beeswax, are used in lip balms, lotions, and creams as emulsifiers and thickening agents. They help to lock in moisture and provide a protective barrier on the skin. Waxes are used as excipients in the formulation of ointments, tablets, and capsules. Beeswax, for example, is used as a binding agent in pill production. Beeswax is often used as a coating for fruits and cheese to preserve freshness. It is also a key ingredient in the production of food-grade polish and edible wrappers. Due to their biodegradable nature, insect waxes are used in the creation of eco-friendly packaging materials and coatings.

6. Insect-Produced Enzymes

Insects are valuable sources of enzymes with applications in biotechnology, agriculture, pharmaceuticals, and food production. Insect-produced enzymes often have unique properties, making them ideal for specific tasks that traditional plant, animal, or microbial enzymes struggle to perform. Digestive enzymes like proteases, lipases, and amylases are highly efficient, adaptable, and useful across various industries. Proteases such as trypsin and chymotrypsin aid in protein hydrolysis, while lipases break down fats, making them suitable for food processing and bioremediation. Amylases from insects can be applied in biofuel and starch processing. [18]

Insects possess detoxifying enzymes that help them break down harmful chemicals in their environment, including pesticides and toxic plant compounds. These enzymes are of interest for applications in bioremediation and pesticide detoxification. Cytochrome P450 Monooxygenases enzymes play a role in the detoxification of xenobiotics (foreign compounds) and are being studied for their use in degrading environmental pollutants. [19] Glutathione S-Transferases **(**GSTs**)** help insects neutralize harmful chemicals and oxidative stress. They have potential in pharmaceutical applications for detoxifying drugs and chemicals. Insects like silkworms produce enzymes that aid in the synthesis and degradation of silk. These enzymes have potential applications in the textile, biomedical, and cosmetic industries. Fibroinase enzyme is involved in the breakdown of silk fibroin, a protein that makes up the silk fibres. Fibroinase is being explored for use in silk processing and textile manufacturing. [20] Sericinase breaks down sericin, the protein surrounding silk fibres, and is used in cosmetics for its moisturizing benefits. Insect enzymes, known for their unique catalytic abilities, are valuable in biotechnology due to their resilience in extreme conditions. Detoxifying enzymes like cytochrome P450s and GSTs are being explored for breaking down pollutants and pesticides, providing eco-friendly solutions. Insect enzymes convert organic materials into biofuels and chemicals, and are also used in drug development for peptide synthesis and protein-based therapies. Chitinase, which degrades chitin, has applications in antifungal drugs and exfoliating cosmetics, while amylase and lipase enzymes are useful in food processing for products like maltose syrup, dairy, and fermented foods. [21]

Extraction and processing techniques

1. Collection and Preparation of Insect Material

The collection and preparation of insect material for extracting valuable compounds such as proteins, oils, waxes, dyes, or enzymes require careful selection of species, proper harvesting techniques, and preparation methods. The following steps outline the key procedures:

a) Selection of Insect Species
b) Methods for Harvesting
c) Preparation of Insect Material
d) Storage of Prepared Insect Material

a. Selection of Insect Species

The choice of insect species depends on the desired product, as different insects yield specific compounds:

- Cochineal (Dactylopius coccus) for carmine dye.
- Lac insects (Kerria lacca) for lac and shellac production.
- Honeybees (Apis mellifera) for beeswax.
- Silkworms (Bombyx mori) for silk and silk-related enzymes.
- Mealworms (Tenebrio molitor) and crickets for proteins and oils.

The insect species chosen must be abundant, ethically sourced, and environmentally sustainable.

b. Methods for Harvesting

i. Wild Collection: Insects can be harvested directly from their natural environments, particularly in the case of cochineal or lac insects. This method requires the identification of insect populations and the use of appropriate tools to ensure minimal disturbance to ecosystems: Cochineal insects are typically brushed off from their host cactus plants and dried in the sun before processing. Lac insects are collected from the twigs they inhabit and processed for resin extraction. [22]

ii. Insect Farming: Raising insects on farms offers a more controlled and sustainable way to gather material. This approach is increasingly being used for insects like crickets, mealworms, and silkworms. Silkworms are reared on mulberry leaves and collected once they form cocoons for silk production. Mealworms and other edible insects are reared in controlled environments to ensure their safety for consumption and further processing. Insect farming helps maintain a stable supply of insect material while reducing pressure on wild populations.

c. Preparation of Insect Material

i. Drying and Preservation: Drying is a crucial step in preserving insect material to prevent spoilage or degradation. Depending on the desired compound, insects are dried using the following methods:

- Sun drying: Traditional and cost-effective but may lead to quality variation.
- Oven drying: Provides controlled conditions and uniform drying, typically at temperatures between 40-60°C to preserve sensitive compounds.
- Freeze drying (lyophilization): Preserves biological activity and structural integrity of proteins, enzymes, and other heat-sensitive compounds.

ii. Grinding and Pulverization: Once dried, insects are often ground into a fine powder to facilitate the extraction of compounds like proteins, lipids, and enzymes. This powder is easier to process and can be stored for longer periods without significant loss of quality.

- For dyes like carmine, ground cochineal insects are processed using water or chemical solutions to extract the colouring agent.
- For proteins and oils, ground insect material is subjected to extraction techniques such as solvent extraction or pressing.

iii. Extraction Techniques

- Solvent Extraction: Organic solvents like ethanol or hexane are used to extract oils, lipids, and dyes from ground insect material.
- Water Extraction: Used for hydrophilic substances like proteins and water-soluble dyes. The insect powder is mixed with water, and the solution is filtered and concentrated.
- Mechanical Pressing: Suitable for oils, waxes, and resins. Pressing methods such as cold-press or hydraulic press are used to extract oils from insects like mealworms and beeswax from honeycombs.

iv. Purification and Filtration

Post-extraction, the raw extracts often undergo purification to separate the desired compound from impurities. Techniques include Filtration which is used to remove solid residues from liquid extracts. Centrifugation separates compounds based on density and chromatography is used for separating specific enzymes, proteins, or pigments.

d. Storage of Prepared Insect Material

The extracted and purified compounds must be stored in appropriate conditions to maintain their stability:

- **Proteins and enzymes**: Stored in refrigerated conditions (4°C) or frozen at −20°C to preserve their activity.
- **Dyes and pigments**: Stored in airtight containers to prevent oxidation and degradation.
- **Oils and waxes**: Stored in cool, dark places to prevent rancidity and loss of quality.

Applications in pharmaceutical formulations

Insects provide a variety of natural materials that can be used as excipients in pharmaceutical formulations. These materials exhibit unique properties that make them valuable in drug delivery, wound healing, topical formulations, and stability studies. Below are the major areas of application.

a. Controlled Release Formulations

Insect-derived materials, particularly those containing proteins, lipids, and polysaccharides, can be utilized in controlled-release drug delivery systems. These systems are designed to release the active pharmaceutical ingredient (API) over a prolonged period, improving therapeutic efficacy and patient compliance. Chitosan, a biopolymer derived from the exoskeletons of insects such as crustaceans and some insect species, has been explored for its ability to form hydrogels, films, and matrices that control drug release. Its biodegradability, low toxicity, and mucoadhesive properties make it suitable for sustained-release formulations, particularly in oral and topical routes. [23]

b. Nanoparticles and Microspheres

Nanoparticles and microspheres are promising carriers for targeted drug delivery, and insect-derived materials offer biocompatibility and functionality in these applications. Insect proteins and chitosan have been widely studied for nanoparticle formulation due to their ease of modification and favourable release profiles. Silk fibroin, derived from silkworms, can be used to create nanoparticles for drug delivery. Silk-based nanoparticles offer a biocompatible, biodegradable matrix that can encapsulate various drugs, enhancing their bioavailability and stability. Chitosan nanoparticles have also been widely explored as drug carriers due to their ability to enhance drug absorption, protect drugs from degradation, and release them at a controlled rate.

c. Wound Healing and Tissue Engineering

Insect-derived materials like chitosan and silk fibroin are gaining attention for wound healing and tissue engineering due to their antibacterial, haemostatic, and regenerative properties. Chitosan, sourced from insect or crustacean exoskeletons, promotes faster wound closure and stimulates tissue formation, making it effective for burn wounds and ulcers. Silk fibroin supports cell attachment and proliferation, making it ideal for skin regeneration scaffolds. Additionally, proteins like sericin from silkworms show promise in tissue regeneration due to their biocompatibility and support for cell growth.

d. Topical and Transdermal Systems

Insect-derived excipients, especially those that are biocompatible and biodegradable, offer unique advantages in topical and transdermal drug delivery systems. As a film-forming agent, chitosan creates a protective barrier on the skin, which enhances drug penetration through the skin layers. Its antimicrobial properties make it particularly useful in topical formulations for treating infections and wounds. Commonly used as a thickening agent in ointments, beeswax provides an occlusive layer that helps in the controlled release of APIs in topical formulations. However, sourcing and standardizing natural insect-derived excipients like beeswax pose challenges in consistency and purity.

Challenges

While insect-derived materials offer promising benefits for pharmaceutical applications, several challenges must be addressed to fully realize their potential. These challenges span regulatory, technical, ethical, and consumer acceptance aspects. Insect-derived materials in pharmaceuticals offer promising benefits, but several challenges must be addressed. Variability in raw materials, lack of standardized extraction methods, and contamination risks complicate quality control. Regulatory frameworks are limited, and issues like allergenicity, immunogenicity, and consumer acceptance pose additional hurdles. Scalability, supply consistency, and production costs also present difficulties, while ethical concerns related to insect farming and environmental sustainability require attention. Stability and compatibility with other excipients can affect formulation success. Overcoming these challenges requires rigorous research, regulatory collaboration, and consumer education to unlock the full potential of insect-derived materials.

Regulatory and ethical considerations

1. Regulatory Framework

Current regulations governing the use of insect-derived excipients are still evolving. Most countries lack comprehensive guidelines for insect-based materials in pharmaceuticals. Regulatory agencies like the FDA and EMA may require rigorous safety assessments, allergen testing, and manufacturing standards to ensure consistency, safety, and quality. The absence of clear categorization for insect-derived excipients complicates their approval and commercialization, emphasizing the need for more robust and specialized regulatory frameworks. [24]

2. Ethical and Environmental Issues

The use of insects in pharmaceuticals raises ethical concerns, including the welfare of insects during mass production and farming practices. Consumer acceptance of insect-based products in healthcare is another potential challenge. Additionally, the environmental impact of large-scale insect farming must be considered, particularly in terms of resource consumption, waste management, and biodiversity preservation. However, insects could offer a more sustainable alternative to traditional sources of excipients, with lower ecological footprints if managed responsibly. Balancing ethical and environmental considerations is crucial for the future of insect-derived materials in pharmaceuticals. [25]

Future directions and research opportunities

1. Innovations in Insect-Derived Excipients

Emerging technologies in biotechnology and materials science are opening new pathways for insect-derived excipients. Advances in nanotechnology, bioengineering, and extraction methods are enhancing the functional properties of insect materials, making them more suitable for pharmaceutical applications like targeted drug delivery, sustained-release formulations, and biodegradable scaffolds in tissue engineering. The integration of these innovations could greatly expand the utility of insect-derived excipients, offering novel solutions for challenges in formulation stability, bioavailability, and drug efficacy.

2. Potential for New Discoveries

The potential for further research in insect-based excipients is vast. Key areas include discovering new bioactive compounds from insect sources, exploring underutilized insect species, and developing scalable production techniques. Future research could also focus on improving the safety, allergenic profiles, and consumer acceptance of these materials. Additionally, interdisciplinary studies on the ecological and economic impact of insect farming could support more sustainable practices, paving the way for broader commercial use in pharmaceuticals.

Conclusion

Insect-derived excipients offer a promising alternative to conventional materials in pharmaceutical formulations. Key points discussed include their potential applications in drug delivery systems, wound healing, and tissue engineering, as well as their compatibility and stability in various formulations. While there are challenges related to regulatory, ethical, and environmental considerations, the growing interest in sustainability and innovative biotechnologies positions these materials as viable options for future drug development. Overall, the use of insect-derived excipients could revolutionize pharmaceutical formulations by providing more sustainable, biodegradable, and efficient alternatives. As research advances and regulatory frameworks evolve, insect-based excipients may become integral to the future of drug formulation, addressing both global resource limitations and the need for innovative delivery systems. Continued research and development are essential for unlocking their full potential.

Acknowledgement

The authors are thankful to Shreeshakti Shaikshanik Sanstha's Divine College of Pharmacy for providing the necessary support for writing this review.

Competing interests

The authors declare no conflicts of interest.

Ethical approval

Not Applicable

Funding

No funding

References

1. Gunjal V, Sonawane D, Ahire S, Jadhav P, Deore Y, Jadhav S, *et al*. A Review on Novel Excipients, International Journal of Pharmaceutical Sciences,2023:1(9):304-320. https://doi.org/10.5281/zenodo.8344687
2. Jadhav S, Patil D, Sonawane D. Formulation of Tablet of Ivermectin Co-Crystal for Enhancement of Solubility and Other Physical Properties. Journal of Pharmaceutical Negative Results,2023:14(1):513–520.
3. Weaver E, O'Hagan C, Lamprou D. The sustainability of emerging technologies for use in pharmaceutical manufacturing. Expert Opinion on Drug Delivery,2022:19(7):861–872. https://doi.org/10.1080/17425247.2022.2093857
4. Rinaudo M. Chitin and Chitosan: Properties and Applications. Progress in Polymer Science,2006:31:603-632. http://dx.doi.org/10.1016/j.progpolymsci.2006.06.001
5. Elieh-Ali-Komi D, Hamblin M R. Chitin and Chitosan: Production and Application of Versatile Biomedical Nanomaterials. International journal of advanced research,2016:4(3):411–427.
6. Kasaai MR. Various methods for determination of the degree of N-acetylation of chitin and chitosan: A review. J Agric Food Chem,2009:57(5):1667-76. https://doi.org/10.1021/jf803001m
7. Kundu B, Rajkhowa R, Kundu SC, Wang X. Silk fibroin biomaterials for tissue regenerations. Adv Drug Deliv Rev,2013:65(4):457-70. https://doi.org/10.1016/j.addr.2012.09.043
8. Kundu J, Poole-Warren LA, Martens P, Kundu SC. Silk fibroin/poly(vinyl alcohol) photocrosslinked hydrogels for delivery of macromolecular drugs. Acta Biomater,2012:8(5):1720-9. https://doi.org/10.1016/j.actbio.2012.01.004
9. Gupta VK. Fundamentals of natural dyes and its application on textile substrates. In: Samanta AK, Awwad NS, Algarni HM, editors. Chemistry and technology of natural and synthetic dyes and pigments. IntechOpen, 2020. https://doi.org/10.5772/intechopen.89964
10. Dapson RW. The history, chemistry and modes of action of carmine and related dyes. Biotechnic Histochem,2007:82(4):173-87.
11. Thombare N, Kumar S, Kumari U, Sakare P, Yogi RK, Prasad N, *et al*. Shellac as a multifunctional biopolymer: A review on properties, applications and future potential. Int J Biol Macromol. 2022;215:203-23. https://doi.org/10.1016/j.ijbiomac.2022.06.090
12. Kolobe SD, Manyelo TG, Malematja E, Sebola NA, Mabelebele M. Fats and major fatty acids present in edible insects utilised as food and livestock feed. Vet Anim Sci,2023:22:100312. https://doi.org/10.1016/j.vas.2023.100312
13. Suryati T, Julaeha E, Farabi K, Ambarsari H, Hidayat AT. Lauric acid from the black soldier fly (Hermetia illucens) and its potential applications. Sustainability,2023:15:10383. https://doi.org/10.3390/su151310383
14. Son YJ, Choi SY, Hwang IK, Nho CW, Kim SH. Could defatted mealworm (Tenebrio molitor) and mealworm oil be used as food ingredients? Foods,2020:9(1):40. https://doi.org/10.3390/foods9010040
15. Orkusz A, Dymińska L, Banaś K, Harasym J. Chemical and nutritional fat profile of Acheta domesticus, Gryllus bimaculatus, Tenebrio molitor and Rhynchophorus ferrugineus. Foods,2024:13(1):32. https://doi.org/10.3390/foods13010032
16. Papa G, Maier R, Durazzo A, Lucarini M, Karabagias IK, Plutino M, *et al*. The honey bee Apis mellifera: An insect at the interface between human and ecosystem health. Biology,2022:11(2):233. https://doi.org/10.3390/biology11020233
17. Ebenebe C, Okweche S, Okore O, Okpoko V, Amobi M, Eze J, *et al*. Arthropods in cosmetics, pharmaceuticals and medicine: A review. In: Arthropods - Are they beneficial for mankind? IntechOpen, 2021. https://doi.org/10.5772/intechopen.96159
18. Mika N, Zorn H, Rühl M. Insect-derived enzymes: A treasure for industrial biotechnology and food biotechnology. Adv Biochem Eng Biotechnol,2013:136:1-17. https://doi.org/10.1007/10_2013_204
19. Nauen R, Bass C, Feyereisen R, Vontas J. The role of cytochrome P450s in insect toxicology and resistance. Annu Rev Entomol,2022:67(1):105-24. https://doi.org/10.1146/annurev-ento-070621-061328
20. Guo P, Wang Z, Wang Q. Fibroinase and its physiological inhibitors involved in the regulation of

silk gland development in the silkworm, Bombyx mori. Insect Mol Biol Biochem,2019:106:19-27. https://doi.org/10.1016/j.ibmb.2019.01.003

21. Santana CC, Barbosa LA, Júnior IDB, Nascimento TGD, Dornelas CB, Grillo LAM. Lipase activity in the larval midgut of Rhynchophorus palmarum: Biochemical characterization and the effects of reducing agents. Insects,2017:8(3):100. https://doi.org/10.3390/insects8030100
22. Liceaga AM. Processing insects for use in the food and feed industry. Curr Opin Insect Sci,2021:48:32-6. https://doi.org/10.1016/j.cois.2021.08.002
23. Shariatinia Z. Pharmaceutical applications of chitosan. Adv Colloid Interface Sci,2019:263:131-94. https://doi.org/10.1016/j.cis.2018.11.008
24. Morrison Foerster. Alternative Protein—A comparison of the regulation of insect protein as food and feed. [Internet]. Available from: https://www.mofo.com/resources/insights/211028-alternative-protein-industry-series. Accessed September 12, 2024.
25. Delvendahl N, Rumpold BA, Langen N. Edible insects as food–Insect welfare and ethical aspects from a consumer perspective. Insects,2022:13(2):121. https://doi.org/10.3390/insects13020121