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Royal Jelly: A Brief Review of Nano and Micro Carriers and Potential Applications

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Abstract

Royal Jelly, a bioactive substance known for its rich composition of proteins, lipids, and minerals, possesses significant antioxidant, antimicrobial, and anti-inflammatory properties. However, its instability in the presence of light, heat, and oxygen limits its practical applications. Recent advancements in nanotechnology, mainly using nanoparticles combined with microencapsulation techniques, have shown promise in enhancing royal jelly's stability, bioavailability, and controlled release. This brief review explores encapsulated royal jelly's biological effects and potential applications across various fields, including pharmaceuticals, cosmetics, and food technology. By integrating royal jelly with nanoparticles, researchers uncover novel approaches to maximize its therapeutic potential, improving efficacy while reducing side effects. This review highlights the key findings from global research, focusing on the synergies between royal jelly and nanoparticles, and discusses the prospects of this innovative combination in biotechnological applications.

Keywords: Biocompatibility, encapsulation, ionic gelification, nanoparticles, Royal Jelly

INTRODUCTION

Royal Jelly, a remarkable substance produced by honeybees, contains a complex mixture of proteins, lipids, and minerals that confer numerous beneficial properties, including potent antioxidant, antimicrobial, and anti-inflammatory activities [1, 2]. Despite its rich nutritional composition and unique therapeutic potential, royal jelly's practical applications and long-term efficacy are significantly hindered by the instability of its bioactive components. Factors, such as exposure to light, temperature fluctuations, and oxygen can lead to degradation, limiting its effectiveness in various applications. In this context, microencapsulation emerges as a promising and viable solution to these challenges, providing a protective barrier that safeguards royal jelly from detrimental environmental factors [3]. Furthermore, microencapsulation enables the controlled release of its bioactive compounds in targeted environments, enhancing their therapeutic effects [4].

The importance of encapsulating royal jelly cannot be overstated, as it significantly enhances its stability and bioavailability. Carriers, or delivery systems, are essential tools that facilitate the encapsulation and transport of active substances across diverse industries, including pharmaceuticals, food, and cosmetics. These systems can take various forms, such as liposomes, nanoemulsions, microparticles, and nanocapsules, each offering distinct advantages tailored to specific

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applications. For instance, liposomes are particularly effective in improving the delivery of lipophilic drugs, while nanoemulsions enhance the solubility of hydrophobic compounds. The choice of carrier type is influenced by factors, such as the nature of the active substance, desired administration routes, and controlled release requirements.

The potential applications of encapsulated royal jelly are extensive, encompassing the pharmaceutical sector, where it can be utilized in dietary supplements and functional foods to promote health; the cosmetics industry, where its antioxidant and anti-inflammatory properties can be harnessed for skincare formulations; and the food industry, where it can be incorporated into nutraceuticals to enhance overall well-being [5, 6].

Moreover, incorporating nanoparticles into microencapsulated royal jelly presents a novel approach to expand its applications further. This synergy improves the efficacy of treatments and reduces the side effects typically associated with conventional therapies [6, 7].

This brief review explores the interactions between royal jelly and nanoparticles, highlighting how this combination can optimize the functional properties of royal jelly. By comprehensively reviewing the literature on the biological effects of royal jelly and its association with nanoparticles, analyzing the efficacy of microencapsulation methods, and discussing future perspectives for the application of this innovative combination across various technological sectors, we seek to underscore the relevance of encapsulated royal jelly containing nanoparticles for enhancing individual health and well-being.

METHODOLOGY

This study aimed to compile a brief literature review analyzing the biological effects and applications of royal jelly combined with nanoparticles. The research was primarily conducted using PubMed, ScienceDirect, Google Scholar, and SciELO databases. The 56 articles were pre-selected based on their alignment with the established criteria. Figure 1 illustrates the four steps in selecting the articles from these databases, utilizing the following descriptors: Royal Jelly, Nanoparticles, Microencapsulation, Ionic Gelification, and Biocompatibility.

The inclusion criteria for this review encompassed studies focusing on microencapsulation using sodium alginate and investigations of royal jelly and its potential applications. Only articles published from 2020 onward were considered, as detailed in Table 1. Conversely, exclusion criteria were established to eliminate publications predating the specified base year, articles that utilized other bee-derived materials, and review papers.

Table 1. Exclusion and Inclusion Criteria of the Articles Found.

Exclusion	Inclusion
Before 2019	Higher than 2019
Articles that discuss other types of materials produced by bees	Articles that discuss royal jelly, its bioapplications, and microencapsulation
Review Articles	Research Articles
Keywords	Keywords

RESULTS AND DISCUSSION

Figure 2 shows the steps in stimulating bee colonies to produce royal jelly on a larger scale. This method ensures the production of substantial quantities while maintaining the quality of bioactive components critical for therapeutic and biotechnological applications. The figure highlights the precision required in this process, showcasing the intricate balance between natural bee behavior and human intervention to achieve sustainable production levels.

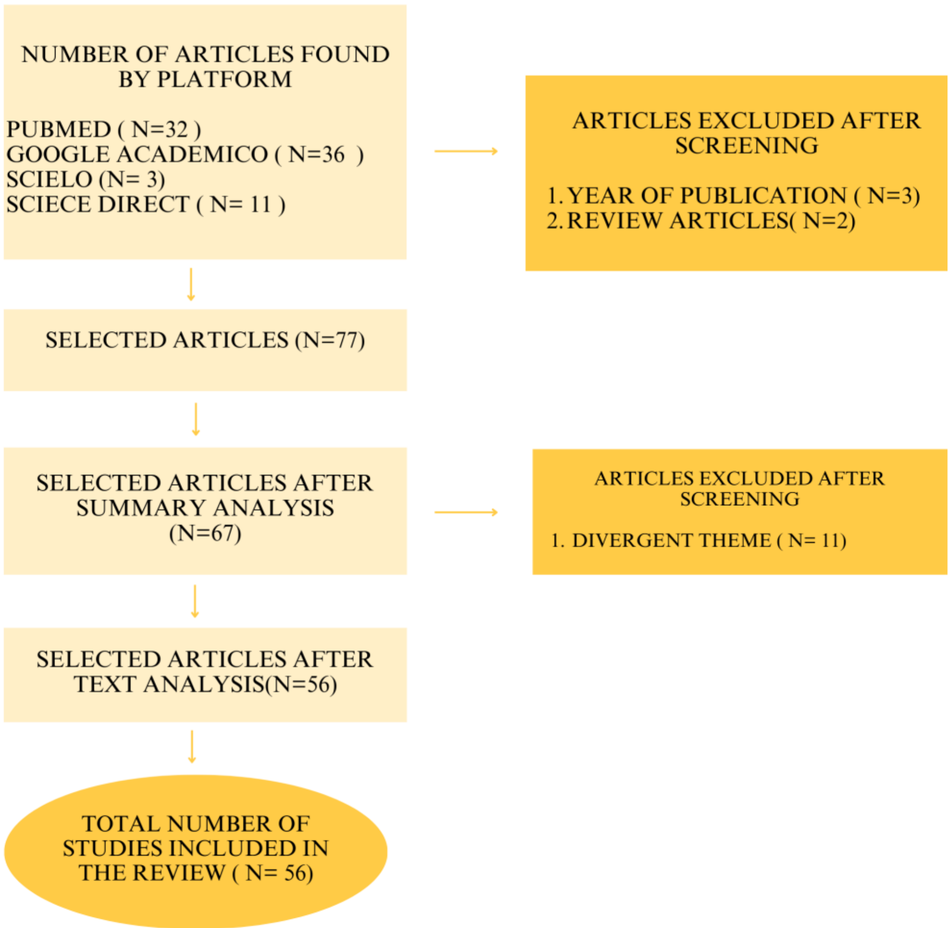

Figure 1. Schematization of the Selection of Articles.

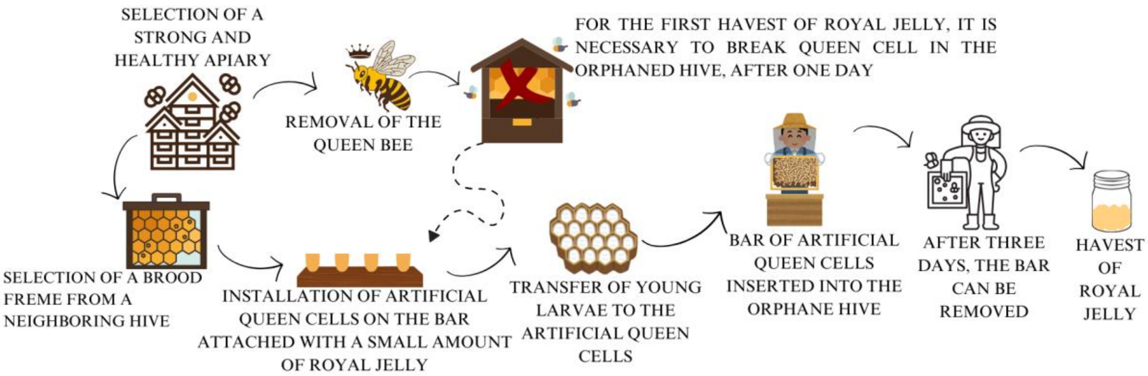

Figure 2. Simplified Representation of the Induction of Artificial Royal Jelly Production.

In the Global landscape of royal jelly production, several countries stand out for their significant contributions, each with unique factors influencing their production capabilities. Brazil, Canada, Russia, South Korea, Malaysia, Vietnam, China, Japan, and Australia have emerged as critical players in this industry, leveraging natural resources, climate, and technological advancements to meet the growing demand for royal jelly. Each country exhibits distinct strengths, which offer valuable insights into the dynamics of royal jelly production on a global scale.

China is the world's largest producer of royal jelly, dominating the global supply due to its extensive apicultural tradition, favorable climate, and large-scale production capabilities. Advanced beekeeping technologies and efficient operations enable China to lead in quality and quantity [8]. In contrast, Japan focuses on premium-quality production, emphasizing purity and bioactive content. Japan's technological advancements and stringent quality controls position it as a leader in high-value markets, especially in pharmaceuticals and cosmetics, where quality is prioritized over volume [9].

Other significant producers include Brazil, South Korea, Vietnam, and Malaysia. Brazil's rich biodiversity and tropical climate support year-round beekeeping, with growing interest in sustainable and organic practices [10]. South Korea specializes in high-quality royal jelly for dietary supplements and traditional medicine, supported by government investment in advanced techniques [11]. Vietnam and Malaysia leverage tropical climates and expanding apiculture investments to enhance production, but they face sustainability challenges [12, 13].

Canada and Australia produce smaller quantities but prioritize purity and sustainability. Canada benefits from clean environments, marketing its royal jelly for health supplements, while Australia's organic methods and biosecurity measures cater to premium markets [14, 15]. In comparison, China and Vietnam focus on large-scale exports, while Japan, Canada, and Australia prioritize quality and sustainability. South Korea excels in niche markets, while Brazil, Malaysia, and Vietnam are poised for growth in organic production.

Research has been notably active across several countries in nanotechnology, particularly in applying nanoparticles combined with royal jelly for microfabrication (Figure 3). The diversity of contributions reflects the global interest in advancing biotechnological applications of royal jelly, with each country bringing unique expertise and research perspectives. Brazil, Chile, Greece, Poland, Iran, Kenya, China, South Korea, Thailand, India, and Japan have made significant strides in exploring the synergies between royal jelly and nanoparticles, offering new insights into their combined potential in various industries.

Figure 3. Articles by Country.

Brazil and Chile are advancing research on nanoparticles and royal jelly, emphasizing sustainability and practical applications. Brazil leverages its biodiversity to create eco-friendly health supplements and cosmetics [10]. Meanwhile, Chile applies nanotechnology in agriculture and food sectors, improving bioactive compound preservation and delivery to enhance food quality and safety [16].

European nations, such as Greece and Poland, concentrate on pharmaceutical and biomedical applications, optimizing drug delivery systems and therapeutic agents by integrating royal jelly's antioxidant and anti-inflammatory properties [17, 18].

Similarly, Iran has emerged as a leader in medical uses, targeting wound healing, cancer therapy, and immune system support through innovative biomedical solutions [19–22]. Kenya contributes by focusing on sustainable agricultural applications, particularly enhancing royal jelly's shelf life under challenging storage conditions [23].

Asia dominates with significant contributions from China, South Korea, Japan, Thailand, and India. China leads globally, using its infrastructure in nanotechnology to push advances in medicine, cosmetics, and food technology [24–28]. South Korea and Japan emphasize cosmetics and pharmaceuticals, particularly anti-aging and therapeutic bioactive delivery [9, 29]. Thailand and India bridge traditional medicine with modern nanotechnology, amplifying royal jelly's properties for health and wellness products[13, 30, 31].

This collective global effort highlights the diverse applications of royal jelly and nanoparticles, spanning agriculture, cosmetics, and medicine. By integrating traditional knowledge with cutting-edge technology, these innovations promise significant impacts across industries, from food to healthcare.

Since ancient times, bee-derived products have been esteemed as natural remedies for various human and animal ailments [16]. Among these, royal jelly, a secretion of the mandibular and hypopharyngeal glands of young worker bees (Apis mellifera), plays a pivotal role in the nourishment of larvae during their initial three days and serves as the sole diet for queen bees throughout their development and adult life [9]. This gelatinous substance is a nutrient-rich aqueous emulsion composed predominantly of proteins, lipids, and sugars alongside bioactive compounds, such as flavonoids (e.g., apigenin, pinocembrin, quercetin, chrysin), polyphenols, phenolic acids, and vitamins. The concentration of these bioactive components varies based on factors like bee species, floral source, season, and production methods [17, 32], as illustrated in Figure 4.

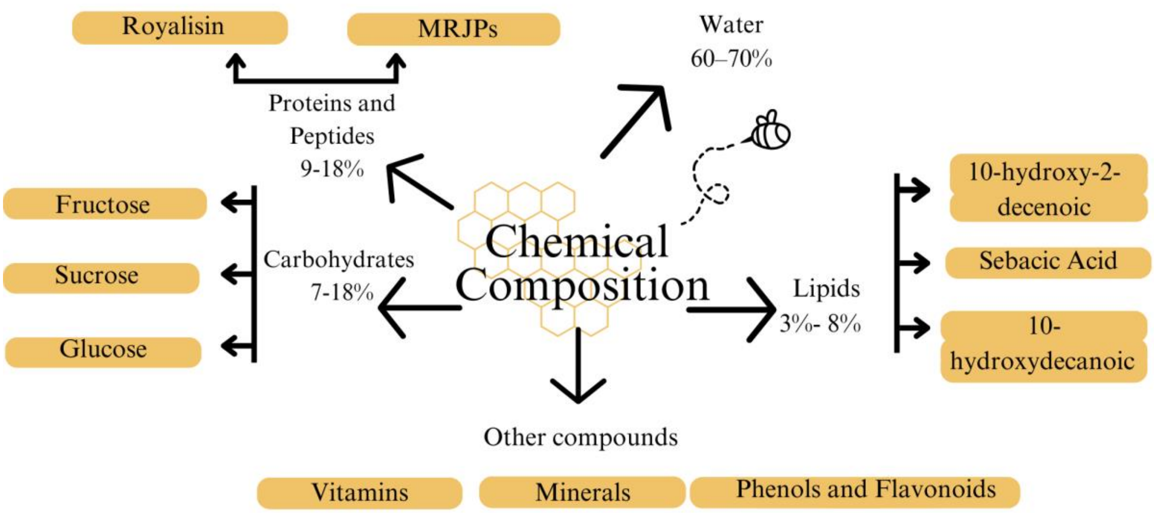

Figure 4. The Chemical Composition of Royal Jelly.

The sustained interest in royal jelly stems from its diverse pharmacological properties and the potential to promote health through its antioxidant, anti-inflammatory, antibacterial, and immunomodulatory effects [23, 24]. Flavonoids primarily contribute to its antioxidant capacity, neutralizing free radicals and mitigating oxidative cellular damage [12, 26].

Meanwhile, royalactin, an essential peptide, and lipids, such as fatty acids support its anti-inflammatory effects [33]. Furthermore, its antimicrobial properties are attributed to proteins like royalisin, which exhibit significant activity against Gram-positive microorganisms, and fatty acids like 10-hydroxy-2-decenoic acid (10-HDA), which combat pathogens, such as E. coli, S. aureus, and Pseudomonas aeruginosa. These attributes underline its relevance in food and pharmaceutical industries, driving innovations for functional products that support a healthier lifestyle [8, 21, 31, 34, 35].

Royal jelly exhibits a wide range of biological properties, supporting its utilization across diverse medicinal fields [36]. Figure 5 summarizes the diverse medicinal uses of royal jelly, emphasizing its role in modern cancer therapies through its biochemical properties and nanoparticle applications.

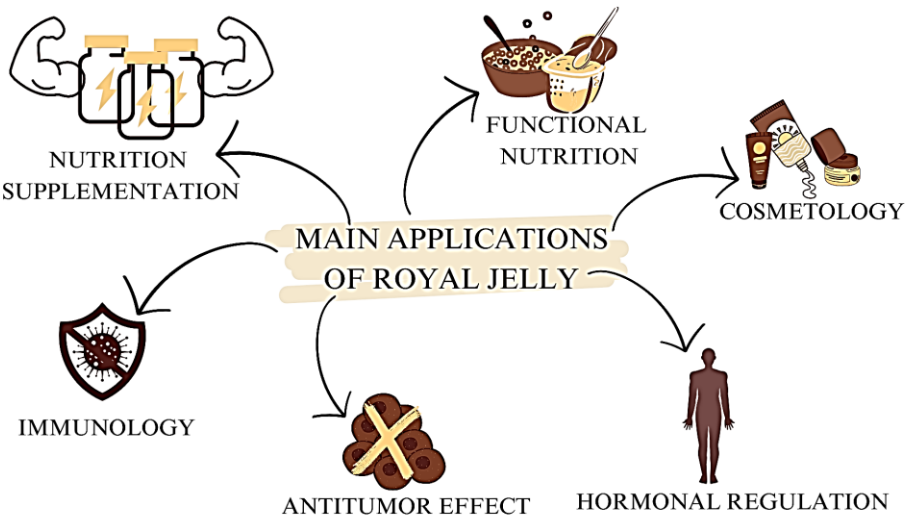

Figure 5. Application of Royal Jelly in Medicine.

One of its key components, 10-hydroxy-2-decenoic acid (10-HDA), shows promise in combating malignancies by inhibiting histone deacetylases (HDACs), enzymes associated with tumor progression [27, 37]. This inhibition promotes histone acetylation, leading to chromatin relaxation and improved accessibility of transcription factors to DNA, thereby enhancing gene expression. Such mechanisms make royal jelly an innovative and less invasive alternative for colorectal cancer therapies [20].

The use of carriers for encapsulating royal jelly is essential for preserving its bioactive compounds, ensuring their stability, bioavailability, and targeted release. Royal jelly is highly sensitive to environmental factors like light, temperature, and oxygen, which can degrade its valuable components, such as proteins, fatty acids, and vitamins [38, 39]. Encapsulation in nano- or microcarriers helps protect these compounds from degradation, preserving their potency during storage and use in functional foods, cosmetics, and pharmaceuticals. Additionally, encapsulation improves the bioavailability of royal jelly's bioactive compounds by enhancing their solubility and stability, thus ensuring better absorption in the body. This approach also facilitates the controlled release of the active ingredients, allowing for more precise therapeutic effects, reduced required dosages, and optimized outcomes in various applications [40–43].

Using nanoparticles and polymeric vesicles (both nano and micro) as carriers for royal jelly offers several key advantages in enhancing its stability, bioavailability, and controlled release. Royal jelly is highly sensitive to environmental conditions, such as light, temperature, and oxygen, which can cause degradation of its valuable bioactive compounds, including proteins, fatty acids, and vitamins [40, 43]. Encapsulating royal jelly in nano- or microcarriers protects these compounds from environmental stressors, maintaining their potency during storage, transportation, and application. This protection is essential for products like functional foods, cosmetics, and pharmaceuticals, where the stability and efficacy of royal jelly are crucial for their success.

Another significant benefit of using nano-and microcarriers for royal jelly encapsulation is the improvement in the bioavailability of its bioactive compounds. Many of these compounds, such as flavonoids and fatty acids, exhibit limited solubility and stability in aqueous environments, hindering their absorption and effectiveness in the body. By encapsulating royal jelly in lipid-based nanoparticles, polymeric microspheres, or metal-organic frameworks, the solubility and stability of these bioactive compounds are enhanced, facilitating their absorption and ensuring their efficient delivery to targeted tissues [44, 45]. This approach optimizes the therapeutic outcomes and reduces the required dosage, making treatments more effective and potentially minimizing side effects. The controlled release of royal jelly's bioactive components is another crucial advantage of nano- and microencapsulation. Utilizing these carriers makes it possible to achieve sustained or targeted release of active compounds, improving their action's precision and effectiveness. This is particularly beneficial in pharmaceutical, cosmetic, and nutraceutical applications, where a specific release profile is essential for maximizing efficacy and enhancing consumer satisfaction.

Overall, encapsulating royal jelly in nano- and microcarriers ensures that its bioactive compounds remain protected, bioavailable, and practical, offering a promising strategy for various applications [46, 48–50].

Table 2 provides a comprehensive overview of studies utilizing royal jelly in encapsulation systems and nanoparticle applications, highlighting their significant potential in enhancing bioactive stability, therapeutic efficacy, and functional properties. Royal jelly, a natural bioactive compound, is widely recognized for its nutritional and medicinal benefits. This table categorizes the research based on the type of vehicle, the presence or absence of nanoparticles, characterization methods employed, and their specific applications.

One study used alginate-pectin to encapsulate royal jelly without incorporating nanoparticles. The encapsulation process was characterized using scanning electron microscopy (SEM), high-performance liquid chromatography (HPLC), and surface characterization (SC). This system was designed to improve the stability of royal jelly products, ensuring their bioactive properties remain intact over time [51]. Alginate and pectin, as natural biopolymers, contribute to creating a biocompatible and biodegradable matrix suitable for food and pharmaceutical applications.

Another notable encapsulation system involves erythropoietin microcapsules containing royal jelly fabricated with poly(lactic-co-glycolic acid) (PLGA) nanoparticles. This formulation focused on optimizing the sustained release and enhancing clinical outcomes. Characterization techniques, such as DLS, HPLC, SEM, TEM, and differential scanning calorimetry (DSC) were utilized to analyze the encapsulation properties, demonstrating the potential for applications in biomedicine and controlled drug delivery systems [52, 54]. Another study explored silver nanoparticles with royal jelly for immunomodulatory supplementation, aiming to enhance immune system responses. However, the characterization methods in this context were not reported [55–57].

DLS – Dynamic Light Scattering; DSC – Differential Scanning Calorimetry; SEM – Scanning Electron Microscopy; FTIR – Fourier transform infrared spectroscopy; TEM – Transmission Electron Microscopy; TGA – Thermogravimetric Analysis; UV-Vis – UV-Vis spectroscopy; MIC – Minimum Inhibitory Concentration; MBC–Minimum Bactericidal Concentration; DRX – X-ray Diffraction; SC – sphericity coefficient.

Further, silver nanoparticles combined with royal jelly were also investigated as alternatives to traditional antibiotics, with properties characterized through techniques, such as UV-Vis spectroscopy, DLS, TEM, X-ray diffraction (XRD), and minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) assays. This approach aims to address the growing challenge of antibiotic resistance by leveraging the antimicrobial properties of silver nanoparticles and the natural bioactivity of royal jelly [58].

Silver nanoparticles have been extensively studied for their unique physicochemical properties when combined with royal jelly. In one application, silver nanoparticles were employed alongside royal jelly, and their properties were analyzed using techniques, such as UV-Vis spectroscopy, dynamic light scattering (DLS), transmission electron microscopy (TEM), Fourier-transform infrared spectroscopy (FTIR), and other methods. These nanoparticles demonstrated a notable anticancer effect, showcasing the potential of combining natural bioactive with advanced nanotechnology for therapeutic applications [59, 60].

Table 2. Types of Vehicle, Nanoparticles, Physics Characterizations, Applications.

Vehicle	**Bioactive**	**Nanoparticle**	**Characterization**	**Applications**	**Reference**
Alginate-Pectin	Royal Jelly	Absent	SEM, HPLC, SC	Stability of Royal Jell Products	51
Absent	Royal Jelly	Silver	UV-Vis, TEM, DLS, FTIR	Anticancer Effect	60
Absent	Royal Jelly	Silver	Absent	Immunomodulatory Supplementation	55
Absent	Royal Jelly	Silver	UV-Vis, DLS, TEM, XRD, MIC, MBC	Alternatives to traditional antibiotics	58
Erythropoietin microcapsules	Royal Jelly	PLGA	DLS,HPLC, SEM,TEM,DSC	Optimize sustained release and enhance clinical outcomes	52
Alginate	Royal Jelly	Absent	FTIR, SEM	Enhancing the therapeutic effects of royal jelly	56
Absent	Royal Jelly	Iron	FTIR, UV-VIS, DRX, SEM	Sun Protection Factor	61

Lastly, Royal Jelly was combined with iron nanoparticles to develop a formulation to improve the sun protection factor (SPF) in cosmetic applications. Characterization techniques, such as FTIR, UV-V is spectroscopy, X-ray diffraction (XRD), and SEM highlighted the formulation's potential to provide enhanced skin protection against UV radiation [61]. These studies collectively underscore the versatility of encapsulation systems and nanoparticle-based delivery mechanisms in enhancing royal jelly's stability, functionality, and therapeutic efficacy across various fields, including biomedicine, cosmetics, and food technology. Integrating advanced characterization techniques ensures precise control over these systems' structural and functional properties, paving the way for innovative applications in diverse industries.

Various characterization techniques play a crucial role in understanding the properties and behavior of nanoparticle-based carriers, particularly those incorporating bioactive compounds like royal jelly. Dynamic Light Scattering (DLS) is a vital method for measuring the size distribution and zeta potential of nanoparticles, providing insights into the stability and dispersion of nanoparticle formulations. DLS helps to evaluate how nanoparticles behave in solution, which is essential for optimizing their performance in drug delivery, nutritional supplements, and cosmetics. DLS confirms that nanoparticles remain stable and uniform for formulations with royal jelly, ensuring that the bioactive compounds are effectively encapsulated for targeted delivery and controlled release.

Differential Scanning Calorimetry (DSC) and Thermogravimetric Analysis (TGA) are essential thermal analysis techniques to assess nanoparticle-based carriers' physical properties and stability. DSC measures the heat flow associated with phase transitions in the material, providing valuable information about the crystallinity, melting point, and thermal stability of nanoparticles encapsulating Royal Jelly. This is crucial for understanding the release profile and stability of the bioactive compounds under different conditions. Conversely, TGA quantifies weight changes in response to temperature, allowing researchers to assess nanoparticle degradation patterns and composition. Together, DSC and TGA offer comprehensive thermal data, ensuring the formulation's stability and performance throughout its shelf life and during physiological conditions.

Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) are critical imaging techniques that provide detailed structural information about nanoparticles. SEM allows for the visualization of surface morphology and the overall shape of the particles, which is essential for understanding how the nanoparticles interact with their environment, such as during the encapsulation of royal jelly. TEM, with higher resolution, offers insights into the internal structure and distribution of the bioactive compound within the nanoparticle matrix. Fourier Transform Infrared Spectroscopy (FTIR) also identifies the molecular interactions between royal jelly and the nanoparticles by detecting characteristic bonds.

UV-Vis spectroscopy monitors the stability and absorption properties of the encapsulated bioactive compounds. Techniques like Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) assess the antimicrobial effectiveness of royal jelly-loaded nanoparticles, ensuring their potential as antimicrobial agents in medical and cosmetic applications. These techniques comprehensively understand nanoparticle carriers' properties, stability, and functionality in delivering bioactive compounds.

Encapsulated royal jelly's applications highlight its potential to enhance its stability, bioavailability, and therapeutic efficacy in several fields. The combination of natural products like royal jelly and advanced nanoparticle technology represents a promising approach to improving the performance of bioactive compounds, particularly in biomedicine, food, and cosmetic industries.

One significant application involves anticancer effects. Studies have shown that incorporating silver nanoparticles with royal jelly can enhance its anticancer properties. The microencapsulation of royal jelly within nanoparticle systems improves the delivery and stability of bioactive compounds, allowing for targeted therapeutic effects. This approach aims to overcome the challenges of traditional anticancer treatments by providing more efficient and selective action against cancer cells [60–62].

Another critical application is immunomodulatory supplementation, where silver nanoparticles are combined with royal jelly to enhance immune responses. Royal Jelly is well known for its immunomodulatory properties, and encapsulating it with nanoparticles ensures better bioavailability and prolonged therapeutic effects. This combination can serve as a natural alternative to synthetic immune boosters, offering a safer and more sustainable solution for immune system support [55, 57].

Royal jelly, in combination with silver nanoparticles, has also been investigated as a potential alternative to traditional antibiotics. With the growing challenge of antibiotic resistance, this formulation provides a promising solution. The silver nanoparticles exhibit strong antimicrobial properties, and when combined with royal jelly, they offer a potent alternative to conventional antibiotics, with applications in treating resistant infections [58, 59].

In the cosmetic industry, sun protection is another area where microencapsulated royal jelly with nanoparticles shows promise. Research has explored using iron nanoparticles in combination with royal jelly to improve cosmetic formulations' sun protection factor (SPF). This combination offers enhanced protection from harmful UV radiation and improves sunscreen products' overall stability and efficacy of sunscreen products [61]. Furthermore, the use of erythropoietin microcapsules containing royal jelly and PLGA nanoparticles has been studied for its ability to optimize sustained release and enhance clinical outcomes. This system provides a controlled release mechanism, allowing for sustained therapeutic effects, which is crucial for applications, such as hormone replacement therapy and controlled drug delivery [52].

Alginate-based microcapsules containing royal jelly have also been explored to enhance its therapeutic effects. The encapsulation in alginate ensures improved bioavailability and stability of royal jelly, making it more practical for use in therapeutic applications related to health and nutrition [56]. This system helps protect the bioactive compounds from degradation and facilitates their controlled release, enhancing their therapeutic benefits.

Lastly, the overall goal of these microencapsulated systems is to achieve sustained release of bioactive compounds, which improves clinical outcomes. The controlled release ensures that the bioactive ingredients are delivered effectively over an extended period, thus enhancing the overall efficacy of treatments and reducing side effects [55, 56].

The broad applicability of microencapsulated royal jelly with nanoparticles across various fields, from anticancer therapies to immunomodulatory supplementation, antibiotic alternatives, sun protection, and sustained drug release as shown in Figure 6. Combining royal jelly with advanced nanoparticle technologies provides a promising way to improve its stability, bioavailability, and therapeutic effects, making it an essential component of modern biomedicine and other related industries [62, 63].

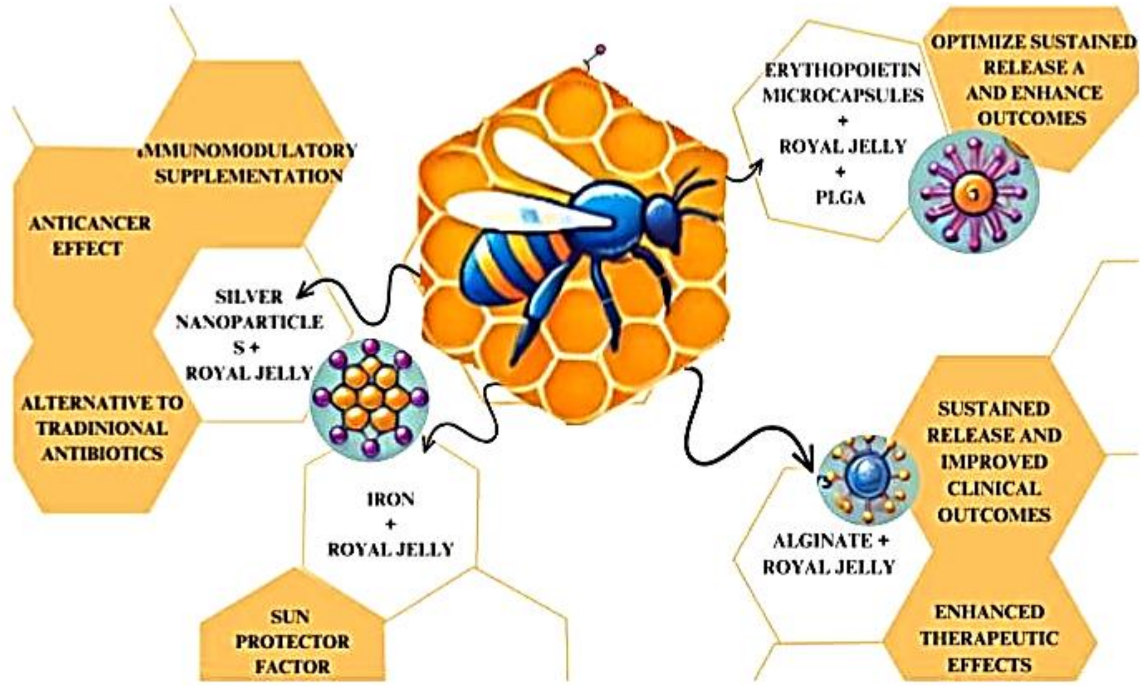

Figure 6. Types and Application of Royal Jelly Carriers.

Despite the increasing volume of literature on the individual benefits of nanoparticles and natural products, more studies must address the synergistic effects of nanoparticles combined with encapsulated natural products. Our research group has systematically explored this synergy and demonstrated that incorporating nanoparticles with naturally derived encapsulated compounds yields numerous advantages. These include enhanced bioavailability, improved stability, and targeted delivery of bioactive substances, collectively contributing to more effective therapeutic outcomes. Our findings underscore the potential of integrating nanoparticles with encapsulated natural products to significantly advance applications across various domains, including pharmacology, nutrition, and cosmetics, thereby emphasizing the necessity for further investigation in this promising area of research.

CONCLUSIONS

This review emphasizes the biotechnological potential of combining royal jelly with nanoparticles, highlighting their synergistic effects in enhancing bioactive properties, such as antioxidant, anti-inflammatory, and antimicrobial activities. The integration of nanoparticles improves the stability, bioavailability, and targeted delivery of royal jelly, making it a promising candidate for use in pharmaceuticals, dietary supplements, and cosmetics. Future research should focus on optimizing microencapsulation techniques, understanding the biocompatibility and mechanisms of these systems, and addressing long-term safety and regulatory challenges. This approach has the potential to lead to innovative health and wellness applications, offering safe and effective solutions for enhancing well-being.

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Data Availability Statement

Not applicable.

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Conflicts of Interest

The authors declare no conflict of interest.

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