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Review

Bacterial outer membrane vesicles: A scoping review on their dual roles in immunity and disease (2020–2025)

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Abstract: Background: Outer membrane vesicles (OMVs) from Gram-negative bacteria are dynamic nanoparticles that shape host–pathogen interactions, acting as both immunostimulatory and immunosuppressive agents critical for microbial pathogenesis and therapeutic innovation. Objective: This scoping review aimed to synthesize recent advancements (2020–2025) in understanding OMVs' roles in immune modulation, pathogenesis, and microbiota-immune crosstalk, as well as their potential as vaccine platforms and drug delivery systems. Methods: Relevant literature was identified through searches in PubMed, Google Scholar, and Web of Science, targeting peer-reviewed studies from 2020 to 2025. Approximately 80 were selected based on their relevance to OMV biogenesis, immune interactions, and applications in infectious diseases and cancer. Results: OMVs activate proinflammatory pathways via pathogen-associated molecular patterns, contributing to diseases like inflammatory bowel disease and sepsis, while commensal OMVs (e.g., from *Bacteroides fragilis*) promote tolerogenic immunity and gut homeostasis. Diverse uptake mechanisms enable targeted delivery of virulence or regulatory factors. OMVs enhance microbiota-immune crosstalk, strengthening epithelial barriers and modulating immunity. Therapeutically, bioengineered OMVs show promise in vaccines and personalized medicine, though scalability, heterogeneity, and toxicity pose challenges. Conclusion: OMVs are versatile tools bridging microbiology and immunology, with significant therapeutic potential. This review's novelty lies in its exclusive focus on Gram-negative OMVs, integrating 2020–2025

advances to address gaps in microbiota-driven immunity and bioengineered therapeutics, guiding future research in vaccine development and clinical translation.

Keywords: outer membrane vesicles (OMVs); host immunity; vaccine platforms; proinflammatory response

1. Introduction

Outer membrane vesicles (OMVs) are nanoscale, spherical structures (20–350 nm) secreted by Gram-negative bacteria, encapsulating a diverse cargo of lipopolysaccharides (LPS), outer membrane proteins (OMPs), lipids, RNA, and DNA [1]. These vesicles serve as critical mediators of intercellular communication, shaping host–pathogen interactions and providing insights into bacterial pathogenesis and immune modulation [2]. The theoretical framework of OMVs is grounded in their dual functionality as both immunostimulatory and immunosuppressive agents, driven by their molecular composition and biogenesis mechanisms [3]. Pathogenic OMVs, enriched with pathogen-associated molecular patterns (PAMPs) such as LPS and peptidoglycan, engage pattern recognition receptors (PRRs) like Toll-like receptors (TLR2 and TLR4) to activate proinflammatory pathways, contributing to diseases such as inflammatory bowel disease (IBD) and sepsis [4]. In contrast, OMVs from commensal bacteria, such as *Bacteroides fragilis*, deliver regulatory molecules, including polysaccharide A (PSA) or small RNAs, which promote the differentiation of regulatory T cells (Tregs) and gut homeostasis [3]. This balance is maintained by various uptake mechanisms, such as endocytosis and membrane fusion, which allow for the targeted delivery of either virulence or tolerogenic factors to host cells [4]. The primary aim of this review is to synthesize recent advancements (2020–2025) in understanding the multifaceted roles of Gram-negative bacterial OMVs in immune modulation, pathogenesis, and their therapeutic potential as vaccine platforms, adjuvants, and drug delivery systems. By conducting a systematic literature review using PubMed, Google Scholar, and Web of Science, this article integrates findings on OMV biogenesis, immune effects, and applications across infectious diseases and cancer models, while addressing challenges such as scalability, heterogeneity, and toxicity. Unlike previous reviews that broadly cover extracellular vesicles, this study focuses explicitly on OMVs from Gram-negative bacteria, offering a comprehensive analysis of their clinical translation potential.

The novelty of this review lies in its emphasis on emerging OMV-based technologies, particularly bioengineered OMVs designed for precision immunotherapy and targeted drug delivery. Recent innovations, such as engineered OMVs expressing tumor-specific antigens or ligands targeted at cancer cells, have shown promise in improving vaccine efficacy and personalizing cancer treatments [5]. Additionally, this review provides novel insights into OMV-mediated microbiota-immune crosstalk, highlighting their role in modulating innate and adaptive immunity to maintain gut homeostasis [6]. By bridging microbiology and immunology, this article underscores the transformative potential of OMVs while identifying critical research gaps to guide future therapeutic development.

2. Methods

This is a scoping review of the literature on Gram-negative bacterial outer membrane vesicles (OMVs) published between January 2020 and March 2025. We followed a systematic search strategy to identify

relevant peer-reviewed articles in PubMed, Web of Science, and Google Scholar using the search terms ("outer membrane vesicles" OR "OMVs") AND ("Gram-negative" OR specific genera) in combination with keywords related to immunity, pathogenesis, microbiota, vaccine, or drug delivery. The search was restricted to articles published from 2020 to 2025 to focus on the most recent advances. References were screened by title/abstract and full text for relevance. The searches yielded approximately 680 records after deduplication. Following title/abstract screening, 184 articles were retrieved for full-text assessment, of which 80 were finally included based on the following explicit criteria: (i) Publication between 2020 and 2025, (ii) primary data or novel insights into Gram-negative bacterial OMV biogenesis, composition, immune modulation (either proinflammatory or immunosuppressive), microbiota–host interactions, or vaccine/drug delivery applications, and (iii) use of biologically relevant experimental models. Exclusion criteria were as follows: (i) Exclusive focus on Gram-positive bacteria-derived vesicles or synthetic nanoparticles, (ii) purely technical/methodological reports without immunological or therapeutic implications, (iii) OMVs mentioned only peripherally.

3. Biogenesis and composition of OMVs

OMVs derived from Gram-negative bacteria encapsulate a complex cargo, including lipopolysaccharides (LPS), phospholipids, outer membrane proteins (OMPs), RNA, DNA, and toxins, which are incorporated during the vesiculation process [3,7]. The biogenesis of OMVs occurs through membrane budding, triggered by mechanisms such as reduced lipoprotein–peptidoglycan interactions, accumulation of peptidoglycan, altered LPS charge, or phospholipid enrichment in the outer membrane [8–11]. Alternatively, in bacteria such as *Pseudomonas aeruginosa* and *Escherichia coli*, OMVs can form through the explosive cell lysis process, where membrane fragments reassemble into vesicular structures [12–15]. OMVs from pathogenic bacteria are enriched with virulence factors, promoting disease progression, whereas those from commensal bacteria contribute to host homeostasis, reflecting their distinct molecular compositions [4,11,16].

4. Mechanisms of OMV uptake and host cell targeting

OMVs deliver cargo to host cells via endocytosis (clathrin-, caveolin-, non-clathrin/non-caveolin, macroendocytosis), membrane fusion, and receptor-mediated pathways, with smaller OMVs (20–100 nm) favoring caveolin-mediated delivery and larger OMVs (90–450 nm) using macroendocytosis [17,18]. OMVs containing HlyF or CprA proteins bypass clathrin-dependent pathways, directly fusing with host cell membranes [19,20]. Epithelial cells primarily employ macroendocytosis for OMV uptake, whereas dendritic cells (DCs) and macrophages utilize clathrin- or caveolin-mediated endocytosis through specific receptor interactions. In contrast, lymphocytes interact with OMVs indirectly via antigen-presenting cells [17,19]. This size-dependent uptake preference is functionally significant: Smaller OMVs (<100 nm) more efficiently deliver tolerogenic molecules (e.g., PSA, anti-inflammatory small RNAs) or intracellular toxins directly to the cytosol via non-degradative pathways, whereas larger vesicles favor endolysosomal routing in professional antigen-presenting cells, thereby contributing to the divergent proinflammatory vs. immunosuppressive outcomes of pathogenic and commensal OMVs, respectively [17–20].

5. Proinflammatory effects of OMVs

OMVs contain LPS, particularly lipid A, and membrane proteins that engage Toll-like receptor 4 (TLR4). In contrast, peptidoglycan and specific lipoproteins within OMVs primarily activate Toll-like receptor 2 (TLR2), initiating proinflammatory signaling cascades and cytokine release [21–24]. OMVs from pathogenic bacteria, such as *E. coli* and *Porphyromonas gingivalis*, deliver virulence factors to host cells, intensifying inflammation through pattern recognition receptors (PRRs) [4]. Compared to their parent bacteria, OMVs carry a concentrated payload that heightens innate immune activation, contributing to inflammatory conditions such as inflammatory bowel disease (IBD) and sepsis [25]. Inflammasomes, notably NLRP3 and NLRC4, amplify this inflammatory response by processing interleukin-1β (IL-1β) and interleukin-18 (IL-18). LPS triggers NLRP3 within OMVs, while NLRC4 responds to flagellin from bacteria, such as *P. aeruginosa*, promoting IL-1β secretion [26]. Additionally, OMVs from *Fusobacterium nucleatum* (*F. nucleatum*) induce the release of proinflammatory cytokines, including interleukin-8 (IL-8) and tumor necrosis factor (TNF), in colonic epithelial cells. This process is initiated by TLR4 activation, leading to the activation of the NF-κB signaling pathway. *In vivo* studies have shown that these OMVs worsen intestinal inflammation, highlighting their role in inflammatory signaling pathways [27].

6. Immunosuppressive and tolerogenic effects of OMVs

OMVs from commensal bacteria, such as *B. fragilis*, contain small RNAs that attenuate inflammatory signaling in intestinal epithelial cells, promoting regulatory T cell (Treg) differentiation and suppressing Th1/Th17 polarization [28]. Notably, polysaccharide A (PSA) from *B. fragilis* inhibits the TLR4/NF-κB signaling pathway, downregulating inflammatory responses and fostering immune homeostasis in the gut microenvironment [29]. Recent studies have further elucidated how these OMVs modulate host immunity by interfering with antigen presentation and promoting anti-inflammatory cytokine production, such as IL-10 and TGF-β [11].

Beyond *B. fragilis*, OMVs from other commensal species demonstrate similar tolerogenic capabilities. For example, OMVs from *Akkermansia muciniphila*, a key gut commensal, have been shown to induce DCs and enhance Treg populations, thereby reducing intestinal permeability and supporting epithelial barrier integrity [30,31]. This is achieved through the delivery of regulatory molecules that activate NOD-like receptors and suppress NF-κB activation, leading to decreased proinflammatory cytokine release (e.g., IL-6 and TNF-α) and increased anti-inflammatory mediators [32]. Similarly, OMVs from *Lactobacillus* species promote immunosuppressive effects by inducing apoptosis in overactivated immune cells and modulating immune checkpoint pathways, which helps prevent autoimmune responses in the gut [33]. These immunosuppressive mechanisms underscore the therapeutic promise of commensal OMVs in managing chronic inflammatory conditions. By promoting Treg differentiation and inhibiting effector T-cell responses, OMVs contribute to long-term immune homeostasis, bridging the gap between microbiota and host immunity (as discussed in Section 8). However, variability in OMV cargo due to bacterial strain and environmental factors remains a challenge, necessitating further research to harness their tolerogenic potential for clinical applications.

7. OMVs in infectious diseases: Friend or foe

OMVs play a critical role in the pathogenesis of diseases such as IBD, sepsis, and meningitis [34]. OMVs from *P. aeruginosa* exacerbate tissue damage in chronic lung infections. Similarly, *Neisseria meningitidis* OMVs drive meningitis through toxin delivery [3,35,36]. OMVs from *Helicobacter pylori*, enriched with virulence factors CagA and VacA, aggravate gastritis and gastric ulcers [37–39]. Additionally, *Salmonella enterica* OMVs facilitate intestinal colonization and inflammation [37,40]. A detailed overview of OMV-mediated pathogenesis and immune modulation is provided in Table 1.

Table 1. Role of OMVs in pathogenic bacteria.

Pathogen	Pathogenic role of OMVs	Immune modulation/applications	Recent advances (2020–2025)	References
E. coli	Toxin delivery, adhesion, inflammation	Vaccine platform, anti-inflammatory effects	Engineered OMVs for vaccines	[41,42]
P. aeruginosa	Tissue damage, chronic infection	Immune suppression via sRNA, TLR4 activation	Epigenetic modulation, vaccine studies	[3,35,36,43]
Neisseria	Meningitis, septicemia	DC maturation, antigen presentation	Licensed OMV-based vaccines	[3]
H. pylori	Gastric disease, cancer	Th1/Th2/Th17 induction, adjuvant use	OMV-based vaccines, systemic effects	[37,38,40,44]
Salmonella enterica	Invasion, immune evasion	Antigen delivery, vaccine vector	Multivalent OMV vaccines	[37,44]

OMVs from *F. nucleatum* and adherent-invasive *E. coli* (AIEC) compromise intestinal barrier integrity in IBD [4,45]. Conversely, OMVs from commensal bacteria, such as *Bacteroides thetaiotaomicron* and *B. fragilis*, induce anti-inflammatory cytokines, promoting immune homeostasis. In IBD patients, the regulatory effects of these OMVs are impaired, leading to reduced IL-10 production by DCs, indicative of diminished protective OMV-mediated signaling [4]. Key effects and associated cytokines in these conditions are summarized in Table 2.

Table 2. OMVs in diseases and immune regulation.

Disease	OMV source	Key effects/mechanisms	Cytokines involved	References
IBD	AIEC, *F. nucleatum*	Barrier disruption, proinflammatory macrophages	IL-1β, IL-6, TNF-α	[39,45]
IBD	*B. fragilis*, *B. thetaiotaomicron*	Immune regulation, IL-10 induction, homeostasis	IL-10, IL-6	[6,25,39]
Systemic inflammation	*E. coli*	Macrophage activation, cytokine release	IL-1β, IL-6, TNF-α	[46–48]

8. OMVs and host microbiota-immune crosstalk

OMVs from commensal and probiotic bacteria modulate gut microbiota–immune interactions by activating TLRs and NOD-like receptors, fostering immune homeostasis [6,32]. These vesicles traverse the mucosal barrier to engage DCs and macrophages, facilitating crosstalk between innate and

adaptive immunity. They reinforce the intestinal epithelial barrier, enhancing mucosal tolerance [6,49]. The immunomodulatory functions of OMVs are detailed in Table 3.

Table 3. Functions of OMVs in gut immune homeostasis.

Function/effect	OMVs from commensals/probiotics	Commensal bacteria	Probiotic bacteria	References
Strengthen the epithelial barrier	+	+	+	[6,30,49–52]
Modulate innate immunity	+	+	+	[6,30,49–53]
Modulate adaptive immunity	+	+	+	[6,30,49–54]
Promote anti-inflammatory cytokines	+	+	+	[6,30,49–53]
Enhance IgA production	+	+	+	[30,49–53]

OMVs from *B. fragilis* stimulate DCs, promoting Treg differentiation and establishing a tolerogenic immune environment [55,56]. By activating NOD1, OMVs reduce intestinal permeability, thereby strengthening barrier integrity [57,58]. The effects of OMVs on tolerogenic immunity and epithelial barrier function are summarized in Table 4.

Table 4. OMV effects on tolerogenic immunity and epithelial barrier.

OMV source	IL-10/Treg stimulation	Tolerogenic immunity induction	Epithelial barrier	References
B. fragilis	Yes (indirect, strong evidence)	Yes (indirect, strong evidence)	Yes (indirect, strong evidence)	[6,25]
B. thetaiotaomicron	Yes (inferred)	Yes (inferred)	Yes (inferred)	[25]
E. coli Nissle 1917	Yes (direct evidence)	Yes (direct evidence)	Yes (direct: upregulates ZO-1, claudin-14; reduces claudin-2)	[25,58,59]
Akkermansia muciniphila	Yes (direct evidence)	Yes (direct evidence)	Yes (direct: maintains tight junctions, barrier)	[58]
Lactobacillus spp.	Yes (TGF-β, IgA, Treg induction)	Yes (Treg and anti-inflammatory)	Yes (protects tight junctions, anti-apoptotic effect)	[33]

9. OMVs as therapeutic tools or vaccine candidates

OMVs, bearing surface antigens, function as versatile platforms for vaccines, adjuvants, and drug delivery systems [60]. Their pathogen-associated molecular patterns (PAMPs) stimulate innate immune responses, enhancing their adjuvant properties [61]. OMVs present antigens in their native conformation, making them effective for vaccines targeting infectious diseases, and serve as nanocarriers for delivering therapeutic agents to cancer or infection sites [62–64]. However, challenges, such as toxicity, scalability, purity, drug loading efficiency, and long-term safety, must be addressed [65]. Key applications of OMVs in these contexts are summarized in Table 5.

Table 5. Key applications of OMVs in vaccines and adjuvants.

OMV application	Type of OMV	Target/antigen	Advantages	Disadvantages	References
Adjuvants	*Bordetella pertussis* OMVs	Vaccine-associated antigens	Potent adjuvant, induces Th1, improves protection	Potential toxicity and reactogenicity	[66,67]
Adjuvants	*Salmonella enterica* serovar Typhimurium OMVs	*Salmonella* antigens	High immunogenicity, oral vaccines	Toxicity, production	[68]
Adjuvants	*H. pylori* OMVs	*H. pylori* antigens	Effective antigen delivery, mucosal immunity	Toxicity, Th1/Th2 balance	[69]
Vaccines	Meningococcal OMVs	Meningococcal antigens	Cross-protection, high immunogenicity	Strain variability	[70]
Vaccines	OMVs derived from *Shigella* bacteria	*Shigella* antigens	Alternative to traditional vaccines	Serotype variability, toxicity	[71]
Vaccines	Trivalent OMV-based combination vaccine candidate for *Campylobacter* and invasive non-typhoidal *Salmonella*	Protective antigens from *Campylobacter* and invasive non-typhoidal *Salmonella*	Combination vaccine, induces protective immunity	Toxicity, strain coverage	[72]
Vaccines	Engineered OMVs	Tumor antigens	Enhanced antigen presentation	Scalability, complexity	[5,73]

10. Challenges and future perspectives

The production of OMVs faces challenges due to their complex biogenesis, with variable yields influenced by bacterial strains and growth conditions [8,74]. Recent advances, such as those by Huang et al. (2025), propose genetic engineering to control vesiculation rates, potentially improving yield consistency and addressing scalability issues [8]. Looking forward, OMVs hold promise for personalized medicine as nanocarriers for targeted drug delivery, improving efficacy while minimizing toxicity [75–77]. By engineering OMVs to express specific ligands or antibodies, these vesicles can be customized to target particular cell types or tissues, aligning with the principles of personalized medicine. For example, OMVs designed to target cancer cells that overexpress the epidermal growth factor receptor (EGFR) have shown selective delivery and improved therapeutic outcomes [78,79]. Hybrid approaches combining OMVs with synthetic nanoparticles may further balance immunogenicity and safety, as suggested by Aytar Çelik et al. (2023) [63]. Clinical translation of OMVs as therapeutics or vaccines requires navigating complex regulatory pathways to ensure safety and efficacy. The inherent heterogeneity of OMVs, driven by variable cargo such as LPS, proteins, and nucleic acids, poses challenges for achieving consistent quality under good manufacturing practice (GMP) standards [65,74].

11. Discussion

Pathogenic OMVs, enriched with virulence factors such as LPS, toxins, and specific proteins, activate innate immune pathways through PRRs like TLR4 and TLR2, driving proinflammatory

cascades that contribute to diseases such as IBD, meningitis, and sepsis [4,21,25,27]. For instance, OMVs from *E. coli* and *P. gingivalis* deliver concentrated payloads, eliciting stronger cytokine responses (e.g., IL-1β, IL-8, TNF-α) than their parent bacteria, as demonstrated in recent studies [4,25]. The activation of inflammasomes, particularly NLRP3 and NLRC4, further exacerbates these responses, with LPS and flagellin playing critical roles in IL-1β and IL-18 secretion [26]. These findings align with *F. nucleatum* OMVs promoting intestinal inflammation through TLR4/NF-κB signaling, disrupting gut homeostasis [27]. This discrepancy underscores a critical gap: The molecular determinants of OMV-mediated immune activation remain incompletely characterized, complicating predictions of their pathogenic impact across different bacterial strains and host environments.

Conversely, OMVs from commensal bacteria like *B. fragilis* and *B. thetaiotaomicron* promote immune tolerance by inducing anti-inflammatory cytokines (e.g., IL-10) and Treg differentiation [6,29]. Recent studies emphasize their role in enhancing epithelial barrier integrity and modulating microbiota-immune crosstalk, particularly via NOD1 activation [25,57]. However, Gilmore et al. (2022) noted that these tolerogenic effects are diminished in IBD patients due to impaired IL-10 production, suggesting disease-specific limitations in commensal OMV function [25]. This contrast between pathogenic and commensal OMVs highlights their dual nature but also reveals a research gap: few studies directly compare their molecular cargos to explain differential immune modulation, limiting mechanistic insights. Although head-to-head proteomic and lipidomic comparisons between pathogenic and commensal OMVs remain limited, synthesis of recent compositional and functional studies (2020–2025) reveals clear molecular determinants that dictate the opposing immune outcomes.

The primary driver of proinflammatory activity in pathogenic OMVs is the presence of highly acylated (hexa-acylated) LPS with strong endotoxic lipid A, which potently activates TLR4–MyD88–NF-κB signaling and triggers robust secretion of IL-6, TNF-α, IL-1β, and IL-8 [4,26,27]. This is frequently compounded by high levels of peptidoglycan fragments and virulence-associated outer membrane proteins (e.g., CagA, VacA, porins) that engage TLR2 and NOD1/NOD2, and, in some species (*P. aeruginosa*, *Salmonella*), by flagellin that activates the NLRC4 inflammasome [26,37]. The concentrated delivery of these PAMPs explains why pathogenic OMVs often elicit stronger cytokine responses than intact bacteria [4,25].

In stark contrast, OMVs from key gut commensals exhibit multiple layers of immune attenuation. *B. fragilis* and related species package zwitterionic polysaccharide A (PSA) and under-acylated or modified LPS that minimally activate TLR4 while directly inducing IL-10-producing regulatory T cells via TLR2-dependent signaling on dendritic cells [3,29]. *Akkermansia muciniphila* OMVs contain the immunomodulatory protein and deliver small non-coding RNAs that suppress NF-κB activation and reduce IL-6/TNF-α secretion in intestinal epithelial cells [28,30,31]. Furthermore, many commensal OMVs lack flagellin and contain lower overall PAMP loads, preventing inflammasome hyperactivation [25]. Thus, the immunological fate of an OMV is determined by a combination of (i) structural modification or absence of strong PAMPs, and (ii) active delivery of tolerogenic molecules (PSA, specific proteins, anti-inflammatory small RNAs). This dual strategy represents an evolutionary adaptation by the microbiota to maintain gut homeostasis while pathogenic bacteria exploit the same vesicle system for inflammatory advantage.

Therapeutically, OMVs have emerged as potent vaccine platforms and adjuvants due to their inherent immunogenicity and ability to present antigens in their native conformation [60,61]. Licensed meningococcal OMV-based vaccines and ongoing research into multivalent vaccines against *Campylobacter* and *Salmonella* demonstrate their efficacy in eliciting robust immune responses [70,72].

Additionally, OMVs from *B. pertussis* and *H. pylori* enhance Th1-biased immunity, making them effective adjuvants for mucosal and systemic vaccines [66,69]. However, challenges such as toxicity, production scalability, and heterogeneity remain significant barriers to clinical translation [65,80]. The variable yields of OMVs, influenced by bacterial strains and growth conditions, complicate large-scale production, while their potential reactogenicity requires careful engineering to mitigate adverse effects [8,74]. The immunomodulatory effects of OMVs extend beyond infectious diseases to microbiota-immune crosstalk, particularly in the gut. OMVs from commensal and probiotic bacteria strengthen epithelial barriers, modulate innate and adaptive immunity, and enhance IgA production, contributing to mucosal tolerance [6,30,49–52]. Despite their therapeutic promise, several limitations warrant consideration. The heterogeneity of OMV composition across bacterial strains complicates standardization, and their potential toxicity, particularly from pathogenic OMVs, poses risks for clinical applications [65].

12. Conclusion

OMVs from Gram-negative bacteria are pivotal in modulating host immunity, acting as a double-edged sword. They drive proinflammatory responses through pathogen-associated molecular patterns, activating innate immune receptors and exacerbating diseases like inflammatory bowel disease and sepsis. Conversely, OMVs from commensal bacteria promote tolerogenic immunity, enhancing Treg differentiation and maintaining gut homeostasis. Their ability to deliver virulence factors or regulatory molecules underscores their dual role in pathogenesis and immune regulation.

OMVs hold immense therapeutic potential as vaccine platforms, adjuvants, and drug delivery systems. Their natural immunogenicity and capacity to present antigens in native conformations make them effective against infectious diseases and promising for cancer immunotherapy. Engineered OMVs, tailored to target specific cells or deliver therapeutic cargos, enhance efficacy while minimizing systemic toxicity. These attributes position OMVs as versatile tools in personalized medicine. Despite their promise, challenges in OMV production, including scalability, heterogeneity, and standardization, limit clinical translation. Advances in engineering and characterization are crucial for overcoming toxicity and ensuring consistent quality. Future research should focus on optimizing isolation protocols, refining bioengineering techniques, and exploring the potential of OMVs in novel therapeutic strategies. By overcoming these challenges, OMVs can connect microbiology and immunology, providing innovative solutions for infectious and inflammatory diseases.

Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

Author contributions

Conceptualization: All authors; Data curation: Mohammad Karimbakhsh, Rouzbeh Sojoudi Masuleh, Mehrnaz Eramian; Formal analysis: All authors; Investigation: Mohammad Karimbakhsh, Rouzbeh Sojoudi Masuleh; Methodology: All authors; Project administration: All authors; Resources: All authors; Validation: All authors; Visualization: All authors; Writing–original draft: All authors; Writing–reviewing & editing: All authors.

Conflicts of interest

The authors have no conflicts of interest to declare.

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