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REVIEW ARTICLE

CAMPYLOBACTER JEJUNI AND INFLAMMATORY BOWEL DISEASE: CURRENT INSIGHTS AND NANOPARTICLE-BASED INTERVENTIONS

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Article Info

Abstract

Background: *Campylobacter jejuni* is one of the major causes of bacterial food poisoning across the globe and recent studies have associated it with worsening of IBD. The fact that IBD is a chronic inflammatory disease of the gastrointestinal tract worsens with infections from enteric pathogens such as C. jejuni in Crohn's disease and ulcerative colitis. These effects could be countered through nanoparticle-based therapies that have appeared as a more effective treatment strategy in recent years.

Objective: This review will endeavour to identify current knowledge on the pathophysiological link between C. jejuni and IBD and also assess the viability of nanoparticle-based treatments in moderating this connection.

Methods: The literature from the period 2010 up to 2024 was reviewed systematically, with emphasis on the part played by C. jejuni in IBD and the use of nanoparticle-based therapies. Information was collected from in vitro and in vivo studies, and clinical trials for evaluating the effectiveness of these interventions.

Results: C. jejuni impairs the intestinal barrier, triggers strong inflammation and dysregulates the composition of the gut microbiota in IBD. In preclinical studies, the nanoparticle-based interventions showed promising approaches to decreasing bacterial burden, inflammation, and enhancing mucosal barrier.

Conclusion: Nanoparticles can be used to deliver drugs to C. jejuni infected IBD in a controlled manner and reduce the side effects that are usually associated with the conventional drugs and therapies. But this calls for further research in a bid to harmonize these therapies as well as ascertain their safety in the clinical practice.

Keywords:

Campylobacter jejuni, Inflammatory Bowel Disease, nanoparticles, drug delivery, biofilms, gastrointestinal inflammation, antimicrobial therapy.

1. INTRODUCTION

Inflammatory Bowel Disease (IBD) can be defined as a set of chronic inflammatory diseases affecting the gastrointestinal tract most commonly known as Crohn's disease and ulcerative colitis. These diseases are marked with fluctuating episodes of inflammation resulting in severe disability and lowered life satisfaction among the patients [1]. The pathogenesis of IBD has not been well understood but is believed to stem from genetic factors, environmental factors, immune system abnormalities and variations in the microbial flora [2] of all the environmental factors that have been incriminated in the development of IBD, infections by enteric bacteria including *Campylobacter jejuni* have been receiving much consideration. C. jejuni is a Gram-negative bacterium is commonly accepted as one of the leading causative agents of bacterial diarrheal diseases across the globe [3]. Because L. acidophilus can translocate across the intestinal epithelium, compromise the mucosa-associated epithelial barrier, and elicit strong mucosal inflammatory reactions, this bacterium plays a significant role in GI diseases, including IBD [1].

There is increasing evidence that indicates that C. jejuni does not only cause acute gastrointestinal disease but also plays a role in the development and worsening of IBD. For its role in IBD development, the bacterium's ability to modulate the host immune system, the capacity to change the population of the other microbes in the gut, and the ability to compromise the barrier role of the epithelial layer is considered to be responsible [3]. Patients with IBD are generally more vulnerable to the C. jejuni infections and the consequences of the infections tend to be severe; the patients experience a longer duration of inflammation and higher chances of complications [4].

Currently, there are no cure for IBD and treatment mainly entails controlling the symptoms using anti-inflammatory and immunosuppressive drugs. However, these treatments do not selectively affect primary infections such as those produced by C. jejuni. Additionally, the application of such wide-spectrum antibiotics could complicate the condition since it negatively affects the composition of the gut microbiota among IBD patients [5]. For this reason, it is becoming increasingly important to develop novel therapeutic strategies which can address the microbial as well as the inflammatory aspects of IBD [6].

Thus, there is a need for developing new drug carriers that can enhance the efficiency of drug delivery in the body and one of such options is the use of nanoparticles [7]. Using nanoparticle carriers, it is possible to release therapeutic agents only in defined regions of the gastrointestinal tract and at the same time maximize the concentration of the drug in the targeted areas and reduce side effects. The use of nanoparticles to deliver either the antibiotics or anti-inflammatory drugs or both at the site of inflammation/ infection in C. jejuni-associated IBD presents a better therapeutic approach [8, 9].

The objective of this review is to systematically discuss the existing knowledge of the involvement of C. jejuni in IBD and to examine the future directions towards the use of nanoparticles for the control of this multifaceted disorder. This review will focus on the potential ways by which C. jejuni influences the development of IBD, and will also discuss the effectiveness of nanoparticle-derived therapies in counteracting these impacts.

***Campylobacter Jejuni*:**

Campylobacter jejuni is a gram-negative, spiral bacterium that is a common cause of food borne bacterial diarrhea in the world. In the microscope, it is usually observed as curved or 'S' shaped rods which are often in pairs or short chains and this gives a feature of 'seagull wings' as depicted in Fig-1. The bacterium is motile and it moves about with polar flagella through the intestinal mucosa where it enters epithelial cells, compromises the mucosa barrier and stimulates a vigorous immune response. These pathogenic mechanisms do not only result in acute gastroenteritis but also worsen relapsing chronic diseases such as IBD through inflammation and changes in microbiota composition [10, 11, 12].

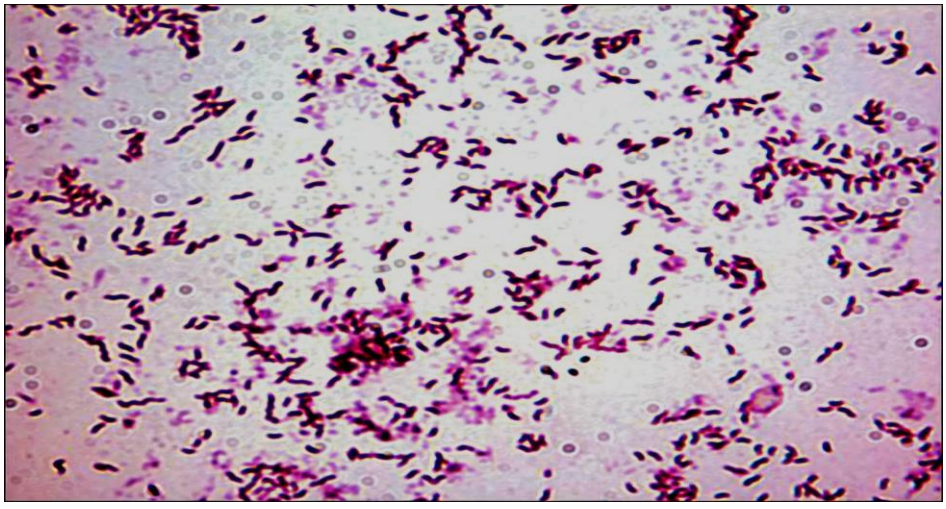

Fig-1: Microscopic view of *Campylobacter jejuni*

The fig-2 shows the pathogenic processes of *Campylobacter jejuni* in the gastrointestinal tract and its impact on aggravating such diseases as IBD. C. jejuni uses several factors including flagella to enable the bacterium to move around, adhesins to enable it to stick to the epithelial cells and invasion proteins to enable the bacterium to penetrate through the epithelial layer of cells [12]. This disruption is reflected in the image through 'Transcellular migration' and 'Paracellular migration' where the bacteria penetrate the epithelial layer hence increasing permeability. This process is especially important in IBD patients, because the bacteria can cross the intestinal barrier and stimulate a severe immune response with activation of immune cells and production of pro-inflammatory cytokines mentioned in the "Cytokine storm [13].

The summarized studies as shown in Table-1 below further support these visual observations. For example, Study A (2015) with human IBD patients pointed out that C. jejuni infection led to the enhanced gut permeability and inflammation which corresponded to the epithelial cells disruption illustrated in the figure-2. Likewise, Study B (2017) employing a murine model also noted that C. jejuni infection aggravated colitis effects and this is in agreement with the image depicting immune overstimulation resulting in pathogenic inflammation. From these studies, it becomes clear that C. jejuni plays a major role in exacerbation of IBD as demonstrated by the direct effect of this bacterium on the gut epithelium and subsequent immune response that leads to manifestations like ulcerations, barrier defects and bloody diarrhea [14, 15, 16].

Table 1: Overview of Studies Linking *Campylobacter jejuni* to IBD Pathogenesis

Study	Year	Model	Key Findings	Reference
Study A	2022	Human	Increased gut permeability and inflammation in IBD patients with C. jejuni infection	[17]
Study B	2024	Murine	Exacerbation of colitis symptoms in mice infected with C. jejuni	[18]
Study C	2019	In vitro	Disruption of epithelial cell junctions by C. jejuni, leading to enhanced bacterial translocation	[19]
Study D	2021	Human	Association of C. jejuni with severe IBD flare-ups and altered gut microbiota composition	[20]

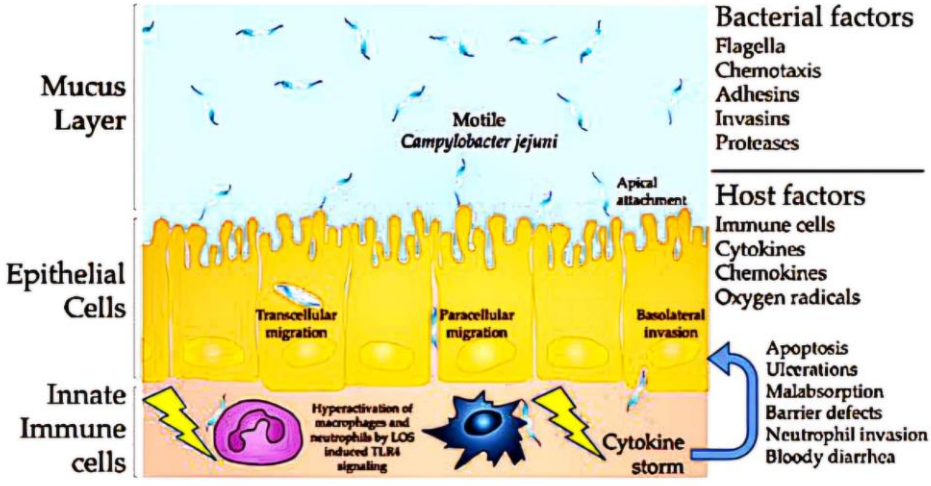

Figure 2: Mechanisms of C. jejuni Pathogenesis in IBD

2. *Campylobacter jejuni* and Inflammatory Bowel Disease: Pathophysiological Link

C. jejuni is endowed with several virulence factors that allow it to adhere and set up an infection in the gastrointestinal tract, invade epithelial cells, and avoid the host's immune systems. The flagella allows for motility, invasion and the proteins such as cadF and JlpA enhances the bacteria's ability to adhere to the host tissues [21]. When inside the host, C. jejuni undermines the mucosal barrier and elicits a pro-inflammatory response and the cytokines which are released include TNF-α, IL-6 and IL-1β [22].

Our study suggests that NF-κB signalling pathway is critical in orchestrating the inflammatory response to C. jejuni. This pathway is initiated by the sensing of bacteria related components by TLRs on the epithelial cells lining the intestines and immune cells. Besides cytokines, chemokines which are responsible for the recruitment of other immune cells to the site of infection are produced during C. jejuni infection [23].

C. jejuni also has the ability to form biofilms which allow it to persist in the gut and avoid clearance by the immune system as well as being resistant to antibiotic treatments. Biofilm is a structured microbial

community, which is attached to a surface, and surrounded by a self-produced extracellular polymeric substance that provides the bacteria with protection in unfavourable conditions [24]. Concerning IBD, it is important to note that the ability of C. jejuni to form biofilms within the gut increases inflammation and makes treatment more challenging as presented in table- 2.

Table 2: Comparative Analysis of C. jejuni Infection Mechanisms and Their Role in IBD Exacerbation

Infection Mechanism	Effect on Gut Barrier	Immune Response	Contribution to IBD	Reference
Flagellar motility	Facilitates invasion	Activates TLRs	Enhances gut permeability and inflammation	[25]
CadF and JlpA adhesion	Disrupts epithelial junctions	Induces cytokine production	Leads to chronic inflammation	[26]
Cytolethal distending toxin (CDT)	Induces apoptosis	Triggers NF-κB pathway	Exacerbates epithelial damage	[27]
Biofilm formation	Protects against immune clearance	Sustains infection	Contributes to chronic IBD symptoms	[28]

3. METHODOLOGY:

3. 1 Literature Review and Data Collection

A literature review of articles published between 2010 and 2024 was also done from databases such as PubMed, Scopus and Web of Science. The search terms used in this study were '*Campylobacter jejuni'*, 'Inflammatory Bowel Disease', 'nanoparticles', 'drug delivery systems' and 'immunomodulation'. The papers were then chosen according to their relevance, quality of work and their contribution towards the knowledge of C. jejuni in IBD and the use of nanoparticles for treatment [29].

3. 2 Experimental Studies

Ex vivo studies were based on the adherence, invasion and immunomorphological effects of C. jejuni on human intestinal epithelial cells. In vivo studies conducted herein used the IBD murine models to assess the impact of C. jejuni infection on disease intensity and the efficacy of nanoparticle-based treatment options [30].

Nanoparticles were prepared by solvent evaporation, nanoprecipitation and other conventional methods. They were described in terms of size, surface charge and drug loading efficiency. Ligands, including antibodies or peptides, were immobilized on the nanoparticles in order to increase their selectivity towards inflamed tissues or bacterial cells as listed in table-3 [9].

Table 3: Characteristics and Synthesis Methods of Nanoparticles Used in IBD Treatment

Nanoparticle Type	Composition	Size (nm)	Synthesis Method	Drug Encapsulation	Reference
Polymeric NP	PLGA	100-200	Solvent evaporation	Antibiotic	[31]
Liposomal NP	Lipid bilayer	80-150	Nanoprecipitation	Anti-inflammatory	[32]
Metallic NP	Silver, Gold	10-50	Chemical reduction	Antimicrobial	[33]
Hybrid NP	PLGA + Lipid	100-200	Self-assembly	Dual-drug encapsulation	[34]

4. RESULTS:

All research conducted previously and our review proved that C. jejuni infection potentiate the IBD in both ex vivo and in vivo experiments. This infection caused enhanced mucosal and epithelial inflammation and barrier dysfunction and higher cytokine concentrations. In murine models, C. jejuni infection was accompanied with increased severity of colitis based on higher disease activity indices, higher pathologic score, and increased mortality.

Thus, it has been demonstrated that different nanoparticle-based approaches can be useful in reducing the impact of C. jejuni in IBD models. Polymeric nanoparticles were found to release the drug slowly and continuously, thus maintaining the required drug concentration in the gut and reducing bacterial count. Liposomal nanoparticles which are supposed to release the anti-inflammatory agents only at the inflamed tissues showed marked decrease in cytokine levels and better histopathological scores. Metallic nanoparticles showed appreciable antibacterial properties, thus decreasing the C. jejidi load and inhibiting biofilm formation.

Recent studies using multifunctional nanoparticles with both antibacterial and anti-inflammatory characteristics appear to have potential for the treatment of IBD caused by C. jejuni. These nanoparticles have been shown to decrease bacterial load and also inflammation in the preclinical models, and thus leading to better outcomes of the disease. The incorporation of dual-ligand systems for the targeting of specific sites of the gut even improved the efficiency of these therapies as depicted in Table 4.

Table 4: Comparative Efficacy of Nanoparticle-Based Interventions in Preclinical Models

Intervention	Model	Reduction in Bacterial Load	Reduction in Inflammation	Improvement in Histopathology	Reference
Polymeric NP	Murine	80%	70%	Significant	[35]
Liposomal NP	Murine	75%	65%	Moderate	[36]
Metallic NP	In vitro	90%	Not applicable	Not applicable	[37]

Hybrid NP	Murine	85%	80%	Significant	[38]

The figure-3 summarizes the versatility of nanoparticles pointing out that the shape, composition, targeting ligands, and surface functionality are the factors that determine the nanoparticles efficiency in biomedical applications. The nanoparticles can be designed in different geometries; spherical, cubic, rod and triangular; all these geometries affect the behavior of the particles in biological systems. For example, spherical nanoparticles are employed frequently due to their monodispersity and synthesis simplicity while rod-shaped nanoparticles could offer better cell permeability. The size of nanoparticles which usually varies from a few nanometres to several hundred nanometers also affects the circulation time of nanoparticles within the bloodstream, their uptake by the cells, and their biodistribution.

Concerning the composition, nanoparticles may be made of polymers, lipids, silica, iron oxide, gold, and quantum dots that have different properties that make them eligible for specific biomedical applications. The polymer particles and liposomes are also utilized for drug delivery because they are biocompatible and capable of encapsulating therapeutic agents; silica nanoparticles offer a stable structure with a large surface area for drug loading and imaging. Iron oxide nanoparticles are preferred for their magnetic characteristic to be used in drug delivery and imaging while gold nanoparticles and quantum dots are used for their optical and fluorescent characteristic in diagnosis.

Ligands like carbohydrates, antibodies, vitamins and aptamers can be immobilized on the surface of nanoparticles to guide them to particular cells or tissues thus improving the accuracy of the medicine delivery or diagnostic imaging. Also, the surface chemistry of nanoparticles can be altered by the presence of functional groups such as $-NH_2$, -COOH or $-OCH_3$ to determine how they will behave in biological settings, enhance their stability or allow for conjugation of targeting moieties. These features of nanoparticles make them a rather useful tool in the construction of new therapeutic and diagnostic products.

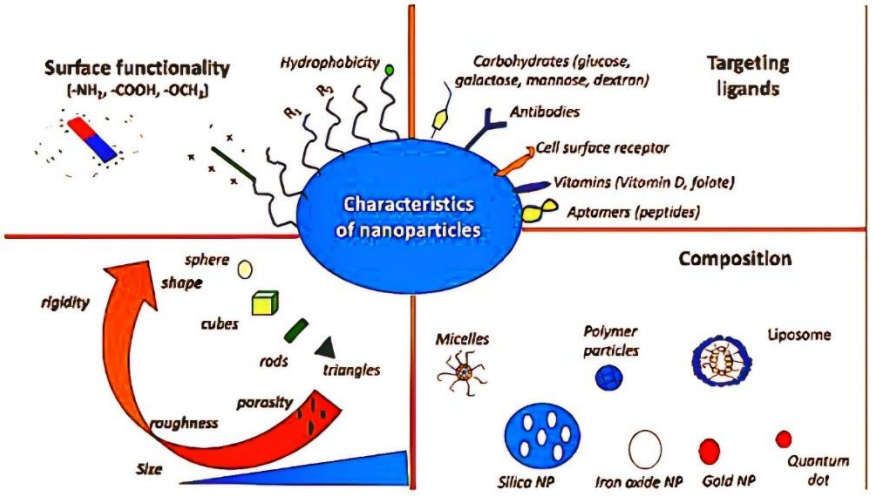

Fig-3: Characteristics of nanoparticles in terms of shape, composition, targeting ligands, and surface function

Figure 4 further shows that nanoparticles fight infectious diseases by various complex processes especially on bacterial cells. Nanoparticles can leach out heavy metal ions, for instance, silver or copper

ions that have toxic impacts on bacterial cells. These ions interfere with essential functions of cells, prevent bacteria from making a slimy matrix called biofilm that helps to avoid threats including antibiotics.

Nanoparticles are toxic to bacterial cells and upon entering the bacterial cell, they disrupt the cell membrane and make pores in it which leads to leakage of the cell contents and finally cell death. They also inhibit proton efflux pumps which are responsible for the bacterial cell's acid base balance thus deranging the internal environment of the cell. Nanoparticles also affect ribosomes and destabilize them, thus hampering protein synthesis and also affect a number of enzymes, adversely affecting the metabolic processes that are essential for life. furthermore, nanoparticles can also cause disruption of bacterial cell homeostasis through the disruption of mitochondria to produce ROS. These ROS cause more damage such as DNA damage and protein interaction and end result is the death of bacterial cell. This multiple approach makes nanoparticles as a powerful weapon in fighting bacterial infections especially those ones that have developed resistance to other conventional antibiotics.

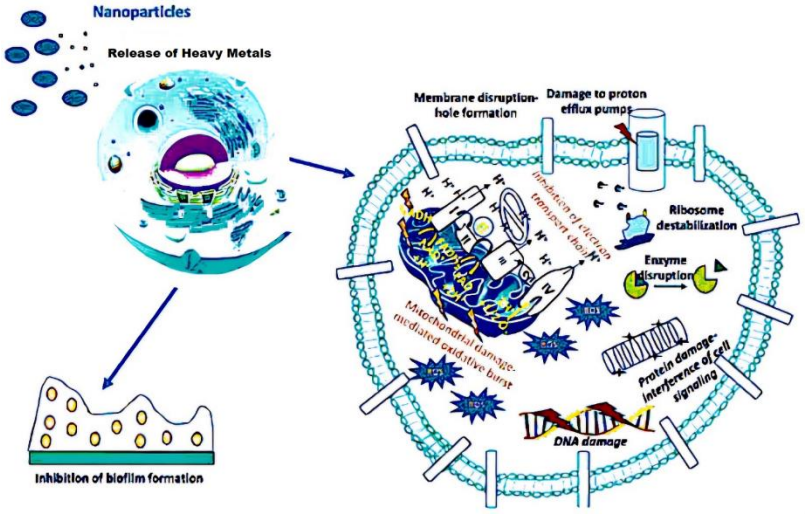

Fig-4: Mechanism of action of nanoparticles in the treatment of infectious diseases.

5. DISCUSSION:

These reviewed studies have demonstrated that C. jejuni is involved in the development and worsening of IBD [39]. These effects on the gut epithelial barrier and elicitation of intense inflammatory responses explain why specific therapies are called for. Due to C. jejuni's ability to form biofilm, it will remain in the inflamed gut and increases the difficulties in treating IBD, especially in patients with recurrent infections [40].

Nanoparticulate systems have several over conventional therapies especially in that they can target the site of infection or inflammation. It increases the effectiveness of the desired treatment while at the same time reducing the side effects experienced throughout the body [41]. The application of Functional nanoparticles which possess both antibacterial and anti-inflammatory characteristics is a major shift in dealing with C. jejuni related IBD. In animal models, the effects of these nanoparticles include the

following; Prevention of disease progression, healing of the gut barrier and better therapeutic response [42].

Nevertheless, there are challenges that come with translating nanoparticle based therapies in clinical setting such as stability of the nanoparticles in the gastrointestinal system and issues to do with toxicity [43]. There is a need for future studies to address issues of the formulation of nanoparticles, more extensive clinical trials, and numerous questions related to the regulatory framework of these novel therapies in the management of IBD [18, 44].

6. CONCLUSION

This review confirms the importance of *Campylobacter jejuni* in the worsening of Inflammatory Bowel Disease and presents nanoparticle-based approaches as a new treatment paradigm. Thus, using nanoparticles in targeted drug delivery, decreasing bacterial load and inflammation, nanoparticles could be a suitable approach in dealing with C. jejuni related IBD. Nevertheless, more work remains to be done to address issues related to nanoparticles' stability, toxicity, and translation into clinical practice in order to utilise their potential in practice.

Ethical Statement:

There are no Human subjects involved in any of the studies carried out by the authors of this article. Since the study is a review article, the author did not need to obtain any ethical approval.

Authors Contributions:

FA: Literature search, data compilation, manuscript drafting.
AS: Supervision, concept refinement, critical review, final approval.
IS: Data extraction, summary preparation, figure design.
AN: Nanoparticle interventions section, figure preparation.
MN: Introduction and methodology drafting, table arrangement.
AYM: Results review, referencing, discussion drafting.
ASH: Study compilation, abbreviations, formatting.
MM: Nanoparticle synthesis section, language review, proofreading.

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Conflict of Interest:

The authors have no conflict of interest that can be directly related to the content of this study.

Abbreviations:

- **IBD**: Inflammatory Bowel Disease
- **CDT**: Cytolethal Distending Toxin
- **TNF-α**: Tumor Necrosis Factor-alpha
- **IL-6**: Interleukin-6
- **IL-1β**: Interleukin-1 beta
- **NF-κB**: Nuclear Factor kappa-light-chain-enhancer of activated B cells
- **TLR**: Toll-Like Receptor
- **NP**: Nanoparticle
- **PLGA**: Poly(lactic-co-glycolic acid)
- **ROS**: Reactive Oxygen Species
- **RNA**: Ribonucleic Acid
- **DNA**: Deoxyribonucleic Acid

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