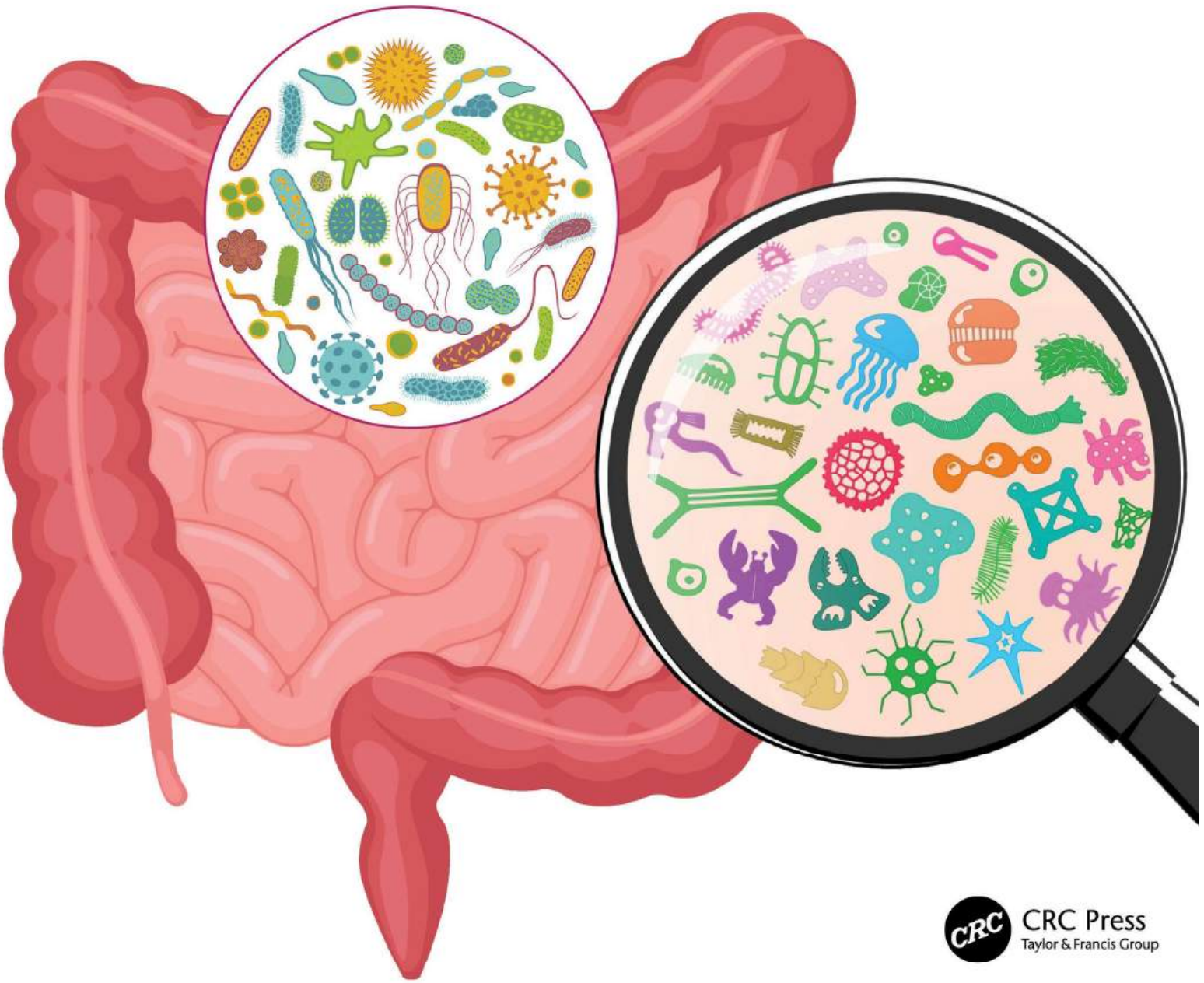
GASTROINTESTINAL INFLAMMATIONS AND GUT MICROBIOTA

Pathophysiology, Management, and Emerging Therapies

Edited by Neeraj Mishra, Sumel Ashique, and Anoop Kumar



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Gastrointestinal Inflammations and Gut Microbiota

This book offers a comprehensive and multi-faceted examination of gastrointestinal inflammations, discussing factors that impact gut health. The initial chapters establish a foundational understanding of gastrointestinal inflammations and the critical role of the gut microbiota. The book then delves into the complex pathophysiology and various risk factors associated with these conditions, offering insights into the latest diagnostic, screening, and prevention techniques. It explores the dynamic interactions between the gut and the brain as well as the biochemical interplays involving short-chain fatty acids, reactive oxygen species, and superoxide dismutases. Additionally, the book thoroughly discusses the impact of genetics on gastrointestinal health, the interactions between antibiotics and gut microbiota, and the pivotal role of the immune system in inflammation. It highlights advancements in diagnostic technologies and gut microbiota-based strategies, along with the use of nanoparticles in treatment. The book also examines the psychological aspects associated with gastrointestinal inflammations, emphasizing the importance of mental health for physical well-being. It assesses the potential of functional foods, various types of nanocarriers, and plant-based bioactives in managing gastrointestinal inflammations. As such, this book is primarily intended for researchers and students in the fields of gastroenterology and microbiology.

Key Features:

- Provides an extensive overview of gastrointestinal inflammations, starting from the basic concepts of the gut microbiota to complex pathophysiological aspects
- Delves into the latest advancements in diagnostic, screening, and prevention techniques, highlighting cutting-edge technologies and approaches in gastroenterology
- Explores the role of the immune system and the impact of genetics and diet on gastrointestinal health
- Examines use of probiotics, prebiotics, postbiotics, and various nanotechnology-based approaches for gastrointestinal inflammation management
- Emphasis on the psychological factors associated with gastrointestinal inflammations

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Preface

Gastrointestinal inflammation pertains to the development of inflammation inside the gastrointestinal tract, encompassing the esophagus, stomach, small intestine, and large intestine. Inflammation within the gastrointestinal (GI) tract can arise from a multitude of factors, and it is frequently linked to conditions such as inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), infectious gastroenteritis, and other related disorders. One of the most common digestive disorders, gastrointestinal inflammations, is characterized by constant, recurrent stomach pain and irregular bowel movements.

The cause of IBS is not fully known and is thought to be extremely complex; consequently, treatments are only somewhat effective. Epidemiologic research on individuals with post-infectious IBS (PI-IBS) has demonstrated a changed microbiota in the human gastrointestinal tract as one of the potential causes of IBS in the last ten years. Previous observational studies have shown that there is a higher risk of developing IBS in the future when the gut microbiota changes because of acute gastroenteritis. Additionally, there is a strong correlation between IBS and antibiotic therapy for extra-intestinal infections, which may change the intestinal flora. IBS is thought to be caused by a complex combination of genetic, environmental, and microbiota-related factors, while its specific cause is yet unknown. Promising therapy options for IBS include nanocarriers and methods that modify the gut microbiota. Therapeutic medicines can be packaged and delivered via nanocarriers like nanoparticles or liposomes right to the damaged parts of the gastrointestinal (GI) tract. By decreasing drug exposure to healthy tissues, this strategy lessens negative effects. The modified NPs (nanoparticles) have boosted medication concentration, decreased systemic adverse effects, and improved the efficacy and safety of local drug delivery. The development of IBD therapies based on nanotechnology is accelerating exponentially. For optimal health, IBS prescription medication is accessible.

The development of various nanoparticles that will aid in the management of IBS and other gastrointestinal illnesses is a major priority for many pharmaceutical companies. However, further research is necessary to fully comprehend how the effects of the nanoparticle on the gut flora could benefit IBD patients' prognoses. By extending the duration of the therapeutic impact and lowering the frequency of medication administration, controlled-release nanocarriers can increase patient compliance. Researchers are investigating the creation of hybrid systems that combine medicines that target the microbiota with nanocarriers for drug delivery. For instance, probiotics or prebiotics can be added to nanocarriers to increase their therapeutic efficiency.

About the Editors

Neeraj Mishra has been serving as a Professor at the Amity Institute of Pharmacy, Gwalior, since July 2019. He brings approximately 20 years of experience in teaching and research. Dr. Mishra has published over 100 papers of international and national significance, focusing on novel drug delivery systems, oral delivery of synbiotics, localized drug delivery, and targeted and controlled drug delivery using nanocarriers and microparticles for treating breast and colon cancer, as well as neurodegenerative disorders. He has also edited more than 15 books and authored 25 book chapters. He is the recipient of the "Distinguished Professor Award" (2019) from DST-NSTMIS, SPAICS, Indore, Madhya Pradesh, and the "Outstanding Scientist Award" (2020) from the 6th International Scientist Awards on Engineering, Science, and Medicine, held in Chennai, India. Further, Dr. Mishra received the "Distinguished Professor Award" in 2021 from the Indian Pharmaceutical Association, MP State Branch, Indore, and the "Best Academician Award" at the Indian Pharmacy Graduate Association's M.P. State International Conference, held on May 6, 2023, at the DAVV Auditorium, Indore, India.

Sumel Ashique has been working as an Assistant Professor at Bengal College of Pharmaceutical Sciences & Research, Durgapur 713212, West Bengal, India. He has 4 years of teaching experience. He has achieved 80 publications in international and national accredited reputed journals. He has knowledge in drug delivery, nanotechnology and targeted treatment strategy. He is working as a potential reviewer for many well-known publishers (Elsevier, Springer, Dove Press, and Bentham Sc.). He has also five granted patents from IP and Australia, 20 published book chapters in Bentham, Springer, Elsevier, Bentham and Taylor & Francis. Currently he is editing 14 books under CRC Press, Elsevier, Taylor & Francis, Wiley, Nova Science and Springer. He has published 80+ papers including research, reviews, column articles, editorials in Scopus, and WOS indexed. He is serving as Guest Editor for *JoVE Journal* (IF 1.2, Scopus & WOS indexed*), Current Probiotics* (Bentham Science) & *Current Indian Science Journal*. He is a potential reviewer for Elsevier, Springer, Taylor & Francis and Wiley journals for expertise in the fields of targeted drug delivery, nanotechnology, gut-microbiome, and postbiotics. Currently, he is pursuing his PhD degree from Lovely Professional University, Punjab, India (NAAC A^{++}) in the Pharmaceutical Science department.

Anoop Kumar is currently serving as an Assistant Professor in the Department of Pharmacology and Clinical Research at Delhi Pharmaceutical Sciences & Research University (DPSRU), New Delhi, India. Previously, he held the position of Assistant Professor in the Department of Pharmacology and Toxicology at the National Institute of Pharmaceutical Education and Research (NIPER), Raebareli. He has also served as an Associate Professor and Officiating Head in the Department of Pharmacology at ISF College of Pharmacy, Moga, Punjab. Additionally, Dr. Kumar has worked as a research scientist in the Medical Affairs and Clinical Research Department at Sun Pharmaceutical Limited, Gurugram, and at the Translational Health Science and Technology Institute (THSTI), Faridabad, India. Dr. Kumar has authored over 80 research and review articles and 15 book chapters in internationally renowned journals. He is also the author of three books. He has received research grants from the Indian government. His research interests include drug repurposing using computational, in vitro, and in vivo techniques, meta-analysis, signal analysis in pharmacovigilance, and pharmacoeconomic studies.

17 Lipid Nanocarriers for the Treatment of Gastrointestinal Inflammations

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17.1 INTRODUCTION

The definition of inflammation has evolved from its four cardinal signs of calor, rubor, tumor, and dolor as proposed by Celsus during the first century A.D. to the addition of the fifth sign of inflammation by Virchow in 1871 as the loss of function. With the advancement of cell-based techniques and molecular biology in the 19th century, the term inflammation has been defined more elaborately. The body's defense response to injury caused by any agent—be it microbial, immunological, physical, or chemical—is called inflammation. Clinically, this definition encompasses a multitude of biological processes (Scott et al., 2004).

Inflammation helps to alleviate harmful substances, flush them out, and promote tissue repair. Two fundamental processes—the early inflammatory response and the subsequent healing process—are involved in inflammation. While both of these processes typically serve as defenses against harmful agents, inflammation and healing can also have serious negative effects on the body(Carton et al., 2006).

The body's initial reaction is known as acute inflammation, which usually goes away quickly after the underlying cause is treated and is followed by healing. It lasts for two weeks or longer. It starts following a particular injury that triggers the migration of neutrophils and macrophages to the site of inflammation by the release of soluble mediators such as cytokines, acute phase proteins, and chemokines. Chronic inflammation develops either immediately after the acute inflammatory stimulation or after a prolonged period of time has elapsed. Chronic inflammation is characterized by its prolonged duration. In chronic inflammation, T lymphocytes and plasma cells go to the site of inflammation (Hannoodee & Nasuruddin, 2023).

Gastrointestinal inflammations are a type of disease that affects the gastrointestinal tract. This tract runs from the oral cavity to the anal cavity. Several conditions can cause inflammation of the gastrointestinal tract, including gastritis, periodontal disease, peptic ulcer disease, Crohn's disease, and ulcerative colitis. All of these conditions involve chronic inflammation in various parts of the gastrointestinal mucosa, which can result in epithelial compromises and tissue damage. There are also autoimmune components associated with the inflammatory bowel diseases along with systemic effects (Bamford, 1999).

17.1.1 Major Types of Gastrointestinal Inflammations

Of the gastrointestinal tract inflammatory conditions associated with inflammatory bowel disease (IBD), the most frequently occurring conditions are Crohn's disease and ulcerative colitis. The pathological mechanisms involve complex interaction of immunological, microbial, environmental, and genetic variables.

Genetic predisposition is just one of the numerous factors causing immune system dysregulation in inflammatory bowel disease (IBD) (Geremia et al., 2014) as well as dietary habits (Keewan et al., 2020) and the gut microbiome (Matsuoka & Kanai, 2015). Potentially, such mechanisms can take into account cytokine modulation, microbiome therapies, or dietary readjustments to manage and treat IBD.

Gastritis is the other condition of the gastrointestinal inflammation. Gastritis is the inflamed, irritated, or eroded stomach lining as a pathological condition that may manifest abruptly (acute) or develop gradually (chronic). Overindulgence in alcohol or long-term use of nonsteroidal anti-inflammatory medicines (NSAIDs), including ibuprofen or aspirin, are common causes of the illness. bacterium infection, especially Helicobacter pylori (HP), persistent bile reflux, stress, and some autoimmune diseases (Elseweidy, 2017).

Eosinophilic esophagitis (EoE) refers to a persistent inflammatory condition affecting the esophagus, primarily observed among the pediatric demographic. EoE is characterized by clinical symptoms of esophageal dysfunction and eosinophilic infiltration of the esophageal mucosa (Sutton et al., 2015).

In genetically susceptible individuals, duodenal inflammation is the hallmark of celiac disease (CD), a multiorgan autoimmune condition of the chronic intestinal disease group that is triggered by gluten consumption. Today, there is a great deal of research on the pathophysiology of celiac disease, which expands the concept beyond autoimmune alone and explains why the condition is hereditary. The

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