



21-22 November, 2024

Synergistic Antioxidant Effects of Metal Nanoparticles and Polyphenols in Alleviating Inflammatory Bowel Disease

Haralambie Mara-Georgiana^{1†}, Haralambie Oana-Roxana^{1†}, Igori Balta^{2†*}, Sanda Andrei^{1†*},

¹University of Agricultural Sciences and Veterinary Medicine, 400372 Cluj-Napoca, Romania

²University of Life Sciences King Mihai I from Timisoara, 300645 Timisoara, Romania

[†]Equal contribution

[‡]Shared correspondence

*Corresponding author's email: balta.igori@usvt.ro

Abstract: Oxidative stress, caused by the accumulation of reactive oxygen species (ROS), is associated with the initiation and progression of inflammatory bowel disease (IBD). This pathology is characterized by intestinal inflammation and the appearance of epithelial lesions. Numerous studies in animal models have suggested that ROS underlie this pathology. Although various treatment methods have been investigated, these lesions remain difficult to treat. As the excessive use of drugs inevitably causes side effects, new methods of developing the therapeutic effect have been attempted. Researchers have fabricated nanoparticles (NPs) with anti-inflammatory potential, liposomes or polymers containing the active substance in the centre of molecular structure. The only drawback of these structures is the need for more accurate knowledge of the beneficial and toxic dose. Various metal and metal oxide NPs, including copper, zinc oxide, and magnesium, have anti-inflammatory properties. Using organic sources for NPs synthesis avoids toxic chemicals, making the process more eco-friendly and cost-effective. Additionally, the gradual release of active substances from these NPs can help minimize side effects. This review aims to provide insights into the antioxidant capacity of NPs with metals and polyphenols as possible therapeutic alternatives for IBD while also addressing future concerns and perspectives in this area of research.

Introduction

Inflammatory bowel disease (IBD) is a chronic inflammatory condition characterized by recurrent episodes, with its prevalence declining in Europe and North America, but increasing in industrialized countries¹. Incidence rates of ulcerative colitis are 505 per 100,000 in Norway and 286 in the United States, with males generally more affected. However, a study in Portugal noted a 12% reduction in IBD incidence from 2017 to 2019, with a higher prevalence among females¹. IBD primarily includes Crohn's disease and ulcerative colitis, which can onset at any age. Genetic predisposition plays a role, as shown in monozygotic twins, with incidences of 30-35% for Crohn's disease and 10-15% for ulcerative colitis⁶. Environmental factors and a weakened intestinal mucosal barrier, along with infections, deficiencies in nutrients, and certain medications, also contribute to IBD's development (Fig. 1A). Clinical symptoms typically include abdominal pain, chronic diarrhea, and hematochezia, with around 50% of patients experiencing extraintestinal manifestations, like anemia and an increased risk of colorectal cancer⁶ (Fig. 1C). While free radicals and oxidative stress can aid in the immune response, excessive levels can lead to inflammatory damage⁴ (Fig. 1B).

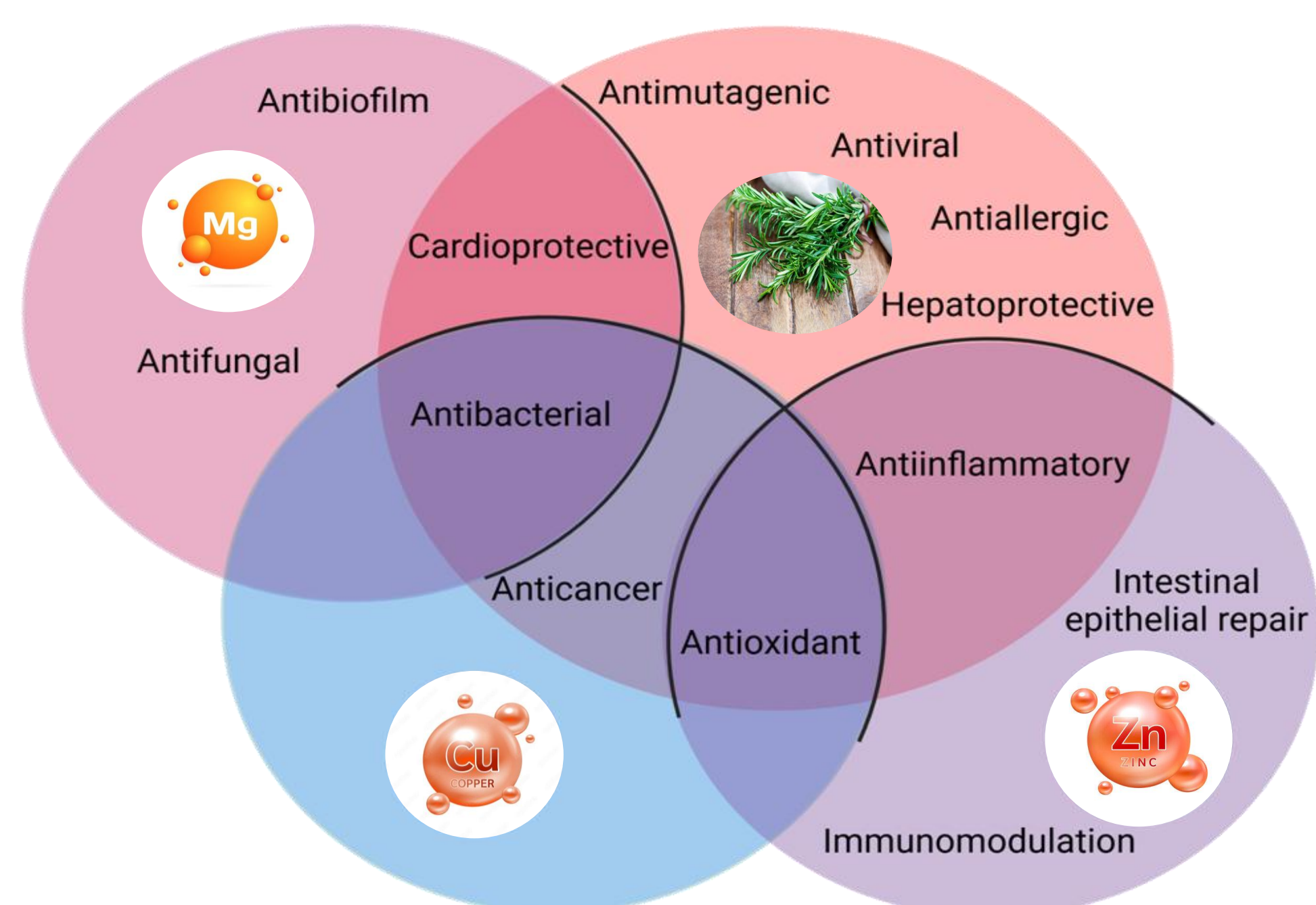


Fig. 2. The synergistic therapeutic benefits of rosmarinic acid and copper, zinc, and magnesium.

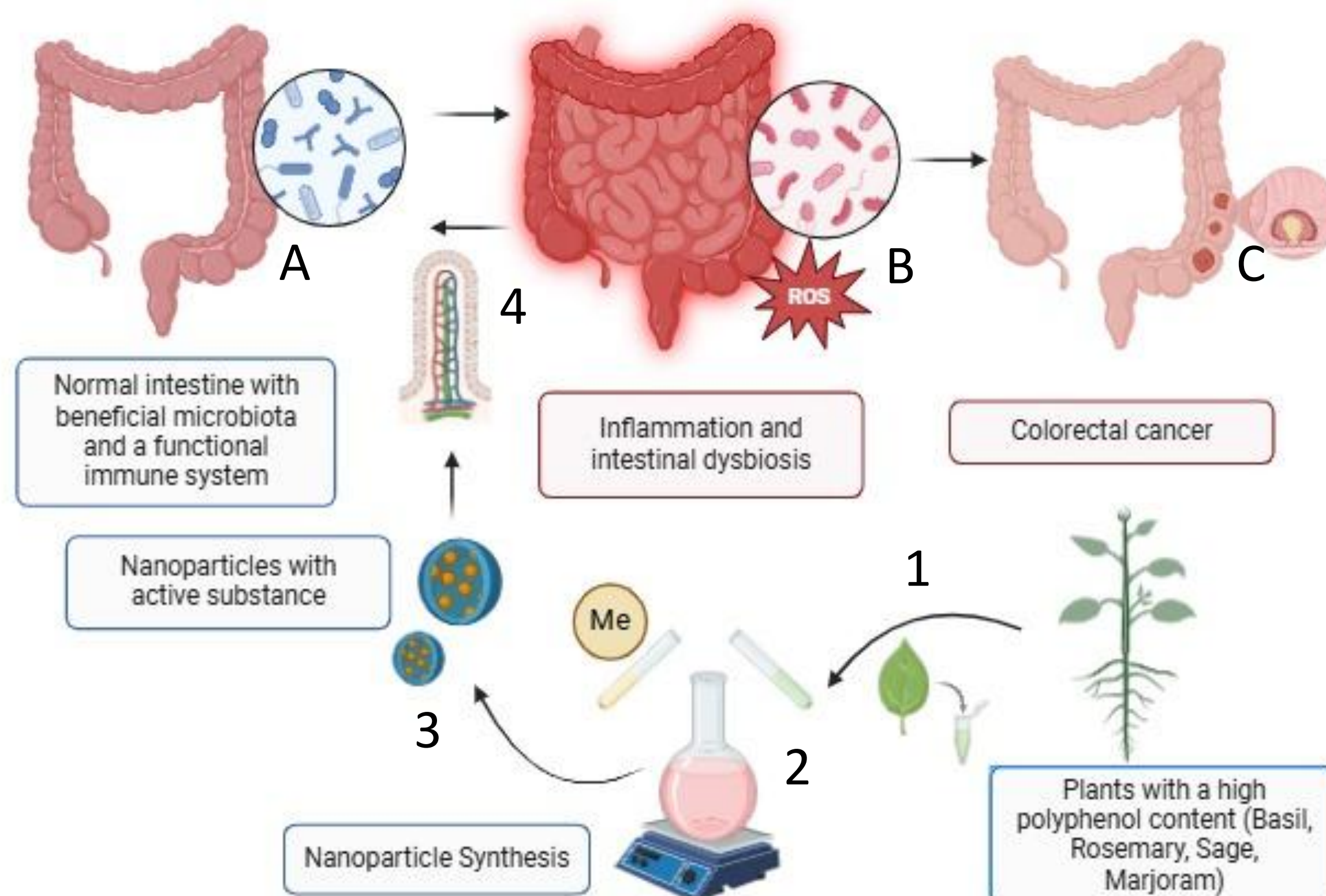


Fig. 1. The effect of ROS on the intestine and synthesis of nanoparticles from plants containing rosmarinic acid and their combination with magnesium, zinc and copper.

- Healthy gut with a balanced microbiota and a functional immune system.
 - Intestinal dysbiosis and subsequent intestinal inflammation.
 - The transformation of the inflammatory process into a neoplastic one.
- To prevent these processes from taking place, it is possible to intervene before the start of intestinal inflammation by administering nutraceuticals with an anti-inflammatory role.
 - In order to increase bioavailability at the intestinal level and reduce the systemic absorption of active substances (rosmarinic acid and various metals), their encapsulation in nanoparticles is used.

Conclusions

It is worthy of note that oxidative stress plays a pivotal role in the pathogenesis of inflammatory bowel diseases. Consequently, in addition to conventional methods, the targeting of oxidative stress in the gut, either by reducing the excess of reactive species or by managing antioxidant pathways, including increased antioxidant enzyme expression: catalase (CAT), glutathione peroxidase (GPx) and reductase, superoxide dismutase (SOD), nitric oxide synthase, reduced DNA damage, decreased amounts of oxygen and nitrogen, has the potential to significantly reduce the disease⁶. The synthesis of plant bionanoparticles containing rosmarinic acid presents a number of advantages and disadvantages. The primary advantage of rosmarinic acid is the variety of beneficial effects it has, including a low cost of materials, a faster production time than other types of NPs, an environmentally friendly nature, a lower toxicity level, and greater control over the size and shape of the NPs.

Antioxidant properties

Antioxidants, particularly phenolic compounds found in all plant parts, are important for protecting organisms from ROS and offer antioxidant, anticancer, antimicrobial, and anti-inflammatory benefits² (Fig. 2). This review focuses on rosmarinic acid (RA), found in plants like rosemary, basil, sage, and perilla. In addition to its bioactivity, RA-containing plant extracts can stabilize metal ions, enabling rapid nanoparticle (NP) formation with controlled size and morphology, bypassing lengthy synthesis processes⁵. However, RA's low water solubility and poor oral bioavailability limit its effectiveness². As a potential drug, RA should undergo testing for acute and chronic toxicity, LD50, and pharmacokinetics, in both animal models and human trials.