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Review Article

Nanoparticulate Formulation for the Treatment of Different Types of Colon Disease Like Ulcerative Colitis: A Comprehensive Review

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ABSTRACT

It is crucial to use a colon-targeted medication delivery system to treat diseases that start in the colon, such as inflammatory bowel disease, colon cancer, amoebiasis, and irritable bowel syndrome. Through colon targeted drug delivery system, we can give localised treatment to the patient which reduces the chance of toxicity and improves its therapeutic efficacy. The bioavailability of medications for the colon has greatly increased because to recent improvements in oral formulations. But because it is intimately linked to GI Inflammation, it is crucial to make some changes to the Gastrointestinal (GI) physiology to increase the therapeutic effect even more. Due to their structural makeup and smaller size, nanoparticles are often used in the administration of drugs that are specifically targeted for the colon. It is designed in such a way that it promotes aggregation time of drugs at the site of action, supporting localized therapy. This review article mainly focuses on oral nanoparticulate formulations that are targeted for treating Colon related diseases.

Keywords: Colon, Ulcerative Colitis, Nanoparticles, Drug delivery, Formulations.

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INTRODUCTION

Nanotechnology is regarded as the most important area of study in the twenty-first century. These so-called nanoparticles are actually very tiny colloidal particles, which have a diameter of about 200 nm and can be either biodegradable or non-biodegradable polymers. It is much more advanced over conventional dosage forms as the formulated drug increases efficacy, improves biodistribution as well as patient compliance, also reducing the toxicity risk. In nanoparticulate formulations the main drug is dissolved, entrapped and encapsulated to nanoparticles matrices. In the digestion process the colonic colonies plays a very important role and it is the site of decomposition of the macromolecule polysaccharides which are difficult to digest.

In these recent days, we can see that oral routed medicines are mostly preferred for treatment of colon diseases. Although it is very difficult to administer polypeptide drugs as because it is endangered by gastric acid or secretory protease degradation resulting in inactivation of the drug in the digestive tract. But oral route is not preferred at the time of emergency as it has slow absorption rate.[1,2]

Ulcerative Colitis

Widespread colonic mucosal inflammation is a hallmark of ulcerative colitis (UC), a kind of inflammatory bowel disease. It affects the rectum and lasts however long it does proximally along the colon. There are two main kinds of the condition (inflammation beyond the splenic flexure): left sided colitis, which produces inflammation up to the splenic flexure, and extensive colitis. When choosing a course of therapy and planning surveillance colonoscopies, which are used to find and treat colorectal cancer, these classifications are important. One in a thousand people in the Western world have colitis.[3]

Causes of ulcerative colitis

Inflammatory bowel disease may arise from environmental factors even though its precise cause is unknown in genetically predisposed people. Most likely, an inflammatory response to gut bacteria causes the autoimmune condition ulcerative colitis. An inflammatory bowel disease (crohn's disease or ulcerative

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colitis) affects 10% to 20% of persons with this condition. Some inflammatory bowel disease patients may experience a flare-up of their condition after taking non-steroidal anti-inflammatory medications. Paracetamol is probably a safer option for analgesia, even though modest non-steroidal anti-inflammatory medicines like ibuprofen may occasionally be administered if patients are informed of the potential for a higher risk of recurrence. Compared to Crohn's disease, ulcerative colitis is less likely to be brought on by smoking. Colitis coexists with gastroenteritis caused by known infections in up to 50% of cases.

Symptoms in patients suffering from ulcerative colitis

A brief history, assessment of endoscopic and radiological appearances, microbiology and histology is required for the diagnosis of colitis. Cardinal symptoms of UC are as follows:

i. Urgency,

ii. Tenesmus (Straining at stool),

iii. Bloody diarrhoea.

Even in individuals who have experienced a known relapse of ulcerative colitis, stool cultures should be taken (especially for Clostridium difficile toxin). Endoscopy should be done if bloody diarrhoea persists for longer than three weeks since it may indicate the existence of inflammatory bowel disease.[4]

Diagnosis of ulcerative colitis

The diagnosis of ulcerative colitis requires both an endoscopy and a mucosal biopsy. Despite the distinctions, there is a significant amount of similarity between the endoscopic findings of Crohn's disease and ulcerative colitis. Except for the typical patch of inflammation around the appendix's base, the rectum is continuously and uniformly afflicted, and the colon develops ulcers. In Crohn's disease, the terminal ileum frequently becomes ulcerated, while the rectum frequently remains unaffected and other parts of the colon frequently remain whole. It may be challenging to identify between isolated colonic Crohn's disease and ulcerative colitis in roughly one-third of instances of colitis; these patients are referred to as having indeterminate colitis.[5]

Nanoparticles for Colon Targeting

Any particulate material with at least one dimension between 1 and 100 nm is referred to as a Nanoparticle (NP). The method employed for a nanoparticle's creation has a significant impact on its size. The only type of medication delivery device that can get past all physiological barriers and function at a specific target spot is a nanoparticle. Except being a drug carrier or a dissolving or an encapsulating form of drug, nanoparticles can also be used by adsorbing or attaching the active substances. There are evidences where nanoparticles have shown improved efficacy, less toxicity and a huge enhancement of biodistribution if compared with conventional dosage forms. Drug delivery systems that are based on nanoparticles, have proven to be pharmacokinetically and pharmacodynamically more advanced.[6,7] Because of their biodegradability, ion and temperature sensitivity, as well as pH levels, they also demonstrated controlled release capabilities. The drug rate of drug release can be interfered by polymer degradation process. Because they avoid any difficulties brought on by the long-term deposition of nanoparticles or any remaining components inside the ulcerated tissue, biodegradable polymers are employed to create nanoparticles.[8,9]

However, dose deterioration resulted to the release of the entrapped drug, so to address this issue, drug-filled nanoparticles were sealed within pH-sensitive microspheres. This allowed the nanoparticles to act right where they were needed, which immediately stopped the drug leakage. In contrast to their bulk counterparts, Nanoparticles (NPs) have a variety of characteristics, including as high surface energy and unusual mechanical, thermal, and optical behaviours. By adding various functional groups to the surface of NPs, one can vary their chemical activity and dispersibility, making them ideal for use in specific environments. Thus, by using a variety of techniques, we may conclude that nanoparticles may be a very effective instrument for targeted medication delivery at particular locations within the inflamed colon.[10,11]

Nanoparticulate Formulation as a Drug Delivery Technniques for Ulcerative Colitis

Nanoparticles use a number of targeting strategies to cross the epithelial barrier and into the UC site. This method of administering drugs allows for the delivery of high local drug concentrations, reduced drug degradation and efficacy loss before to site of action, and a reduction in systemic medication adverse effects.[12,13]

Nanoparticulate formulation as Drug delivery techniques for UC

- Depending on the pH of the location following ingestion, nanoparticles target the epithelium of the inflammatory colon.
- Targets the inflamed colon epithelium based on the level of Reactive Oxygen Species (ROS) there.
- Used to deliver nanoparticles to the inflamed colon after oral treatment.
- Directed at the inflamed colonic epithelium via a ligand-receptor interaction. (Oral therapy).[14,15]

Nanoparticles used for Colonic Ulcerative colitis

Artificial nanoparticles have proved effective in treating Ulcerative Colitis (UC) in the pre-clinical stage. Despite its popularity, it has two shortcomings. Each of these nanoparticles' potential toxicities

must be assessed before clinical procedures. The product's scale is also limited.[16,17] Contrarily, it is believed that nanoparticles obtained from natural sources are inexpensive, risk-free, and may be able to get around the limitations of synthetic nanoparticles. Extracellular Vesicles (EVs) protected from mammalian cells and factory-derived nanoparticles have recently demonstrated significant preclinical potential for the treatment of UC. These findings suggest that naturally occurring nanoparticles might offer a cutting-edge UC treatment approach.[18,19]

Plant-Derived Nanoparticles

Finding out whether artificially produced nanoparticles can contribute to interspecies communication and have a direct beneficial impact on fatal illnesses, particularly intestinal inflammation, is of great interest.[20,21] Grape Nanoparticles (GELNs) that are ingested orally and contain proteins, lipids, and micro-RNA are designed to pass through the gut and be absorbed by intestinal stem cells. Similar to how they were resistant to degradation by slaver, the stomach's acidic environment, and the intestinal tract's abundantly active proteolytic enzymes.[22,23] These results suggested that edible factory-ground nanoparticles might be taken up by intestinal cells and supplied orally to the intestine, where they might provide conditioning akin to intestinal rejuvenescence. Combustible factory-produced nanoparticles with anti-inflammatory properties that naturally target the colon may thus constitute a novel natural delivery method that could effectively be used to treat patients with digestive tract diseases like IBD.[24,25]

pH-dependent Nano-delivery Systems

Methacrylic acid copolymers (Eudragit) are the pH-dependent coating polymers most frequently utilised for oral administration. The pH at which the side chains become soluble can change depending on how they are made. For instance, pH-sensitive nanoparticles containing the topically active corticosteroid Budesonide (BSD) (Eudragit S100) were produced using poly- (lactic-co-glycolic acid) and methacrylate copolymer combinations. At both acidic and neutral pH levels, these nanospheres showed strong drug release properties that were pH dependent, with a sustained release phase occurring at pH 7.4.[26,27] Studies on animals utilising a TNBS-induced colitis model revealed that BSD-loaded nanospheres were superior to BSD alone as a therapeutic agent. These nanospheres showed *in vivo* stronger and more targeted adhesion to ulcerated and inflamed rat mucosal colonic tissue than conventional enteric-coated microparticles.[28,29] Additionally, their systemic toxicity was reduced.

There are still numerous reasons for caution despite the promising results of these pH-dependent nano-delivery systems for the colon. These consist of both the typical intra- and inter-individual pH variations and alterations in luminal pH brought on by diseases. Therefore, for improved disease therapy, researchers should consider the individual inflammation status while devising a delivery system to target the colon based only on pH.[30,31]

ROS-responsive Nano Delivery Systems

Drug carriers that respond to changes in redox potential may also show clinical benefit in the treatment of UC. Reactive Oxygen Species (ROS) production is out of balance, and antioxidant defence mechanisms deteriorate under oxidative stress. Due to the considerable ROS production by inflammatory cells like neutrophils and macrophages, oxidative stress is a hallmark of inflammatory processes. ROS overproduction has been linked to UC.[32,33] For instance, in biopsies collected from the sites of people with UC compared to those without the disease, mucosal ROS concentrations are 10- to 100-fold higher, and ROS concentrations are linked with disease development. By leveraging the pathological characteristics of the disease, redox-responsive nano-delivery technologies provide significant potential for IBD therapy.[34-40]

CONCLUSION

We have primarily concentrated on the benefits of nanotechnology for treating ulcerative colitis in this review study. However, nanotechnological approaches may be used to treat Crohn's disease by administering drug-loaded nanoparticles to both the large intestine and the small intestine (another source of this disease).Targeting and maintaining nanoparticle-loaded drugs in the small intestine present two challenges due to the need to specifically release nanoparticles from the hydrogel to this organ and/or decorate the nanoparticles with ligands specific to receptors expressed mostly in epithelial cells of the small intestine.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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