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Review Article

NANOSPONGES FOR EFFECTIVE TREATMENT OF ULCERATIVE COLITIS

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ABSTRACT

In modern years, nanosponges (NS) have gained marvelous impetus in drug delivery through nanotechnology. Nanosponges are capable of providing solutions for several formulation related problems. Through this review, scientists working in the ground of nanotechnology can have an insight into the techniques of preparation, characterization and applications of NS. Owing to their small size and spongy nature they can bind poorly-soluble drugs within their matrix and recover their bioavailability. They can be crafted for targeting drugs to precise sites, prevent drug and protein deprivation and prolong drug release in a controlled manner. This appraisal attempts to convoluted different schemes of synthesis of NS and their characterization. Factors affecting drug loading and release have been enumerated. Due to their compensation, NS have not only been explored for their pharmaceutical applications but also have large attractiveness in allied sciences, especially in water purification.

Keywords: Nanosponges, Cyclodextrin inclusion complex, Solubility enhancement, Protein and enzyme stabilization, Tumor targeting.

1. INTRODUCTION

Ulcerative colitis (UC) and Crohn's disease (CD) are the disorders collectively known as IBD. While Crohn's disease can influence every part of the intestinal part and frequently affecting the colon and distal ileum, while Crohn's disease influences only the colon [1]. The two types of IBD are highlighted by exacerbated uncontrolled intestinal inflammation that prompts low quality of life and requires delayed therapeutic or surgical interventions [2]. In Europe, IBD affecting more than 2.5 million peoples (~0.5 %) and is getting progressively common in Asia and emergent nations [3]. The frequency of IBD is expanding, specifically emergent nations. Even though the etiology of these inflammatory disorders isn't completely understood, there is a developing body of evidence that morbidity of IBD is related to a hereditary inclination. The additional factors might be related to unsettling influence in the immune system, and irregular intestinal microflora (quantitatively and qualitatively), which has been affirmed in murine models of IBD [4-5]. The significance of these complex interactions results in disturbed intestinal homeostasis and an unbalanced inflammatory microflora. CD is characterized by a transmural inflammation that may influence the layers of the GI wall, while UC is a mucosal inflammation and delineated to the colon [6-7]. There is a developing enthusiasm for multi-particulate modified delivery systems, particularly for site-specific targeting of the gastrointestinal tract (GIT). The systems of modified release were very complex, and their huge scale assembling requires numerous abilities and innovative advancement [8-9]. Among the various kinds of different unit dosage forms, nano-sponges shown up very fascinating dose structures from the monetary process advancement and scale-up perspectives. Nano-sponges having a colloidal structure in which a small solid particle is incorporated in the cavities and mesh-like system- to encapsulate wide assortments of molecules like anti-cancer, proteins, DNA, etc. [10-11]. Nano-sponges are 3D systems with a backbone of the naturally long-length polymer. The nano-sponges are prepared by an interaction between cross-linking polyesters and peptides, contrasted with a few other nano dimensions medicate drug delivery systems. Nano-sponges are lipid in nature, and also, they can scatter in the aqueous transporting fluid. They can be used to overcome the bitter taste of drugs. The medication discharge from the nano-sponge system can be changed by modifying cross-linker to polymer proportions. Nano-sponge binds to the surface of the target site in their circulation process in the body and discharges the

medication in a controlled and anticipated way [12-15]. Budesonide (BUD) is the locally acting corticosteroid with a brilliant affinity for glucocorticoid receptors with the strong anti-inflammatory activity. It offers many benefits over old steroids. Budesonide has 200 times higher topical potency than hydrocortisone and only 10 % of systemic bioavailability. It was reported that budesonide showed less systemic side effects than prednisone. Positively BUD is an ideal drug for the local therapy of IBD includes low oral bioavailability, quick clearance and toxic metabolites [16, 17]. BUD is available in many formulations in the market, such as ileal release formulation, tablets, and enema, etc. In the account of the beneficial effects of nano-sponge, and due to drawbacks of traditional topical drug delivery, and absence of availability of nano-sponges based DDS; present research work was intended to figure out and assess novel nano-sponges based budesonide formulation for its promising effects in the treatment of IBD [18].

1.1. What is Ulcerative Colitis?

Ulcerative colitis is an idiopathic inflammatory bowel disease that affects the colonic mucosa and is clinically characterized by diarrhea, abdominal pain and hematochezia. The extent of disease is variable and may involve only the rectum (ulcerative proctitis), the left side of the colon to the splenic flexure, or the entire colon (pancolitis). The severity of the disease may also be quite variable histologically, ranging from minimal to florid ulceration and dysplasia. Carcinoma may develop. The typical histological (microscopic) lesion of ulcerative colitis is the crypt abscess, in which the epithelium of the crypt breaks down and the lumen fills with polymorphonuclear cells. The lamina propria is infiltrated with leukocytes. As the crypts are destroyed, normal mucosal architecture is lost and resultant scarring shortens and can narrow the colon.

1.2. Systemic and Extra-Colonic Manifestations

Arthritic complication may arise in as numerous as 26 % of patients with ulcerative colitis. Spondolylitis occurs in 3 % of these patients. The arthritics symptoms may appear before the inflammatory bowel disease and do not necessarily pursue the course of the intestinal disease. Twelve to 23% of patients with ulcerative colitis have peripheral arthritis, which affects large, weight-bearing joints such as knees or ankles. Arthritis signs and symptoms usually accompany exacerbations of ulcerative colitis. Nineteen percent of patients with ulcerative pancolitis experience dermatological changes. Erythemianodosum and pyodermagangrenosum are commonly associated with this disease. Other dermatological sequelae include dermatitis, erythematous rash, psoriasis, carcinoma, urticaria, pityriasis, lupus erythematosus, vitiligo and ecchymosis. Ocular manifestations of ulcerative colitis occur in 5 % of patients with extensive disease or with Crohn's disease, and may include anterior uveitis, episcleritis and keratoconjunctivitis. Symptoms of these complications include headache, photophobia, blurred vision, burning and increased secretions from the eyes.

2. CLASSIFICATION

The extent of colonic mucosal participation and severity of disease correlate with the clinical manifestations of ulcerative colitis. Approximately one-third of all patients with ulcerative colitis have involvement limited to the rectum (the distal 15 cm of the large intestine) or ulcerative proctitis. Ulcerative proctitis is endoscopically characterized by edema, erythema and loss of vascular markings. Granularity, friability, and frank ulceration are also seen in more severe disease. Distal or left-sided colitis is found in patients in whom the inflammatory process extends from the rectum 40 cm. Disease activity does not extend beyond the splenic flexure, and there is evidence of chronic inflammation and chronic architectural distortion. Pancolitis involves the portion of the colon beyond splenic flexure. It is characterized by hematochezia and diarrhea, and may be accompanied by abdominal pain and cramps, fever, and/or weight loss with persistent inflammation. Normal haustral markings disappear with generalized shortening and tubularization of the colon. In severe disease, the mucosa may be described as nodular with pseudopolyps, a reticular pattern, and discrete ulcer craters.

3. OCCURRENCE AND SYMPTOMS

The occurrence of ulcerative colitis has remained fairly constant in those areas for which data are available for a number of years. Ulcerative colitis has been reported between 1.0 and 15.0 cases per 100,000. In general, the rates are highest in the Scandinavian countries, Great Britain and North America. The disease is uncommon in Asia, Africa and South America, although good data are generally lacking from underdeveloped countries where the rates seem to be low. Prevalence is higher among Jewish people born in Europe and the United States (Ashkenazi Jews) than among those born in Asia and Africa. The literature reports a slightly higher incidence

of ulcerative colitis in females than males. It is most likely to occur in early adulthood, but disease presentation can occur in the fifth or sixth decade, and occasionally in the seventh or eighth decade. Diet, breast-feeding, oral contraceptives, and the cessation of cigarette smoking have been implicated as risk factors for ulcerative colitis. Studies indicate a decreased risk of ulcerative colitis for current smokers, however, former smokers are at increased risk of developing the disease.

The predominant symptom in ulcerative colitis is diarrhea, which can be associated with frank blood in the stool. The patient has frequent bowel movements, which may be small in volume, as a result of irritability of the inflamed rectum (proctitis). Other symptoms include abdominal or rectal pain, fever and weight loss. Although diarrhea is the dominant complaint in patients with ulcerative colitis, some patients may complain of constipation and rectal spasm.

4. ULCERATIVE COLITIS: CAUSES

Genetics Inheritance on a polygenetic basis seems to play a role in the etiology of ulcerative colitis in about 12-15 % of cases. The most firmly established and quantitatively greatest risk factor for developing ulcerative colitis is a family history. The factors responsible for variable expression of this heritable susceptibility are not known. Also, the fact that migrants to developed countries appear to develop higher rates of disease, and the rates among Jews vary by country, support an important environmental component to risk as well. Evidence of higher rates of ulcerative colitis in urban areas raises the issue of a transmissible agent that may be responsible for disease expression or increased susceptibility. Environmental Environmental factors that may potentiate the onset of ulcerative colitis are currently under investigation. Such risk factors include diet, breast-feeding and other perinatal events, occupation and social class, oral contraceptive use, and, most impressively, the cessation of cigarette smoking. Although the "protective" factor in tobacco smoke is unknown, several preliminary trials have shown promising results. Pathogenesis The pathogenesis of ulcerative colitis remains unknown. Several theories have been proposed that implicate vascular impairment, autoimmune mechanisms, bacterial-immunological interactions, and allergic or hypersensitivity reactions. Recent literature on inflammatory bowel disease (IBD), Crohn's disease, and ulcerative colitis reports an intensive search for the antigens that trigger the immune response in inflammatory bowel disease. There are three major hypotheses as to these antigenic triggers. One hypothesis is that these triggers are microbial pathogens, as yet unidentified. According to this theory, the immune response in IBD is an appropriate but ineffective response to these pathogens. The second hypothesis as to the antigenic trigger in IBD is that there is some common dietary antigen or nonpathogenic microbial agent to which the patient mounts an abnormal immune response. It has been hypothesized that patients with IBD are genetically programmed to mount an intense immune response to some common luminal antigen (dietary or microbial) to which most people do not respond. Diet is a major source of antigens in the intestinal lumen. Dietary antigens are capable of triggering immune responses. One of the foods implicated in the pathogenesis of IBD is cow's milk. Patients with IBD and Crohn's disease demonstrate an increased incidence of antibodies to cow's milk protein. In patients with IBD, cow's milk proteins and other dietary antigens have abnormal access to the lamina propria because of the defect in the epithelial cell monolayer caused by inflammation. Normally, the intestinal epithelium is a barrier between the immune cells of the lamina propria and luminal antigens; however, in IBD, the immune cells of the lamina propria are exposed to numerous luminal antigens. These luminal antigens are capable of triggering immune responses. As a result, specific immune responses to the etiological agent may be overwhelmed by immune responses to thousands of luminal antigens that pass through the damaged epithelium. The third hypothesis relating to antigenic triggers postulates that an antigen is expressed on the patient's own cells, particularly on intestinal epithelial cells. Theoretically, the patient mounts an appropriate immune response against some luminal antigen; but because of similarities between proteins on the epithelial cells and the lumen antigen, the patient's immune system also attacks the epithelial cells. Under this autoimmune theory, the immune response is directed toward the epithelial cells, and the cells are destroyed by one of two immune effector mechanisms-either antibody-dependent cellular cytotoxicity or direct cell-mediated cytotoxicity.

Diagnosis Overview Evaluations at initial presentation, at the beginning of each subsequent attack, and at multiple points during each attack are required to assess the clinical picture. The extent of the evaluation should be guided by the presentation. The milder the presen-

tation, the less extensive or invasive the evaluation. The frequency and severity of diarrhea is a good indicator of the severity of disease. Six or more bowel movements per day are associated with severe disease. The increase in frequency of bowel movements during an attack, as compared to the normal number of bowel movements, is more informative than the absolute number. Fever, hypotension, and tachycardia are markers for the presence of severe disease and necessitate more extensive evaluation in a hospital setting. Nocturnal bowel movements are also crucial in the history to determine severity. The differential diagnosis in ulcerative colitis includes other forms of inflammatory bowel disease, including Crohn's disease, diverticular inflammation and hemorrhage, collagenous colitis, ischemic bowel disease, radiation colitis, and infectious etiologies including the following organisms: Campylobacter, Shigella, Clostridium difficile, amebiasis, and *Escherichia coli*.

Non-Invasive Diagnostic Imaging Plain abdominal x-rays demonstrate the gaseous outline of the transverse colon in the acutely ill patient. Shortening of the colon and loss of haustral markings can also be demonstrated by plain films, as well as a double-contrast barium enema. Indications of ulcerative disease include loss of mucosal detail, cobblestone filling defects, and segmental areas of involvement. Contrast studies are a sensitive radiological diagnostic tool to determine the extent of ulcerative colitis. Currently, the most common radiological procedures include the small-bowel series, enteroclysis, barium enema and upper gastrointestinal films. Small-Bowel Series This is a fast, safe procedure for visualization of the small bowel. The patient drinks a barium suspension and overhead abdominal radiographs are taken at 20-30 minute intervals. When the barium reaches the right colon, fluoroscopy is performed while moving the patient in various positions to unwind superimposed bowel loops. Compression spot radiographs are obtained with attention to the terminal ileum. Enteroclysis Enteroclysis is more sensitive for focal lesions (such as adhesions), but has a higher rate of complications and technical difficulty. With the patient mildly sedated, a tube is passed through the nose and advanced into the jejunum. Under constant fluoroscopic imaging, barium is infused through the tube with a methylcellulose solution, resulting in distension and coating of small-bowel loops. The appearance is similar to a double-contrast enema. Barium Enema this is a safe, effective tool for evaluation of patients with ulcerative colitis. It demonstrates ulcer depth and fistulas. A high-density barium preparation is administered through a rectal tube. Under fluoroscopy, air is introduced until the entire colon is distended and coated with barium. Spot films are taken during the filling of the colon and a series of overhead films are taken after the patient has been positioned to demonstrate the whole colon. Post-evacuation films are also obtained.

5. NANOSPONGE

The pharmaceutical and health care industry has been creating and using nano-scale materials for solving many physical, chemical and biological problems associated with the treatment of disease. Since 1950's, nano-technology has dominated technology. During the same period extensive research on cyclodextrins (CD) became a "hot topic" owing to their toxicological safety and widespread applications. Cyclodextrins are nonreducing cyclic oligosaccharides having 6-8 glucose molecules bonded with a 1, 4-α-glucosidicic bond, having a characteristic truncated cone structure. The outer molecule is hydrophilic while the internal cavity is hydrophobic. It is the hydrophobic cavity which provides the CDs with the unique ability to form inclusion complexes and stabilize organic molecules of suitable polarity and size in solution. CD are capable of reversibly trapping substances which are hydrophobic in nature of any state of matter. Among the natural cyclodextrins, the most prominently used type is β-CD, due to their low cost. They can be administered parenterally and are nonirritating on intra-muscular administration. CDs have been exhaustively reported in various pharmaceutical, cosmeceutical, agricultural, biotechnological, industrial and environmental applications. But, they suffer from two major limitations namely, easy dissociation of complex on dilution and specific polarity and size requirement of guest molecule. For this reason CDs have been modified and frequently used as building blocks by linking β-cyclodextrin with substituents in a regioselective manner. They can be predictably hyper-branched using different cross-linking agents to produce tiny nano-sized sponge like structures likened to a "honeycomb". Cross-linkers have two or more reactive groups capable of covalently attaching chemically to specific groups present in CDs to produce cross-linking [5]. On the same principle cross-linked hyper-branchedcyclodextrins gave birth to nanosponges (NS). NS gained popularity by the work started by Chemist

De Quan Li and a graduate student Min Ma, who successfully developed a polymer that could absorb and trap organic contaminants in water using "cyclodextrinnanosponges" (CD-NS). These were successfully utilized for cleaning water [6.] In the field of pharmaceuticals, the era of nanoporous materials comprised of cyclodextrins, started in 1992, the first studies on cyclodextrin microparticles were reported by Loftsson et al [7]. Many drugs are hydrophobic and present a confront for effective in vivo delivery. Shrinking materials to nano size has overpoweringly enhanced the effectiveness of such drugs. A number of polymers have been investigated and used as Novel drug delivery systems (NDDS). NS when used for target specific drug delivery can improve therapeutic response resulting in minimum side-effects. "Tagging" drug-loaded NS ensures desired pharmacological response by targeting disease affected cells, while leaving the healthy ones unharmed [10]. Drugs included within the NS pores are shielded from premature destruction and drug stability is enhanced [11 ,12, 13] This article focuses on cyclodextrin based nanosponges since cyclodextrin is a widely used excipient in pharmaceutical dosage form development and has a well established history of toxicological safety in humans and animals.

5.1. Properties of nanosponges

Nanoporous structures have been broadly classified into nanoporous membranes, nanoporous hydrogels and nanoporous particles. NS fall into the category of nanoporous particles. CD-NS have been reported as white fine powders, insoluble in water and common organic solvents. The academia and pharmaceutical industry have found nanosponges to be effective drug delivery systems. Nano-sized carriers have recently been applied for adsorption, separation, and catalysis due to their considerable internal surface areas and pore volumes 14. The thin line of distinction among nanoparticles and NS is the difference in porosity and size. Nanoparticles have size in nanometer whereas NS have pores in nanometers while their overall size can extend up to micrometers, and are usually smaller than 5μm. Many times NS have been reported as Nano-porous nanoparticles/microparticles. CD-NS have colloidal dimensions which form clear or opalescent suspensions in water depending on their concentration. NS show different domains in their structure, since they have both hydrophobic and hydrophilic groups. 15 Toxicological consideration All toxicity studies have demonstrated that orally administered cyclodextrin inclusion complexes are practically non-toxic in rats, a phenomenon attributed to lack of absorption from the gastrointestinal tract.16 Haemolytic activity studies on normal blood cells have shown that CD-NS were non-haemolytic up to 20 mg/mL. The cytotoxicity of NS on HT-29 cells showed that exposure for 24 and 48 h did not cause decrease in cell viability, whereas a slight decrease in cell viability was observed when the cell lines were exposed to NS for 72 h.

5.2. Advantages of nanosponges

1. Current research into novel nanomaterials aims at improving properties of existing materials such as having greater control over the size, homogeneity, high drug loading and predictable/controlled drug release [15, 16, 17]. NS are envisioned as materials having great potential because of the attractive features summarized below.
2. Being amphiphilic in nature, NS, can simultaneously carry both hydrophobic molecules in the hydrophobic cyclodextrin cavity and hydrophilic molecules in the spaces between the single cyclodextrin moieties. Hydrophobic drugs can be loaded into the NS structure to consequently increase their solubility.
3. An attractive feature is the simplicity of chemistry of particles. CD can be cross-linked to form nanopores which serve as sites for drug loading.
4. The superior properties of NS have been attributed to 'tunability', that is the ability to control the structure of particles and control the nature and size of aperture. By varying the proportion of cross-linker to polymer, the degree of cross linking can be modulated, which ultimately affects drug loading and release.
5. One of the major advantages of this system is the ability to produce predictable/controlled drug release.
6. NS can be tagged with specific linkers to target diseased cells hence achieving greater efficacy while reducing side-effects, decreasing dose and dosing frequency and in turn increasing patient compliance.

5.3. Preparation of Nanosponge

5.3.1. Emulsion solvent diffusion method

In this method, dissimilar proportion or quantity of ethyl cellulose and polyvinyl alcohol are used to prepare nanosponges. Two phases are used in this method dispersed and permanent. The dispersed phase consists

of ethyl cellulose and the drug, which is then dissolved in 20 ml of dichloromethane and some quantity of polyvinyl alcohol (PVA) is added to 150ml of the continuous phase (aqueous). Then, the mixture is stirred at the speed of 1000 rpm for about 2h. The product *i.e.* the nanosponges are collected by filtration. To conclude, the product is dried inanoven at a temperature of 400°C [11].

5.3.2. Loading of drug keen on nanosponges

To obtain the particle size less than 500 nm, nanosponges should be pre-treated. To obtain this range, the nanosponges are dissolved or suspended in water. The suspended nanosponges are sonicated vigorously to prevent the accumulation. The suspension is centrifuged to produce a colloidal fraction. The supernatant is separated and the sample is dried using a freeze dryer.

An aqueous suspension of nanosponges is prepared. An excess amount of drug is added to the suspension and continuously stirred for the certain period of time for the complexation to occur. After the complexation has taken place, the uncomplexed drug is separated from the complexed drug by using centrifugation. The solid crystals of the nanosponges are obtained by using a freeze dryer or by evaporating the solvent.

This Solid Crystal structure of nanosponges has a crucial rule in complexation of the drug. The drug loading capacities of paracrystallinenanosponges is lesser when compared to crystalline nanosponges. The drug loading takes place as a mechanical mixture in weakly crystalline nanosponges [12].

5.3.3. Mechanism of drug release from nanosponges

Since the nanosponges have an open structure (in the surrounding of nanosponges they do not have any continuous membrane), the active substance is added to the vehicle in an encapsulated form. The encapsulated active substance is talented to move freely from the particles into the vehicle awaiting the vehicle gets saturated and the equilibrium is obtained. As soon as the product is applied on to the skin, the vehicle containing the active ingredient gets unsaturated causing a commotion in the equilibrium. Thus, the flow of active substances from nanosponge particles into vehicles starts to epidermis awaiting the vehicle is either absorbed or dried. Still after the retention of the nanosponge particles on the surface of skin i.e. the stratum corneum, the release of active substance continues to skin for a long period of time.

5.4. Factors influencing in the formulation of nanosponges

5.4.1. Nature of polymer

The polymer used in the preparation of nanosponges can influence its formation and can also affect the pre-formulation. The size of the cavity of a nanosponge should be big enough to entrap a drug molecule of a particular size into it for complexation [13].

5.4.2. Drug

To be complex with nanosponges, the drug molecules should have some specific characteristics as mentioned below:

- The molecular weight of the drug molecule should be in range ranging from 100-400 Daltons.
- Structure of drug molecule should not consist of more than 5 condensed ring.
- The solubility of thedrug in water should be<10 mg/ml.

The melting point of the drug should be <250°C.

5.4.3. Temperature

Changes in the temperature can affect the complexation of drug or nanosponges. Increasing the temperature generally decreases the extent of the stability constant of the drug or the nanosponge complex which may be due to the reduction of interaction forces such as hydrophobic forces and Van der Waal forces of drug/ nanosponges with an increase in the temperature [14].

5.4.4. Degree of substitution

The number, position, and type of the substituent of the parent molecule can affect the ability of complexation of the nanosponges to a greater extent.

5.4.5. Method of preparation

The method of drug loading into the nanosponges can cause a change in the complexation of drug and the nanosponges. Although, the success of a method mainly depends on the nature or the characteristics of the drug and polymer; in some cases, freeze drying has also been known to affect the drug and nanospongecomplexation.

5.5. Characterization of nanosponges

The characterization methods for the complexed drug/ nanosponges are listed below:

5.5.1. Solubility studies

Inclusion complexes is a technique by which can determine the solubility and bioavailability of the drug.

This technique is the most widely approached technique for analysis of the inclusion complexes of nanosponges. Degree of completion can be known by the plot of phase solubility. Solubility studies are conducted to access the pH of the drug, solubilization outline and to evaluate the factors affecting drug solubility [16].

5.5.2. *Microscopic study*

Microscopic studies of nanosponges/drug can be conducted by using scanning electron microscope and transmission electron microscope. Inclusion complex formation is indicated by the difference in the crystallization state and the product seen under an electron microscope.

5.5.3. *Zeta potential determination*

Zeta potential can be defined as the difference of potential between two layers (dispersion medium and immobile layer) of fluid locked up with dispersed particles. Zeta potential is the major key indicator for the stability of the colloidal dispersion. By adding extra electrode on particle size equipment or zeta seizer, the zeta potential can be measured. Higher the value of zeta potential of a colloidal dispersion more is its stability.

5.5.4. *Thermodynamical method*

If any changes occur in drug molecules or particles undergoes some changes earlier then the thermal degradation of nanosponges it can be determined by the thermo-chemical method. The changes of drug particles can be melting, evaporation, oxidation and decomposition and polymeric changes. The changes in the drug molecules indicate the formation of a good complex.

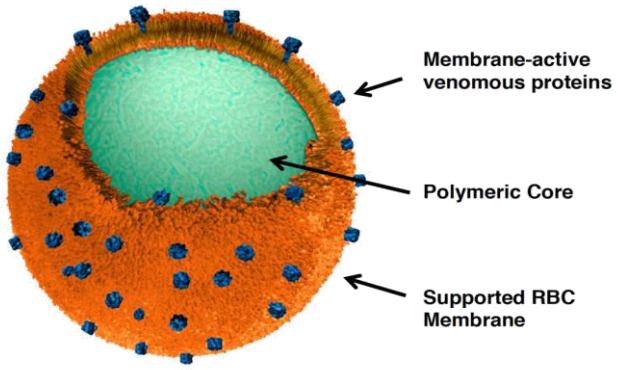

Fig. 1: Nanosponges: Tiny Particles Coated With Cell Membranes Sop Up Toxins In The Blood-stream

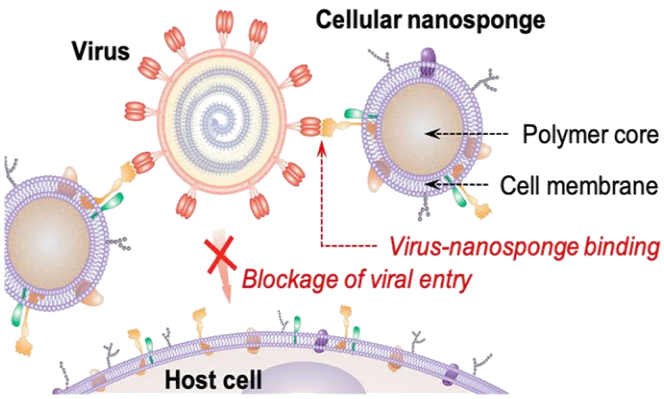

Fig. 2: Working Principal of Nanosponges

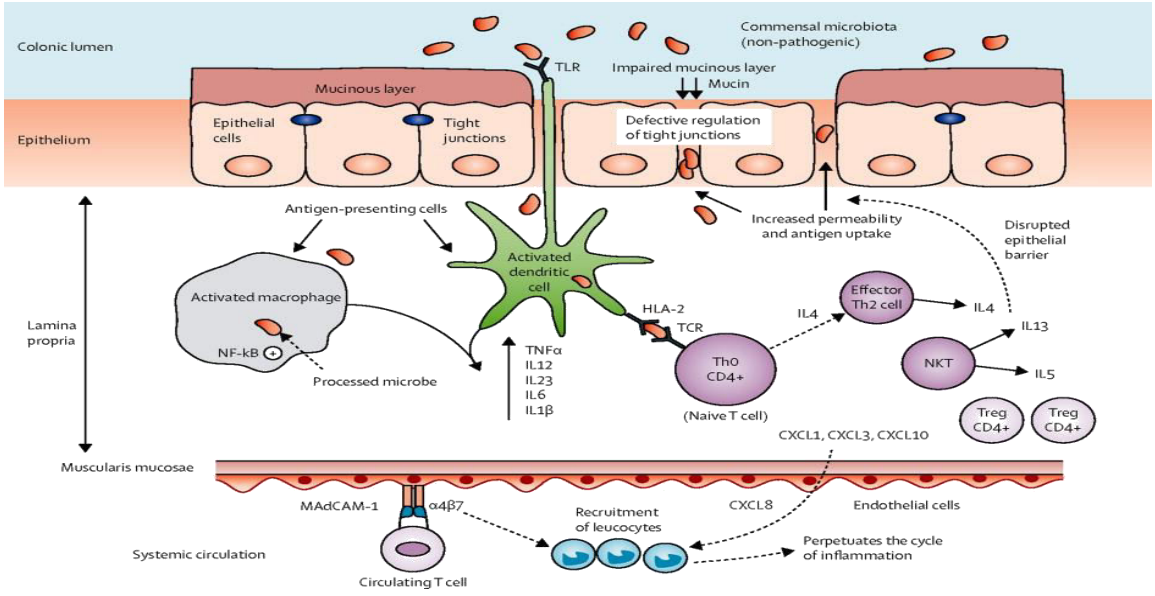

Fig. 3: Ulcerative Colilis

5.5.5. Particle size and polydispersity

Particles size is determined by the process of dynamic light scattering using 90Plus particle size determining software. Dynamic light scattering (DLS) is defined as a technique used to find out the size distribution profile of nanoparticles. At last, the final diameter of the particles and poly-dispersity index (PDI) can be found.

5.5.6. Thin layer chromatography (TLC)

TLC can be defined as a technique which can be used to separate the non-volatile or evaporative mixture. In this technique, if the Rf value of a particular drug molecule is of an acceptable range then it is helpful in recognizing the formation of a complex between drug and nanosponges.

5.5.7. Infrared spectroscopy

The interaction between nanosponges and the drug in the solid state can be determined by using infrared spectroscopy. Nanosponge bands can slightly change during formation of complexes. Few guest molecules attached in the complexes which are less than 25%, the drug spectrum can be easily masked by the spectrum of nanosponges. The technique is not appropriate to identify the inclusion complex over the other methods [19].

5.5.8. Loading efficiency

The loading efficiency of a nanosponge particle can be determined by the estimation of drug loaded into the nanosponge using UV spectrophotometer and high-performance liquid chromatography method for the nanosponges. The loading efficiency of nanosponges can be calculated by using the following equation.

LE = (Actual drug content in nanosponges/Theoretical drug content) x 100

5.6. Applications of nanosponges

Nanosponges have a wide range of application in the pharmaceutical field, because of its biocompatibility and versatility. In the pharmaceutical industry, nanosponges can be used as an excipient for the formulation of tablets, capsules, granules, pallets, suspensions, solid dispersions and topical dosage forms. Nanosponges can accommodate bothlipophilic and hydrophilic drug molecules, basically, those drugs substances which belong to the biopharmaceutical classification system (BCS-class II) as well as the poorly water-soluble drug [20-25].

6. CONCLUSION

Nanosponges can carry the water-insoluble drug because of their tiny porous structure. To increase the dissolution rate, solubility and permeability of drug nanosponges complexes play a major role. This is reported that β-cyclodextrine based nanosponges are three or five times more effective to deliver the drug to the targeted site. Nanosponges are generally solid in nature and can be prepared for oral, parental, topical and inhalation dosage form. For the preparation of tablet, capsule *i.e.* oral administration the nanosponges complexes are dissolved in a suitable excipient like lubricants, diluents and anti-cracking agent.

Conflict of interest

None declared

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