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# Liposome Targeted Drug Delivery for the Treatment of Colon Cancer

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**Abstract**

Cancer is an illness that can kill you, which kills millions of people worldwide every year. Smoking, obesity, processed meat consumption, radiation, family history, mental stress, environmental variables, radiation and chance are all factors to consider which causes cancer. Surgical excision of solid tumors, radiation therapy, and chemotherapy are the initial treatments for cancer. For treating disorders like inflammatory bowel disease, local distribution to intestinal tissue with oral medication is a difficult but desirable goal (IBD) for cancer. The medicine should be protected throughout the journey to the colon by a colon-specific drug delivery system. Targeted drug delivery to the colon is a hot topic in colon disease research because it has the potential to improve therapeutic efficacy for disease. Rectal formulations may appear to be ideal for colon-targeted medicine delivery; nevertheless, their efficacy is restricted to ailments of the rectum and distal colon, as well as patient administrative problems. In the treatment of more widespread colon inflammation, such as that observed in inflammatory bowel disease, they are unsuccessful (IBD) for colon.

***Keywords:*** *Liposome, Liposome in Cancer, Design of Liposome, Stability of Liposome, Cancer Therapy*

## 1. Introduction:

At the Babraham Institute in Cambridge, Dr. Alec D. Bangham, a British haematologist, first described liposomes in 1961 (published in 1964). The word liposome mainly derives from two Greek words: lipo, which means fat, and soma, which means body. A liposome is a synthetic vesicle that is made mostly of natural phospholipids that may also contain mixed lipid chains which behave like surfactants. The global prevalence of colonic diseases has risen in recent decades, necessitating better local treatment of colonic disorders in order to develop more effective and safer pharmaceutical regimens. Colon cancer is most often caused by colorectal cancer (CRC). Approximately 3% of people will be diagnosed with it at some point in their lives (more than 200,000 deaths per year) [1], also, it's the third most popular fatal disease in Europe (more than 200,000 fatalities per year) [1, 2]. Inflammatory bowel disease (IBD) is also on the rise in traditionally low-incidence regions such as Asia [3].The uncontrolled multiplication of abnormal cells in the body is classified as cancer. Malignant cells are the ones that cause cancer [4, 5]. Many anticancer medications target cancer cells that divide at a quicker pace than normal cells, causing them to expand out of control. In rare circumstances, normal, healthy cells may expand rapidly, and chemotherapy may damage these cells, resulting in chemotherapy side effects. Because of the diversified a good vascular supply and high interstitial pressures tumour especially when referring to tissue or cells in the necrotic zone, medicine penetration is hampered in solid tumours. Drug delivery systems are made to release macromolecular drugs gently via tumour cells or

tissues. These devices are designed to promote tumour tissue permeability and retention. This is due to the dysregulated nature of tumour angiogenesis, which is characterised by structural and physiological abnormalities that result in hypermeability. Chemicals having a high molecular weight, a small distribution volume, and a long circulation potential extravasate from abnormalities with a greater frequency artery and concentrate on cancer cells or tissues [5, 6, 7].

## 2. Colon Targeted Drug Delivery:

Traditional non-targeted therapy has been extensively studied for the local treatment of colonic illnesses due to the possibility of unwanted owing to adverse effects and low efficacy medication before reaching the target, there is systemic absorption region [8, 9]. Colon-targeted drug delivery devices are used for the local treatment of colonic illnesses due to the possibility of unwanted owing to adverse effects and low efficacy medication systemic absorption before reaching the target region. Instead of releasing medicine prematurely into the upper GI tract, colon focused the release of drugs is the goal of drug delivery systems, medicine selectively as a result of the colonic environment. It is critical to examine the colon's physiological features as well as the environment surrounding the illness a place where colon-targeted medicine delivery devices can be successfully developed (s). The motility of the GI tract fluctuates throughout time, fluid levels, enzyme activity, and pH as it travels the stomach to the small intestine [10]. The micro-environment around diseased tissues in the colon differs significantly from the microenvironment surrounding normal and healthy tissues. Reactive oxygen species (ROS) and inflammatory cytokines are elevated in patients with colonic diseases, as well as an antioxidant deficiency and mucosal damage [11]. Nanomedicinal formulations are nanometer-sized carriers that improve drug tissue bioavailability, allowing chemotherapeutic medicines to be used more effectively. Liposomes are a cutting-edge nanoscale drug delivery device that consists of a spherical vesicle with a phospholipid bilayer membrane for drug delivery. By enhancing medication absorption and stability while simultaneously minimizing adverse effects through site-specific targeted administration, liposomes overcome the limitations of conventional chemotherapy. As a result, cancer chemotherapy obtains more advantages [12, 13, 14]. Liposomes offer a variety of pharmacological and biological applications, and their amphipathic nature allows them to entrap both hydrophilic (polar) and hydrophobic (non-polar) molecules in aquatic settings. Hydrophobic substances, for example, encircle the watery core [15]. Because of their flexible structure, biocompatibility, and natural nontoxicity, non-immunogenicity, and biodegradability, liposomes are used as DDDs [16]. Medication solubility has been demonstrated to be improved by liposomes [17].

## 3. Design of Liposome:

Water soluble when dissolved solutes have a difficult time letting go through the liposome's aqueous solution area because it is coated with a hydrophobic barrier. Liposomes can contain both hydrophobic and hydrophilic substances because hydrophobic medicines can be dissolved into the membrane. This lipid bilayer joins with another type of cell membrane bilayers to transport the liposome's contents to the site of action, where medications are delivered. We can make liposomes out of a DNA solution that can't pass through the membrane to get the drug over the lipid bilayer. Liposomes with a low or high pH neutralise on their own, allowing the medicine inside to flow freely over the membrane. As a result, liposomes administer drugs via diffusion rather than direct cell fusion. Biodegradable & biocompatible phospholipids and sphingolipids are the most frequent lipids used to produce liposomes. Cylindrical molecular lipids include phosphatidylcholine, phosphatidylserine, phosphatidylglycerol, and sphingomyelin. They produce a stable bilayer in aqueous solutions, making them appropriate for liposome compositions. Phosphatidylcholines are the most widely used of these lipids because of their remarkable stability and the ability to react to changes in the pH or salt concentrations of the product or biological environment [18, 19].

## 4. Liposomes and Cancer:

Liposomes have the ability to target cancer in its natural state. Endothelium cells are kept contained in all human blood vessels by tight connections in the endothelial wall. Because of the tight connections, large blood particles can not escape the vessel. In the event of a tumor vessel, this type of arrangement does not exist, making it diagnostically "leaky." The improved permeability and retention effect is the name of this capacity. Liposomes with

a diameter of less than 400 nm can quickly penetrate tumor from the bloodstream, whereas healthy tissue on the endothelium wall holds them there [20, 21, 22].

## 5. Formulation Approaches for Colon Targeted Drug Delivery:

Colon targeted medication delivery is a hot topic in the field of colon illness research, as it has the potential to improve treatment efficacy while lowering systemic toxicity. The bioavailability of medications in the colon has unquestionably improved as a result of enhanced oral drug delivery systems. Rectal formulations may appear to be ideal for colon-targeted medicine delivery, but their efficacy is restricted to disorders affecting the distal colon and rectum, as well as patient administration problems. They are inefficient in the treatment of more widespread colon inflammation, such as that seen in Irritable Bowel Disease and other diseases (IBD). Treatments might be delivered locally or systemically using oral formulations. The medicine must be transported to a specific location within the gastrointestinal (GI) tract in order to produce a localized effect, yet it must not be absorbed or be absorbed in a bad manner. Orally administered drugs require systemic absorption in the intestines before being dispersed throughout the body. A formulation that is taken orally, (ii) can reach the colon, (iii) delivers high drug concentrations at the site of inflammation, and (iv) is not absorbed systemically would be ideal for illnesses characterized by localised inflammation in the colon's tissues . The effectiveness of current formulations in targeting sick vs. healthy colon tissue selectivity is limited. Furthermore, there is no guarantee that the drug will be absorbed entering the tissue and cells of the inflamed area, even if it is administered into entire the colon's surface (including sick tissue)). As a result, researchers have looked at employing nanotechnology in formulation design to improve therapeutic efficacy allowing focused targeting and incorporation into inflammatory the colon's tissue [23,24]. Inflammatory bowel disease (IBD), cancer, and infections have all been treated with nanoformulations [25,26]. By adding polymer coatings to the liposomal surface, liposomes can be manipulated to target the gastrointestinal system. The GI tract's hostile environment, which includes enzymes (e.g., pancreatic lipases) and bile salts that would typically the lipid bilayer is broken down [27,28,29], protects oral liposomal formulations from breakdown. Chitosan and pectin are non-toxic, biodegradable, and mucoadhesive natural polymers. GI tract targeting is aided by adhesion to the mucosa because it promotes liposome direct contact with the mucosal surface, allowing for better cellular absorption and medicine release. When intestinal motility is elevated, as it is in IBD, liposome clearance is reduced [30,31,32,33,34]. Chitosan-coated liposome formulations have exhibited better drug uptake in colon tissue ex vivo, as well as increased stability in simulated stomach and intestinal fluids , when compared to uncoated liposome formulations [24.34, 35, 36,37] . Eudragit® is a copolymer made from synthetic materials covering that has mucoadhesive properties as well as pH-dependent release mechanisms to increase oral drug delivery to the colon. Eudragits® are methacrylic co-polymers with a variety of side groups that modify their pH solubility [38]. In vitro, the pH-dependent release characteristics of Eudragit®-coated liposomal and microsphere formulations were good [39]. For example, the medicine release from Eudragit®-coated liposomes was greatly reduced at pH 6.3 (small intestine) and pH 1.4 (stomach), but there was at pH 7.8, there is a considerable medication release (ileocaecal region) [40]. In vitro, bile salts damaged the Eudragit® coating, reducing its efficacy in vivo by inducing premature liposome disintegration and drug release in the duodenum, according to the study. Liposomes coated with Eudragit® have better mucoadhesion properties than other popular polymers such as chitosan and carbopol, as demonstrated using freshly excised pig intestinal tissue [41]. These results imply that coating nanoparticles with Eudragit® can target the colon and enable effective drug release. However, more formulation design is needed to overcome the coating's bile salt vulnerability.

## 6. Stability of Liposomes:

Chemical deterioration of liposomal phospholipids, such as oxidation and hydrolysis, is possible. -tocopherol (Vitamin-E), a common non-toxic dietary lipid, is the most commonly employed anti-oxidant at the moment, but tocopherols may also be used because they are more effective as long-term anti-oxidants [42]. At pH values near to neutral, ester linkage hydrolysis is the slowest. Hydrolysis can be prevented entirely by using lipids with ether rather than ester connections, such as those found in halophilic bacterium membranes [43]. The use of sphingomyelin or

phospholipid derivatives with the 2-ester linkage substituted by a carbomyloxy activity can prevent hydrolysis in vivo as a result of enzyme attack [44]. The physical and chemical stability of the liposomes in terms of size distribution, entrapment efficiency, and low degradation of liposomal apparatuses is the key limiting step for drug administration with this method. Liposomes are primarily degraded chemically at the level of their phospholipid bilayers, where two processes can take place: I hydrolysis of the ester linkages between fatty acids and the glycerol backbone, and ii) peroxidation of any unsaturated acyl chains that are accessible [45]. Due to physical instability, liposomes may aggregate/flocculate and fusion/coalescence, affecting the size of the vesicle and resulting in considerable loss of the contained API [46]. Lyophilization [47], spray drying [48], and superficial fluid [49] are examples of methods for stabilising liposomal compositions that are expandable. To preserve liposomal stiffness and the phospholipid: cholesterol molar ratio, liposomal composition (e.g., phospholipids – lipids with high phase transition temperatures), fatty acid side chains, polar head chemistry, chain length, and degree of unsaturation are chosen (essential for liposomal stability and medication release management). Briuglia et al. (2015) found that a 70:30 molar ratio of phospholipids (using 1,2 – Dimyristoyl – sn- glycerol – 3 – phosphocholine (DMPC), dipalmitoyl phosphatidylcholine (DPPC), dipalmitoyl phosphatidylcholine (DPPC), and distearoyl phosphatidylcholine (DSPC) : cholesterol has developed a liposomal formulation that ensures medication release stability and control [50].

## 7. Conclusion:

Liposomes, a potential delivery technology, can be used to deliver anticancer drugs to specific areas. On a local level, colon-focused drug delivery is an important technique for treating colonic disorders such as IBD and colorectal cancer. It may have a variety of advantages over typical dose formulations in terms of their efficacy, safety, and adherence by patients. Delivery to the colossus methods can also be utilized to boost systemic exposure to drugs that are acid-and/or enzyme-labile, including macromolecules. These nanocarriers minimize undesirable side effects on normal tissues, such as headaches and cytotoxicity, while also extending circulation time and boosting bioavailability. They reduce chemotherapeutic medicine elimination and toxicity while also shielding them from the environment and transporting them to the desired location where the action is taking place. Because of the digestive system limited permeability and physicochemical and metabolic instability, the majority of biologics and pharmaceuticals are still sold as parenteral formulations, despite advancements in biotechnology and protein engineering, which have broadened the therapeutic potential of proteins and peptides. As a result, colon-targeted delivery is gaining traction as a viable technique for increasing macromolecule bioavailability in the mouth.

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