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Review Article

Nanotechnology Approaches for Colon Targeted Drug Delivery System: A Review

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ABSTRACT

Compared to non-targeted medications, targeting drugs to specific sites of action has various advantages. Colon-designated drug conveyance improves the adequacy of therapeutics and empowers confined treatment. Because of this, it is a functioning space of examination for neighborhood sicknesses influencing the colon. The advances for planning oral medication conveyance have altogether expanded the bioavailability of medications to the colon and likewise worked on the remedial viability during infection. Presently a day's nanotechnology assumes a significant part in oral dose plans as methodologies to additional upgrade take up into ailing tissue inside the colon. This exploration work manages the life systems and physiology of the colon, different methodologies for the colon focusing on, and assessment of medication discharge in the colon to give refreshed data for the need and improvement of medication stacked nanoparticles for various sorts of colonic infection.

Keywords: Colon targeting, Nanoparticle, Bioavailability Therapeutics, Nanotechnology.

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INTRODUCTION

The conveyance of the medications explicitly to the colon without being assimilated first in the upper gastrointestinal (GI) lot considers a higher convergence of the medication to arrive at the colon with insignificant fundamental retention. The colonic substance has a more drawn-out maintenance time (as long as 5 days), and the colonic mucosa is known to work with the digestion of a couple of prescriptions, making this organ an ideal site for drug transport. Oral measurement structures are the most favored conveyance course for colon-explicit conveyance because of their accommodation. Oral Controlled release drug delivery system(CDDS) needs to shield the medication from being delivered to the stomach and small digestive system. Along these lines, the methodologies utilized in fostering a CDDS are pointed toward deferring the medication discharge until the framework arrives at the colon, for certain procedures exhibiting preferable accomplishment over others.[1,2]

Nonetheless, many mixtures are fruitless and come up short in investigation and advancement given their low ingestion and low bioavailability upon oral administration.[3] Some clarifications for helpless bioavailability are as per the following: (a) improper segment steady since it impacts the penetration of the medication through the lipid layer; (b) the principal pass digestion causes the digestion of medication which winds up in helpless ingestion and low bioavailability of the medications; (c) P-glycoprotein (P-GP) intercede outpouring furthermore was displayed to change the material of medication; the presence of P-glycoprotein inside the liver, kidney, and gut causes a decrease in the assimilation of the medication.[4] Many approaches are applied to support the oral bioavailability of ineffectively water-solvent medicine, strong scatterings, and micronization. Lately, nanocarriers are acquiring colossal intrigue and have shown outstanding advantages over regular portion structures in oral medication conveyance of hydrophobic medication.[5-7]

At present, novel medication conveyance frameworks have increasingly been investigated to upgrade remedial usefulness and support medication unharness properties through defeating the issues like helpless solvency and low oral bioavailability of medication. The classifications of ACE inhibitors: Expert inhibitors, metallic component channel blockers, vasoconstrictors, focal sympathomimetics, diuretics, α-adrenergic blockers, β-adrenergic blockers, and vasodilators. The greater part of that medication has some imperative downsides like low bioavailability, nearly short half-life, low penetrability, and unfavorable future impacts. For viable conveyance of such medication frameworks region unit is required which might give the resulting attributes: (a) low dosing recurrence, (b) expanded bioavailability, (c) increased activity, and

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(d) decreased aspect effects.[8] Designing science-fundamentally based oral medication conveyance frameworks give another procedure to direct medicament specialists with further developed bioavailability and restorative impact.

Physiology of colon and colon-specific diseases

The internal organ is about 1.5 meters long, starting from the caecum in the right iliac fossa and ending at the rectum and a channel somewhere down in the pelvis. Its lumen is bigger than that of the small digestive tract. For spell-binding purposes, the colon is isolated into the caecum, rising colon, cross-over colon, plunging colon, sigmoid or pelvic colon, rectum, and butt-centric channel. The caecum is the initial segment of the colon.[9-11] It is an enlarged piece that has a visually impaired end poorly and is constant with the climbing colon superiorly. It is ordinarily around 13cm long and has a similar design as the dividers of the colon however contains more lymphoid tissue Table 1. The rising colon passes upwards from the caecum to the level of the liver where it twists intensely to one side at the hepatic flexure (right colic flexure) to turn into the cross-over colon. The cross-over colon is a circle of the colon that reaches out across the stomach before the duodenum and the stomach to the space of the spleen where it shapes the splenic flexure (left colic flexure) by twisting intensely downwards to turn into the rising colon.

Anatomy of the colon

The colon is essentially arranged in the midsection. It is a cylinder-formed chamber that is lined by a soggy, sensitive pink covering called the mucosa; the pathway is known as the lumen and is around 2-3 drags in distance across. The colon shapes the lower part of the gastrointestinal plot and stretches out from the ileocecal intersection to the butt. The colon is the upper five feet of the inward organ and the rectum is the lower six inches. The convergence of the little stomach-related lot (ileum) and the colon is in the lower right midriff. The accompanying piece of the colon, in the solicitation wherein substance stream, is the point or turn is known as the hepatic flexure, found just under the rib keep. In the left lower piece of the mid-region, the colon makes an S-molded bend from the hip over the midline known as the sigmoid colon. Lymph hubs are structures found in the flowing lymphatic arrangement of the body that produces and store cells that battle contamination, irritation, unfamiliar proteins, and malignancy.[12-14]

Existing novel drug delivery approaches for colon

Designated drug conveyance portrays the release of medication towards specific a piece of the body like tissue and elective organs, or at a particular retention site, in this manner expanding remedial adequacy. A befittingly planned maintained or controlled release drug conveyance framework is regularly a meaningful step forward towards tracking down the matter identified with the current medication conveyance framework. The design of indefinite quantity forms has many objectives, one among those is to endeavor to realize drug unleash at sites that will guarantee the most therapeutic benefits.

Colon as a site offers distinct benefits on account of a close to neutral pH scale, away longer transit time, reduced organic process accelerator activity, and a way bigger responsiveness to absorption enhancers. Colonic drug delivery is additionally helpful for general absorption of the medicine, particularly macromolecule and amide medication, attributable to the less hostile surroundings prevailing within the compared with the abdomen and tiny intestine. Colonic drug delivery could also be achieved by either oral or body part administration. Body part indefinite quantity forms like enemas and suppositories don't seem to be perpetually abundant and effective because of high variability within the distribution of drugs administered by this route. Delivery through the oral route has perpetually been thought of as the favored and therefore the most convenient manner for drug administration having the best degree of patient compliance. Above all, high patient acceptance and a high degree of flexibility in indefinite quantity type style further as on dosing.[15]

The conventional indefinite quantity forms square measure delivering an inadequate quantity of drug because of the absorption or degradation within the hostile higher Gastrointestinal tract (GIT). Designated drug conveyance to the colon has drawn bountiful interest as of late for local treatment of the scope of colonic infections.

Drug targeting can also be used once a delay in drug absorption is desired from the therapeutic purpose of dosing, like the treatment of diseases that have peak symptoms within the early morning nocturnal asthma attack, angina, or arthritis.

Various systems are developed for targeting drug delivery, embody coating with pH scale-dependent systems, valence linkage of a drug with a carrier i.e., prodrugs system, style of regular unleash indefinite quantity forms, and therefore the use of carriers that square measure degraded solely by colonic bacteria.[16-18]

Advantages of colon targeted drug delivery system

Further developed oral nanoparticulate drug conveyance framework has very worked on the colonic bioavailability of medications, that is, these definitions are powerful at coming to and delivering drugs explicitly in the colon. In any case, for a medication to have remedial adequacy it should be restricted to the site of activity inside the colon. Traditional oral definitions have restricted adequacy and explicitness for unhealthy colon tissue. Nanotechnology has been utilized in oral measurements definition plans as a methodology to additionally further develop take-up into infected tissue inside the colon. Contrasted with the regular oral organization of medications, nanoparticles can shield the medication from delivery and digestion in the stomach

Table 1: Different parts of the Colon.

Region of Gastrointestinal tract	Characteristics
Large intestine	Length in cm
Caecum	6-7
Ascending colon	20
Transverse colon	45
Descending colon	30
Large intestine	Intestinal diameter (cm)
The pH of the Caecum and colon	5.5-7
Rectum	7
Colon	Redox potential
Right	-415
Left	-380

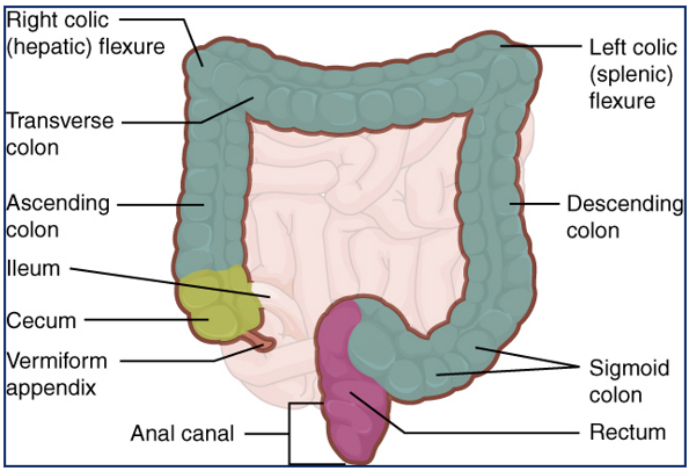

Figure 1: Large Intestine.

and small digestive system, along these lines expanding the measure of medication accessible for fundamental assimilation or confined conveyance inside the colon. Moreover, despite the inclusion of the colonic surface (counting infected tissue), there is no assurance that the medication is viably taken up into the tissue and cells at the site of irritation. Drug procedures using nanoparticulate frameworks as transporters for dynamic mixtures have shown promising outcomes intending to the physiological changes during colonic sickness. These frameworks are more gainful than regular details because their size prompts a more powerful focus on, better bioavailability at ailing tissues, and diminished foundational unfavorable impacts. In this way, nano-transport systems have been found to have relative or chipped away at healing practicality at lower drug obsessions interestingly, with conventional plans Figure 1. Nano-conveyance frameworks stay away from fast transporter disposal by being promptly taken up into kindled tissue and cells.[19-21]

Nanotechnology at a glance

Nanoliposomes are submicron vesicles that consist of phospholipids bilayer for encapsulating and delivery of active pharmaceutical ingredients. Unique properties of nanoliposome can give controlled delivery attributes of a few medications and bioactive specialists. They can work on the adequacy and cell take-up of typified drugs. Owing to their biocompatible and biodegradable properties with their nano size, nanoliposomes show their improved bioavailability, *in vivo, in vitro* stability and reduced unwanted interaction with other molecules. They can deliver the medication in a controlled way to the site of activity and upgrade remedial proficiency. Critically like liposome, nanoliposomes doesn't go through fast corruption and freedom by liver macrophages.[22] Among various nanomedicines, nanoliposomes have demonstrated a successful platform with several FDA-approved marketed formulations. So, in our work, an attempt has been made to prepare a drug-loaded nano liposomal formulation with a combination of various phospholipids and polymers to achieve Controlled-release properties.

Nanotechnology is the study of issues and materials that arrangements with molecule size in nanometers. Nanoparticles are strong colloidal particles going in size from 1 to 1000 nm (1 μm) and made out of manufactured or semi-engineered polymers. Nanoparticles were created around the 1970s. They were at first conceived as transporters for antibodies and anticancer medications. To upgrade tumor take-up, the technique of medication focusing was utilized, and as a first significant advance, research zeroed in on the improvement of strategies to diminish the take-up of the nanoparticles by the cells of their Articular-endothelial system.[23] Nanoparticles had the option to accomplish, with progress, tissue–the focus of many medications. Nanoparticles are comprised of non-biodegradable and biodegradable polymers. The idea of medication focusing on controlled medication conveyance can be accomplished by surface adjustments and the decision of fitting molecule materials.[24] Nanoparticles made out of transient polymers region unit got ready for application in oral treatment. For the nano size of nanoparticles, the region unit is suitable for the endo-venous organization. Applied science is being used inside the drug field for a few reasons, nonetheless, perhaps the main objectives region unit is to help drug dissolvability/bioavailability as well as a conveyance to shifted locales of activity Figures 2 and 3.

Oral nano-delivery system for colon

Further developed oral nanoparticulate drug conveyance framework has a great influence on the colonic bioavailability of medications, that is, these plans are viable for coming to and delivering drugs explicitly in the colon. In any case, for a medication to have helpful viability it should be confined to the site of activity inside the colon. Traditional oral details have restricted viability and explicitness for sick colon tissue.

Table 2: Different types of the Colonic disease.

Colonic Disease	Types
Colorectal cancer	Colonic polyps
	Ulcerative colitis
	Diverticulitis
	Irritable viscus syndrome
	Chronic inflammatory viscus diseases
	Crohn's sickness (CD)
Inflammatory bowel disease(IBD)	Ulcerative colitis
	Crohn's disease

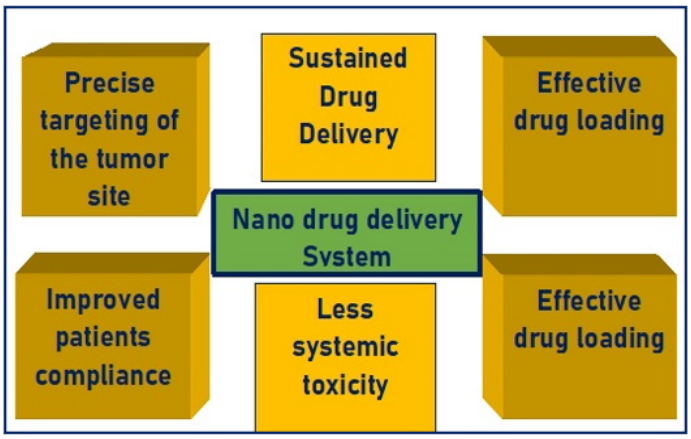

Figure 2: Advantages of Nano drug delivery system.

Nanotechnology has been utilized in oral dose detailing plans as methodologies for additional expansion take-up into unhealthy tissue inside the colon.

Contrasted with the ordinary oral organization of medications, nanoparticles can shield the medication from delivery and digestion in the stomach and small intestine, subsequently expanding the measure of medication accessible for fundamental assimilation or confined conveyance inside the colon. Additionally, NP compositions can be tailored to provide effective delivery of loaded drugs to the desired location.[26-28]

Nano-conveyance frameworks have been intended to inactively or effectively focus on the site of the objective. Because of their smaller size, these systems are more effective at targeting diseased tissues, have better bioavailability in diseased tissues, and have fewer systemic side effects than traditional formulations. In contrast with ordinary details, nano-conveyance frameworks have been accounted for to have the same or improved remedial adequacy at lower drug fixations. This size decrease empowers improved and specific conveyance of dynamic atoms into the colon tissue by applying an epithelial upgraded penetrability and maintenance (eEPR) impact and permits the particular take-up of the nano-sized particles by resistant cells that are profoundly expanded in number at the ailing districts. Nano conveyance

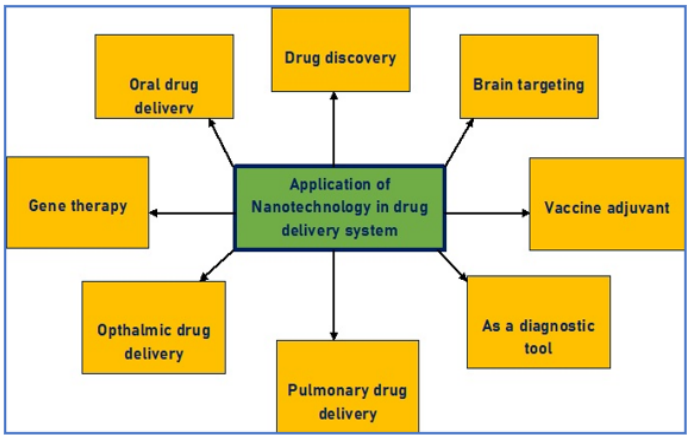

Figure 3: Application of Nanotechnology in drug delivery.

frameworks keep away from quick transporter disposal by being promptly taken up into aggravated tissue and cells.[29]

Nanotechnological approaches for colonic medication conveyance

Nanoparticles utilized as medication conveyance vehicles square measure regularly < 100 nm in at least one measurement, and fuse distinctive short-lived materials like normal or fake polymers, lipids, or metals. Nanoparticles square measure fixated by cells extra with proficiency than bigger miniature atoms and thus might be utilized as successful vehicle and conveyance systems. For remedial applications, a delivery system will either be coordinated inside the lattice of the molecule or associated with the molecule surface. Nanosystems with entirely unexpected creations and natural properties are widely researched for medication and conveyance applications.[30,31]

Size-dependent nanoparticulate system for colon

Size-dependent drug delivery systems are one example of delivery systems for the treatment of IBD. The specific size of the drug particulate can cross the infiltration of immune and inflammatory cells like macrophages, dendritic cells, and neutrophils. They are capable of uptaking the specific particles and helping to retain the drug in the inflamed sites and helping to get rid of the effect of Inflammatory Bowel Disease (IBD).[32]

Enzyme-dependent nanoparticles for colon

Enzyme-activated delivery systems are the most promising colon-targeted drug delivery systems. These nanoparticulate systems are dependent on the specific enzyme activity bacteria found in colonic regions and the polymers degraded by them. Like as polysaccharides (pectin, guar gum) inulin, and chitosan as they can retain their integrity in the upper GI tract and help to release the entrapped medicament.[33]

Surface charge-dependent nanoparticulate systems

It includes positive and negative charges of nanoparticles (NPs) that are being researched for use in clinical gadgets, particularly

in imaging furthermore, quality and medicine conveyance. Cell take-up is regularly needed for these applications, furthermore, it is impacted by surface properties like hydrophobicity and charge, notwithstanding size. The surface charge has been shown to alter nanoparticle fate after intravenous delivery in numerous research; however, few studies have looked at the effect of surface charge on nanoparticle bioavailability and absorption after oral administration. The electrostatic association of nanocarriers with parts in the GI parcel can be impacted by changing the surface charge of nano-conveyance frameworks, which hypothetically ought to give selectivity to wiped-out tissue. In any case, during GI travel, there is a risk of electrostatic coordinated efforts and coming about limiting of these nanoparticles with other charge-changing manufactured substances (for instance bile acids and dissolvable mucins).[34]

Pegylation-dependent nanoparticulate system

PEGylation, or covering the outside of nanoparticles with polyethylene glycol (Stake), is a common technique for upgrading medicine and quality conveyance proficiency to target cells and tissues. The effect of Stake coatings on the destiny of foundationally conveyed nanoparticle details has been widely explored, following the accomplishment of PEGylating proteins to upgrade fundamental course time and limit immunogenicity. Nanoparticles with Stake coats shield the surface from collection, opsonization, and phagocytosis, taking into consideration longer fundamental dissemination times.[35]

Quantum dots

Different kinds of nanoparticles can be utilized in mild research, with Quantum Dots (QD) being the most ordinarily utilized up until this point. QDs are semiconductor light-transmitting nanocrystals with interesting optical capacities because of their nanometer-sized developments. They exhibit brilliant fluorescence, are bleach-resistant, and can emit fluorescent light of various wavelengths. These characteristics make QD ideal for visualizing brain regions and the systems that underpin their operations. Because of the unique features of QDs, even single molecules under investigation can be detected. QDs can also be utilized to deliver drugs to the brain.[36]

Future prospect of nanotechnology for colon disease

In recent decades, the event of engineering science has provided a chance to beat the old aspect of conventional drugs. Mixing of varied nanomaterials (NMs) with chemical analysis, organic chemistry, and optical strategies has allowed the event of advanced strategies for tumor medical aid, which can revolutionize the treatment of tumors. NMs have performed flawlessly in shifted parts of antitumor therapy and accumulated extreme examination interest, and they have offered the pleasant potential for antitumor treatment by upgrading the viability of medicines and lessening general angle impacts. Likely clinical utilization of NMs is perceived to possess excellent biocompatibility. Nanoparticles (NPs) with appropriate breadths change regions demonstrated by having the alternative to enter the blood spread and endure endocytosis into cells. In like manner, research shows that NM-based clinical strength incorporates good potential in the treatment of tumors, diabetes, sickness, neurodegenerative confusion, and disturbance. The mixing of tumor medical aid with NMs is predicted to motivate breakthroughs for engineering science within the field of drugs.[37-39]

Needs for colon-targeted drug delivery

Thus, by utilizing a site-specific medication delivery system, various colonic diseases can be effectively and safely treated Table 2.

The therapeutic benefits of administering the medication to the affected organ include.

Drug delivery is as close as feasible to the target spot in its complete form.

The capacity to reduce the standard dose.

Decreased incidence of adverse side effects.[40]

CONCLUSION

The importance of colon target drug delivery is that the drug released from the system must be sensitively active in the colon. Medication focusing on the unhealthy colon is invaluable in diminishing the fundamental incidental effects, bringing down the portion of the medication and providing the medication just when it is required, and keeping up with the grouping of medication as feasible for colon-designated drug conveyance. There is a need to foster an original methodology that is explicit for the colon to focus on. Colon explicitness is bound to be accomplished with frameworks that use normal materials that are corrupted by colonic bacterial catalysts. The test stays to create and approve a disintegration technique that joins the physiological provisions of the colon. In the future, various multifunctional novel nanoparticle-based drug delivery may be designed and developed for treating colon cancer.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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