



## Advancement of Targeted Drug Delivery Over Conventional Drug Delivery System Targeting to Colonic Region

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### ABSTRACT

Colon-targeted drug delivery is a wonderful drug delivery system targeting the lower parts of the GI tract to treat several colonic diseases such as inflammatory bowel diseases subdivided as ulcerative colitis, Crohn's disease, amoebiasis, chronic diarrhea, colon cancer, vaginal infection, and bacterial infections, etc. A conventional drug delivery system can be referred to as a release of the drug, particularly to the targeted organ with a predetermined rate in a controlled manner. To achieve the prolonged therapeutic effect with predictable drug release kinetics, reduction of fluctuation in the steady-state concentration, increasing the therapeutic efficacy that convenient to patient and reduction of the patient compliance. Conventional drug delivery systems have some disadvantages which can be overcome by target-specific drug delivery systems. A targeted drug delivery system is a wonderful approach to target the pharmacological and therapeutical active moiety to target a specific region, and not to target non-targeted areas such as organ or tissue and accumulate to the targeting region only to show pharmacological activities. Some important criteria can be noticed under targeted drug delivery such as they are selectively and effectively targeting local as well as systemic regions and also involved in the pre-identified target can be set to deliver the active moiety, increase or enhancement of therapeutic concentration at the targeting region and accumulation of the active moiety to the target region and show high concentration, targeted drug delivery can enhance of therapeutic activity with less adverse effect with less adverse events. The review discusses the advancement of targeted drug delivery over conventional drug delivery targeting the colonic environment to treat colonic diseases.

**Keywords:** Targeted drug delivery systems, nanotechnology, conventional drug delivery systems, Colon-targeted drug delivery systems, Drug development.

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### INTRODUCTION

Drug delivery target to the colonic environment is a very challenging task. The maximum drugs available in the market, involved in the treatment of colonic diseases are failed to achieve therapeutic efficacy due to the altered environment as before reaching the targeted area, premature drug release in the upper GI tract.<sup>1</sup>

A colon-targeted drug delivery system is a wonderful approach to overcome the problem related to stability in the gastric environment. The colon-targeted drug delivery systems refer to the drug delivery system which can provide proper medication at the diseased colon and stable at the altered gastric environment and fewer side effects. They ensure the drug must be able at the target site, prolong drug therapy to the colonic environment,

dose requirement less than reducing the patient compliance.<sup>2</sup>

There are a variety of strategies used to target the drug in the colonic environment and the purpose of the development is to attained high drug concentration at the target site and achieve therapeutic efficacy with fewer side effects. pH-dependent or pH-sensitive strategy as pH-dependent materials help to transfer the drug at the particularly colonic environment and can able to withstand in altered GI environment and disintegrate in the colonic pH. Time-dependent drug delivery approach help to reduce immediately burst release and maintain steady concentration by releasing the drug in a controlled and predictable manner. Microbially triggered drug delivery plays an important role in the colonic drug delivery system. Colon targeted drug delivery particularly disintegrate by several microflorae such as *E. coli*, *P. Vulgaris*, *B. mycoides*, *Clostridia*, etc. by their different enzymatic activity in the colonic environment.<sup>3,4</sup>

### Importance of Colon targeted Drug Delivery System

Colon-targeted drug delivery is a wonderful drug delivery system targeting the lower parts of the GI tract to treat several colonic diseases such as inflammatory bowel diseases subdivided as ulcerative colitis, Crohn's disease, amoebiasis, chronic diarrhea, colon cancer, vaginal



infection, and bacterial infections, etc. Importance of colon-targeted drug delivery system as follows -

- Colon-targeted drug delivery mainly provides target specificity to the colonic disorders such as inflammatory bowel diseases subdivided into ulcerative colitis and Crohn's diseases, amoebiasis, colorectal cancer, chronic constipation, chronic diarrhea, etc.<sup>5</sup>
- Colon-specific drug delivery systems involved in less enzymatic activity with a reduced dose frequency which reduces patient compliance.<sup>6</sup>
- Colon-targeted drug delivery system involved in the treatment of local as well as systemic treatment and also, they are suitable for protein and peptides. Targeting protein and peptide drug delivery to the colonic environment is very difficult due to premature release at the upper GI tract and increasing the adverse reaction due to excessive doses involved in protein and peptide delivery.<sup>7</sup>
- Colon-targeted drug delivery reduced gastric irritation (NSAIDs) and drug therapy can be prolonged and involved in drug utilization during drug therapy.<sup>8</sup>

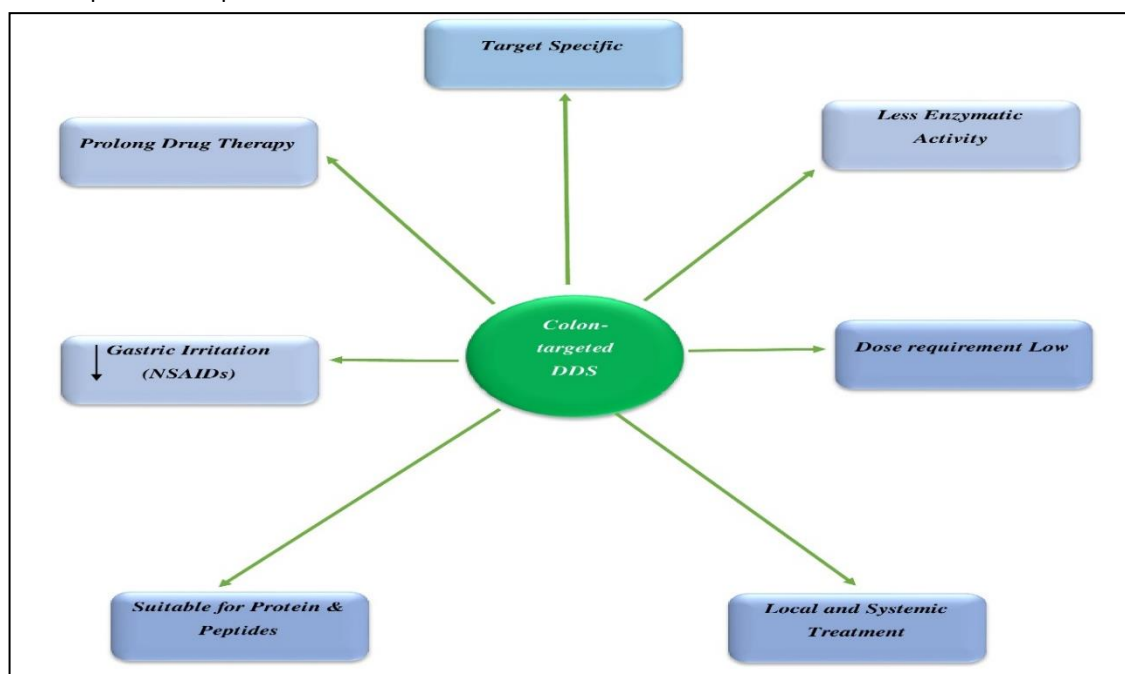


Figure 1: Importance of Colon-targeted Drug Delivery System<sup>9</sup>

#### Advantage of colon-targeted drug delivery

- Colon-targeted drug delivery is providing direct treatment in the colonic environment and provides proper therapeutic efficacy with fewer side effects.
- Protein and peptides are suitable in colon-specific drug delivery without premature release at the different environments on the gastrointestinal side.
- Colon-specific drug delivery is involved in the reduction of dose frequency and enhancement of extension of action to the target area.
- Fluctuation of the plasma concentration at the target site can be reduced through colon-specific drug delivery systems.
- Colon-specific drug delivery system in reduction of degradation at upper GI tract and protect the drugs from degradation.
- Increasing the bioavailability due to the high absorption rate.<sup>10,11</sup>

#### Drawback/ Disadvantages of Colon-targeted drug delivery

- Manufacturing cost is high compared to conventional drug delivery systems and difficult in manufacturing due to multiple steps involved.
- Due to several microflorae present in the colonic environment, drugs may be degraded and the effectiveness of drug action can be reduced.
- In appropriate polymers and the non-availability of in-vitro dissolution methods, the biggest difficulty is in the treatment of colonic disorders.
- Colon-specific drug delivery system impacts gastro retention time as well as colonic transit time and it varies with different environmental conditions such as pH, diseases, food habit, temperature as well as genetic conditions.<sup>12,13</sup>

A conventional drug delivery system can be referred to as a release of the drug, particularly to the targeted organ with a predetermined rate in a controlled manner. To achieve the prolonged therapeutic effect with predictable drug release kinetics, reduction of fluctuation in the steady-state concentration, increasing the therapeutic efficacy that

convenient to patient and reduction of the patient compliance.<sup>14,15</sup>

#### Importance of Conventional drug delivery system

- 1) Reduction of the fluctuation of the dose at the target site to maintain steady-state concentration.
- 2) Reduction of unwanted side effects during therapy.
- 3) Prolong drug release and shows the optimum effect in the target site.
- 4) Dosing frequency can be reduced.
- 5) Improvement of patient compliance.<sup>16,17</sup>

**Table 1:** Advantages and Disadvantages of Conventional Drug Delivery Systems<sup>18,19</sup>

Advantages of conventional drug delivery systems	Disadvantages of Conventional drug delivery systems
High therapeutic efficacy and controlled release delivery to the target site.	Permeability is low and followed first-pass metabolism.
Delivery drug to the local as well as systemic action.	Degradation at different pH conditions.
Reduction of fluctuation of plasma drug concentration.	Solubility and half-life are low.
Simple and convenient instrumentation as well as easy to operate.	Leakage can be seen
Drug absorption and bioavailability can be increased.	Stability problem
Production cost is low	Drug absorption low, less bioavailability
The dose must be accurate and measured dose to the patient.	High adverse effects with increased patient compliance.

#### Targeted Drug Delivery system

A targeted drug delivery system is a wonderful approach to target the pharmacological and therapeutical active moiety to target a specific region, and not to target non-targeted areas such as organ or tissue and accumulate to the targeting region only to show pharmacological activities.<sup>20</sup> Some important criteria can be noticed under targeted drug delivery such as they are selectively and effectively targeting local as well as systemic regions and also involved in the pre-identified target can be set to deliver the active moiety, increase or enhancement of therapeutic concentration at the targeting region and accumulation of the active moiety to the target region and show high concentration, targeted drug delivery can enhancement of therapeutic activity with less adverse effect with less adverse events.<sup>21</sup>

#### Ideal Characteristic of Targeted Drug Delivery Over Conventional Drug Delivery

- Targeted drug delivery to the targeting region is followed as biochemically inert, non-toxic, non-immunogenic as well as non-irritant.
- They are physical as well as chemical stability.
- Rate of drug can be followed through a controlled and predictable manner and accumulate at the target region and not interfere with the non-target region.
- Drug release can be predictable and drug action can be seen properly and pharmacokinetics study can be easily observed with high therapeutic values.
- Targeted drug delivery leakage of the drug can be reduced compared with conventional drug delivery systems.
- Targeted drug delivery or target specific drug delivery can be overcome fluctuation of dose as well as fluctuation of blood plasma level and low dose enough to produce high therapeutic efficacy.<sup>22,23</sup>

#### Advantages and disadvantages of targeted drug delivery systems over conventional drug delivery systems

- Dose frequency reduction, fluctuation of dose reduced compared to conventional drug delivery systems.
- Enhancement of absorption to the target region, increase bioavailability and site-specificity.
- Smaller amount of dose is enough to excrete high therapeutic value with low side effects.
- Stability of dose and storage of the active moiety is much higher compared with conventional drug delivery systems.
- Dose administration is more simplified than the conventional approach and targeting the specific area and showing proper therapeutic effectiveness is quick.<sup>24,25</sup>

Some disadvantages of targeted drug delivery systems as,

- Clearance of the drugs is rapid compared to conventional drug delivery systems.
- Sometimes insufficient to localization of targeted area and show may be shown immune reaction.
- High sophisticated with the highly skilled personnel required to manufacture the dosage form.
- Stability difficulties compared to conventional drug delivery.
- Fixed dose of drugs is still unknown and complex in the administration compared to the conventional drug delivery systems.
- Yield of the drugs is less compared to conventional drug delivery.



- Cost of the formulation is highly expensive compared to traditional drug delivery systems.<sup>26,27</sup>

### Future prospective of Targeted drug delivery in the treatment of colonic diseases

Targeted drug delivery is gaining much more attention over conventional to upcoming researchers for various advantages such as target specificity, enhancement of bioavailability, stability, reduction of premature drug release, enhancement of absorption to colon regions, and reduction of adverse effects.<sup>28</sup> The upcoming targeted drug deliveries such as nanoparticles, liposomes, microsphere, microspoon, noisome, aquasomes, etc. are successfully targeting the predetermined target region to show high stability with predictable release rates. Targeting drug delivery to the colonic environment, nanoparticles play an important role over others carriers available in the market. Nanoparticles are such a carrier that provides high bioavailability of poorly soluble drugs as highly lipophilic, target specificity, low dose as well as low dose frequency, dose dumping and leakage of the dose can be reduced through carriers.<sup>29,30</sup>

### CONCLUSION

Colon-targeted drug delivery is a wonderful approach to targeting drugs into the colonic region. Marketed drugs are unavailable to target the colon region due to premature drug release before reaching the target region. A targeted drug delivery system is recently gaining much more interest to the researcher to show target specificity and high therapeutic activity. The present review is focused on the advancement of drug delivery over conventional drug delivery or traditional approach to providing target specificity, enhancement of bioavailability, accumulation of drug to the colonic environment in a controlled and predictable manner without premature drug release before reaching the goal. To show the proper therapeutic efficacy and accumulation of drugs in the particularly colonic environment various strategies can be applied such as proper designing of the dosage form, methodologies that can be successfully delivered the dosage form at the colonic environment.

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