

## Development of colon targeted matrix tablets of Metformin HCl using various concentration of selected polymers

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**Received date:** November 30,2017;**Accepted date :** December 20,2017; **Published date:** December 09,2017.

**Citation for this Article:** Swathi Goli. Development of colon targeted matrix tablets of Metformin HCl using various concentration of selected polymers. J. Gastroenterology Pancreatology and Hepatobiliary Disorders. 1(1). Doi: [10.31579/2641-5194/002](https://doi.org/10.31579/2641-5194/002)

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### Abstract

The aim of the present study was to develop colon targeted matrix tablets of Metformin HCl using various conc. of selected polymers such as HPMC, Ethyl Cellulose Guar gum and combination of the same. Tablets were prepared by direct compression method and both pre-compression and post-compression parameters for all batches shows in the acceptable ranges.

Short term accelerated stability studies was performed according to ICH guidelines temperature of  $400 \pm 20$  and relative humidity of  $75 \pm 5\%$  RH to study any physical changes and chemical decomposition of drug, no formulation shown any physical or chemical changes.

The compatibility of drugs, polymers and excipients were determined by FT-IR Spectroscopy results showed that the drug was compatible with polymers and all excipients.

Dissolution studies were performed for 12 hours study in 1.2 pH for first 2 hrs then in 7.4 pH for next 3 hrs followed by 6.8 pH phosphate buffer at the temperature of  $37 \pm 0.50^\circ\text{C}$  at 100 rpm.

The dissolution data so obtained was fitted to various mathematical kinetic models and the drug release followed mixed order and Higuchi's model. To study release mechanism of drug from matrices the data were fitted to Korsmeyer-Peppas model and the release.

In-vitro release profile of Metformin HCl from various polymers showed that drug increasing the conc. of polymers resulted in reduction in the release rate of drug (MTF1 to MTF12).

Formulation containing combination of E.C-G.G, HPMC-G.G and E.C-HPMC showed drug release profile for MTF-12 about 38.72% after 12 hrs, MTF-11 about 40.66% after 12 hrs, for MTF-10 about 45.45% after 12 hrs. This is an indicative of retardation of drug release when polymer combination was changed.

Results showed that the tablets with higher binding concentration showed minimum drug release. Combination of polymers shows greater retarding of drug release.

### Key Words

colon targeted; matrix tablets; metformin HCl; HPMC; guar gum; ethyl cellulose

### Objective

#### Need for the study

The aim of the present research work was to develop matrix tablets of Metformin HCL targeted to colon.

The delivery of drugs to colon for systemic action or a local effect is valuable in a variety of circumstances. These include the topical treatment of diseases such as ulcerative colitis, Chron's disease, irritable colon syndrome, infectious disease, colon cancer and the potential for the oral delivery of peptides and other labile drugs. Targeting of drugs to the colon via oral route can be achieved by different approaches including different formulation system. For which the drug release is controlled by different pH conditions, transit time and microbial flora.

Metformin HCL is a BCS class-III (highly soluble-poorly permeable) biguanide derivative that has been used worldwide for the treatment of type-II diabetes. In spite of its favorable clinical response chronic therapy with Metformin HCL suffers from certain specific problems of which, the most prominent being the high dose (1.5-2.0 g/day), half life is about 1.5-3.5 hours, low bioavailability(60%) and high incidence of GI side effects(30% cases). The situation is complicated further with decrease in absorption of drug with food that delays tmax by up to 35mins.

Colon targeted drug delivery systems are developed to increase the bioavailability of drugs since colon is composed of large amount of lymphoid tissue the drug by passes.

The first-pass metabolism and enters into the systemic circulation. However Metformin HCL cannot cross the colonic epithelial layer since it belongs to BCS class-III. In order to increase the bioavailability of Metformin HCL permeation enhancers like succinic acid is used. Thus it improves bioavailability there by frequency of dosing is reduced, minimize the GI side effects and improves the patient compliance through CDDS.

### Methods and Materials

#### Description

Visual inspection of drug was done and description as per specification was checked.

#### Melting point

Melting point of drug was determined by capillary method in triplicate. The melting point was found to be in the range of  $222^\circ\text{C}$ - $226^\circ\text{C}$ .



### Solubility in different dissolution media

Excess amount of the drug is added to 100 ml distilled water, 100 ml phosphate buffer pH 7.4 (intestine), 100 ml phosphate buffer pH 6.8 (colon). After adding maximum amount of the drug shake the each volumetric flask in a shaker for more than 12 hrs for maximum saturation of the solution. Then 5 ml of solution was removed from each flask and dilution was made as required. Absorbance was taken at 233 nm in UV-Visible spectrophotometer.

### Summary

Targeting of drug to the colon is recognised to have several therapeutic advantages because colon is rich in lymphoid tissue, uptake of antigens in to the mast cells of the colonic mucosa produce rapid production of antibodies and thus helps in effective vaccine delivery. The colon has longer retention time and appears highly responsive to an agent that enhances the absorption of poorly absorbed drugs. Absorption of drug molecules from the colon like other regions of GIT is a result of a complex series of events. Successful colonic uptake of a drug species require both enzymatic stability and has to transport from the mucosal surface to the venous and or lymphatic capillaries located in the sub mucosa. The colonic epithelial permeability is insufficient to allow for the transport rate required for a therapeutic delivery. Then the co-administration of an absorption enhancing agent offers a potential means of overcoming this barrier mostly through the use of chemical enhancers like chelating agents, surfactant and dicarboxylic acids (succinic acid, lauric acid..etc).

The delivery of drugs to colon for systemic action or a local effect is valuable in a variety of circumstances. These include the topical treatment of diseases such as ulcerative colitis, Chron's disease, irritable colon syndrome, infectious disease, colon cancer and the potential for the oral delivery of peptides and other labile drugs. Targeting of drugs to the colon via oral route can be achieved by different approaches including different formulation system. For which the drug release is controlled by different pH conditions, transit time and microbial flora.

Colon targeted drug delivery systems are developed to increase the bioavailability of drugs since colon is composed of large amount of lymphoid tissue the drug by passes the first-pass metabolism and enters into the systemic circulation. However Metformin HCL cannot cross the colonic epithelial layer since it belongs to BCS class-III. In order to increase the bioavailability of Metformin HCL permeation enhancers like succinic acid is used. This increases bioavailability and reduces dosing frequency by minimize the GI side effects and improves the patient compliance through CDDS.

### Results And Discussions

In the present work colon targeted matrix tablets were prepared by direct compression technique using Metformin HCl as a model drug for the treatment of oral diabetes. Tablets were prepared by using different polymers like Ethyl cellulose, Guar gum, HPMC alone and in combinations. The prepared formulations were evaluated for both pre-compression and post- compression parameters. The absorbance was measured in UV spectrophotometer at 233nm against 1.2 pH buffer.

### Conclusion

Metformin HCL belonging to BCS class-III (highly soluble-poorly permeable) biguanide derivative that has been used worldwide for the treatment of type-II diabetes.

The objective of the present study was to develop and investigate the colon targeted matrix tablets of Metformin HCl using some selected polymers as the release controlling matrices.

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