RAFT FORMING SYSTEM A VALUABLE EXPANSION IN GRDDS

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ABSTRACT
Gastroretentive drug delivery system plays a vital role among novel drug delivery systems. The retention of oral dosage forms in the upper GIT causes prolonged contact time of drug with the GI mucosa, leading to higher bioavailability, and hence therapeutic efficacy, reduced time intervals for drug administration, potentially reduced dose size and thus improved patient compliance. Gastroretentive drug delivery system is facing many challenges which can be overcome by upcoming newly emerging approach i.e. raft forming system. The present study provides valuable information & highlights advances in this raft forming system. This review focuses on various factors aspects of the raft forming system, different types of smart polymers used for their formulation, mechanism, formulation and evaluation of raft forming system.

KEYWORDS: Raft, Gastric residence time, Gastroretentive, Floating, Effervescent; applications etc.

INTRODUCTION
Gastroretentive drug delivery system (GRDDS) can be defined as a system which retains in the stomach for a sufficient period of time and releasing active moiety in a controlled manner and finally metabolized in the body. Over the last two decades, numbers of GRDDS have been designed to prolong GRT. The main aim of preparing GRDDS is to minimize the problem associated with existing oral sustained release dosage form and to develop patient benefited drug delivery.[1]

Approaches To Achieve Gastric Retention
1. Low density approach:
   A. Effervescent system:
      a. Gas generating system: Single layer floating tablet, Bilayer floating tablet, Multiparticulate system.

2. High density approach.
3. Mucoadhesive approach
4. Expansion by swelling approach and
5. Raft forming system.[2-3]

Raft forming system
Gastroretentive drug delivery system is facing many challenges which can be overcome by upcoming newly emerging approach i.e. raft forming system.

Raft forming systems have received much attention for the delivery of antacids and drug delivery for gastrointestinal infections and disorders. The mechanism involved in the raft formation includes the formation of viscous cohesive gel in contact with gastric fluids, wherein each portion of the liquid swells forming a continuous layer called a raft.

Raft forming systems have received much attention for the delivery of antacids and drug delivery for gastrointestinal infections and disorders. A simple meaning of Raft is a flat structure, typically made of planks, logs, or barrels, that floats on water and is used for transport or as a platform for swimmers.[4]

Mechanism of action of Raft forming system
The Raft forming system is the one which on swallowing slides down the esophagus into the stomach. Raft forming system contains sodium alginate and calcium carbonate, where sodium alginate forms a complex with Ca2+ ion and forming a gel like structure, due to low density of gel form a barrier on stomach. Sodium bicarbonate was used to produce carbon dioxide and gives bouncy to the dosage form.[5]
Potential candidates for Rafting drug delivery system
1) Drugs that are primarily absorbed in the stomach eg. Amoxicillin.
2) Drugs that are poorly soluble in alkaline pH eg. Furosemide, Diazepam.
3) Drugs that have narrow absorption window eg. Levodopa, Methotrexate.
4) Drugs that degrade in the colon eg. Ranitidine, Metformin HCl.
5) Drugs that disturb normal colonic microbes eg. Antibiotics against Helicobacter pylori.[6-7]

Drugs suitable for Raft forming system
1) Drugs with narrow absorption window in GIT, e.g., Riboflavin and Levodopa.
2) Drugs that primarily absorbed from stomach and upper part of GIT, e.g., Calcium supplements, chlordiazepoxide and cinnarazine.
3) Drugs that act locally in the stomach, e.g., Antacids and Misoprostol 135.
4) Drugs that degrade in the colon, e.g., Ranitidine HCl and Metronidazole.
5) Drugs that disturb normal colonic bacteria, e.g., Amoxicillin Trihydrate.[8-9]

Significance of Raft systems
1) Rapid and Long-duration of action can easily achieved by raft formation.
2) High level patient compliance can be achieved and it is well tolerated.
3) It will not interfere with function of pyloric sphincter.
4) It decreases the frequency of drug administration.
5) Increase the desired residence of drug at the site of action mainly in the stomach.
6) It Minimize the side effects.
7) It Minimize the cost of treatment.
8) It does not interfere with the activity of promotility agent, antisecretory agents such as cimetidine.[10-13]

Approaches of Raft forming system
Raft forming drug delivery systems are a revolution in oral drug delivery. These systems are liquids at room temperature but undergo gelation when comes in contact with body fluids or change in pH. These have a unique property of temperature dependent and cation-induced gelation. Gelation involves formation of the double helical junction zones followed by aggregation of the double helical segments which form three dimensional networks by complexation with cations and hydrogen bonding. Different approaches based on their mechanisms used for triggering the raft formation in the GIT are as follows.[14-15]

1. Raft formation based on physical mechanism.
   a) Swelling,
   b) diffusion,
   c) crosslinking.

2. Raft formation based on physiological stimuli mechanism
   a) pH dependent gelling;
   b) Temperature dependent gelling:

Polymers used for formulation of Raft forming system
- Alginic Acid
- Gellan Gum
- Xyloglucan
- Chitosan
- Carbopol.[16-18]

Applications of Rafting drug delivery system
1) In Novel drug delivery system
   Rafting drug dosage forms can remains in the stomach for prolong time and enhance the GRT of numerous drugs. Also, these dosage forms are large in size due to which don’t pass through pylorus (0.9-1.9 cm opening). So, GRDDS provides sustained drug delivery.
2) Site-specific drug delivery Some drugs such as furosemide, riboflavin.
3) To improve Bioavailability, Rafting dosage form can be beneficial to prolong the GRT, hence it increases the bioavailability.
4) Local action in stomach The GRDDS are beneficial for drugs that are desire to produce local action in the stomach. For example: antacids.
5) Reduce irritation of acidic drugs Acidic drugs, after administration may cause irritation on the stomach wall. Hence Rafting dosage forms may be advantageous for the administration of acidic drugs such as aspirin and other.
6) Advantageous to drugs which are unstable in intestine environment Drugs such as captopril, ranitidine HCl, metronidazole which are unstable in the intestinal or colonic environment can be administered by making Rafting dosage forms.
7) Beneficial to drugs that show low solubility at high pH Some drugs such as diazepam, chlordiazepoxide, and verapamil show low solubility at high pH. GRDDS can be useful because it enhance the GRT of these drugs and hence increase the bioavailability of these drugs by increasing absorption.
8) To improve patient compliance since it increases the bioavailability high level of patient compliance is associated with Raft forming system.[19-23]

In vitro in vivo characterization of Raft forming system
a) Total floating time
b) Floating lag time
c) Water uptake
d) Resultant weight
e) Swelling Study
f) Specific gravity/Density;
g) In Vitro drug release studies
In vivo studies
a) Radiology;
b) Scintigraphy;
c) Gastroscopy;
d) Magnetic Marker Monitoring;
e) 13C octonoic acid breath test;
f) Pharmacokinetic study.[24-27]

Marketed brands of Raft forming system
1. GAVISCON ADVANCE TABLETS ® (Reckitt and Colman)
2. GASTROCOTE ® (Boeringer Mannheim)
3. BISODOL ® (White Hall)
4. GASTRON ® (Sanofi Winthrop)
5. LIQUID GAVISCON ® (Reckitt Benckiser Healthcare)
6. ALGICON ® (Rorer).[28-30]

CONCLUSION
Gastroretentive drug delivery is prepared with the intention to retain drug in the gastric region for prolonged time and release incorporated drug candidates and thereby enable sustained and prolonged input of the drug to the upper part of the GIT thus leading its optimal bioavailability. Gastroretentive drug delivery system is facing many challenges which can be overcome by upcoming newly emerging approach i.e. raft forming system.

The raft system contains a gel forming agent and alkaline bicarbonates or carbonates responsible for the formation of CO2 to make the system less dense and float on the gastric fluids. The system contains a gel forming agent sodium bicarbonate and acid neutralizer, which forms a foaming sodium alginate gel (raft) when in contact with gastric fluids.

The raft thus formed floats on the gastric fluids and prevents the reflux of the gastric contents into the esophagus by acting as a barrier between the stomach and esophagus.

Raft forming system promises to be a potential approach for heartburn, oesophagitis & various diseases. Thus by looking all above aspects we can conclude that Raft forming system is valuable expansion in Gastroretentive drug delivery system.

REFERENCES


