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USE OF POROUS CARRIERS IN THE DEVELOPMENT OF INTRAGASTRIC FLOATING DRUG DELIVERY SYSTEMS: REVIEW

Sharma Saurabh[1]* and Nanda Arun[2]
[1]Pharmaceutics Research Lab., Vivek College of Technical Education, Bijnor, Uttar Pradesh, India
[2]Dept. of Pharm. Sciences, M.D.University, Rohtak, Haryana, India

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*Email: saurabhmpharm@rediffmail.com

ABSTRACT
Considerable research efforts have been used in the development of floating drug delivery system including gas generation system, swelling systems and low density systems. In the development of low density systems the porous carriers are used because of its characteristics such as stable uniform porous structure, high surface area, tunable pore size and well-defined surface properties. This review focused on the use of porous materials in the development of intragastric floating DDS.

KEYWORDS: Gastroretentive, Intragastric, Floating and Porous carriers.

INTRODUCTION

Oral delivery of drugs is by far the most preferable route of drug delivery due to the ease of administration, patient compliance and flexibility in formulation, etc. From immediate release to site-specific delivery, oral dosage forms have really progressed[1].

However, oral administration has only limited use for important drugs, from various pharmaceutical categories, that have poor bioavailability due to incomplete absorption and/or degradation in the GI tract. Some of these drugs are characterized by narrow absorption window at the upper part of gastrointestinal tract. This is because the proximal part of small intestine exhibits extended properties. Despite the extensive absorption properties of the duodenum and jejunum, extend of absorption at these site is limited because the passage through this region is rapid. Enhancing the gastric residence time of a narrow absorption window drug, may significantly improve the net extent of its absorption. To increase the GRT of drugs, a gastroretentive dosage form can be developed[2].

Dosage forms with a prolonged GRT, i.e., gastroretentive dosage forms (GRDFs), will provide us with new and important therapeutic options[1].

Gastroretentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment. It has applications also for local drug delivery to the stomach and proximal small intestines. Gastroretention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patients[3].

Floating drug delivery system is one of the gastroretentive dosage forms which could prolong GRT. The system basically floats in the gastric fluid because of its lower bulk density compared to that of aqueous medium[4]

During the past decade, a diversity of inert polymeric carriers has been developed to control temporal or distributional drug delivery to oral. Recently, there has been exponential growth in the investigations related to the use of porous material in pharmaceuticals. Porous material possess several attractive features, such as stable uniform porous structure, high surface area and tunable pore size with narrow distribution as well as well defined surface properties. This will allow them to absorb drug and release them in a more reproducible and predictable manner. Due to wide range of useful properties, porous carriers have been used for many purposes includes development of novel drug delivery system like floating drug delivery system (because of low mass density), sustained drug delivery system, improvement of solubility of poorly soluble drugs and enzyme immobilization etc[5,6].

Examples of pharmaceutically exploited porous carrier are Porous calcium silicate (Florite ®) poly propylene foam powder (Accurel ®), magnesium aluminometa silicate (Neusilin ®), Porous ceramic and porous silicon dioxide (Sylysia®) etc[6].

Calcium Silicate (Florite®)

Calcium silicate posses many interparticle and intraparticle pores, particularly of size 12 and 0.15 micro meter respectively on its surface. Calcium silicate is easily dispersible in all aqueous fluids and has been used to absorb oily and other drugs, as a compressive agent in pharmaceuticals, and to improve solubility[7].

Poly Propylene Foam Powder

It is highly porous with open cell structure and having low inherent density. It is practically insoluble in cold organic solvents and resistant to alkalies. For pharmaceutical process it is used as packaging material and approved for parental dosage forms[8].

Magnesium Alumino Metasilicate (Neusilin ®)

Neusilin is a synthetic amorphous form of Magnesium aluminometasilicate. It is a multifunctional excipient that can be used in both direct compression and wet granulation of solid dosage forms. Neusilin is widely used for improvement of the quality of tablets, powder, granules and capsules. It is stable against heat and has a long shelf life[9].

Porous Ceramics

Porous ceramics are bodies comprised of a three-dimensional array of hollow polygons, known as cells. If the individual cells are interconnected the porous ceramic is termed open-cell, while if they are isolated from each other, the porous ceramic is termed closed-cell. They can also be partly open or partly closed. These properties have found many applications including catalyst supports, filters for molten metal's and hot gases, refractory linings for furnaces, and porous implants in the area of biomaterials[10].

Previous Work on Porous Carriers

Calcium silicate (Florite®)

Yuasa et al., prepared the intragastric floating granules using calcium silicate (Florite, FLR) as a floating carrier which has floating ability due to air present in the pores when they are covered with a polymer. The prepared granules showed a longer floating time and they suggested that the FLR is a useful carrier for the development of a floating sustained release drug delivery systems[11].

Sharma S and Pawar A, prepared a multi-particulate floating pulsatile drug delivery system using calcium silicate and sodium alginate for time and site specific release of meloxicam. The floating beads were prepared by absorbing the meloxicam on porous calcium

silicate and drug absorbed calcium silicate was used to prepared beads by ionotropic gelation method. The prepared beads were evaluated for yield, entrapment efficiency, and buoyancy and dissolution studies. It was observed that the prepared beads showed a lag period ranging from 1.9 to 7.8 hours in acidic medium followed by rapid release of meloxicam in simulated intestinal fluid without pepsin[6].

Jain A K et al., developed floating granular drug delivery system of ranitidine hydrochloride using Calcium silicate as porous carrier, HPMC and ethylcellulose as metrix forming agent. The prepared granules were evaluated for particle size, *in vitro* floating behavior and *in vitro* drug release. The formulation demonstrated favorable *in vitro* floating and drug release characteristics and they suggested that calcium silicate is a useful carrier for the development of floating and sustained release preparations[12].

Jain S K et al., prepared floating Orlistat microsphere using calcium silicate as porous carrier and eudragit S as polymer by solvent evaporation method and evaluated for *in vitro* floating behavior, drug entrapment and in vitro drug release studies. The floating microsphere showed best floatability (88 % buoyancy) in simulated gastric fluid and drug release pattern followed Higuchi matrix and Peppas- Korsmeyer model[13].

Jain S K et al., developed a porous carrier based floating granular delivery system of Repaglinide using calcium silicate, HPMC and Carbapol and evaluated for in vitro floating behavior, drug content and in vitro drug release. The optimized formulation demonstrated favorable in vitro floating and release characteristic and relative bioavailability of repaglinide loaded granules increased 3.8 times than marketed product[14].

Poly propylene foam powder (Accurel)

Strubel A et al., prepared a single unit floating drug delivery system consisting of poly propylene foam powder and matrix forming polymers like HPMC, sodium alginate and guar gum and it was observed that the floating behavior of low density drug delivery system could successfully be combined with accurate control of drug release pattern[15].

Strubel et al., developed a multiparticulate gastroretentive drug delivery system using poly propylene foam powder, Eudragit RS and Ethylcellulose as polymer. The prepared microparticle were characterized for drug loading, *in vitro* floating behavior and *in vitro* drug release kinetics and it was observed that the micro particles were irregular in shape and highly porous, drug entrapment efficiency closed to 100% and showed good in vitro floating behavior[8].

Garg and Gupta prepared floating tablets of Silymarin by using polypropylene foam powder, matrix forming polymer HPMC, Carbapol, xanthum gum and sodium alginate. In vitro drug release studies were performed and drug release kinetics evaluated using the linear regression method and it was found that the tablets followed both the Higuchi and Korsemeyer and Peppas equation. The drug release mechanism was found fickian type in most of the formulations. The developed floating tablets of Silymarin may be used in clinic for prolonged drug release for at least 24 h, thereby improving the bioavailability and patient compliance[16].

Baskar G V et al., formulation gastro-retentive floating multi-particulate system of metoprolol tartarate by using by solvent evaporation using Eudragit, polypropylene foam powder, and dichloromethane as release-rate modifying polymer, floating aid and solvent respectively and evaluated for floatability and *in-vitro* drug release. The dried free-flowing, white coloured highly porous microparticles were obtained and *in-vitro* drug release from the particles followed a biphasic pattern with zero-order kinetics. The microparticulate system exhibited good floating ability with t1/2 of 300 min over the duration of the *in-vivo* study (6 h)[17].

Magnesium alumino metasilicate (Neusilin ®)

Boldhane S P et al., prepared gastroretentive controlled release matrix tablets of metoprolol succinate by using novel combination of sodium alginate, sodium carboxymethyl cellulose and magnesium aluminometasilicate (MAS) as independent variables. The prepared tablets were evaluated for floating lag time, mechanism of drug release and amount of drug release and it was observed that the tablets exhibited non-Fickian diffusion of metoprolol succinate with floating for 16 h[18].

Boldhane S P et al., developed gastroretentive drug delivery system of quetiapine fumarate by using Eudragit, calcium sulphate dihydrate, lactose anhydrous and Magnesium aluminometasilicate and evaluated. It was observed that the tablets containing magnesium aluminometesilicate were close to the required attributes of gastroretentive tablets in terms of t50, t90 and floating lag time[19].

Porous ceramic

Byrne R S. developed a sustained release drug delivery system by using commercial porous ceramic and it was observed that during the in vitro dissolution testing the microparticle showed initial burst release and followed by sustained release. It was also observed that the release was influenced by the surface pore size distribution of the ceramic[20].

CONCLUSION

Porous carriers have a major role to play in the pharmaceutical industry. Their inner structure consists of unidirectional channel like pores that forms a hexagonal pattern. The presence of porous structure makes them suitable in the development of floating drug delivery systems.

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