ISSN: 2279 - 0594

Journal of Biomedical and Pharmaceutical Research 1 (3) 2012, 01-04

REVIEW ARTICLE

A short Review on Stomach Specific Floating in-situ gel

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ABSTRACT

Oral drug delivery is a one of the simplest routes of delivery of drugs for systemic and in certain cases local effect. Liquid oral dosage forms are convenient to administer as compared to solid dosage forms but cannot achieve sustained effect due to less residential time in gastrointestinal tract. In-situ gel provides the best way to overcome problems of immediate release and short gastrointestinal residence of liquids. The in situ gel dosage form is a liquid before administration and after it comes in contact with gastric contents due to one or more mechanisms gets converted to gel which floats on gastric contents. This achieves increased residence as well as sustained release. This approach is useful for systemic as well as local effect of drugs administered. This review gives a short idea about floating oral in-situ gel formation and research done by various scientists on a number of drugs and polymers.

KEY WORDS: Oral, In-situ gel, Floating drug delivery.

INTRODUCTION:

Floating drug delivery system (FDDS) was first described by Davis in 1968. FDDS is an effective technology to prolong the gastric residence time in order to improve the bioavailability of the drug. FDDS are low-density systems that have sufficient buoyancy to float over the gastric contents and remain in the stomach for a prolonged period. Floating drug delivery systems meant for gastric retention, float on the surface of the gastric fluids, due to their low density and produce prolonged effect by showing the controlled release. This type of delivery system is of great value for drugs which get absorbed from upper part of the stomach i.e. their absorption window resides in upper part of stomach. It is also useful for drugs which are inserting at alkaline pH of intestine and remains unabsorbed or causes side effects due to insolubility. The FDDS are particularly useful for drugs required for their local effect in stomach. Though, immediate floating of the delivery system can only be achieved if the density of the delivery system is on lower side. Delivery system with higher density, initially settle down in stomach and then absorbed water, swell and then float due to decrease in density of the system. But, with such system, there may be a possibility of gastric emptying of system, before the floating starts. Low density of system, which leads to floating, rendered either by incorporation of low density excipients or by providing a mechanism which leads to air entrapment within the system may have their own certain limitations.

NEED OF FLOATING DRUG DELIVERY SYSTEM[1, 2]:

Oral dosage forms pose low bioavailability problems due to their rapid gastric transition from stomach, especially in case of drugs which are less soluble at alkaline pH of intestine. Similarly, drugs which produce their local action in stomach get rapidly emptied and do not get enough residence time in stomach. So, frequency of dose administration in such cases is increased. To avoid this problem floating drug delivery system has been developed.

INTRODUCTION TO FLOATING ORAL IN SITU GEL[3, 4, 5]:

Oral in situ gel forming system also known as stomach specific or raft forming systems have provided a suitable way of providing the controlled drug delivery within stomach with enhanced gastro-retention. The tablet/capsule floating dosage forms are stable as compare to liquids but the problem with them is that they are needed to swallow as whole unit. In case of dosage adjustment these cannot be broken in halves as these are also designed for controlled release and floating ability also depends on dimensions of tablets. Elderly patients, children some adult persons and patient with certain conditions suffer from dysphasia, so it becomes difficult for them to swallow tablet/capsule dosage forms. Also in case of dosage adjustments these floating solid dosage forms are needed to be available in different strengths. Where an environment specific gel forming solution, on conversion to gel, floats on the surface of the gastric fluids (due to less density than gastric contents). In this technique, a solution of low viscosity is used which on coming in contact with the gastric fluids, undergo change in polymeric conformation

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and a viscous gel of density lower than the gastric fluids is produced. This low density gel formation called as raft not only provide the much desired gastro retention to prolong the contact time, but also produce the continuous and slow drug release. Diagram shows floating in situ gel[6].

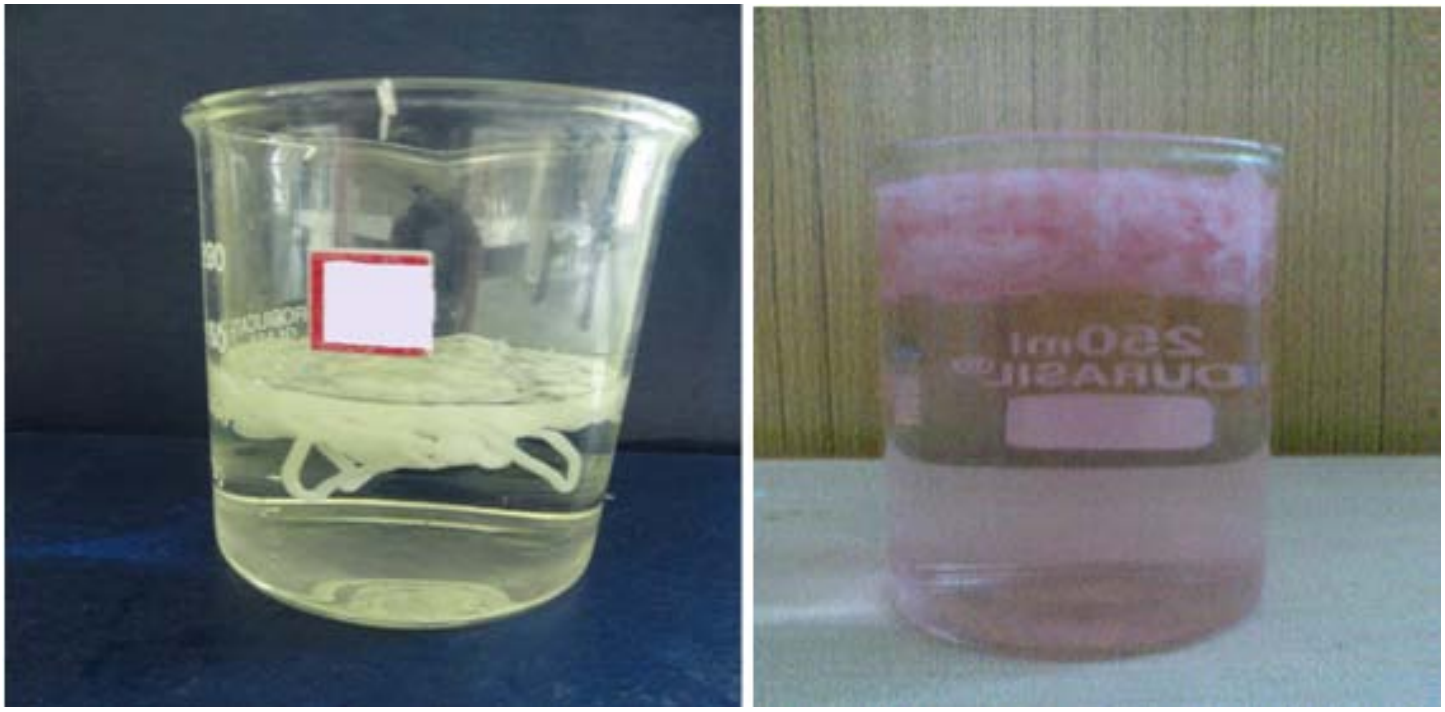

Figure No.1: In-situ formation of floating gel

DIFFERENT APPROACHES FOR IN SITU GELLING SYSTEM:

There are different mechanisms used for triggering the in-situ gel formation: Chemical reactions (e.g., Ionic Cross linking) and Physiological stimuli (e.g., temperature and pH).

A. IN SITU GELLING BASED ON CHEMICAL STIMULI:

IONIC CROSS LINKING[7, 8, 9]:

Certain ion sensitive polysaccharides such as carrageenan, Gellan gum(Gelrite®), Pectin, Sodium Alginate undergo phase transition In presence of various ions such as K^+ , Ca^{+2}, Mg^{+2}, Na^+. For e.g., Gelation of the low-methoxypectins can be caused by divalent cations, especially Ca^{2+}., Alginic acid undergoes gelation in presence of divalent/polyvalent cations e.g. Ca^{2+} due to the interaction with guluronic acid block in alginate chains.

E.g. Formulation Evaluation and optimization of stomach specific in situ gel of Ranitidine hydrochloride[9].

B. IN SITU GEL FORMATION BASED ON PHYSIOLOGICAL STIMULI:

pH DEPENDANT GELLING[8]:

Another formation of in-situ gel is based on Change in pH. Certain polymers such as PAA (Carbopol®, carbomer) or its derivatives, Polyvinylacetal diethylaminoacetate (AEA), Mixtures of poly (methacrylic acid) (PMA) and poly (ethylene glycol) (PEG) shows change from sol to gel with change of pH. Swelling of hydrogel increases as the external pH increases in the case of weakly acidic (anionic) groups, but decreases if polymer contains weakly basic (cationic) groups.

E.g. The influence of variation of gastric pH on the gelation and release Characteristics of in situ gelling sodium alginate formulations[10].

TEMPERATURE DEPENDANT IN SITU GELLING[11, 12]:

These are liquid aqueous solutions before administration, but gel at body temperature. These hydro gels are liquid at room temperature (20^0C-25^0C) and and undergo gelation when in contact with body fluids (35^0C-37^0C), due to an increase in temperature. This approach exploits temperature-induced phase transition. Some polymers undergo abrupt changes in solubility in response to increase in environmental temperature (lower critical solution temperature, LCST). Polymers such as Pluronics (poly (ethylene oxide)-poly(propylene oxide)-poly (ethylene oxide)(PEO-PPOPEO) Triblock), Polymer networks of poly(acrylic acid) (PAA) and polyacrylamide (PAAm) or

poly(acrylamide-co-butyl methacrylate). Polymer solution is a free flowing liquid at ambient temperature and gels at body temperature. It remains at the site of injection providing absorption times from less than one week to many months. Such a system would be easy to administer into desired body cavity. A positive temperature- sensitive hydrogel has an upper critical solution temperature (UCST), such hydrogel contracts upon cooling below the UCST. Polymer networks of poly (acrylic acid) (PAA) and polyacrylamide (PAAm) or poly (acryl amide-co-butyl methacrylate) have positive temperature dependence of swelling.

E.g. In situ gelling formulation based on methylcellulose /pectin system for oral-sustained drug delivery to dysphagic patients[11]

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Natural		Synthetic	
Na Alginae	Tara gum	HPMC K4M	Polyvinyl ethers
Pectin	Moi gum	HPMC K 15M	Esters and halides
Tragacanth	Gum damber	HPMC K 100M	Polymethacrylic acid
Gelatin	Gum copal	Carbopol 934 p	Polymethyl Methacrylic acid
Carrageenan	Sesbenia gum	Ethyl cellulose	HPC
Tamarind gum	Chitosan	Methyl cellulose	
Hibiscus rosasinensis	Gellangum	Sod. Carboxy methyl cellulose	HEC
Okra gum	Xyloglucan	Polyvinyl alcohol	
Guar gum	Xanthum gum	Polyamides	
Locust gum	Carbopol	Polycarbonates	
Isapgulla (Psyllium)	Pluronic F-27	Polyalkylene glycols	

Table No. 1: Polymers used in floating drug delivery system

Author	Drugs	Category	Reference No.
Jayswal et al	Cimetidine	Antihistaminic	06
Patel et al	Ranitidine HCl	Antihistaminic	09
Jivani et al	Baclofen	Skeletal muscle relaxant	10
Itoh et al	Paracetamol	NSAID	11
Wamorkar et al	Metoclopramide	Anti-emetic	15
Bhimani et al	Clarithromycin	Antibiotics	16
Patel et al	Chlordiazapoxide	Antidepressant	17
Rajinikanth et al	Clarithromycin	Anti-H. pylori	18
Rajalakshimi et al	Levofloxacin Hemihydrate	Anti-H. pylori	19
Rathod et al	Ambroxol hydrocloride	Secretolytic agent	20
Patel.et al	Hydrochlorothiazide	Antihypertensive/Diuretic	21
Patel. et al	Famotidine	Antihistaminic	22
Lahoti et al	Ofloxacin	Antibiotics	23

Table No.2: Recent research activities on Stomach specific floating in-situ gel:

CONCLUSION:

In-situ drug delivery provides a great potential for development of liquid orals for their sustained drug release. This floating in-situ gel approach is suitable for drugs having absorption window in stomach or drugs showing local effect in stomach. These types of drugs which are currently present in market as their solid dosage forms (tablets or capsules) will be available as their floating in-situ gel in near future.

REFERENCES:

1. G Umamaheswara Rao, Murari P. Buoyant sustained release drug delivery systems current potentials advancements and role of polymers: a review. Pharmacie Globale (IJCP) 2012; 2 (01):1-7.

2. Rabadia N, Tiwari A, Patel G, Virani V. The floating drug delivery system and its impact on calcium channel blocker: A review article. IJPRD.2011; 3(12):107-131.

3. Shah SH, Patel JK, Patel NV. Stomach specific floating drug delivery system: a review. International Journal of PharmTech Research.2009; 1(3):623-633.

4. Bhardwaj L, Sharma PK, Malviya R. A Short Review on Gastro Retentive Formulations for Stomach Specific Drug Delivery: Special Emphasis on Floating In situ Gel Systems. African Journal of Basic & Applied Sciences 2011; 3 (6): 300-312.

5. Tripathi P, Ubaidulla U, Khar RK, Vishwavibhuti. Floating drug delivery system. International Journal of Research and Development in Pharmacy and Life Sciences.2012; 1(1): 1-10.

6. Jayswal BD, Yadav VT, Patel KN, Patel BA, Patel PA. Formulation and Evaluation of Floating In Situ Gel Based Gastro Retentive Drug Delivery of Cimetidine. International Journal for Pharmaceutical Research Scholars (IJPRS). 2012; 1(2):327-337.

7. Shah S, Upadhyay P, Parikh D, Jinal Shah. In Situ Gel: A Novel Approach of Gastroretentive Drug Delivery. Asian Journal of Biomedical and Pharmaceutical Sciences 2012; 2(8):01-08.

8. Parekh HB, Rishad J, Jivani NP, Patel LD, Ami M, Krunal S. Novel insitu polymeric drug delivery system: a review. Journal of Drug Delivery & Therapeutics 2012; 2(5): 136-145.

9. Patel RP, Baria AH, Pandya NB, Tank HM. Formulation Evaluation and optimization Of stomach specific in situ gel of Ranitidine hydrochloride. International journal of Pharmaceutical sciences and Nanotechnology 2010; 3(1): 834-843.

10. Jivani RR, Patel CN, Jivani NP. The influence of variation of gastric pH on the gelation and release characteristics of in situ gelling sodium alginate formulations. Acta Pharmaceutica Sciencia. 2010; 52: 365-369

11. Itoh K, Hatakeyama T, Shimoyama T, Miyazaki S, D'Emanuele A, Attwood D. In situ gelling formulation based on methylcellulose/pectin system for oral-sustained drug delivery to dysphagic patients. Drug Development and Industrial Pharmacy 2011; 37(7): 790–797

12. He C, Kim SW, Lee DS. In situ gelling stimuli-sensitive block copolymer hydrogels for drug delivery. Journal of Controlled Release 2008; 127:189–207.

13. Kumar SA, Dubey V, Arora V. Role of natural polymers used in floating drug delivery system. Journal of Pharmaceutical and Scientific Innovation 2012; 1(3):11-15.

14. Hardenia SS, Jain A, Patel R, Kaushal A. Floating Drug Delivery Systems: A Review. Asian Journal of Pharmacy and Life Science 2011; 1(3): 284-293.

15. Wamorkar V, Varma MM, Manjunath SY.Formulation and Evaluation of Stomach Specific In-Situ Gel of Metoclopramide Using Natural, Bio-Degradable Polymers. International Journal of Research in Pharmaceutical and Biomedical Sciences 2011; 2(1):193-201

16. Patel RP, Dadhani B, Ladani R, Baria AH, Patel J. Formulation, evaluation and optimization of stomach specific in situ gel of clarithromycin and metronidazole benzoate. International Journal of Drug Delivery 2010; 2: 141-153.

17. Patel RP, Ladani R, Dadhaniya B, Prajapati BG. In situ gel Delivery systems for Chlordiazapoxide using Artificial Neural Network. Int. J. Pharm. Health Sci.2010; 1 (1): 10-22

18. Rajinikanth PS, Mishra B. Floating in situ gelling system for stomach site-specific delivery of clarithromycin to eradicate H. pylori. J Control Release. 2008; 125 (1):33-41.

19. Development and Evaluation of a Novel Floating Insitu Gelling System of Levofloxacin Hemihydrate. Rajalakshmi R, Sireesha A, Subhash KV, Venkata PP, Mahesh K, Naidu KL. International Journal of Innovative Pharmaceutical Research. 2011, 2(1):102-108.

20. Rathod H, Patel V, Modasiya M. Development, evaluation, and optimization of gellan gum
Based in situ gel using 32 factorial designs. International Journal of Biomedical Research. 2011; 2(4):235-245.

21. Patel RR, Patel JK. Development and evaluation of in situ novel intragastric controlled-release formulation of hydrochlorothiazide. Acta Pharm. 2011; 61: 73–82

22. Patel JK, Chavda JR, Modasiya MK. Floating In Situ gel based on Alginate as Carrier for Stomach-Specific Drug Delivery of Famotidine. International Journal Of Pharmaceutical sciences and Nanotechnology.2010; 3(3):1092-1104.

23. Lahoti SR, Shinde RK, Ali SA, Gulecha B. PH triggered sol-gel transition system of ofloxacin for prolonged gastric retention. Der Pharmacia Sinica, 2011, 2 (5): 235-250