Formulation and Evaluation of Floating Dosage Forms: An Overview

Sabale V, Sakarkar SN¹, Pund S², Sabale PM³

Department of Pharmaceutics, Baroda College of Pharmacy, Limda, Vadodara - 391 760, ¹Millenium College of Pharmacy, Nathu Barkheda Road, Neelbud, Bhopal - 462 011, ²B. V. Patel Pharmaceutical Education and Research Development (PERD), Centre, S. G. Highway, Thaltej, Ahmedabad - 380 054, ³Department of Pharmacy, Faculty of Technology and Engineering, The M.S. University of Baroda, Vadodara - 390 001, India

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A B S T R A C T

Floating dosage forms are emerging as a promising novel dosage forms. Floating dosage forms can be prepared as tablets, capsules by incorporating suitable excipients as well by adding certain gas-generating agents, which in turn give the buoyancy to the dosage form in gastrointestinal fluids. The various excipients such as poloxamer 188, carbopol 934P, hydroxypropylmethylcellulose, polyethylene glycol 6000, beta-cyclodextrin, polyvinyl acetate, purified shellac, Eudragit RS, or polymethyl methacrylate, alginate beads and casein-gelatin beads in combination provide buoyancy to the dosage form. The degree of drug embedded in dosage form determines its release. The hydrated layer slowly releases the drug from the dosage form by diffusion. Due to the hydrated gel layer, floating dosage forms can remain afloat in stomach for 6-8 h and release the active pharmaceutical ingredients for extended period of time in gastric environment. These systems have more flexibility in dosage design than conventional dosage form. For the optimization of the drug release pattern in vivo, floating devices such as InteliSite capsule can be used as it provides noninvasive determination of drug absorption and bioavailability at specific sites by gamma scintigraphy. This review summarizes various techniques adopted in the development of floating dosage forms, in vitro and in vivo studies to evaluate the performance and application of floating dosage forms.

In general, the drug release is governed by various polymers, which are used in the formulation. These polymers entrap the drug material in the matrix form or form a membranous sheath around the drug. The polymer in either case controls the release rate of drug by diffusion or by erosion method. Such drug delivery systems are termed as controlled drug delivery systems, which release the drug(s) with a predictable kinetics. Other approaches and materials that have been reported are highly swellable hydrocolloids and light mineral oils, a mixture of sodium alginate and sodium bicarbonate, multiple unit floating pills that generate carbon dioxide when ingested, floating minicapsules with a core of sodium bicarbonate, lactose and polyvinyl pyrrolidone coated with hydroxypropyl methylcellulose (HPMC) and floating systems based on ion-exchange resin technology. Excipients used most commonly in these systems include HPMC, polyacrylate polymers, polyvinyl acetate, polyethylene glycol (PEG)-6000, Carbopol, agar, sodium alginate, calcium chloride, polyethylene oxide and polycarbonates. Drugs used in the formulation of floating dosage forms and some of the marketed preparations are given in Tables 1 and 2.

The oral dosage forms taken orally are very much affected by the gastric physiology. As it is the gastric residence time (GRT), which decides the retention time of oral dosage form in GIT, the gastric emptying (GE) of liquids in the fasted state is a function of

Introduction

Drug delivery systems are used for maximizing therapeutic index of the drug and reduction in side effects due to site-specific drug delivery. With the recent developments and advances in pharmaceuticals, frequently taken medicaments are incorporated in a single unit dosage form. This reduces the frequency of administration of medicament to the patient. The real challenge in the development of a controlled drug delivery system is not just to sustain the drug release but also to prolong the presence of the dosage form in the stomach or the upper small intestine until all the drug is completely released in the desired period of time.¹ ² The residence of a drug delivery system in the upper part of the gastrointestinal tract (GIT) can be accomplished by several drug delivery systems, such as intragastric floating systems,³ swelling and expandable systems,⁴ bioadhesive systems,⁵ modified shape systems,⁶ high-density systems,⁷ delayed gastric-emptying systems⁸ and low-density super porous systems.⁹ This review deals with floating dosage forms, an oral novel drug delivery system.

Correspondence:
Mrs. Vidya Sabale; E-mail: vidyasaabale@yahoo.co.in
the volume administered. The normal GE _t_ is 46.5 ± 5.5 min.\cite{11-14} This sets an approximately 10 h limit for the delivery of drugs absorbed solely from the small intestine region. The various factors affecting GE include age, diseased state and diet. Normal aging is associated with various changes in gastrointestinal motility. The important factor is the impact of various age-related diseases on gastrointestinal motility in elderly patients; for example, long-standing diabetes mellitus may reduce GE in about 50%, depression significantly prolongs whole gut transit time, hypothyroidism may prolong orocecal transit time and chronic renal failure is associated with impaired GE. (Gastrointestinal transit time Figure 1) In addition, various frequently used drugs in elderly patients cause disordered gastrointestinal motility. These drugs include anticholinergics, especially antidepressants with an anticholinergic effect, opioid analgesics and calcium antagonists.\cite{15} Delayed GE or gastrointestinal symptoms occur in 30%-50% of patients with diabetes\cite{16} as well as in chronic liver diseases.\cite{17} High electrolyte content tends to decrease GE.\cite{18} Glucose supplementation accelerates GE of glucose,\cite{19} viscous polysaccharides show delayed GE and slow transit through the small bowel.\cite{20} The GE is significantly slow during dehydration\cite{21} and at times the GE is very rapid as with liquid diet, emotional stress and exercise. Thus, oral controlled release drug delivery systems have limited use in the gastrointestinal controlled administration of drugs if the system cannot remain in the vicinity of the absorption site for lifetime of the drug delivery. The transit time for the mouth to the anus varies with each individual. Oral delivery for 24 h is possible for many drugs; however, the substance must be adequately absorbed throughout the whole GIT. A significant obstacle may arise if there is a narrow window for drug absorption in the GIT or if a stability problem exists in GI fluids or the drug is poorly soluble in the intestine or acts locally in the stomach. Taking these factors into consideration, investigators formulated a novel drug delivery system for controlled drug delivery at the stomach level, termed as floating tablets or Hydrodynamically Balanced Systems (HBS) or gastroretentive drug delivery systems to prolong the residence of the dosage forms in the stomach or somewhere in the upper small intestine until all the drug is released for the desired period. 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 intestine. Gastroretention helps provide better availability of new products with new therapeutic possibilities and substantial benefits for patients. Different techniques used for gastric retention are mentioned in Figure 2.

**Hydrodynamically balanced systems**\cite{22}

Sheth and Tossounian\cite{23} developed an HBS system containing a homogeneous mixture of drug and the hydrocolloid in a capsule, which upon contact with gastric fluid acquired and maintained a bulk density of less than 1, thereby being buoyant on the gastric contents of stomach until all the drug was released.

The HBS is the novel dosage form, which when in contact with gastric fluid and after dissolution of the outer exposed surface of the dosage form, forms a hydrated gel layer and maintains bulk density less than 1 g/cm³. Thus, this system remains buoyant in the gastric fluid inside the stomach for 6 h. Conventional dosage form

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**Table 1: Drugs reported to be used in the formulation of floating dosage forms**

<table>
<thead>
<tr>
<th>Dosage forms</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Floating microspheres</td>
<td>Aspirin, Griseofulvin, p-Nitroaniline, Ibuprofen, Terfenadine and Tranilast</td>
</tr>
<tr>
<td>Floating granules</td>
<td>Diclofenac sodium, Indomethacin and Predisolone</td>
</tr>
<tr>
<td>Films</td>
<td>Cinnarizine</td>
</tr>
<tr>
<td>Floating capsules</td>
<td>Chlorzoxazone hydrochloride, Diazepam, Furosemide, Misoprostol, L-DOPA, Benserazide, Ursodeoxycholic acid and Pepstatin</td>
</tr>
<tr>
<td>Floating tablets and pills</td>
<td>Acetaminophen, Acetylsalicylic acid, Amoxicillin, Amoxicillin trihydrate, Atenolol, Diltiazem, Fluorouracil, Isosorbide mononitrate, p-aminobenzoic acid, Piretanide, Theophylline and Verapamil hydrochloride</td>
</tr>
</tbody>
</table>

**Table 2: Marketed preparation**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Brand name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diazepam Floating capsule</td>
<td>Valreleasing</td>
</tr>
<tr>
<td>Benserazide and L-DOPA</td>
<td>Madopar</td>
</tr>
<tr>
<td>Aluminum-Magnesium antacid</td>
<td>Topalkan</td>
</tr>
<tr>
<td>Antacid preparation</td>
<td>Almagate Flot-Coat</td>
</tr>
</tbody>
</table>

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*Figure 1: Gastrointestinal motility pattern*  
*Figure 2: Physiology of gastrointestinal tract*
disintegrate completely within 60 min and are emptied totally from the stomach shortly afterward. This dosage form releases the drug through the hydrated layer by diffusion principle. This system is valuable for drugs, which are soluble at lower pH and have absorption window in the upper GIT. By varying the composition of the excipient between 20% and 75% w/w of one or more gel-forming hydrocolloids such as hydroxyethylcellulose, hydroxypropylcellulose, HPMC and sodium carboxymethylcellulose, the granules are prepared and compressed into tablets or encapsulated into capsules, which results in the desired release rate of the drug. This hydrated gel controls the rate of solvent penetration into the device and the rate of drug release from the device.

In the early 70’s, Michaels first introduced floating drug delivery device with self-activated mechanism for retaining the device in the stomach, which released the drug under controlled osmotic pressure. The device was found to consist of two chambers, one for the drug reservoir and the other for the osmogen. In the stomach the gastric fluid dissolves the osmogen, which creates pressure on the drug reservoir compartment. This pressure tends to reduce the total volume of drug reservoir compartment, thereby leading to the continuous release of the drug material from the device. In another attempt, Michaels sustained the release of drug in stomach by incorporation of liquid such as ether in an inflatable chamber. In the gastric fluid, the chamber inflates and retains the drug reservoir in stomach. The drug solutes are continuously released from the reservoir into the gastric fluid. Harrigan formulated a drug delivery device with a chamber, which contained vacuum or filled with air or harmless gas. This made the dosage form to float in gastric fluids. The fluids enter the microporous aperture, dissolve the drug and carry the drug solutes out of the drug delivery system for absorption.

Later, Mao et al. prepared oral controlled-release system of metoprolol (M-HBS) with first-order in vitro release kinetics. The gamma scintigraphy (GS) study indicates that after oral ingestion, M-HBS was retained in human stomach for longer time (5-6 h) than the conventional metoprolol tablet (1-1.5 h). The values of \( t_{\text{max}} \) and \( C_{\text{max}} \) were 5.247 h and 125.1 ng/ml, respectively. Moreover, the fraction of the dose absorbed from M-HBS in vivo is well correlated with dissolution rate in vitro.

Sawicki formulated 40 mg verapamil floating tablet, which had a \( C_{\text{max}} \) of 28.27 ng/ml, \( t_{\text{max}} \) 3.75 h and AUC 364.65 ng/ml h, whereas the conventional tablets have 33.07 ng/ml, 1.21 h and 224.22 ng/ml h, respectively. Thus, the formulation had higher AUC and \( Ke \), and therefore had a sustained release pattern.

A HBS-controlled drug delivery tablet of miocamycin was developed by Diao et al. The GS study after oral ingestion showed that miocamycin HBS remained in human stomach for more than 7 h, which is much longer than the conventional tablet (3-4 h). The in vitro release characteristics showed first-order kinetics. The serum concentration time course of miocamycin HBS exhibited typical sustained release characteristics.

Krogel et al. investigated the release behavior of the different devices as a function of HPMC viscosity grade, HPMC content, type of drug (chlorpheniramine maleate or ibuprofen), matrix weight, position of the matrix within the polymeric cylinder, addition of various fillers (lactose, dibasic calcium phosphate or microcrystalline cellulose) and agitation rate of the release medium. The drug release increased with a reduced HPMC viscosity grade, higher aqueous drug solubility, decreased HPMC content and increased surface area of the matrix. The release was fairly independent of the agitation rate, the position of the tablet within the polymeric cylinder and the length of the cylinder. With the pulsatile device, the lag time prior to the drug release could be controlled through the erosion rate of the matrix.

Wu et al. prepared a solid dispersion of nimodipine with poloxamer 188 and added excipients (HPMC and PEG 6000) to formulate floating-sustained release tablet. Increasing the HPMC content and decreasing PEG 6000 content led to decrease in nimodipine release in vitro. The optimized formulation showed gastrointestinal residence time (GRT) of 5 h under fed condition, while GRT was only 3 h under fasting condition. GRT of nimodipine conventional tablet under fed and fasting conditions was 3 and 2 h, respectively. Relative bioavailability of nimodipine floating tablet was 391.46% and GRT over twice that of nimodipine conventional tablet, which appeared to have prolonged GRT and improved bioavailability. Similarly, captopril floating tablets were prepared by Nur et al. using HPMC (4000 and 15,000 cps). With this the release profile of captopril from floating tablets could be apparently prolonged and as a result, a 24-h controlled-release dosage form of captopril could be achieved.

Furosemide (FR) is a weakly acidic drug and has a greater absorption window on the upper GIT. The bioavailability was enhanced by Ozdemir et al. by preparing an inclusion complex of FR with beta-cyclodextrin (beta-CD) in a 1:1 proportion using the kneading method. After adding the excipients, floating tablets were prepared, which showed retention time of 6 h and AUC of about 1.8 times of the conventional dosage form. Similarly, Menon et al. observed around 15% increase in the bioavailability of FR by preparing monolithic modified release dosage form. Klausner et al. reported the absorption phase of levodopa (narrow absorption window) was significantly prolonged following gastroretentive dosage forms (GRDF) administration in comparison with Sinemet CR, which was solely depended on size and rigidity of the novel GRDF.

For the treatment of Helicobacter pylori-associated peptic ulcers a floating device was formulated by Yang et al. with triple drug regimen (tetracycline, metronidazole and bismuth salt). HPMC and poly (ethylene oxide) were the major rate controlling polymeric excipients. Tetracycline and metronidazole were incorporated into the core layer of the triple layer matrix for controlled delivery, while bismuth salt could be included in one of the outer layers for instant release. Results demonstrated that sustained delivery of tetracycline and metronidazole over 6-8 h could be easily achieved while the tablet remained in floating state.

Eight healthy volunteers were observed in a pharmacokinetic and hemodynamic study by Hou et al. of diltiazem floating tablet. Floating tablets showed that the \( t_{1/2} \) (6.4 ± 4.4 h) and \( C_{\text{max}} \) (56 ± 23 ng/ml) were longer and lower than normal tablets as (2.3 ± 1.1 h and 96 ± 30 ng/ml, \( P < 0.01 \), respectively. Streubel et al. prepared floating microparticles consisting of (i) Polypopylene foam powder; (ii) verapamil HCl as model drug; and (iii) Eudragit RS, ethylcellulose (EC) or polyethyl methacrylate (PMMA) as polymers and were prepared with oil in water solvent evaporation method. The microparticles exhibited good in vitro floating behavior. The drug release rate increased with increasing drug loading and with decreasing polymer amounts.

Hydrodynamically balanced capsules

Apart from HBS tablets many investigators also formulated HBS capsules. The pharmacokinetics of the new drug delivery system named Madopar HBS was developed, which was characterized by lower and delayed plasma peak concentrations but a longer-lasting
concentration of L-DOPA and benserazide than standard Madopar. Therefore, this new controlled release system reduced the clinical fluctuations occurring in parkinsonian patients with "wearing-off" and "on-off" phenomena.[37-39] The drug is released and absorbed over a period of 4-5 h, thus maintaining substantial plasma concentrations for 6-8 h after dosing. The presence or absence of food in the stomach has no effect on the absorption of L-DOPA from Madopar HBS, but administration of antacids reduces the bioavailability. Thus, Madopar HBS showed improvement in the clinical condition by about 86% on average as compared with standard Madopar.[40]

Khar[41] formulated sustained-release floating capsules containing salbutamol sulfate, using different combinations of hydrocolloids of natural and semi-synthetic origin. The floating capsule formulated showed a Higuchi release profile, while the marketed product released only about 80% of the total dose in the stipulated 12 h in the dissolution medium. In vivo x-ray studies of the abdomen indicated a residence time up to 8-9 h in the stomach greater than for the non-floating capsule.

A bilayer floating dosage unit composed of HPMC was formulated by Oth et al.[42] to achieve local delivery of misoprostol (a prostaglandin E1 analog) at the gastric mucosa level. The use of a large capsule increases the GRT, as it impedes passage through the pylorus opening. GS studies revealed the average GRT was 199 ± 69 min after a single meal (breakfast) and 618 ± 208 min after a succession of meals.

### Hydrodynamically balanced systems with gas-generating agents

Buoyancy in tablets and capsules could be achieved by incorporating hydrophilic matrix or by incorporation of some inorganic salts that generate gas when in contact with the gastrointestinal fluids.

Baumgartner et al.[43] developed the floating matrix tablets with HPMC and by incorporating gas-generating agent together with microcrystalline cellulose in the formulation. The tablet composition and mechanical strength were retained and the floating characteristics as well the drug-release pattern were maintained by properly optimizing the formulation. The floating time was optimized with floating lag time of approximately 30 s and the duration of floating was more than 8 h. Radiological evidence suggests that, the formulated tablets did not adhere to the stomach mucus and that the mean GRT was 4 h.

Ichikawa et al.[44] developed an oral floating dosage system, which generated carbon dioxide gas. The system was composed of sustained release pills as seeds and double layers on the sustained release pills. The inner layer comprised an effervescent layer containing both sodium bicarbonate and tartaric acid separated by an inert layer. The outer layer was a swellable membrane layer containing mainly polyvinyl acetate and purified shellac. When the system was immersed in water, it formed swollen pills like balloons with a density much lower than 1.0 g/cm³. The reaction was due to carbon dioxide gas generated by neutralization in the effervescent layer with the diffusion of water through the swellable membrane layer. The buoyancy lag time was approximately 10 min and 80% remained floating over a period of 5 h irrespective of pH and viscosity of the test medium. The release rate of the drug from the system depends on the sustained release characteristics of the system.

Minitablets formulated by Rouge et al.[45] achieved buoyancy either by the swelling of the expipient or by incorporation of the gas-generating agent sodium bicarbonate. The buoyancy of the minitablets containing atenolol was greatly improved by adding gas-generating agent sodium bicarbonate to the floating layer as well as by a wet granulation. Atenolol minitablets containing 7% sodium bicarbonate and coated with Eudragit NE30D:RS 70:30 yielded satisfactory results regarding buoyancy and drug release rate for 6 h.

A bilayer floating tablet for gastric retention with cisapride as a model drug was developed by Wei et al.[46] Sodium bicarbonate was added to the floating layer. The tablet when immersed in simulated gastric fluid (SGF) expanded and rose to the surface and eventually the drug was found to release gradually. The in vitro drug release of this type of bilayer dosage was controlled by the amount of HPMC in the drug loading layer. Generally, more the HPMC, slower the drugs release. As cisapride has greater solubility in SGF than simulated intestinal fluid (SIF), its in vitro drug dissolution is faster as compared with SIF.

Frances et al.[47] formulated floating calcium alginate beads, designed to improve drug bioavailability from oral preparations compared with that from many commercially available and modified release products, have been investigated as a possible gastroretentive dosage form. They incorporated riboflavin as a model drug into the formula.

Bhise and Alooarkar[48] formulated floating capsules of theophylline using HBS approach.

### In vitro evaluation method

#### Flow-through USP IV dissolution apparatus

The numerous tests developed for characterizing the biopharmaceutical properties are generally based on two distinct methodologies, namely, closed system (beaker method) and an open system (flow-through method). The most common procedures to evaluate the drug release from the floating dosage forms are the paddle and basket methods. In dissolution testing, according to the U.S. Pharmacopoeia, a nonreactive stainless steel wire helix is typically used to sink dosage forms that would otherwise float. Depending on the type and shape, four classes of sinker shapes were defined, namely, longitudinal, lateral, screen enclosures and internal weights. Longitudinal sinkers contact the dosage form on the long axis. Lateral sinkers either wrap around or contact capsule dosage forms in the middle, such as the line where the top and bottom halves of a capsule shell come together. Screen enclosures are of two types, a wire cage that holds the entire capsule or a circular piece of wire screen placed on top of the capsule.[49]

An alternative method, the flow-through method, was also introduced into the pharmacopoeias. The advantages of the flow through method are evidenced from testing and assessing different types of dosage forms and active ingredients of very slight solubility. Also changes in testing fluids (e.g. change to the pH) can be easily performed during the test. Another advantage is seen in the positioning of the specimen. Capsules even when floating initially or pellets can be tested using the same equipment and requires no additional devices such as sinkers.[50] The USP IV assembly (Flow-through Cell) consists of a reservoir and a pump for the dissolution medium, a water bath that maintains the dissolution medium at 37 ± 0.5°C. The pump forces the dissolution medium upward via the flow-through cell. The pump has a delivery range of 240-960 ml/h with standard flow rates of 4, 8 and 16 ml/min. The volumetric flow...
must be delivered at a constant rate that is independent of flow resistance in the filter device; the flow profile is sinusoidal with a pulsation of 120 ± 10 pulses/min. The flow-through cell is made of transparent and inert material and is mounted vertically with a filter system (specified in the individual monograph) that prevents the escape of undissolved particles from the top of the cell. Standard cell diameters are 12 and 22.6 mm. The bottom cone is usually filled with small glass beads of diameter about 1 mm, with 1 bead of diameter about 5 mm positioned at the apex to protect the fluid entry tube. A tablet holder is available for positioning of special dosage form and the temperature is maintained at 37 ± 5 °C.

By modifying USP dissolution apparatus I and II, Durig et al.[51] evaluated floating and sticking extended-release delivery systems by preparing swellable hydrocolloid (guar) matrix tablets containing verapamil HCl. Two additional configurations were used, one with an additional single ring and another with mesh device or a double mesh device, which was located below the paddle in the dissolution vessel. Tablets were placed on top of the single mesh device or in the compartment formed between the two mesh surfaces of the double mesh device. In all cases, near linear (n ≥ 0.82) release profiles were observed. By using apparatus I, it was observed that the highly swellable tablets were fully constricted by the basket within 5-7 h. This prevented further independent movement and unimpeded swelling and coincided with a departure from linear release and increased variability (SD ≤ 9.5%). By using apparatus I, two of three tablets adhered to the bottom of the dissolution vessel for the duration of the experiment. Consequently, their release profiles were found to differ markedly from those obtained under apparatus I conditions (similarity factor, f(2) = 30.5), with the release rate being approximately half of that obtained under apparatus I conditions. Adhesion to the dissolution vessel was also observed when paddle speed was doubled to 100 rpm, thus again resulting in large variability (SD ≤ 34%). Although the average single and double mesh configuration profiles were similar to the apparatus I profile (f(2) = 57.36 and 61.38, respectively), large variability (SD ≤ 11%) occurred with the single mesh configuration due to floating and random adhesion of tablets to the paddle or sampling tubes. When the tablets were located in the compartment formed by the double mesh device almost superimposable profiles were obtained (SD < 3%). Use of a double mesh device may therefore provide an alternative to current compendial dissolution methods when the reliable determination of the true release kinetics of floating and sticking delivery systems is desired.

**In vivo evaluation method**

**Gamma scintigraphy**

The study of residence in gastrointestinal transit time became necessary to evaluate the drug-release pattern at various levels of GIT by tracking the location of the dosage form. This provided the insight for formulation of a programmable drug dosage form, which would then release the drug at specific levels of the GIT. In earlier days for measurement of in vivo GRT, x-ray studies were used.[32] Radiographs of BaSO₄ were taken after ingestion of the dosage form, to locate the floating and non-floating (fabricated) dosage forms at various periodic time intervals.

Heidelberg capsule technique was introduced for monitoring GRT by radiotelemetry.[33-35] Ewe et al.[58] developed a new method for studying a large variety of physiological, pathophysiological and pharmacological questions concerning gastrointestinal transit by a metal sphere of 6 mm diameter, which can be located accurately in the body by a metal detector at a distance of 2-12 cm from the abdominal surface. This procedure had a correlation of r = 0.99, with pH-sensitive radiotelemetry Heidelberg capsule for recording gastric emptying.

Presently, in vivo evaluation of floating dosage forms is done by gamma scintigraphy (GS). GS is a technique, whereby the transit of a dosage form through its intended site of delivery can be noninvasively imaged in vivo via the judicious introduction of an appropriate short-lived gamma-emitting radioisotope. The observed transit of the dosage form can then be correlated with the rate and extent of drug absorption. Information such as the site of disintegration or dispersion can also be obtained.

Specific site delivery in the GIT can be done by using the Intelisite capsule. The Intelisite capsule is a radiofrequency-activated, non-disintegrating drug-delivery device. It is capable of noninvasively controlled delivery of drug formulations to the GIT for determining regional differences in drug absorption and bioavailability. Radiolabeling permits determination of the capsule location within a specific region of the GIT via GS. When the capsule reaches the desired location in the GIT, external activation opens a series of windows to the capsule drug reservoir. The release and degree of dispersion of the solution or powder contents from the capsule can be visualized. The transit of dosage form or the site of release of drug can be easily correlated with drug absorption. It facilitates neutron activation and standard radiolabeling techniques with regulatory compliance and expert consultation.

Success in formulation and development depends on defining the variables that affect the performance of a drug-delivery system. Often, in vitro testing methods are not predictive of in vivo results. For oral dosage forms, altered gastrointestinal transit due to individual variation in physiologic or pharmacologic factors or the presence of food may influence bioavailability. Disintegration, erosion or drug release may be premature or delayed in vivo. Similarly, altered deposition or clearance from other routes of administration such as nasal, ocular or inhalation may explain drug absorption anomalies. GS combined with knowledge of physiology and dosage form design helps to define these variables. The resulting insight can be used to accelerate the formulation development process and help ensure success in early clinical trials.

Standard radiolabeling techniques will incorporate the radioactive marker in a finished product shortly before dose administration. Alternatively, neutron activation is a technique in which a small amount of stable isotope is incorporated in the dosage form at the time of manufacture. The stable isotope is then converted to a radioactive isotope appropriate for GS by a short exposure to a neutron flux.[39] Hence, GS is a rapid and effective method for determining the rate and extent of drug absorption within specific regions of the GIT under pharmacologically and physiologically relevant conditions and also it saves time and avoids wastage of resources during the drug-development process by defining formulation objectives.

The radionuclides are used because it is not possible to radiolabel drug molecules for GS. A radionuclide must therefore be used in a carrier or in the formulation, which is having radiation energy (Ideal about 150 KeV) with suitable half-life period. Also it should be easily available and should emit only pure gamma rays. Furthermore, it should be nontoxic and nonabsorbable (for nonparenteral routes).

The metal ion nuclides are most commonly used radionuclides [Table 3].[30-32] 99mTechnetium (99mTc) is the most popular nuclide due to
its optimum energy, easy availability (through portable generator), versatile chemistry, low radiation dose and short half-life period.

Conclusion

Drug absorption in the GIT is a highly variable procedure and prolonging gastric retention of the dosage form extends the time for drug absorption. Floating dosage forms promises to be a potential approach for gastric retention. These systems consisting of swelling and expanding systems, floating and inflating systems and bioadhesive systems are also useful for drugs, which are poorly soluble or unstable in intestinal fluids. The floating properties of these systems help in retaining these systems in the stomach for a long time. This review summarizes the various attempts, which have been made to develop a floating system, in vitro and in vivo evaluation studies and application of floating dosage forms.

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