

## Floating drug delivery systems: A review

Abhishek Ravindra Gadge \*, Ganesh Jayram Lamkhade, Sayali Ulhas Vishe, Mayur Maruti Varpe and Moin Mehboob Kazi

*Department of Pharmaceutics, Samarth Institute of Pharmacy, Belhe, Pune 412410, Maharashtra, India.*

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### Abstract

To boost medication bioavailability, target the stomach mucosa, and lengthen gastric residence time, a multi-unit oral floating drug delivery system was created. Due to their potential to enhance drug delivery, floating tablets have become more significant in pharmaceutical formulation. In the upper GIT, where the environment is acidic, tablets absorb poorly. The bioavailability shows 50% when administered orally. An H<sub>2</sub>-receptor antagonist called tablets is frequently prescribed to treat gastrointestinal issues brought on by excess stomach acid. With the right excipients and polymers, floating tablets are meant to float on the contents of stomach over an extended length of time, extending medication release and bioavailability. This review examines the advantages, disadvantages, and in vitro or in-vivo evaluation of famotidine floating tablets with an emphasis on their potential to improve treatment outcomes and patient compliance.

**Keywords:** Bioavailability; Formulation; Resistance; Floating

### 1. Introduction

Since oral medication is simple to give, affordable, and patient-friendly, it is the most widely utilized delivery method. Observance and adaptability in creating, etc. Over the previous few decades, a number of oral medication administration techniques have been created that serve as drug repositories where the active component is able to be let go at a predetermined rate under strict control over a predetermined amount of time. (Lannuceli & Coppi, G, 2011) There is currently interest in new dosage forms for oral controlled release that are meant to remain in the gastrointestinal tract (GIT) on a regular, extended basis, as evidenced by current patent and scientific literature. (Garg & Gupta, G, D, 2011) These days, there are several ways to prolong the gastrointestinal residence durations (GRT), including floating drug distribution networks (FDDS). (Deshande & Shah, N, 2011) high-density systems (Redniek & Tucker, S, J, 2011), superporous hydrogels, (Hwang & Park, H, 2011) magnetic systems, bioadhesive or mucoadhesive systems, vessels systems using gels made of alginate, low-density systems (Kawashinia & Niwa, T, 2011), and elevated density systems. One of the most cutting-edge methods for creating gastroretentive medication formulations is the FDDS, which is briefly covered in this article.

#### 1.1. Mechanisms of Gastroretentive Drug Delivery

Gastroretentive processes, which can continue to stay in the stomach area for a few hours, can extend the time spent in the stomach period of drugs. Extended stomach Retention lowers medication waste, boosts bioavailability, and makes pharmaceuticals more soluble that, at high pH, are less soluble settings. Moreover, it might be utilized to locally supply medication to the stomach and the first few inches of the small intestine. Concurrent medication distribution that employs pharmaceutical excipients or inhibits the motility of the gastrointestinal tract increases the amount of medication held in the stomach. (C.G & Washington N., 2012).

\* Corresponding author: Abhishek Ravindra Gadge

## 2. Methods of Developing Gastroretentives Medication Delivery Systems

Numerous methods have been attempted to enhance the stomach keeping an oral dosage form.

Among these systems are

- System that float
- System of bioadhesion
- Expanding and swelling structures
- System with elevated densities

### 2.1. Floating Drug Delivery Systems

The system that is hydrodynamically balanced (HBS) is another term regarding the floating methods of delivering drugs. Because drug delivery systems that float (FDDS) possess a density significantly lower compared to stomach juice, they can float for a while in the stomach longer duration of time without slowing down the stomach's removing process. As you float atop the contents of the stomach, the drug is progressively emitted from the system at the fixed rate. Once the drug has been discharged, any remaining medication is removed from the stomach. The results of this are enhanced control over variations in drug concentration in plasma and increased GRT. Those methods of delivery fall into two categories: effervescent (Gas Generating System) and non-effervescent.

#### 2.1.1. Non Effervescent Systems

- Colloidal Gel Barrier

The system with hydrodynamic balance (HBS), which comprises drugs containing hydrocolloids that gelled, was initially developed in 1977 by Sheth and Tossounian. High concentrations of polysaccharides, matrix-forming polymers, and cellulose-based hydrocolloids that gel and are highly soluble are present in these systems (20–75%w/w). When stomach fluid comes into contact with the within the system's hydrocolloids, they drink plenty of water and create a barrier made of colloidal gel surrounding the fluid's exterior. How quickly liquids enter the apparatus and, consequently, the rate at which the drug is released is controlled by this gel barrier.

- Micro Porous Compartment Systems

This method's core involves enclosing a drug storage container inside a microporous chamber with holes positioned correspondingly the walls at the top and bottom. The walls surrounding the medication reservoir compartment is tightly sealed to avoid any possibility of direct interaction between the stomach surface mucosa and the drugs that haven't dissolved.

- Multiparticulate Systems

#### Floating Beds

Most oral dosage forms used in drug delivery systems with multiple particles are composed of multiple small, discrete units, each of which exhibits a desired feature. In these arrangements, the amount of the therapeutic chemicals is split across many subunits, each of which is typically made up of thousands of spherical particles, each measuring between 0.05 and 2.00 mm in diameter. Several-part dosage forms are therefore defined as pharmaceutical formulations containing several small, separate subunits of the active component. To provide the required total dosage, these components are put into a sachet.

- Microballons

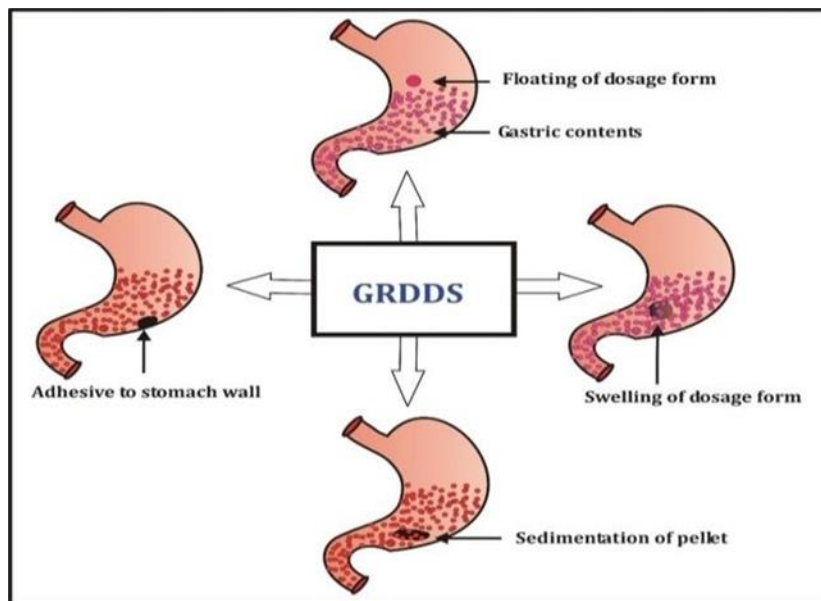
Drugs can be delivered to the desired location using a variety of controlled release techniques. The use of polymeric microballons to transport medication is one of these techniques. A hollow microsphere is referred to as a "microballoon". Microballons immersed in an aqueous solution were able to float *in vitro* for a period of twelve hours. Research utilizing radiography showed that when microballons were given orally to people, they were scattered throughout the region above the stomach and stayed three hours there against the movement of the peristalsis.

### 2.1.2. Effervescent System

A pharmaceutical floating chamber can be added to a control delivery system to make it float in the stomach. that can be loaded with air, inert gas or vacuum. Systems for Containing Volatile Liquids: These feature an inflatable chamber. that expands to enclose the abdomen and is filled with a liquid that gasifies at body temperature, such as ether or cyclopentane. These are floating, osmotically controlled devices with a deformable, hollow unit inside. The medication is kept in one chamber of the device, and the volatile liquid is kept in the other.

### 2.1.3. Gas-Generating System

The buoyant distribution methods rely on the effervescent interaction between carbonate and bicarbonate. CO<sub>2</sub> is released by salts and tartaric/citric acid. After that, these CO<sub>2</sub> is trapped within the hydrocolloid layer of the system, It reduces its specific gravity and produces the system float over the bell. Furthermore, several unit floating tablets that generate CO<sub>2</sub> has been created. There are two layers to the sustained release (SR) pill that acts as the system's seed. Tartaric acid and sodium bicarbonate are present in within the effervescent inside layer. External layer of the swellable membrane layer contains PVA, shellac, and other components. One more fizzy Furthermore, a collapsible spring mechanism has been developed to control the medications' release from the polymer matrix. These system are made using the standard resin beads that are covered in ethyl cellulose and loaded with bicarbonate. The coating is permeable however insoluble, allowing water to pass through. Within the stomach, the beads float. due to the emission of carbon dioxide. (SR. & John Willey , 2002)



**Figure 1** Gastro Retentive Drug Delivery System

## 2.2. Floating Drug Delivery System

### 2.2.1. Definition

Floating system, also called in a dynamic manner regulated system, are systems with low densities that have sufficient ability to float above the information of the stomach and continue there. float in the stomach over an extended length of time without causing the stomach to empty more quickly. Figure 2. As a result, the stomach retention period is prolonged and the changes in drug concentration in plasma are better managed. Numerous buoyant structures founded on laminated films, hollow microspheres, tablets, powders, granules, and powders have been developed.

### 2.2.2. Basic GIT Physiology

The antrum (pylorus), the body, and the fundus are the three anatomical regions that make up the stomach. The proximal portion's body and fundus act as a storage space for unprocessed substances. On the other hand, the antrum acts as a pump to force the stomach to empty and is the primary location for motion mixing. (S., 2011). emptying of the stomach occurs with both food and fasting. Nonetheless, the two states differ in a few ways. motility designs. When following a quick, interdigestive electrical A series of events cycle through the stomach and intestines every three to four hours. (GR & peeters TL,, 2005). The interdigestive myoelectric cycle (IMC) or migrating myoelectric cycle (MMC)

is the term used to describe this process. The remaining four stages are separated into the following divisions: by Wilson and Washington. (CG. & Washington N., 2005).

- Sporadic contractions occur throughout the 40–60 minute Phase I (base phase).
- The second preburst period, which lasts for 40–60 minutes.
- Phase III, often known as the blast lasted between four and six minutes. It is made up of short, forceful contractions that happen a lot. Wave transports every piece of undigested food that passes through the small intestine from the stomach. It's also referred to as the cleaning wave.
- Phase 4 of two successive cycles lasts from 0 to 6 min and occurs in the space between phases 3 and 1.

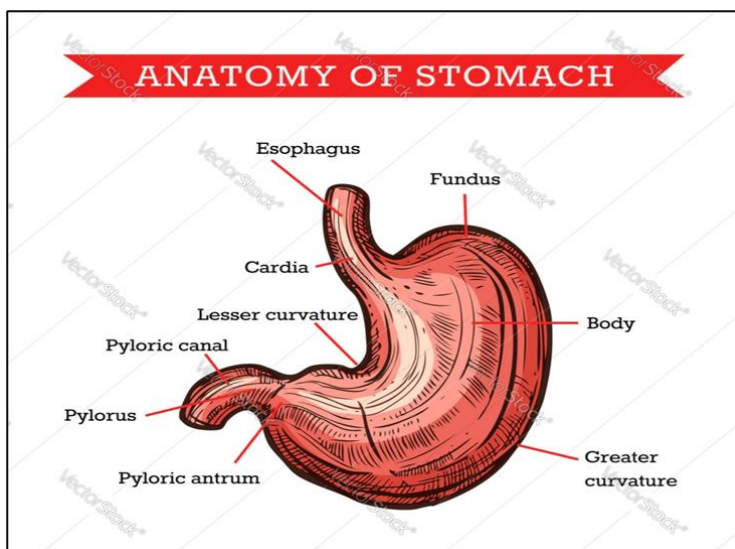


Figure 2 Human stomach

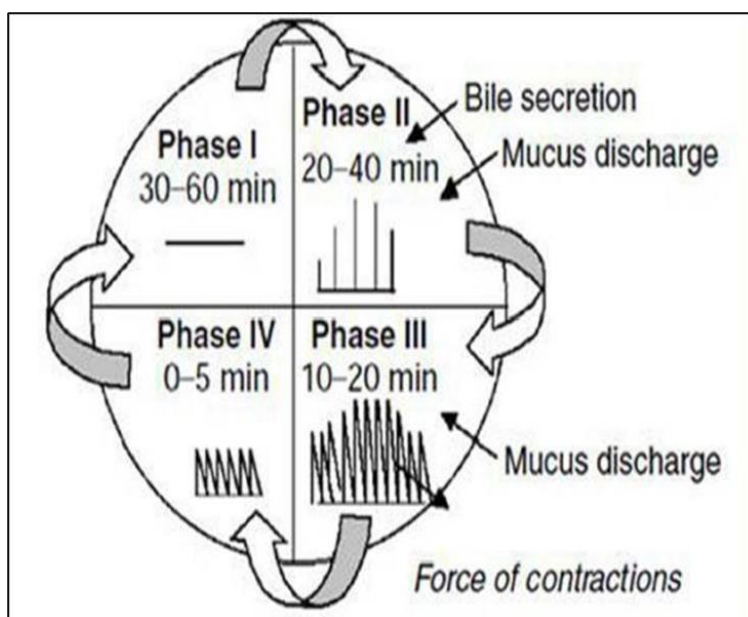


Figure 3 Gastro Intestinal Motility Patterns

After a combination meal is consumed, contraction design changes from at a fast of the federal state. This pattern of continuous contractions, which is sometimes called the "digestive motility pattern," is akin to those that occur during phase II of a fast. Food fragments are produced by these contractions. to shrink to a less than 1 mm in size. which migrate in the direction of the pylorus in a suspension state. Stomach emptying proceeds more slowly during the fed state due

to the delayed onset of MMC. 16 Short stomach residence periods and inconsistent gastric emptying rates are the main issues with oral controlled release dose forms, according to scintigraphic examinations examining the rates of gastric emptying. (S & Bolton S., 2005).

#### Figure Gastrointestinal Motility Patterns

##### Benefits Of Floating Medication Delivery System

- Forms of floating Dosage like a pill or capsule, will float even at an alkaline intestinal pH, for an extended period of time in the solution.
- FDDS are helpful for pharmaceuticals like antacids those are meant to behave locally in the stomach.
- In cases of diarrhea and strong intestinal movement, FDDS dose forms help to keep the medication floating in the stomach to obtain a comparatively improved reaction.
- 4. In order to prevent irritation of the stomach wall brought on by aspirin and other acidic substances, HBS/FDDS formulations are able to be useful when giving aspirin and other comparable medications.
- FDDS are helpful for pharmaceuticals like antacid and ferrous salt that are absorbed by the stomach. (N.H & Laxmi S., 2012).

##### The drawbacks of floating medication delivery devices

- Floating devices should not be used with medications that have problems with stability or solubility in the stomach. (Kawashinia Y, Niwa T, Takcuchi H, , & Hino T., 2012).
- Because delayed stomach emptying may result in decreased systemic bioavailability, some drugs, like nifedipine, which have significant first-pass metabolism and effectively absorbed throughout GI section, are not good contenders for FDDS. The use of FDDS with medications that irritate the stomach mucosa is also restricted.
- One disadvantage of floating is that there needs to be enough liquid in the stomach to support the medication doses to form and float efficiently. (N.H & Laxmi S., 2012)

##### A floating drug delivery system's limitations is

Medicine must dissolve and work effectively in the stomach if there are sufficient liquids present. Growing Higher Systems are impractical for medications that possess problems with steadiness or soluble in stomach fluid. (Atyabi F, Sharma H.L., Mohammad H. AH., & Fell J. T., 2012). Because delayed stomach emptying may result in decreased systemic bioavailability, some medications, like nifedipine, may not be the best choices for FDDS. Nifedipine has minimal first-pass metabolism and is highly absorbed throughout the GI tract. The use of FDDS with medications that irritate the stomach mucosa is also restricted. (EL-Kamel A.H, Sokar M.S., & Algamal S.S., 2012)

##### Affected Factors for Both Floating and Floating Time

- Density Being afloat is determined by medication form buoyancy which depends on density. (M., Watanabe S, & Miyake Y, 2012)
- Design and Form of the dose The ring- and tetrahedron-shaped apparatuses are said to have 48 and 22.5 flexural modules kilograms units of square inch (KSL) respectively, which increases their buoyancy.
- simultaneous medication administration Anticholinergic such as Prokinetic agent atropine and propantheline such as cisapride and metoclopramide, and opioids such as codeine may affect the moment of floating.
- State: Fed Or Unfed The GI moment during fasting is characterized by bursts of high movement or the relocating myoelectric signal (MMC), which happened each one to two hrs. (T.H, 2012).
- Type Of Meal By consuming the stomach fatty acid salt or indigestible polymer, the stomach's movement pattern can be changed as a fed condition, which will slow down stomach emptying and prolong the time that medication is released. (N., Cole E.T., Doelker E., & Buri ., 2012).
- Calorie Content and Frequency of Feeding: Having a high-fat, high-protein lunch can prolong floating for up to ten hours. There can be a 400-minute increase in floating when consecutive meals are provided in contrast to a single meal because MMC occurs infrequently.
- Age Older peoples, particularly those older than 70, live noticeably more extended because of diseases like diabetes and Crohn's disease, among other things. influence the way that medications are delivered as well. (H.R., Zia H., & Rhodes C.T, 2012).
- Posture: The patient could be lying down or floating in an upright walking posture. (A.O & Zhang J.S., 2012).

- Single or multiple unit formulation: It is possible to co-administer units with different formulations. different outcomes and offer a more predictable outcome in the event that a unit fails. There is a greater safety buffer against dosage form malfunction with release profiles or those containing incompatible ingredients as opposed to dosage forms in single unit.

### 3. Evolution of drug delivery systems that float

Many factors, including floating length, dissolving specific gravity, profile, homogeneity, friability or hardness of the substance in the instance of solid dosage forms, must be taken into account when assessing gastroretentive formulations. For (MDDS) additional tests include (DSC), analysis of particle size and flow parameters, surface structure and mechanical characteristics. (Timmermanns.J & Moes A., 2012).

#### 3.1. *In-vitro* method

##### 3.1.1. *Lag time and floating time in floating*

Floating time measurement test is typically carried out in 37 °C stimulated stomach juice or 0.1 % N HCL. Utilizing a dissolving USP device 900 cc of 0.1 N HCL at 37 °C in the dissolve media, the decision is made. The duration of time required for the dosage form for floating is called its float lag time, as well as the length of time remains Afloat is referred to as its Time spent for flotation or floating. The apparatus utilized to track continuous floating-like actions consists of a basket made of stainless steel that is fastened to a metallic object rope and hung from an electronic Sartorius balance. A Lotus Spreadsheet might be able to pick up the balance reading right away. For the floating kinetics studies, 900 cc of simulated stomach fluid was used as the test medium. Every 30 seconds, data was collected, and each measurement was subtracted from a baseline (1.2 PH) that was kept at 37 °C. Dissection At the base of the basket was an holder used to gauge the descending force. (Chen, 2012)

##### 3.1.2. *Dissolution studies*

In order to assess a floating drug delivery system, Gohel and associates, suggested more pertinent in vitro dissolution technique (for tablet doses form). In order to facilitate sample collection and retain 70 milliliters of 0.1 mole HCl lit-1 dissolving moderate, A side arm was incorporated into a 100 milliliter glass beaker. To replicate the rate of stomach acid secretion, Above the beaker, a burette was placed, and used to supply the melting media at an flow two milliliters per minute. A comparison was made between the USP dissolving Device No. 2 (paddle) and the modified apparatus's performance. USP dissolving equipment had an issue employing the tablet adhering to the paddle's shaft. (N.M, Afifi N.N, & Ghorab D.M, 2012). Tablet didn't dissolve in the flurry of activity according to The recommended method. drug release strategy that was recommended made use of kinetics at zero order. suggested test might show a strong in vitro in vivo association because efforts are made to replicate in-vivo settings for example, stomach acid secretion rate, stomach volume, and stomach emptying. (Basak.B, 2012).

##### 3.1.3. *Swelling Index*

Using an in vitro measurement device, the true buoyant doses form' floating qualities as a function of time have been ascertained. It Measured is the force equal to the force F needed to maintain the item fully immersed in the liquid. The force can be used to quantify an object's ability to float or not float by determining the object's weight after submersion. (Ritschel.W.A, 2012). This force, which is determined by the object's weight after submersion, can be used to determine if the object is floating or not. Capacities. The vector total off the force of gravity (F grav) and buoyancy (F buoy) acting on the object corresponds to the force's magnitude, direction, and resulting weight, demonstrated by Eq-  $F = F \text{ buoyancy} - F \text{ gravity}$ .

$$F = F \text{ buoyancy} - F \text{ gravity}$$

$$F = d_f gV - d_s gV = (d_f - d_s) gV$$

$$F = (d_f - m / V) gV$$

where g is the object's gravitational acceleration, d f is its fluid density, d s is its item density m means mass or v means volume. F is the object total vertical force, or weight as a result. (Taludekar.R & Fassihi.R, 2012).

### 3.2. *In vitro* method

#### 3.2.1. X-ray method

One of the most popular evaluation metrics for floating dosage forms these days is X-ray.<sup>54</sup> locating the amount given inside the gastrointestinal system and the process for calculating time difference between the amount given passing via the GIT or stomach clearing out. Because that radio-opaque substance was added to the amount given form in this instance, is visible on an X-ray. (Klausner.EA, Lavy.E, Steensky.D, Friedman.M, & Hoffman.A, 2012).

#### 3.2.2. Gamma-Ray Scintigraphy

Emitting gamma radiation radioisotope compounding in the CR-DFs are now the most advanced-the-artwork for evaluating the gastro-retentive mixture in willing and good subjects, One trace of a stable isotope like sm, is mixed with it to create DF. The radiation is one of the primary disadvantages of gamma-ray scintigraphy. exposure that the seek person experiences, restricted topographic data available, the method's inherent low resolution, or challenging radio-pharmaceutical require costly preparation. (Fell.J & Digenis.C.G, 2012).

#### 3.2.3. Gastroscopy

Includes oral endoscopic when paired along fiberoptic or equipment. According to suggestions, the impact of extended stomach environment occupancy on FDDS might be visually examined via gastroscopy. Alternative (FDDS) could be taken departing from the abdomen for a increase in-depth examination. (Jao.F & Edgren.DE, 2012)

#### 3.2.4. U-Sonography

U-sonographic wave reflect considerably varying sound impedance throughout interfaces, making it possible to see several abdominal organs. When interacting with the physiological environment, the majority of DFs do not display detectable acoustic incompatibilities. Thus, ultrasonography is typically not used to evaluate (FDDS). characterisation incorporated an analysis of the hydrogels' location within the stomach, solvable penetration, and interactions with while peristalsis is occurring, the stomach wall as well as (FDDS).

- Medications assembled within creation of particular

**Table 1** A list of medications in adjustable dosage forms

Different kind of doses form	Medications investigated in float dose form
Microsphere	Aspirin
Granules	Indomethacin
Films	Cinnarizine
Capsules	Diazepam
Tablets/Pills	Riboflavin

- Marketed Products

**Table 2** A few commercial formulations of gastro-retentive floating

Tablet Product	Tablet Content	Tablet Manufacturer	Tablet Formulation
Valrelease	Diazepam (15 Mg)	Hoffmann-LaRoche USA	Floating Capsule
Madopar	Levodopa (100 Mg)	Roche Product USA	Floating CR Capsule
Almagate floatcoat	Al-Mg antacid	-	Floating Doses Form
Convion	Ferrous sulphate	Ranbaxy India	Colloidal gel form (fdds)

#### 4. Conclusion

Increased stomach retention of the dose form results in a long duration for gastrointestinal tract's extremely varied drug absorption process. drug consumption. FDDS seems to be a good method for stomach retention. Dosage formulations for GRT that function slowly will create a great deal of new therapeutic opportunities. The existing polymer-mediated (FDDS) that is both effervescent and non-effervescent appear to be a very successful way of regulating controlled oral medication delivery, based regarding principles of postponed stomach discharge and floating. The quantity of commercialized the number of patents in this domain attest to it. (FDDS) turns into an added benefit regarding medications that are primarily swallowed in the top gastrointestinal tract. namely, stomach, jejunum, and duodenum. Not settled, significant issue include the quantifiable efficacy of delivery system that are float in both fed and test of fasting, the function buoyancy plays in improving FDDS GRT, or most importantly, the development of the optimal form of doses that should be applied regionally to eliminate *H. pylori*, The bacteria that causes stomach ulcers worldwide. Because pharmacokinetic and pharmacodynamic characteristics are complex, It takes in vivo research to determine the ideal doses form for a certain medicine.

#### Compliance with ethical standards

##### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

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