REVIEW ARTICLE JPAR 2018

Journal of Pharmaceutical Advanced Research
(An International Multidisciplinary Peer Review Open Access monthly Journal)
Available online at: www.jparonline.com

Dispersible Tablets: A review

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Received: 05.04.2018 Revised: 16.04.2018 Accepted: 24.04.2018 Published: 30.04.2018

ABSTRACT: Now-a-days, dispersible drug delivery systems are extensively used to improve bioavailability and patient compliance. Over the past three decades, dispersible tablets have gained considerable attention as a preferred alternative to conventional tablets and capsules due to better patient compliance, improved solubility and stability profiles. Dispersible tablets could be preferred choice especially with those drugs sensitive to GI fluids, for masking bitter taste of drug and for patients under category of pediatrics, geriatrics, bedridden, postoperative and who may have difficulty in swallowing the conventional tablets and capsules. These types of tablets disintegrate quickly in the water to produce the suspension. The superdisintegrants are the important constituent of dispersible tablet. Dispersible tablet on contact with water get wet and swell extensively so that the tablet disintegrate quickly. This review includes a detail updated concept on dispersible tablet.

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Key words: Dispersible, Tablets, Patient compliance, Superdisintegrates, Taste masking, disintegration time.

INTRODUCTIONS:

The basic aim behind development of any drug delivery system (DDS) is to achieve a safe and effective therapy for the human being. For decades oral drug delivery has become the major segment in the global pharmaceutical market. It is growing day by day because of being a favorite route for drug administration [1]. A large number of developments in the field of pharmaceutical technology have made manufacturing of tablet a science. In recent days tablets become the most favorable dosage form as compared to other available dosage forms [2]. The popularity of this dosage form is because of

advantages such as ease of manufacturing, convenience in administration, and high accuracy in dosage, stability and safety. Despite all the advantages, conventional tablets generally do not prove useful in certain situations. The elderly face difficulties in taking conventional oral dosage forms because of hand tremors and dysphagia [3,4]. Swallowing is also a common problem in the young individuals because of their under developed muscular and skeletal system. Other groups that may experience problems using conventional oral dosage form include mentally ill, developmentally disabled patients and patients who are uncooperative or who are suffering from severe nausea [4,5].

Table 1. Some dispersible tablets available for common diseases.

Disease condition	Dispersible tablets available
Tuberculosis	Rifampicin/Isoniazid
Diarrhoea	Zinc sulphate
Malaria	Artemether/Lumefantrine.
Pneumonia	Amoxicillin, Amoxicillin/ Clavulanate, Sulphamethoxazole/ Trimethoprim
Rheumatoid arthritis	Prednisolone
Pain and fever	Paracetamol

For the administration of suspension to children a special oral syringe or dossator needs to be provided which requires care during administration such as proper calculation of dose, cleaning of the syringe after use, etc. Therefore, an alternative dosage form is desired that has advantages of both solid and liquid dosage forms. Solid oral dosage forms are most convenient, from patient as well as from manufacturing chemist's perspective. They ensure uniformity of dosage, are more robust and have less microbial issues when compared to liquid dosage forms. However immediate release tablets cannot act as a substitute for suspensions. Thus there is a need for a formulation, which overcomes the problems associated with the swallowing of solid dosage forms and act as a viable substitute for suspensions. One such dosage form is Dispersible tablet.

Fast dispersible tablets are categorized into two types, such are dispersible tablets (These types of tablets disintegrate quickly in the water to produce the suspension) and Mouth dissolving tablets (These types of tablets are differentiated by dissolving in mouth).

DISPERSIBLE TABLETS:

Dispersible tablets as defined in European Pharmacopoeia are uncoated or film coated tablets intended to be dispersed in water before administration giving a homogeneous dispersion. Typically a dispersible tablet is dispersed in about 5 to 15 ml of water (e.g. in a tablespoonful or a glass of water) and the resulting dispersion is administered to the patient. Dispersible tablets are required to disintegrate within 3 min in water at 15 to 25˚C. Also the dispersion produced from a dispersible tablet should pass through a sieve screen with a nominal mesh aperture of 710 µm. The dispersion properties of dispersible tablets can be facilitated by the inclusion of an acid/ base couple in which the base liberates carbon dioxide when the components of the couple are dissolved in water [6].

Ideal characteristics of dispersible tablets [7-9]:

- They require water or other liquid at the time of administration.
- Should easily disintegrate and dissolve.
- Mask or overcome unacceptable taste of drug.
- They should have high drug loading capacity
- They should have special feel in mouth.
- They should have low sensitivity against environmental conditions like moisture etc.
- Ease of administration to patients who are mentally ill, disabled and uncooperative.
- Should be portable without fragility concern.

Special features of dispersible tablets [10-13]:

Dispersible are not intended to be chewed or swallowed whole. They should not be dispersed in carbonated drinks or milk due to foaming or slow dispersion. The purpose of dispersible tablets is to provide a unit dosage form of medication which can be easily administered to infants and children or to elderly, who may have difficulty in swallowing an intact tablet.

Advantages of dispersible tablets [10-13]:

- They are particularly suitable for elderly persons with swallowing difficulties and for children.
- Rapid disintegration and absorption of drug, which will produce quick onset of action.
- Certain dispersible tablets can also be divided.
- The bitter taste of the active substance must be masked in advance. Owing to the number of possible applications, the patient compliance is improved.

- Quick absorption from the g.i.t. improves bioavailability and reduces unwanted effects caused by the drug. E.g. GI irritation caused by NSAID.
- New business opportunities like product differentiation, line extension and life cycle management. Exclusivity of product promotion.
- Although chewable tablets have been in the market for some time, they are not same as the new dispersible tablets. Patients for whom chewing is difficult or painful can use these new tablets easily. Dispersible tablets can be used easily in children who have lost their primary teeth, but do not have full use of their permanent teeth.

Limitations of dispersible tablets [14]:

One common limitation of these formulations is settling of the insoluble solid at the bottom or sides of the container of the prepared dispersion, which may lead to a loss of part of the drug during administration, resulting in suboptimal dosing.

Disadvantages of dispersible tablets [10-13]:

- Drugs absorbed at specific site cannot be given in these dosage forms.
- These tablets show high friability, less hardness than conventional tablets.
- Hygroscopic properties of formulation require extra moisture protection with special packaging for proper stability and safety of the products.

Recommendations for use of dispersible tablets [15]:

- To be dispensed in a small amount (5 to 10ml) of liquid (clean water or milk).
- The liquid can be gently stirred to aid dispersion before swallowing.
- A proportion of the medicine may remain in container after swallowing. Therefore, it is advisable to rinse with a small amount of water or milk and swallow again.
- Careful handling of these tablets is necessary as they are much more fragile than the regular tablets (more fragile, less resistant to rubbing).
- Once removed from the blister packaging, they should be used immediately as their stability outside the blister cannot be guaranteed.

DEVELOPMENTAL IN DISPERSIBLE DRUG DELIVERY [15-17]:

Taste of the active ingredient:

Some drugs have relatively no taste and simply by adding a suitable flavour can mask any unpleasant sensation. However, most drugs do require taste masking if they are to be incorporated into dispersible formulations. Numerous methods exist to achieve this, including simple wet granulation or roller compression with other excipients to minimize the presented surface area of the drug. If further taste masking is needed, there resultant particle can be sealed with a suitable coating material (HPMC, ethyl cellulose, methacrylate and PVP).

Table 2. List of excipients used in the formulation of dispersible tablets.

Excipient	Function	Example
Diluents	Make required bulk of tablet, improve cohesion, flow, compatibility, stability	Lactose, Spray dried lactose, MCC, Mannitol, Sorbitol, Dibasic calcium phosphate.
Binders	Impart cohesive qualities to powdered materials.	Gelatin, glucose, lactose, MC, EC, HPMC, starch, Povidone, Sodium alginate, CMC, Acacia.
Superdis-integrants	They facilitate tablet breaking when it comes in contact with water in oral cavity/GIT	Croscarmellose sodium, Crospovidone, SSG, starch.
Lubricants	Prevent adhesion of tablet material to surface of dies and punches, reduces inter particulate friction.	Insoluble- Steric acid, Magnesium stearate, Talc, Paraffin, Soluble-SLS, Sodium benzoate, PEG.
Glidants	Improve flow characteristics of powder mixture.	Colloidal Silicon dioxide, Corn starch, Talc etc.
Anti-adherents	Prevent adhesion of tablet material to punches and dies.	Talc
Sweet-eners	Produce a palatable dosage form	Sucrose, Sucralose, Saccharin, Aspartame, etc.
Flavours	Improve taste of dosage form	Peppermint, Vanill, Orange, Banana, Cinnamon, Mango
Colours	These are added for better appearance of dosage form	Sunset yellow(Supra)

The choice of coating material will determine the mechanism of taste masking. Other taste masking methods are namely coating methods including electrochemical, hot melt and supercritical fluids. Coacervation has also used to encapsulate certain drug.

Dose:

As mentioned previously, drug may require coating, which will result in an increase in the particle size. The

extent to which this increase will affect the mouth feel and tablet size will depend on the dose of the drug and the amount of coating material required for masking its taste.

Hygroscopicity:

Several dispersible tablets are hygroscopic and cannot maintain physical integrity under normal conditions of temperature and humidity. Hence, they need protection from humidity that calls for specialized product package.

Friability:

In order to allow dispersible tablets to disintegrate rapidly in the mouth, they are made of either very porous or soft molded matrices or compressed into tablets with low compression force, which makes the tablet friable and/or brittle which are difficult to handle and often require specialized peel-off blister packing.

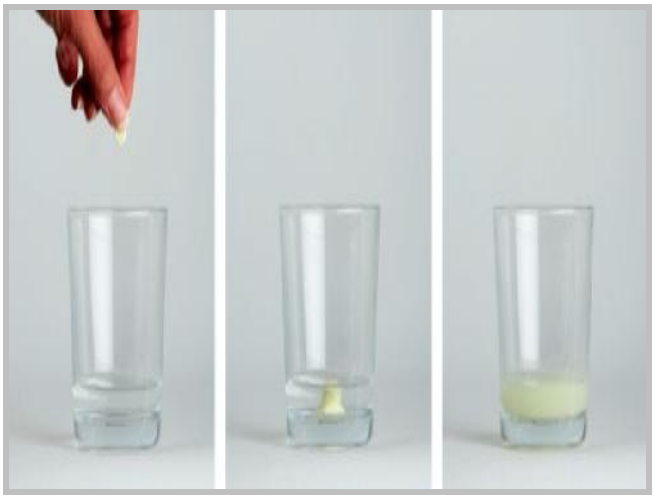

Fig 1. Step by step representation of disintegration process of a dispersible tablet.

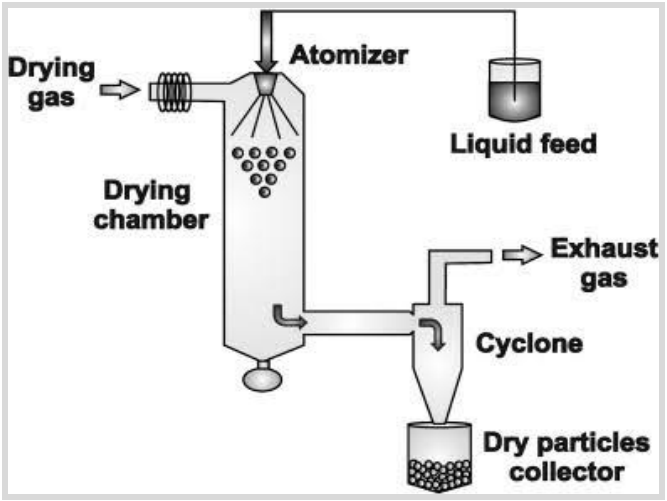

Fig 2. Spray drying.

METHOD OF PREPARATION OF DISPERSIBLE TABLETS:

Spray drying:

Spray drying is one of the oldest forms of drying and one of the few technologies available for the conversion of a liquid, slurry, or low-viscosity paste to a dry solid (free-flowing powder). The spray-drying process is carried out in three fundamental stages. The first stage is atomization of a liquid feed into fine droplets. In the second stage, spray droplets mix with a heated gas stream and the dried particles are produced by the evaporation of the liquid from the droplets. The final stage involves the separation of the dried powder from the gas stream and collection of these powders in a chamber. The components included supporting agents like non hydrolyzed and hydrolyzed gelatin, a bulking agent like mannitol and a volatilizing agent [16,17].

Lyophilisation or freeze drying:

It is a process in which solvent is removed from a frozen drug solution or a suspension containing structure forming excipients. Freeze drying process normally consists of three steps: a) Material is frozen to bring it below the eutectic point, b) Primary drying to reduce the moisture around 4% w/w of dry product and c) Secondary drying to reduce the bound moisture up to required final volume. The resulting tablets are usually very light and have highly porous structures that allow rapid dissolution or disintegration. This process may result in a glassy amorphous structure of excipients as well as the drug substance leading to the enhanced dissolution rate [16,18-20].

Sublimation:

In this technique, highly volatile substances like camphor, urea and urethane are added to the blend before compression. When highly volatile substances are compressed, they can be easily removed by sublimation. This improves the dissolution rate as the end product is a porous structure due to the evaporation of the volatile substances [16, 21].

Molding:

The powder blend is moistened with the solvent and the tablet is molded. This process is called solvent molding. The low compression pressure used results in a porous structure which leads to enhanced dissolution rate; the powder blend is generally passed through a very fine screen. The major drawback of the molded tablets is that they lack the mechanical strength. The molded forms

have also been prepared directly from a molten matrix in which the drug is dissolved or dispersed (known as heat molding) or by evaporating the solvent from a drug solution or suspension at ambient pressure (no-vacuum lyophilisation) [16].

Cotton candy process:

Cotton candy process involves formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to have improved flow properties and compressibility. This candy floss matrix is then milled and blended with active ingredients and excipients and subsequently compressed to dispersible tablets. This process can accommodate high dose of drug and high process temperature limits the use of this process [22,23].

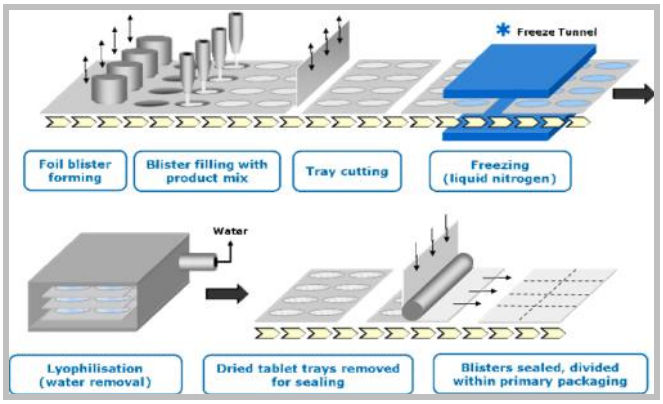

Fig 3. Lyophilisation or freeze drying.

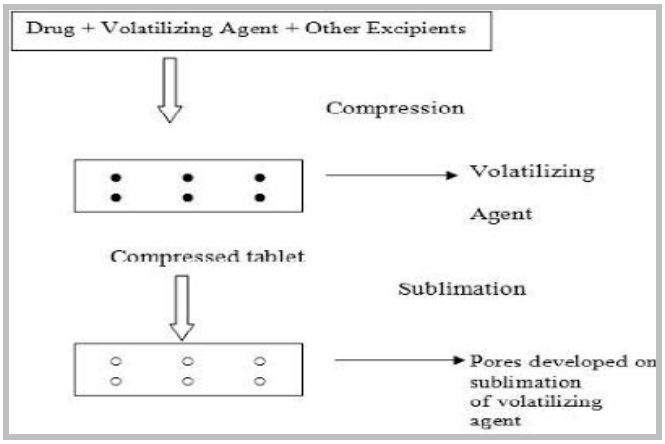

Fig 4. Steps involved in sublimation.

Direct compression:

This method can be applied to manufacture dispersible tablets by choosing appropriate combinations of excipients which can provide fast disintegration and good physical resistance. This technique is mainly preferred because of the availability of improved excipients especially superdisintegrants and sugar based excipients [24].

Superdisintegrants:

The addition of superdisintegrants principally changes the rate of disintegration and hence the dissolution. Tablet disintegration time can be optimized by concentrating the disintegrants. Below critical concentration tablet disintegration time is inversely proportional to disintegrants concentration. Above the critical concentration level, however, disintegration time remains approximately constant or even increases [25]. As the superdisintegrants are of prime importance, a careful selection of superdisintegrants based on the following factors is critical in the formulation [16]. The disintegrant should possess quick wicking action for generating the hydrostatic pressure required for faster disintegration. Smaller particles are preferred over larger particles as the latter produce gritty mouth feel. The gel forming superdisintegrants are generally avoided for patient non-compliance. A more compactable superdisintegrant is preferred to avoid friability.

METHOD OF ADDITION OF SUPERDISINTEGRANTS [25,26]:

Internal addition:

In wet granulation method, the disintegrant is added to other excipients before wetting the powder with the granulating fluid to incorporate it within the granules whereas in dry granulation method, the disintegrant is added to other excipients before compressing the powder between the rollers.

External addition:

In both wet and dry granulation methods, the superdisintegrant is added to the granules during dry mixing prior to compression.

Internal and External Addition:

In this method, disintegrant is divided into two portions. One portion is added before granule formation (intra) and remaining portion is added to granules (extra) with mixing prior to compression. If both intra granular and extra granular methods are used, extra granular portion break the tablet into granules and the granules further disintegrate by intra granular portion to release the drug substance in to solution.

Mechanism of action of superdisintegrants [24,25]:

Swelling: High swelling force is observed in the tablets with low porosity and vice versa. During swelling, the

adhesiveness of the other ingredients is considerably reduced, there by facilitates disintegration of the tablet.

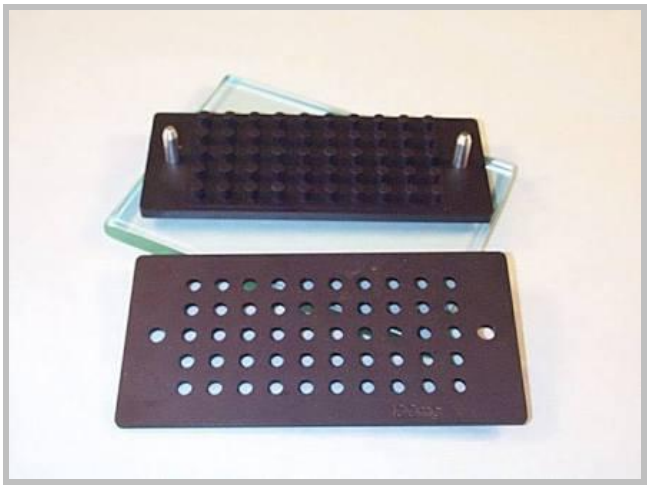

Fig 5. Molding method.

Wicking: The main principle involved here is porosity and capillary action. Liquid is drawn upon "wicked" into these pathways through capillary action and rupture the interparticulate bonds causing the tablet to break apart.

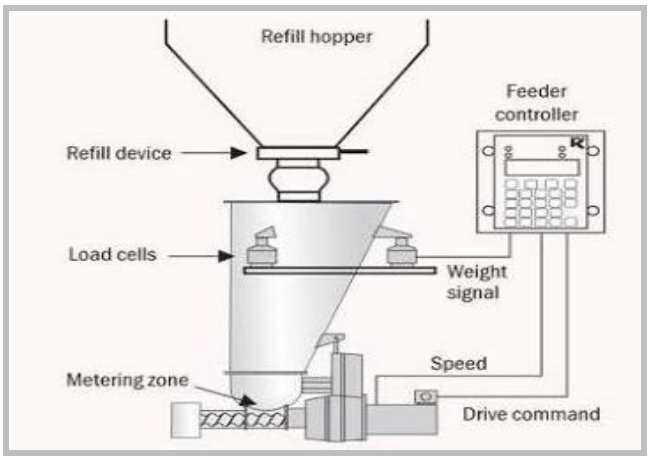

Fig 6. Direct compression.

Electrostaticrepulsion: In this mechanism, water is required for disintegration which is mainly due to the electrostatic repulsions between the particles. Wicking may sometimes be the secondary mechanism of disintegration in such cases.

Sugar based excipients:

These have been widely used as bulking agents because of their high aqueous solubility, sweetness, pleasing mouth feel and good taste masking. Nearly all formulations for dispersible tablets incorporate some sugar materials in their formulations. The use of sugar based excipients especially bulking agents like dextrose, fructose, and xylitol which display high aqueous solubility and sweetness and hence impart taste masking property [17].

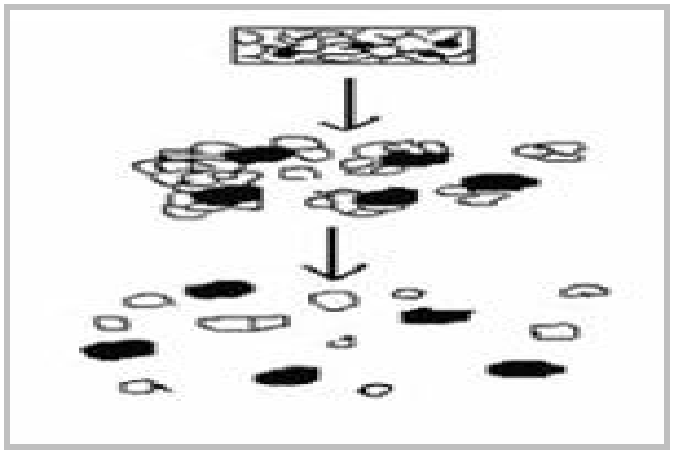

Fig 7. Swelling action: particles swell and break up.

NANONISATION:

A recently developed nano melt technology involves reduction in the particle size of drug to nano size by wet milling technique. Surface adsorption of the nano crystals of the drug is done on selected stabilizers for stabilizing them against agglomeration, which are then incorporated in to the dispersible tablets. This technique is mainly suitable for poor water soluble drugs and wide range of doses (up to 200 mg of drug per unit) [20,21].

EXCIPIENTS USED IN THE FORMULATION OF DISPERSIBLE TABLETS [27,28}

All of these must meet certain criteria as follows:

- They must be physiologically inert.
- They must be acceptable to regulatory agencies.
- They must be physiologically and chemically stable.
- They must be free of any bacteria considered to be pathogenic or otherwise objectionable.
- They must not interfere with the bioavailability of the drug.
- They must be commercially available in the form and purity commensurate to pharmaceutical standards.
- Cost must be relatively inexpensive.
- They must conform to all current regulatory requirements.
- To assure that no excipient interferes with the utilization of the drug, the formulator must carefully and critically evaluate combinations of the drug with each of the contemplated excipients The screening of drug-excipients and excipient-excipient interactions should be carried out routinely in the pre-formulation studies.

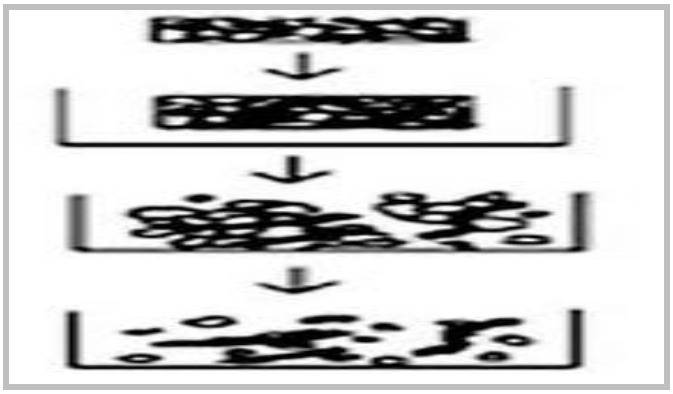

Fig 8. Wicking action in dispersible tablet.

PACKAGING OF DISPERSIBLE TABLETS [6]:

Some of the dispersible tablets are stable during storage, e.g. for 2 years or even 3 years in conventional packaging and these type of dosage forms are stored in High Density Polyethylene bottles, blister and strip packs.

CONCLUSION:

Dispersible tablets are an upcoming trend of using solid dosage form in oral route. The ODTs have potential advantages over conventional dosage forms, with their improved patient compliance; convenience, bioavailability and rapid onset of action had drawn the attention of many manufactures over a decade. Significant more research emphasis has to be given for enhancing porous nature of dispersible tablet to achieve rapid tablet disintegration in the oral cavity along with good taste-masking properties and excellent mechanical strength.

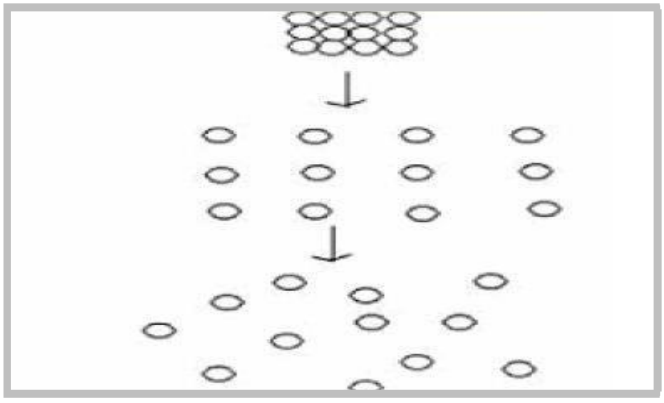

Fig 9. Repulsion force in breaking dispersible tablet.

ACKNOWLEDGEMENTS:

Authors wish to thanks the authority of Mother Theresa Post Graduate and Research Institute of Health Sciences for providing library facility to carry out this review article.

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Conflict of Interest: None

Source of Funding: Nil

Paper Citation: Nandhini J, Rajalakshmi AN. Dispersible Tablet – A review. J Pharm Adv Res, 2018; 1(3): 148-155.