



DISPERSIBLE TABLET AS A FORMULATION FOR ORAL DRUG DELIVERY SYSTEM

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ABSTRACT

Dispersible drug delivery methods are widely utilized nowadays to increase patient compliance and bioavailability. Over the past years, dispersible tablets have gained a lot of attention as a preferable alternative to conventional tablets and capsules due to increased patient compliance, improved solubility, and improved stability profiles. Dispersible tablets may be a better option, particularly for medications that react negatively to GI fluids, to cover up a medication's bitter taste, and for patients, who fall into the paediatric or geriatric categories, are bedridden, have recently undergone surgery, or may have trouble swallowing conventional tablets and capsules. These tablets instantly break down in the water to create the suspension. The key component of a dispersible tablet is the super disintegrants. When a dispersible tablet comes into touch with water, it becomes moist and swells significantly, quickly disintegrating.

Keywords: Dispersible Tablets Disintegration, Super disintegrants, Direct compression.

1. INTRODUCTION

The primary goal of any drug delivery system (DDS) development is to provide a safe and effective therapy for humans. Oral medication administration has been the most important part of the global pharmaceutical market for decades. It is rising in popularity as a preferred route for medication administration. A huge number of advancements in pharmaceutical technology have made tablet manufacture a science. Tablets have recently emerged as the most advantageous dose form when compared to other possible dosage forms. This dosage form's popularity stems from benefits such as ease of production, ease of administration, high dose precision, stability, and safety. Despite their many advantages, traditional tablets are typically ineffective in some scenarios. Because of hand tremors and dysphagia, the elderly has difficulty taking traditional oral dosage forms. Swallowing is also a prevalent problem in children due to their underdeveloped muscular and skeletal systems. Patients, who are mentally ill, developmentally impaired, or cooperative suffering from acute nausea may also have difficulty using conventional oral dosage forms.

1.1. Dispersible tablet

Dispersible tablets are uncoated or film-coated tablets, as specified by the European pharmacopeia, designed to be

dispersed in water before administration, resulting in a homogenous dispersion. A dispersible tablet is typically dispersed in about 5 to 15 ml of water (e.g., a tablespoonful or a glass of water) and then provided to the patient.

In water at 15 to 25°C, dispersible tablets must dissolve in 3 minutes. A dispersible tablet's dispersion should also pass through a sieve screen with a nominal mesh aperture of 710 m. The presence of an acid/base couple in which the base liberates carbon dioxide when the couple's components are mixed can aid the dispersion qualities of dispersible tablets [1, 2].

1.2. Ideal properties of dispersible tablets [1, 3]

- They must be administered with water or another liquid and should break down and dissolve easily.
- Mask or eliminate the drug's unpleasant taste.
- They should be able to load a lot of drugs.
- They should have a distinct taste in the mouth.
- They should be resistant to most things.
- Wetness and other environmental factors.
- Ease of administration to mentally ill individuals.
- Ill, crippled, and unwilling to cooperate
- Should be portable without being fragile.

1.3. Dispersible tablet characteristics

Dispersible tablet should not be chewed or ingested whole. Due to froth and slow dispersion, they should not be used in carbonated drinks or milk. Dispersible tablets are designed to provide a unit dosage form of medication that can be readily administered to infants, children, and the elderly, who may have trouble swallowing an unbroken tablet.

1.4. Advantages of dispersible tablets [4-6]

- They are especially good for older people who have difficulty swallowing and youngsters.
- They have a rapid disintegration and absorption of the medicine.
- Will have a rapid onset of action
- Some dispersible tablets can be separated as well.
- The active ingredient must have a bitter flavor masked ahead of time because the large quantity of patient compliance is one of the conceivable applications improved.
- Rapid gastric absorption increases bioavailability and reduces drug-related adverse effects. NSAID-induced GI pain is one example.
- Chewable tablets have been available for some time, but they differ from the new dispersible tablets. These new medicines can help patients who have trouble chewing or find it unpleasant.
- Dispersible medications can be helpful for kids who have lost their primary teeth but still do not have access to all of their permanent teeth.
- Dispersible tablets' negative aspects [7]
- Rapid dissolving tablets must be kept in a humidified, temperature-controlled environment since they are hygroscopic.
- Special packaging is needed for dispersible tablets in order to effectively stabilise and protect the stable product.
- There is typically a lack of mechanical strength. Therefore, utmost caution is necessary.
- Leave an unpleasant taste and/or grittiness on the tongue if improperly made.

1.5. Limitation of dispersible tablet [8]

- In the dispersible tablet, drugs with moderately greater dosages are difficult to manufacture.
- The hygroscopic qualities of the composition necessitate further moisture protection with particular packaging to ensure product stability and safety.

- These tablets have a lower hardness and friability than traditional tablets, making them fragile and difficult to handle. They sometimes require special packaging in peel-able blisters.
- These dosage forms cannot be used to give drugs that are absorbed in a specific place.
- Anticholinergic medication-using patients might not be excellent candidates for dispersible tablets.
- For soluble pharmaceuticals, the dose of the drug product in freeze-dried dosage forms must be less than 60 mg, and for insoluble drugs, it must be less than 400 mg.

1.6. Dispersible tablet usage recommendations [1]

- To be administered in a small volume of liquid (5 to 10ml) (clean water or milk).
- Before swallowing, gently mix the beverage to let it disperse.
- After ingesting, a portion of the drug may stay in the container. As a result, rinsing with a tiny amount of water or milk and swallowing again is recommended.
- These tablets must be handled with care because they are substantially more fragile than conventional tablets (flimsier, and less resistant to rubbing).
- Since their stability outside the blister packaging cannot be ensured, they should be utilized straight away after being taken out of the blister packaging.

1.7. Mechanism of drug release [9]

When a tablet comes into contact with moisture, it disintegrates and shatters into small pieces. The next step is de-aggregation or disintegration into primary particles smaller than the initial granule size. Because the available surface area is enormous, primary particles dissolve more quickly, whereas complete tablets and aggregates created during tablet breakdown dissolve more slowly. In less than three minutes, the rest should disperse or disintegrate. The basis for development is the use of super disintegrants such carboxymethyl cellulose, polyvinylpyrrolidone, and sodium starch glycolate.

2. CHALLENGES IN THE FORMULATION OF DISPERSIBLE TABLET [6, 10, 11]

2.1. Time to disintegrate and mechanical strength

Many dispersible tablets are delicate, and there is a risk that they will shatter during packaging, transit, or patient

handling. Tablets based on Zydis technology necessitate specialized packaging. As a result, there must always be a strong balance between mechanical strength and packaging.

2.2. Taste masking

A bitter pharmaceutical tablet that dissolves/disintegrates in the mouth will have a substantial impact on patient compliance. Bitter drugs require effective taste masking to ensure that the drug's flavour is not noticed in the oral cavity. Several approaches have been developed to disguise the bitter taste of most medications.

2.3. Sensitivity to environmental variables

Dispersible tablets should be less sensitive to environmental factors like humidity and temperature because the majority of the components used in them are designed to dissolve in a tiny amount of water.

2.4. Feel in the mouth

In the mouth, dispersible pills shouldn't crumble into bigger pieces. The dispersible tablet should produce the tiniest possible particles once it dissolves. Dispersible tablets should leave little to no aftertaste in the mouth after oral intake. Additionally, flavourings and cooling components like menthol heighten the tongue's sensation.

2.5. Aqueous solubility

Water-soluble drugs pose several problems because they produce a eutectic mixture, which causes freezing point depression. An amorphous composite can be made stiffer and more crystalline by using excipients that form a matrix, like mannitol.

2.6. Organoleptic characteristics

The creation of dispersible tablets requires the presence of organoleptic qualities. The mouth feel of a tablet dispersion must be adequate, which is governed by particle size and viscosity. Flavourings and sweeteners can be applied to change and hide the taste.

2.7. Hygroscopicity

When exposed to normal temperature and humidity, oral disintegration dosage forms become hygroscopic and lose their physical integrity. They must therefore be protected from moisture, which calls for the usage of unique product packing packages.

2.8. Cost

Dispersible Tablet technology should be cost-effective in terms of the final output. Costs are greatly increased by

techniques like Zydis and Orasoly, which demand specific packaging and technology.

3. THE BASIC COMPONENT OF DISPERSIBLE TABLETS FORMULATION

3.1. Drugs

The drugs that are particularly water-soluble, weakly compressible and hygroscopic are the hardest to manufacture into dispersible tablets. Excipients must be carefully chosen to provide a tablet matrix with high compressibility.

3.2. Binders

When making tablets using the direct compression method, these fillers/binders are crucial in improving flowability and compressibility.

3.3. Disintegrants

A compound known as a disintegrant quickens the pace at which a pill dissolves in water. The so-called super disintegrants used in this work are so-called because of their exceptional capacity to absorb water and swell, which is connected to their high disintegrant efficiency *e.g.* cross povidone, sodium starch glycolate.

3.4. Diluents

A diluent or filler helps to compress a formulation and adds strength and aesthetic appeal to the finished tablet. Diluents are categorised according to how well they dissolve in water, and they are chosen based on the physio-chemistry of the medicine, including its solubility, hygroscopicity, compression properties, instability, and production process. Mannitol with microcrystalline cellulose, for instance.

3.5. Lubricants

Because stearic acid salts, such as magnesium stearate, are hydrophobic and can create scum with an unattractive look, they are possibly undesirable in dispersible tablet compositions. Surprisingly, magnesium stearate is the lubricant of choice for most commercial dispersible pills.

3.6. Excipients used in the preparation of dispersible tablets

All of these must adhere to the following requirements:

- They must be amorphous biologically
- The requirement for regulatory agencies to approve them.
- They must be physiologically and chemically stable.
- They must be devoid of any microorganisms that are either pathogenic or offensive in any other way.

- They must not impede the medication's bioavailability.
- They need to be offered commercially in a form and purity that meet pharmaceutical requirements.
- The price must be reasonably low.
- They must adhere to all applicable legal and regulatory obligations.
- The formulator must thoroughly and critically evaluate combinations of the medicine with each of the suggested excipients to ensure that no excipient interferes with the drug's use. Pre-formulation studies should routinely screen for drug-excipient and excipient-excipient interactions.

3.7. Dispersible tablet manufacturing

The creation of fast-dispersing tablets, fast-dissolving tablets, and/or orally-dispersible pills can be split into two categories based on current advancements. The first type involves using traditional methods to make tablets, followed by using modern technology.

4. MANUFACTURING OF THE DISPERSIBLE TABLETS WITH CONVENTIONAL METHOD

4.1. Lyophilization or freeze-drying [12, 13]

Lyophilization, often known as freeze-drying, is the most widely used conventional production process for the formulation of quickly dispersible tablets. Lyophilization is used in the production of more than 40% of quick dispersible tablet formulations. After the product has been frozen, water is sublimed from it in this procedure. The freeze-drying of formulations for quick disintegration is the basis for the many patented technologies of Zydus, Quick Solv, and Lyon. These technologies are mostly employed in the production of ODTs.

4.2. Granulation method

Various granulation techniques, such as wet granulation and dry granulation, are used in the production of rapidly dispersible tablets or Fast dissolving tablets. The most popular granulation technique is known as wet granulation, which involves sizing wet grains, wet massing the powder mixture with a granulating liquid containing an appropriate binder, and then drying the granules in an appropriate drier. The creation of rapidly dispersible granules appropriate for ODT formulation has attracted a lot of attention.

4.3. Tablet moulding

Solvent and heat are the two different sorts of moulding techniques. The solvent process involves moistening the

powder mixture with a hydroalcoholic solvent, compressing it in moulded plates at low pressures to form a wetted mass, removing the solvent by air drying, and producing fewer compact tablets with a porous structure that dissolve more quickly than compressed tablets.

4.4. Direct compression [14]

The direct compression method is the most widely utilized form of tablet manufacture. It is very cost-effective and easy, and it does not require the use of any additional equipment such as a granulator or drying equipment.

4.5. Spray drying

Spray drying can result in thin, porous particles that disintegrate quickly. Supporting ingredients include hydrolysed and non-hydrolysed gelatin, mannitol, sodium starch glycolate or croscarmellose sodium, citric acid and/or sodium bicarbonate, sodium starch glycolate or sodium starch glycolate, sodium bicarbonate, sodium starch glycolate, sodium starch glycolate, sodium starch glycolate, sodium starch glycolate, sodium starch glycolate, sodium starch glycolate, sodium starch glycolate, sodium starch glycolate, sodium starch glycolate. A tablet made of spray-dried powder that was submerged in an aqueous medium fell apart in 20 seconds.

4.6. Material extrusion

The active mixture is softened with methanol in this approach, and the softened mass is then ejected through an extruder or syringe to produce a product cylinder in uniform segments, using heated sheets to create the tablet. The dried cylinder can be used to coat pharmaceutical grains to mask their unpleasant flavour.

4.7. Sublimation [15]

The tablet dissolves when it comes into contact with saliva because pores in the tablet's structure were created during the sublimation process to remove volatile components. This method was used to create rapidly dissolving tablets with a highly porous structure and good mechanical strength.

4.8. Cotton candy process

This technology derives its name from the fact that it uses a unique rotating mechanism to create a crystalline structure that looks like cotton candy and resembles floss. The simultaneous action of immediate melting and spinning results in the production of a saccharide or

polysaccharide matrix in this approach. To improve flow and compressibility, the matrix's form has been moderately recrystallized. The active components in this candy floss matrix are crushed and varied before being compacted into tablets that dissolve quickly. This method is capable of handling large medication doses while also providing greater mechanical strength. The high temperature of the procedure, however, limits its application.

5. MANUFACTURING OF THE DISPERSIBLE TABLETS WITH NOVEL TECHNOLOGY [15]

5.1. Zydus technology

The medication is lyophilized or freeze-dried in a gelatin-based matrix to create a Zydus pill. The Zydus solution should dissolve within 2 to 3 seconds when placed on the tongue. The flavour of the dosage form is enhanced by the addition of flavours and sweets.

5.2. Orasolv technology

The Orasolv technology consists of a somewhat effervescent pill that dissolves quickly on the tongue. Tablets are created using a direct compression method to reduce the time required for oral dissolution. The pills are delicate and soft, and they are packaged in specific containers for collecting and placement.

5.3. Duracell technology

Duracell is a second-generation rapid-dissolve/disintegration tablet formulation by CIMA Lab. Duracell has significantly stronger mechanical strength than its predecessor. Duracell is so durable that it can be packaged in conventional blisters or glass vials.

5.4. Pharma burst technology

This invention was patented by SPI Pharma, of New Castle. Pharma burst ODT makes use of a proprietary disintegrating product (Pharma burst) based on Mannitol and standard tableting aids. It formulates ODT, which dissolves in 30-40 seconds, using co-processed excipients. The dry mixing of medicines, lubricants, and flavours is followed by tablet compression.

5.5. Flash tab technology

Technology for Flash tabs is patented by the Prographarm lab. The diluents employed in this technology fall into two categories: dissolving agents and swelling agents. These tablets have adequate physical strength. They take a minute to dissolve in the mouth.

5.6. Wow tab technology

Yamanouchi Pharmaceutical Co. was the first to patent the Wow tab technique. The abbreviation 'WOW' stands for 'without water'. Up to 50% of a tablet's weight may be made up of its active ingredients. The highly formable substance dissolves slowly due to its high compressibility.

5.7. Oraquik technology

This creation has a patent that belongs to K.V Pharmaceuticals. Due to its technology for dissolving and dissolving, Oraquik is suitable for drugs that are sensitive to heat. To hide the flavour and provide a better oral experience, it uses a microspheres technology known as a micro mask.

5.8. Nanocrystal technology

Elan's Nano Crystal technology aids in the improvement of compound activity and final product qualities. Nano Crystal particles are minuscule pharmaceutical particles with a diameter of less than 1000 nm that are produced by wet grinding components.

5.9. Frosta technology

The first technology employs low-pressure compression of highly plastic grains to produce fast-melting tablets. Malt dextrin, corn syrup solids, a wet binder, and a water-penetration enhancer are all included in malt dextrin tablets. To produce tablets with a quicker disintegration time and greater strength, each of the three components is essential.

5.10. Flash dose technology

The Fuisz Corporation obtained a patent for the Flash dose method. Flash dose tablets are made of a self-powered dental floss-shaped matrix. Instead of using silk-like material to deliver the drug, small saccharide spheres can be created.

6. PRE-COMPRESSION PARAMETERS [14, 15]

6.1. Angle of repose

It is common practise to measure non-cohesive (free-flowing) granular material's maximum slope angle when assessing interparticle force. It is the angle created between a horizontal plane and the cone-shaped slope of such material.

- Follow these steps to properly weigh 30g of granules and feed them into the funnel, which is 10cm from the base.
- The funnel's tip should now be adjusted such that it just touches the top of the pile as you manually draw a circle around the pile.

- Calculate the heap's height, radius, and angle of repose using the formula below.

$$\text{Angle of Repose } (\theta) = \tan^{-1} \{h/r\}$$

6.2. Bulk density

The bulk density of a substance is the mass-to-volume proportion of an untapped powder sample, which takes into account the interparticulate void volume.

- Follow these steps to correctly weigh 30g of granules and add them to the graduated cylinder.
- Mark the area in the cylinder that the bulk takes up, then use the formula below to determine the bulk density.

$$\text{Bulk Density } (D_b) = M/V_b$$

Where, D_b = Bulk Density, M = Weight of the dried granules, V_b = Bulk Volume

6.3. Tapped density

The mass-to-volume proportion of the tapped powder sample determines a material's tapped density.

Procedure:

- Transfer 30g of carefully weighed grains to the graduated cylinder.
- Mark the portion of the cylinder's volume that the bulk occupies, then use the formula below to get the density of the bulk.

$$\text{Tapped Density } (D_T) = M/V_T$$

Where, D_T = Tapped Density, M = Weight of the dried granules, V_T = Tapped Volume

6.4. Carr's index

It shows how easily the powder or grains can be compressed. It is calculated as a percentage proportion using the following formula.

$$\text{Carr's Index } (\% \text{ Compressibility}) = (V_b - V_t) \times 100 / V_b$$

Where, V_b = Bulk Volume, V_t = Tapped Volume

6.5. Hausnor's ratio

Is a term that is widely used to describe the flow properties of a powder or granule. The ratio of bulk volume to tapped volume is what determines this.

$$\text{Hausner's Ratio} = V_b / V_t$$

Where, V_b = Bulk Volume, V_t = Tapped Volume

7. POST COMPRESSION PARAMETERS

7.1. Weight variation

This test makes sure that each tablet has the right amount of medication in it. Using an analytical weighing scale, 20 tablets were weighed independently. The average weight and percent weight variation were then determined.

$$\% \text{ Wt. Variation} = \{(\text{Individual Wt.} - \text{Average Wt.}) / \text{Average Wt.}\} \times 100$$

7.2. Hardness

It is a method for determining the breaking point and structural integrity of a tablet. It is used to calculate the strength of the granules. The hardness of the tablets is determined using the Monsanto hardness tester. Dispersible tablets are softer than traditional tablets. Uncoated tablets are thought to have a hardness of 3-5.

7.3. Friability

It represents the proportion of weight loss caused by mechanical activity on the pill during the test. The Roche friabilator is used to determine tablet friability. The friabilator is a plastic chamber that spins at 25 rpm and drops tablets at a height of 6 creeps in each upset. A sample of tablets that had been pre-measured was placed in the friability and rotated 100 times. The tablets were cleaned and reweighed using delicate muslin fabric.

$$\% \text{ Friability} = \{(W1 - W2) / W1\} \times 100$$

$W1$ = Initial Weight of the Tablets, $W2$ = Weight of tablets after the test

7.4. Thickness

It allows for precise measurement and provides information on tablet variation. Six tablets were measured in thickness using a Vernier calliper. The pill thickness should be kept within 5% of the prescribed value. Millimetres are used to measure.

7.5. Disintegration test

It determines whether the tablets dissolve sufficiently in the liquid medium. Six tablets were placed in the tubes of the disintegration test apparatus (which was filled with dispersion medium, i.e. pH 6.8 Phosphate Buffer at $37^\circ\text{C} \pm 5^\circ\text{C}$), and the disintegration test apparatus was operated until no tablet residue remained onscreen.

7.6. Dissolution test

The purpose of this check is to make sure that solid indefinite quantity forms that are administered orally comply with the dissolution requirement. This is a critical test because it provides the drug-release profile. The USP dissolution test apparatus as well as the USP dissolution test method can be used. Dissolvable pills dissolve quickly. A USP type-2 apparatus at 50-100 rpm is used for dissolution studies. The USP Type I basket apparatus has a disadvantage in that some tablet residue adheres to the spindles, whereas the USP Type 2

apparatus does not. Type-2 equipment is preferred due to the reproducible-dissolution profile.

8. CONCLUSION

Dispersible tablets are a new development in the use of solid oral dosage regimen form. The greater patient compliance that dispersible tablets offer over conventional dose forms, together with their comfort, bioactivity, and rapid start of action, have attracted the interest of numerous manufacturers during the past decade. Dispersible tablets are a superior dose form not just for adults but also for children, the elderly, and patients who are bedridden since new approaches are being developed by researchers on a daily basis. We tried to summarize the fundamental ideas and fundamental methods used in the creation of dispersible tablets in this review.

Conflict of interest

None declared

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