Rapid disintegrating tablets: an effective method for accelerating the therapeutic action of poorly soluble Drugs

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Abstract

The ease of administration and increased patient compliance are critical factors in the design of oral drug delivery systems, which continue to be the dominant method of drug delivery despite numerous shortcomings. The rapid disintegrating tablet (RDT) could be a great alternative to traditional tablets because it dissolves quickly when it comes into contact with saliva. Rapid disintegrating tablets (RDTs) are currently more widely available than other tablets to treat various disorders. Due to its ease of manufacture and administration, oral administration is being investigated as the most frequently used route. Due to its rapid disintegration features, water-free use, and simplicity of swallowing, RDTs, particularly for pediatric patients, are effective drug delivery devices. Rapid disintegrating tablets are solid dosage forms that disintegrate in the mouth without water in less than 60 seconds. Rapid disintegration of tablets results in rapid dissolution and, thus, immediate action. The primary objective of this review paper is to discuss the benefits, drawbacks, formulation issues, manufacturing methods, patented technology and evaluation tests. Spray drying, freeze drying, direct compression, moulding, and sublimation are all traditional ways of preparation, however new technologies have been created for the production of RDTs.

Keywords: Rapid disintegrating tablets, patient compliance, spray drying, freeze drying, direct compression.

INTRODUCTION

Oral administration is the most often used method of drug administration due to its ease of absorption, discomfort prevention, adaptability (to handle a variety of drug candidates), and, most significantly, patient compliance. Oral medication delivery methods are less expensive to develop since they do not require sterile conditions. Numerous innovative oral administration technologies have recently become available to improve drug’s physicochemical and pharmacokinetic properties while also increasing patient compliance 1-2. Pharmaceutical drugs intended for oral administration, independent of their physical shape, require varying degrees of optimization of the dosage form’s properties within the constraints of GI physiology 3. Thus, a fundamental understanding of multiple disciplines, including gastrointestinal physiology, pharmacokinetics, pharmacodynamics, and formulation design, is critical for the oral pharmaceutical dosage form to be established successfully in a systemic approach. The more advanced a delivery system is, the more complicated the numerous disciplines involved in the system’s design and optimization. In any case, the scientific framework necessary for the effective development of an oral drug delivery system includes a fundamental understanding of the factors mentioned above 4-5.

Nowadays, research and development operations for new active pharmaceutical ingredients (API) are significantly reduced compared to the development of new dosage forms for existing compounds. Formulation scientists face several challenges when developing new dosage forms for previously approved APIs that meet regulatory requirements 6. The standard tablet appears to be the most prevalent medicinal dose type. However, regular tablets provide swallowing issues for the elderly and newborns, whereas liquid dosing versions are preferable 7.

When considering the history of oral solids, it can be claimed that the disadvantages of one dosage form were used as a springboard for developing a new dosage form. Chewable pills have been accepted for patients who have difficulty swallowing tablets, but their disadvantages include a chalky flavor, gritty particles, and an unpleasant taste of the active ingredient 8-9. While dispersible and effervescent tablets that were pre-dissolved in a glass of water before consumption addressed some of these issues, the use of insoluble lubricants resulted in a "scum" or dirty insoluble residue floating on the surface of the solution or the container’s sides, causing patient discomfort 10.

To combine the benefits of tablets and liquids, research has been focused on developing rapid disintegrating tablet (RDTs), which are solid oral formulations that rapidly disintegrate in the oral cavity within one minute, providing...
increased ease of administration for patients who are physically disabled, uncooperative, mentally ill, pediatric, or geriatric. Due to these advantages, the pharmaceutical industry mainly uses rapid disintegrating tablet, orodispensible tablets and oral wafers or films for fast-release formulations.  

Orally rapid disintegrating tablet (RDT) has increased acceptance and safety profile compared to regular tablets. When it comes into contact with saliva, it rapidly disintegrates and releases its active ingredient, allowing it to be swallowed without additional liquid.

According to the US Food and Drug Administration (US FDA), RDTs should have a rapid disintegration time (less than 30 seconds) and a tablet weight of at least 500 mg. These are the two most critical characteristics of this oral dosage form, and they have posed some difficulties for the formulation. Along with its ease of ingesting, high dosage accuracy, and cost-effectiveness, RDTs may offer other advantages over conventional formulations. Rapid onset of action and avoiding first-pass metabolism can be favourable because they allow for a reduction in the total dose of the active component, resulting in a formulation with fewer potential side effects and ultimately better patient compliance and outcomes.

However, because many active components are bitter, patient compliance may be compromised, prompting the pharmaceutical industry to develop innovative taste-masking technologies to improve the palatability of RDTs. Among these strategies, the most accessible and widely used is the introduction of flavours or sweetening compounds; nevertheless, this strategy may not be effective when a particularly bitter medicine or a substance administered at large doses is present. Alternatively, complexation or coating with taste barrier polymers such as Eudragit E can conceal the taste. Due to the inclusion of moisture-sensitive excipients in RDTs, they are sensitive to humidity, necessitating the usage of better protective packs. Depending on the RDT preparation procedure, some of these techniques may result in delicate tablets, such as those prepared via lyophilization.

These tablets are also referred to as orodispensible tablets, rapid disintegrating tablets, mouth dissolving tablets, rapid dissolving tablets, porous tablets, and rapimelts. Nevertheless, the United States Pharmacopoeia (USP) has accepted these dose forms as ODTs (orally disintegrating tablets). RDT is a solid dosage form that dissolves or disintegrates in the oral cavity without water in less than a minute and has a nice flavor. FDT is also referred to as an orally dissolving tablet, a fast-melting tablet, a mouth-melting tablet, or a fast-dissolving tablet.

**CHARACTERISTICS OF RDTs**

- Does not require water for swallowing but should dissolve or disintegrate in seconds in the mouth.
- Compatibility with other excipients
- Be portable without regard for fragility.
- Have a pleasantly textured mouth feel.
- After oral administration, leave little or no residue in the mouth.
- Demonstrate a low sensitivity to environmental variables such as temperature and humidity.
- Enable the tablet to be manufactured at a reasonable cost using normal processing and packaging equipment.
- Ease of administration in patients who cannot swallow, including the elderly, stroke victims, bedridden patients, patients with renal failure, and individuals who refuse to swallow, including pediatric, geriatric, and psychiatric patients.
- The dose form does not require water to be swallowed, which is a handy feature for traveling patients who do not have immediate access to water.
- Rapid dissolution and absorption of the medication, resulting in a rapid commencement of the action.
- Pre gastric absorption can increase bioavailability and reduce dosage; it can also improve clinical performance by reducing adverse effects.

**ADVANTAGES OF FAST DISSOLVING TABLETS**

- Greater ease of administration and dosage accuracy when compared to liquids.
- The dosage form does not require water to be swallowed, which is extremely handy for traveling patients who do not have fast access to water.
- The pleasant mouth feel of these tablets contributes to the widespread perception of medication as a "bitter pill," particularly among pediatric patients.
- Rapid dissolving and absorption of the drug, resulting in a rapid commencement of the action.
- Capability to give the benefits of liquid medication in a solid form.
- Increased bioavailability, particularly for insoluble and hydrophobic medicines, due to tablets' fast disintegration and dissolving.

**LIMITATIONS OF FAST DISSOLVING TABLETS**

- If the tablets are not properly formed, they may leave an unpleasant taste or grittiness in the mouth.
- It is more challenging to construct drugs with relatively significant dosages into ODTs, for example, antibiotics such as ciprofloxacin, which has an adult dose tablet containing around 500 mg of the medicine.
- For insoluble medications, the dose must be less than 400mg; for soluble pharmaceuticals, the dose must be less than 60mg.
- The tablets are typical of modest hardness. As a result, they are brittle and/or friable, making them difficult to handle. They frequently require specific peel-off blister packaging and demand extra attention during handling.
- Because RDTs are hygroscopic, they must be protected from humidity.
- Delivery of drug from the fast dissolving formulation would not expect to avoid first pass metabolism since the unit disintegration rapidly and the drug would be swallowed.

**FORMULATION CONSIDERATIONS OF RAPID DISINTEGRATING TABLETS**

Important ingredients that are used in the formulation of RDTs should allow quick release of the drug, resulting in faster dissolution. This includes both the drug and the excipients.
Selection of drug candidate:

Several factors may be considered while selecting an appropriate drug candidate for development of orally disintegrating tablets. The ultimate characteristics of a drug for dissolution in mouth and pregastric absorption from fast dissolving tablets include:

1. Free from bitter taste
2. Dose less than 400 mg
3. Small to moderate molecular weight
4. Good solubility in water and saliva
5. Partially unionized at oral cavity pH
6. Ability to diffuse and partition in to the epithelium of upper GIT
7. Ability to permeate oral mucosal tissue.

In contrast, the following characteristics may render unsuitable for delivery as an orally disintegrating tablet:

1. Short half-life and frequent dosing.
2. Require controlled or sustained release.
3. Very bitter or otherwise unacceptable taste because taste masking cannot be successfully achieved.
4. Combination with anticholinergics.

Fast disintegration

RDTs needed to disintegrate rapidly within a few seconds in the oral cavity upon contact with saliva, resulting in the administered medication being solved or suspended. Superdisintegrants such as crosspovidone, croscarmellose sodium, and sodium starch glycolate are included in the formulation to achieve rapid disintegration. By swelling, wicking, effervescence, deformation, or combination of all these processes, superdisintegrants act.

Taste masking

Taste is an essential parameter in RDTs development. A dissolving / disintegrating bitter drug tablet in the mouth can seriously affect patient adherence and acceptance of the dosage type. Through extracting or incorporating rival taste masking chemicals, the taste masking of the drug can be accomplished by avoiding drug penetration to the tongue. Active techniques such as coating, microencapsulation, and product granulation in conjunction with the sweeteners can better taste. Using flavors and cooling agents like menthol can improve the palatability and mouth feeling of RDTs.

Tablet strength and porosity

RDTs are formulated to obtain disintegration within a few seconds. Maintaining good mechanical strength is a significant challenge while doing so. The necessary compression force should be applied during output to achieve good mechanical power. RDTs usually contain several excipients are involved in a dynamic dissolution cycle that starts when the solvent reaches the solid and penetrates the tablet matrix. It is believed that the excipient effect is related to the particle surface properties and solid matrix structure.

Hygroscopicity

RDTs should have low moisture sensitivity. This issue can be particularly challenging because, in the formulation, some highly water-soluble excipients are used to improve fast-dissolving properties and create a good mouth feeling. Those highly water-soluble excipients are susceptible to moisture; some will even deliquesce at high humidity. To protect RDTs from various environmental factors, a good package layout or another strategy should be developed.

METHODS OF PREPARING RAPID DISINTEGRATING TABLETS

Many methods can prepare rapid disintegrating tablets, but the resultant products may differ in their physical properties like swallow-ability, dispersion and dissolution in saliva, bioavailability, stability, mechanical properties, and taste masking. Compaction, molding, freeze-drying, melt granulation, spray-drying, effervescent technology, cotton candy, and phase transition are widely accepted for the preparation of rapid disintegrating tablets.

Conventional techniques

a) Freeze drying

A system in which, after freezing, water is sublimated from the material, leaving a highly porous solid with a high specific surface area that dissolves quickly and shows enhanced absorption and bioavailability. Nevertheless, lyophilization-formed FDT has low mechanical strength, temperature stability, and humidity. In addition to the above problems and their expensive equipment, it is observed that the use of freeze-drying is limited.

b) Direct compression

It is the easiest way to produce tablets. Direct compression involves conventional devices, commonly available excipients, and a limited number of processing steps. High doses can also be accommodated, and the final tablet weight can easily exceed that of the other production method. Nevertheless, problems associated with powdered blend separation can be minimized by matching the particle size and density of the active drug material with excipients.

c) Spray drying

The formulations included hydrolyzed and unhydrolyzed gelatin as a matrix supporting agent, mannitol as a bulking agent, and glycinate/ croscarmellose as a disintegrant sodium starch. Using an acid (e.g., citric acid) or an alkali (e.g., sodium bicarbonate) further increased disintegration and dissolution. The suspension of the above excipients was spray-dried to produce a compact porous powder into tablets. Tablets produced using these methods have been disintegrated into an aqueous medium in < 20 sec.

d) Tablet molding

Molded tablets are prepared using water-soluble ingredients to dissolve the tablets completely and quickly. The powder mixture is moistened with a hydroalcoholic solvent and formed under low pressure into tablets compared to conventional table compression. Instead, air drying eliminates the solvent. Molded tablets are much less lightweight than tablets that are compressed. These have a porous structure that increases dissolution.

e) Sublimation

Sublimation was used to produce high porosity FDTs. A porous matrix is created by compressing the volatile ingredients into tablets and other excipients that are eventually subjected to a sublimation cycle. For this reason, high volatility inert solid ingredients (e.g., ammonium bicarbonate, ammonium carbonate, benzonic acid, camphor, hexamethylene tetramine, naphthalene, phthalic anhydride, urea, and urethane) were used. Often suggested are solvents such as cyclohexane and benzene to produce porosity in the matrix.
Figure 1: Methods of preparing rapid disintegrating tablets

f) Effervescent method
Mouth dissolving tablets are also prepared by an effervescent method using 12% w/w concentration of sodium bicarbonate and tartaric acid and superdisintegrants such as pregelatinized starch crospovidone, croscarmellose, sodium starch glycolate. First, to remove absorbed/residual moisture, sodium bicarbonate and tartaric acid were preheated at a temperature of 80ºC and thoroughly mixed in a mortar. The blends are eventually condensed in the punch.39

g) Phase transition process
In this process, the combination of low and high melting point sugar alcohols, along with a transition of phase in the manufacturing process are important for formulating MDTs. MDTs prepared by compressing xylitol at melting point; 93-95ºC and erythritol at melting point; 122ºC are the example of this technology.31

h) Melt granulation
Meltable binders such as PEG-6-stearate and Superpolystate are used for efficient agglomeration with pharmaceutical powders in this process. Compared to traditional granulation, the benefit of the technique is that water or organic solvents are not required as it does not require a drying phase. The process is less time-consuming compared to wet granulation and uses less energy. This technique can increase the dissolution rate of drugs with poor water solubility, such as griseofulvin.31

Patented techniques
a) Zydis technology
Zydis, the best-known tablet preparation for fast-dissolving/dispersing, was the first new technology tablet on the market. In seconds after putting on the tongue, the tablet dissolves in the mouth. In a matrix usually consisting of gelatin, a Zydis tablet is formed by lyophilizing or freezing the drug. The material is very light and delicate and needs to be delivered in a special blister pack. The freeze-dried framework disintegrates immediately when Zydis units are held in the mouth and do not require drinking liquid. Polymers like gelatin, dextran or are incorporated during handling to give strength.31

b) Flash dose technology
Fuisz patented the invention of the flash dose. The first commercial product introduced by Biovail Corporation is Nurofen melt release, a new form of ibuprofen as melt-in-mouth tablets, prepared using flash does technology. Flash dose tablets consist of a matrix of the self-binding shear form called "floss." Shear form matrices are generated by processing flash heat.30
c) Flash tab technology

This process involves excipient granulation by wet or dry granulation system accompanied by tablet compression. In this process, two types of excipients are used. Some of the disintegrating agents included are reticulated polyvinyl pyrrolidine or carboxymethyl cellulose, starch, altered starch, microcrystalline cellulose, carboxymethyl starch, etc. Physical resistance is satisfactory in these tablets.

d) Durasolv technology

Durasolv is the fast-dissolving or disintegrating tablet formulation of the second generation of CIMA to produce stronger tablets in traditional blisters or bottles for packaging. Durasolv’s mechanical strength is much lower due to the higher compaction stress during tableting. One of Durasolv’s drawbacks is that the system is not compatible with larger drug doses as the formulation is subjected to high compaction pressure. The drug powder coating in Durasolv may become fractured during compaction, exposing the bitter-tasting drugs. This technology is suitable for tablets having a low amount of active ingredients.

e) Orasolve technology

Orosolve software has been developed in CIMA laboratories. The active drug is masked in this process. It also contains a disintegrating agent that is effervescent. Tablets are made with direct compression at low pressure to reduce oral dissolution time. The tablets are produced using conventional blenders and tablet machines. The tablets produced are soft and packaged in a pick and place device specially designed.

f) Wow tab technology

The WOW in the WOWTAB means that the tablet is to be provided without water. This technology uses excipients such as caffeine and water. The two different types of saccharides are combined to obtain a tablet formulation with sufficient hardness and rapid dissolution speed. The two main saccharides are high moldability, such as maltose, mannitol, sorbitol, and oligosaccharides, and low moldability, such as lactose, fructose, mannitol, xylitol (fast dissolution). Tablets produced from this technology will have sufficient hardness to maintain the physical characteristics of the dosage form during production until it comes in contact with moisture such as saliva in the mouth.

g) Cotton candy technology

This method is named because it uses a unique spinning mechanism to create floss, such as a crystalline structure that imitates cotton candy. The process of cotton candy is also known as candy floss. A tablet that dissolves the mouth is created using a matrix of candy floss or shear type. This requires the creation of polysaccharide matrix or saccharides by flash melting and spinning simultaneously. The matrix formed is partially recrystallized to improve flow properties and compressibility. This candy floss matrix is then milled and blended with active ingredients, excipients and subsequently compressed to RDT.

h) Pharmaburst technology

SPI Pharma is patenting pharmaburst software. Pharmaburst technology uses co-processed excipients off the shelf to produce an FDT that dissolves within 30-40 seconds, depending on the active ingredients and processing type. The amount of pharmaburst used in tablet formulation depends on the active ingredients. The process involves a dry mixture of a drug flavor, and lubricant found in a tablet on a regular tablet press with stock tooling.

EVALUATION OF FAST DISSOLVING TABLETS

Organoleptic properties:

The tablet’s dimensions can be described, monitored, and controlled dimensionally. When employing filling equipment, the thickness of a tablet is an important factor to consider. The constant thickness of the tablets serves as a counting mechanism in some filling machinery. A micrometre was used to measure the thickness of ten different tablets.

Hardness:

Significant strength in RDT is difficult to acquire due to the specific manufacturing procedures and ingredients employed. The RDT’s hardness limit is often kept low to promote early dissolution in the mouth. The tablet’s hardness can be determined using conventional hardness testers.

Friability:

To keep the percent friability of an RDT within acceptable ranges is difficult for a formulator, as all techniques of manufacturing RDT increase the percent friability values. Thus, it is vital to analyse this parameter and ensure that the results are within acceptable bounds (0.1-0.9%).

Wetting time:

Wetting time indicates the inner structure of the tablets and the hydrophilicity of the excipients. Thus, the wetting time of a dosage form is related to the contact angle. The lower the wetting time, the quicker the disintegration of the tablets. The wetting time can be measured using five circular tissue papers 10 cm in diameter, placed in a Petri dish of 10 cm diameter. Ten milliliters of water-soluble dye like eosin solution are added to the Petri dish. The tablet is carefully placed on the surface of tissue paper. The time required for water to reach the upper surface of the tablet is noted as the wetting time.

Dissolution test:

For dissolution experiments on RDTs, USP apparatus 1 or 2 may be utilized. Apparatus 1 will clamp the pores on the tablet and cause some dissolution profile errors if a tablet-forming part is used. This is why the paddle procedure known as apparatus 2 is widely used for ODT dissolution testing. Usually, rotation of 50 rpm is desired, but the rotation speed can be up to 100 rpm for masked RDT formulations. Ultraviolet spectroscopy and high-pressure liquid chromatography are widely used to determine the quantity of the dissolved active agent using analytical methods. According to the FDA, a minimum of 85% should be dissolved within 30 min of the active ingredient in ODT formulations.

CONCLUSIONS

RDTs have significant advantages over conventional oral dosages forms because they improve bioavailability, have a faster onset of action, are more convenient, and are more consistent, which are important to pharmaceutical producers. The possibility of decreasing prices when customers seek alternatives to make new product types and the ability to mask the taste and increase mechanical efficiency are all issues that could arise for various RDT manufacturers. Even bitter drugs can be incorporated in
RDTs by using taste-masking agents. The research for RDTs is still going on. Patient demand and availability of different technological options have increased the acceptance of RDTs.

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REFERENCES

1. Rathore R, Gupta AK, Parashar AK. Formulation and Evaluation of fast dissolving films of Granisetron Hydrochloride. JDDT [Internet]. 2014 Apr 29; cited [Jan 2022]; 9(2-A):36-8. Available from: http://jddtonline.info/index.php/jddt/article/view/2768
2. Chang R, Guo X, Burnside BA, Couch RA. A Review of Fast Dissolving Tablets. Pharm Tech. 2000; 2(4):52-58.
3. Mohire NC, Yadav AV, Gaikwad VK. Novel approaches in development of metronidazole orodispersible tablets. Res J Pharm Technol. 2009 Jun 28; 2(2):203-6.
4. Parashar AK, Kakde D, Chadvar V, Devayali R, Shivratav V, Jain UK. A review on solid lipid nanoparticles (SLN) for controlled and targeted delivery of medicinal agents. Curr Res Pharm Sci. 2011; 1(2):37-47.
5. Jire DS, Gosavi NS, Badhe RB, Jagdale DH. Mouth dissolving tablet: A novel drug delivery system. Asian Journal of Pharmaceutical Research. 2021 Aug 14; 11(3):180-6. https://doi.org/10.52711/2231-5691.2021.00033
6. Parashar AK, Patel P, Gupta A, Jain N, Kurni B. Synthesis Characterization and in vivo Evaluation of PEgylated PPI Dendrimer for Safe and Prolonged Delivery of Insulin. Drug Del Letters. 2019; 9:248-63. https://doi.org/10.21742/2210303109666190401231920
7. Gehel M, Patel M, Amin A, Agrawal R, Dave R, Bariya N. Formulation design and optimization of mouth dissolve tablets of nimesulide using vacuum drying technique. AAPS Pharm SciTech. 2004 Sep; 5(3):10-5. https://doi.org/10.1208/pst050336
8. Parashar AK, Singh G. Synthesis and characterization of ligand anchored polypropyleneimine dendrimers for the treatment of brain glioma. J of Med. Physical & Allied Sci. 2021; 10(3):2784-2789. https://doi.org/10.22270/jmpas.v10i3.1084
9. Reddy LH, Ghosh B, Rajneesh. Fast dissolving drug delivery system: A review of literature. Indian J Pharm Sci 2002; 64(4):331-336.
10. Parashar AK, Nema RK. A Review on novel techniques for drug delivery to the brain. Current Research in Pharmaceutical Sciences. 2012; 5:13-41.
11. Lopez FL, Ernest TB, Tuleu C, Gul MO. Formulation approaches to pediatric oral drug delivery: benefits and limitations of current platforms. Expert opinion on drug delivery. 2015 Nov 2; 12(11):1727-40. https://doi.org/10.1517/17425247.2015.1060218
12. Abay FB, Ugurlu T. Orally disintegrating tablets: a short review. Journal of Pharmaceutics & Drug Development. 2015 Jun 25; 3(3):303. https://doi.org/10.15174/2348-9782.3.303
13. Comoglu T, Unal B. Preparation and evaluation of an orally fast disintegrating tablet formulation containing a hydrophobic drug. Pharm Dev Technol [Internet]. 2015; 20(1):60-4. Available from: http://dx.doi.org/10.3109/10873540.2015.862636
14. Parkash V, Maan S, Deepika, Yadav SK, Hemlata, Jogpal V. Fast disintegrating tablets: Opportunity in drug delivery system. J Adv Pharm Technol Res [Internet]. 2011; 2(4):223-35. Available from: http://dx.doi.org/10.5403/japtr/2011-2-4-223-235
15. Parashar AK, Kurni B, Patel P. Preparation and characterization of ligand anchored polymeric nanoparticles for the treatment of epilepsy. Pharmaspirit 2021; 13(1):1-5.
16. Bradoo R, Shahani S, Poojary S, Deewan B, Sudarshan S. Fast dissolving drug delivery systems. JAMA India 2001; 4(10):27-31.
17. Biradar SS, Bhagavati ST, Kuppadas IJ. Fast dissolving drug delivery systems: A brief overview. The Int J Pharmaco 2006; 4(2). https://doi.org/10.5580/0897-9620
18. Parashar AK, Nema RK, Preparation and Characterization of Polymeric Nanoparticles for Sustained Delivery of Insulin. Curr Res Pharm Sci.2012; 153-159.
19. Bhaskaran S, Narmada GV. Rapid Dissolving tablet: A Novel dosage form. Indian Pharmacist 2002; 1: 9-12.
20. Devrajin PV and Gore SP, Melt- in-mouth tablets: innovative oral drug delivery system. Express Pharma Pulse 2000; 7(1):16.
21. Tiwari G, Tiwari R, Bannerjee S, Bhati L, Pandey S, Pandey P, et al. Drug delivery systems: An updated review. Int J Pharm Investig [Internet]. 2012; 2(1):1-2. Available from: http://dx.doi.org/10.4103/2230-973x.96920
22. Ghosh T, Ghosh A, Prasad D. A review on new generation orodispersible tablets and its future prospective. International Journal of Pharmacy and Pharmaceutical Sciences 2011; 03(01):1-7.
23. Vishali T, Damodharan N. Orodispersible tablets: A review. Res J Pharm Technol [Internet]. 2020; 13(5):2522. Available from: http://dx.doi.org/10.5958/0974-360X.2020.00449.7
24. Govind A, Menden MB, Narayana Swami VB. Formulation and evaluation of mouth dissolving tablet Asian J. Pharm Tech. 2016; 6(2): 91-98. https://doi.org/10.5958/2231-5713.2016.00013.1
25. Watanabe Y, Koizumi K, Zama Y, Kiriyama Y, Mastumoto Y and Mastumoto M. New compressed tablet rapidly disintegrating in saliva in the mouth using crystalline cellulose and a disintegrant. Bio Pharm Bull 1995; 18(9):1308. http://dx.doi.org/10.1248/bpb.18.1308
26. Panighraji D, Baghel S, Mishra B. Mouth dissolving tablets: An overview of preparation techniques, evaluation and patented technologies. J Pharm Res 2005; 4(3):35-38.
27. Seager HJ. Drug delivery products and zidov fast dissolving dosage forms. Pharmarcol 1998; 50:375-382. http://dx.doi.org/10.1111/j.1748-6042.2002.tb02466.x
28. Sahadev AK, Purwa S. Process involve in the formation of novel drug delivery system. Asian J. Res. Pharma. Sci 2018; 8(4):203-209. https://doi.org/10.5958/2231-5659.2018.00034.6
29. Kaushik D, Dureja H, Saini TR. Mouth dissolving tablets: A Review. Indian Drugs. 2004; 41(4):187-192.
30. Bhowmik D, Chiranjib B, Krishnananth, Pankaj, Chandria RM: Fast dissolving tablets: An overview. Journal of Chemical and Pharmaceutical Research 2009; 01(01):163-177.
31. Deshpande KB, Ganesh NS. Orodispersible tablets: An overview of formulation and technology. International Journal of Pharma and Bio sciences 2011; 02(01):726-734.
32. Rahane RD, PR Rachh PR, A review on fast dissolving tablet. Journal of Drug Delivery and Therapeutics 2018; 8(5):50-55 http://dx.doi.org/10.22270/jdtt/v8i5.1888
33. Momin S, Khan S, Ghadage DM, Yadav AV, Wagh A, Formulation and evaluation of bilayer tablets of propanolol hydrochloride, Journal of Drug Delivery and Therapeutics. 2017; 7(2):50-57 http://dx.doi.org/10.22270/jdtt/v7i2.1399