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ORAL DISPERSIBLE TABLETS: A REVIEW

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ABSTRACT

The need for delivering of drugs to patients efficiently with minimum side effects has prompted pharmaceutical industries to be engaged in the development of new drug delivery systems. Oral route is presently the gold standard in the pharmaceutical industry where it is regarded as the safest, most economical and most convenient method of drug delivery resulting in highest patient compliance. ODT has advantages such as patient compliance, quick onset of action, improved bioavailability, etc. Usually, elderly people experience difficulty in swallowing the conventional dosage forms like tablets, capsules, solutions and suspensions because of tremors of extremities and dysphagia. In some cases such as motion sickness, sudden episodes of allergic attack or coughing, and an unavailability of water, swallowing conventional tablets may be difficult. In recent past, several manufacturing technologies such as sublimation technique, spray drying technique etc. are employed to overcome the limitations of conventional tablet dosage forms. Once the mouth dissolving tablets are prepared they are required to be evaluated for various parameters so as to have long term stability and better therapeutic efficacy.

KEYWORDS: Fast Dissolving Tablets, Superdisintegrants, Oral Route.

INTRODUCTION

Tablets are solid preparations each containing single dose of one or more active substances and usually obtained by compressing uniform volume of particles. Tablet is intended for oral administration. Some are swallowed whole, after being chewed , some are dissolved or dispersed in water before being administered and some are retained in the mouth where the active substances is liberated. Tablets are widely used dosage form because of its convenience in terms of self administration, compactness and ease in manufacturing. But

paediatrics and geriatric patients may encounter inconvenience in swallowing it. To overcome this problem, in recent years, increasing attention has been focused in formulating fast dissolving and dispersible tablets that are intended to dissolve or disintegrate rapidly in mouth. Tablet disintegration has been considered as the rate limiting step in faster drug release. Recent advances in novel drug delivery system (NDDS) aims to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for administration and to achieve better patient compliance. Tablets are the most widely utilized oral dosage forms.

The performance of ODTs depends on the technology used in their manufacture. The orally disintegrating property of these tablets is attributable to the quick ingress of water into the tablet matrix, which creates porous structure and results in rapid disintegration. Hence, the basic approaches to develop ODTs include maximizing the porous structure of the tablet matrix, incorporating the appropriate disintegrating agent and using highly water-soluble excipients in the formulation.[1, 2, 3]

Advantages [4]

- Improved patient compliance.
- Improved bioavailability.
- Patients that having difficulty to swallowing (dysphagia) the tablet can easily administered.
- They are lightest and most compact of all oral dosage form.
- Disintegration time is faster than the regular compact tablets that is within few seconds to 3 minutes.
- Chemical stability is good.
- Improving the dissolution of poorly soluble drugs by using various superdisintegrants available.
- Dispersible tablets are more convenient for medicines which are unstable in water. Nowadays, dispersible tablets are gaining more importance in the market of taste masking property. For poorly soluble orally administered drugs the rate of absorption is often controlled by rate of dissolution. The rate of dissolution can be increased by various techniques (micronization, complexation solid dispersion etc). Another pre-requisite for the fast dissolution may be disintegration time of the tablets. Because dispersible tablets delivers a fine suspension of drug particles and thus favours the greater dissolution of the drugs.

CHALLENGES IN FORMULATION OF ODTS[5]

1. Disintegration time and mechanical strength

ODTs are formulated to obtain disintegration time usually less than a minute. While doing so, maintaining a good mechanical strength is a prime challenge. Many ODTs are fragile and there are chances that such fragile tablet will break during packing, transport or handling by the patients. Tablets based on technologies like Zydis need special type of packaging. It is very natural that increasing the mechanical strength will delay the disintegration time. So a good compromise between these two parameters is always essential.

2. Taste masking

Many drugs are bitter in taste. A tablet of bitter drug dissolving/ disintegration in mouth will seriously affect patient compliance and acceptance for the dosage form. So effective taste masking of the bitter drugs must be done so that the taste of the drug is not felt in the oral cavity.

Number of techniques are developed for masking the bitter taste of most of the drugs, that includes formation of pellets by extrusion, spheronization or mass extrusion[6], coating of drug using a taste masking polymer[7,8], spray drying the drug dispersed in a polymeric solution[9], complexation of drug by inclusion in cyclodextrin[10,11], drug-resinate complex formation[12,13], microencapsulation of drug by polymer[14].Chandira R.M et al.[15] enhanced solubility of carvidiol by β- cyclodextrin as a complexing agent. Solubility studies were performed to investigate the drug carrier interaction. I.R. and D.S.C studies carried out to investigate any interaction and stability of formulation. Tablets were prepared by direct compression technique. Prepared tablets were evaluated for thickness, uniformity of weight, hardness, friability, wetting time, in-vitro disintegration time, drug content and in vitro drug release. It can be concluded that Carvedilol can be successfully complexed with Beta-cyclodextrin to prepare fast dissolving tablets in the ratio of 1: 4.

3. Sensitivity to environmental conditions

ODTs generally should exhibit low sensitivity to environment conditions such as humidity and temperature as most of the materials used in ODTs are meant to dissolve in minimum quantity of water.

4. Mouth feel

ODTs should not disintegrate into larger particles in the oral cavity. The particles generated after disintegration of the ODTs should be as small as possible. ODTs should leave minimal or no residue in mouth after oral administration. Moreover addition of flavours and cooling agents like menthol improve the mouth feel.

5. Cost

The technology used for ODTs should be acceptable in terms of cost of the final product. Methods like Zydis and Orasolv that require special technologies and specific packaging increase the cost to a remarkable extent.

CRITERIA OF SELECTION[16]

The ideal characteristics of a drug for in vivo dissolution from an FFDT include.

- No bitter taste
- Dose lower than 20mg
- Small to moderate molecular weight
- Good stability in water and saliva
- Partially non ionized at the oral cavities pH
- Ability to diffuse and partition into the epithelium of the upper GIT (log P>1, or preferably>2)
- Ability to permeate oral mucosal tissue
- Passive diffusion drug absorption
- BCS-class 2
- Molecular weight below 500 da.

MECHANISM OF DRUG RELEASE

Overall Mechanism of drug release of ODT: According to official publication European Pharmacopoeia the ODT should be disperses or disintegrates in less than three minutes. The fundamental approach used in development of ODT is the use of superdisintegrants like sodium starch glycol ate (Primo gel, Explotab) carboxymelhylcellulose (Crosscarmellose), Poly vinylpyrrolidone (Polyplasdone) etc. provides rapid disintegration of tablet after putting in mouth, and release the drug in saliva. Bioavailability of certain drugs may be increased due to absorption of drugs in oral cavity and may be due to pre-gastric absorption of saliva which

contains dispersed drugs which pass down into the stomach. The amount of drug which is subject to undergo first pass metabolism is reduced.

1. Superdisintegrants[1]

As ODT require faster disintegration. So, pharmacist needs to formulate Disintegrates i.e. Superdisintegrants which are effective at low concentration and have greater disintegrating efficiency and they are more effective intragranularly. But have one drawback that it is hygroscopic therefore not used with moisture sensitive drugs. And this superdisintegrants act by swelling and due to swelling pressure exerted in the outer direction or radial direction, it causes tablet to burst or the accelerated absorption of water leading to an enormous increase in the volume of granules to promote disintegration.

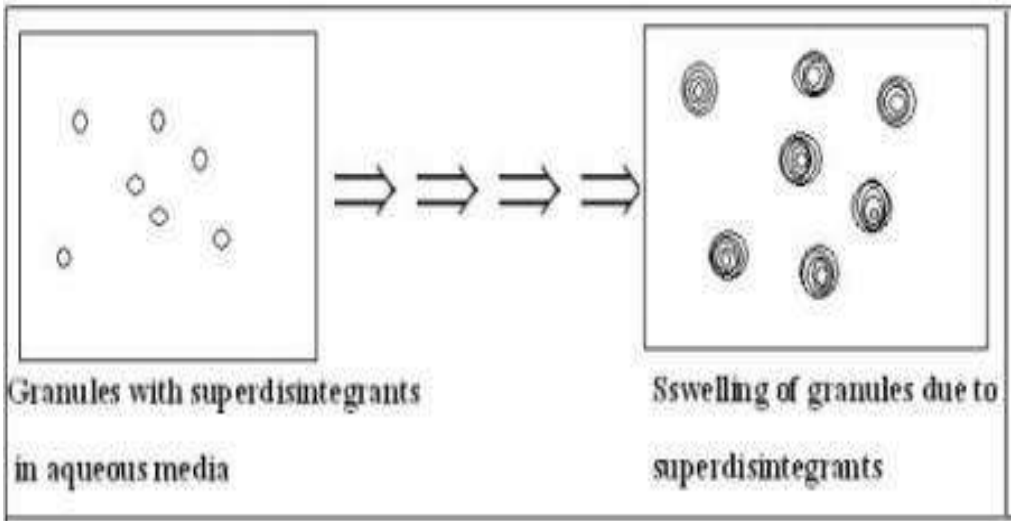

Table: List of superdisintegrants.

Superdisintegrants	Examples
Crosspovidone	Crosslinked PVP
Sodium starch glycolate	Crosslinked starch
Alginic acid NF	Crosslinked alginic acid
Soy polysaccharides	Natural super disintegrant

TECHNIQUES USED IN PREPARARTION OF ODTs

1. Freeze drying/ Lyophilisation

Lyophilisation means drying at low temperature under condition that involves the removal of water by sublimation. Drug in a water soluble matrix which is then freeze dried to give highly porous structure. The tablets prepared by lyophilisation disintegrate rapidly in less than 5 seconds due to quick penetration of saliva in pores when placed in the oral cavity. Lyophilisation is useful for heat sensitive drugs i.e. thermo-labile substances.[17,18]

Freeze drying process normally consists of three steps: Material is frozen to bring it below the eutectic point. Primary drying to reduce the moisture around 4% w/w of dry product. Secondary drying to reduce the bound moisture up to required final volume.

Advantages: More rapid dissolution than other available solid products.

Disadvantages: High cost of the equipments & lack of physical resistance in blister packs. Ahmed I.S. et.al.[19] prepared ODTs by freeze-drying an aqueous dispersion of nimesulide containing a matrix former, a sugar alcohol, and a collapse protectant. Development of a lyophilized orally disintegrating tablet (ODT) enhanced the in vitro dissolution and in vivo absorption of Nimesulide, a drug with poor solubility and poor bioavailability.

Bhoyar P.K. et al.[20] formulated rapid disintegrating tablet in the blister packs using Freeze Drying Method. Eudragit EPO polymer was used for complexation with drug Trimetazidine HCl for overcoming taste problem. The Lyophilisation method was used to form the drug polymer complex in a tablet. 1:3 ratio of the drug to polymer was effectively masked the bitter taste of drug.

2. Spray drying

This technique is based on a particulate support matrix, which is prepared by spray drying an aqueous composition containing support matrix and other components to form a highly porous and fine powder. This then mixed with active ingredients and compressed into tablets. The formulations are incorporated by hydrolyzed and non hydrolyzed gelatins as supporting agents, mannitol as bulking agent, sodium starch glycolate or crosscarmellose sodium as disintegrating and an acidic material (e.g. citric acid) and / or alkali material (e.g. sodium bicarbonate) to enhance disintegration and dissolution. Tablet compressed from the spray dried powder disintegrated within 20 seconds when immersed in an aqueous medium.[21]

Advantages

Rapid disintegration of tablets.

Masareddy R et al. [22] studied the effect of co-processed excipients bases in formulation of orodispersible tizanidine HCl tablets by direct compression method. Co-processed excipients of microcrystalline cellulose with SSL hydroxypropylcellulose was prepared using spray drier in 1:1, 1:2 and 1:3 ratio. Formulated tablets were evaluated for hardness, friability, in vitro disintegration time and in vitro drug release. Granules obtained by spray drying

technique were found to be more spherical which improved its flow property and was supported by scanning electron microscope studies. Inclusion of coprocessed excipients base in formulation of orodispersible tablets enhanced disintegration significantly.

3. Molding

Tablets prepared by this method are solid dispersions. Molded tablets offer improved taste due to water soluble sugars present in dispersion matrix. Molding process is of two type's i.e. solvent method and heat method. Solvent method involves moistening the powder blend with a hydro alcoholic solvent followed by compression at low pressures in molded plates to form a wetted mass (compression molding). The solvent is then removed by air-drying. The tablets manufactured in this manner are less compact than compressed tablets and posses a porous structure that hastens dissolution. The heat molding process involves preparation of a suspension that contains a drug, agar and sugar (e.g. mannitol or lactose) and pouring the suspension in the blister packaging wells, solidifying the agar at the room temperature to form a jelly and drying at 30^{o}C under vacuum.

Advantages: Molded tablets disintegrate more rapidly and offer improved taste because the dispersion matrix is, in general made from water soluble sugars.

Disadvantages: Moulded tablets do not possess great mechanical strength. Erosion & breakage occur during handling & opening of blister packages.

4. Sublimation

In this method a subliming material like (Ammonium bicarbonate, Ammonium carbonate, Urea, Benzoic acid, Naphthalene, camphor) is removed by sublimation from compressed tablets and high porosity is achieved due to the formation of many pores. Where camphor particles previously existed in the compressed tablets prior to sublimation of the camphor. A high porosity was achieved due to the formation of many pores where camphor particles previously existed in the compressed mannitol tablets prior to sublimation of the camphor. These compressed tablets which have high porosity (approximately 30%) rapidly dissolved within 15 seconds in saliva.[23]

Advantage: Tablets dissolve in 10-20 sec. and exhibit sufficient mechanical strength.

Kumar R et al.[24] developed FDT with improved Haloperidol dissolution by sublimation of tablets containing camphor as subliming agent. Orodispersible tablets of haloperidol were

prepared by wet granulation technique using camphor as subliming agent and sodium starch glycolate together with crosscarmellose sodium as superdisintegrants. Camphor was sublimed from the granules by exposing the granules to vacuum. The porous granules were then compressed in to tablets.

Alternatively, tablets were first prepared and later exposed to vacuum. Sublimation of camphor from tablets resulted in superior tablets as compared with the tablets prepared from granules that were exposed to vacuum. The results revealed that the tablets containing subliming agent had a good dissolution profile.

5. Mass Extrusion

This technology involves softening of the active blend using the solvent mixture of water soluble polyethylene glycol and methanol and expulsion of softened mass through the extruder or syringe to get a cylindrical shaped extrude which are finally cut into even segments using heated blade to form tablets. This process can also be used to coat granules of bitter drugs to mask their taste.[25,26]

Advantage: Mask bitter taste by coating the granules.

Mansing G. Patil et al.[27] prepared orally disintegrating tablets of Tramadol hydrochloride for achievement of quick onset of action of the drug. An attempt was to prepare bitterless orally disintegrating tablet using Eudragit E 100 as a taste masking agent. Mass extrusion was the technique used for preparing taste masked granules and tablet was prepared using superdisintegrants like crospovidone, crosscarmellose sodium and sodium starch glycolate. The extrusion technique represents a novel application of polymer processing technology to prepare pharmaceutical dosage forms. The process involves embedding a drug in a polymeric carrier while shaping the composite material to form a pharmaceutical product. The drug release from orally disintegrating tablets increased with increasing concentration of superdisintegrants and was found to be highest with formulations containing Crospovidone..

6. Direct compression [28]

The process by which tablets are compressed directly from mixtures of the drug and excipients without any preliminary treatment. It offers advantages over the other manufacturing Processes of tablets, such as wet granulation and delivers high Efficiency. The mixture to be compressed need have Satisfactory flow properties and cohere under pressure

thus making pre-treatment as wet granulation unnecessary. In many cases, the superdisintegrants have a major role in the disintegration and dissolution process of mouth dissolving tablets made by direct compression. The choice of a suitable type and an optimal amount of disintegrates is vital for ensuring a high disintegration rate. The addition of other formulation mechanisms such as water soluble excipients or Effervescent agents can further enhance dissolution or disintegration properties.

Characterisation and evaluation parameters [29-32]

Pre- compression parameters

- **Bulk density**: Bulk density is the weight of soil in a given volume. Soils with a bulk density higher than 1.6 g/cm3 tend to restrict root growth. Bulk density increases with compaction and tends to increase with depth.

$$\text{Bulk density} = \frac{\text{mass}}{\text{unsettled apparent volume}}$$

- **Tapped density**: The tapped density is an increased bulk density attained after mechanically tapping a container containing the powder sample. The tapped density is obtained by mechanically tapping a graduated measuring cylinder or vessel containing the powder sample.

$$\text{Tapped density} = \frac{\text{mass}}{\text{final tapped volume}}$$

- **Compressibility index**: The volume of powder from bulk density and tapped density testing were used for calculate compressibility index follow equation.

$$\text{Compressibility index} = \frac{\text{unsettled apparent volume} - \text{final tapped volume}}{\text{unsettled apparent volume}}$$

- **Angle of repose**: The angle of repose of a granular material is the steepest angle of descent or dip relative to the horizontal plane to which a material can be piled without slumping. The angle of repose can range from 0° to 90°.

$$\tan\theta = \frac{\text{Height}}{\text{Radius.}}$$

- **Hausner's ratio:** The Hausner's ratio is a number that is correlated to the flow ability of a powder or granular material.

$$\text{Hausner's ratio} = \frac{\text{unsettled apparent volume}}{\text{final tapped volume}}$$

Post Compression parameters

- **Hardness test:** The prepared tablets were subjected to hardness test. Hardness indicates the ability of tablet to without mechanical shocks while handling. The hardness of tablets was determined using Monsanto hardness tester and expressed in kg/cm2. Five tablets can be randomly picked from each batch and the hardness of the tablets can determined. The mean and standard deviation values can be calculated for each batch.
- **Thickness test:** The tablet dimensions can be measured using a calibrated dial calliper. Five tablets of each batch can be picked randomly and its thickness was measured. Tablet thickness should be controlled within ±5% variation of a standard value.
- **Friability Test:** The friability was determined using Roche friabilator and expressed in percentage (%). Ten tablets have to be initially weighed and placed into the friabilator. The friabilator should be operated at 25 rpm for 4 minutes or run up to 100 revolutions, and then the tablets were weighed again. The loss in weight due to abrasion or fracture is the measure of tablet friability.

$$F = \frac{W(final) - W(initial)}{W(final)} X100$$

% friability of less than 1% is considered acceptable (Subramanyam CVS. Textbook of physical pharmaceutics, 2001).

- **Weight Variation Test:** 20 tablets were taken and their weight was determined individually and collectively on an electronic balance and the mean weight taken. Each tablet can weighed individually and the standard deviation in weight can calculated for each batch. The average weight of one tablet was determined from the collective weight.

$$\% \text{ of weight variation} = \frac{\text{individual wt.} - \text{Average wt.}}{\text{Average wt.}} X100$$

- **Wetting Time:** This was carried out to measure the time required for the complete wetting of tablet formulations. A piece of tissue paper folded twice was placed in small petridish containing 6ml of purified water. A tablet having small amount of Rosaline dye powder on the upper surface of the tablet was recorded as the wetting time. The same procedure without Rosaline dye powder was followed for determining the water absorption ratio R and it was determined using the following equation;

$$R = \frac{Wa - Wb}{Wb} X100$$

Where, Wb & Wa were the weights of the tablets before and after.

- **Disintegration test:** introduced one tablet into each tube. The disc Wa added to each tube. The assembly is suspended in beaker containing buffer and operated the apparatus for 3 minutes. Water is used as medium at temperature of 26^0C.
- **Uniformity of dispersion:** this test is applicable only for dispersible tablets. Placed one tablet in 100ml of water and stirred gently until completely dispersed. A smooth dispersion was obtained which passes through a sieve screen with a nominal mesh aperture of 710 μm (sieve no. 22).
- **Drug content uniformity:** percent drug content uniformity can be determined spectrometrically**.**
- **In- vitro dissolution study :** this study was carried out on USP XXIII tablet dissolution apparatus using ph 6.8 buffer 900ml at 100 rpm for 20 min at 37^0C, employing paddle method. Single tablet from each formulation can use for the studies. A 1ml sample from dissolution medium was withdrawn at different time intervals and diluted approximately so as to get a concentration of 10μg/ml. The withdrawn sample is replaced by same amount of fresh dissolution medium to maintain sink conditions. The absorbance was measured on UV spectrophotometer.
- **Scanning electron microscopy:** SEM has been used to determine particle size distribution, surface topography, texture and to examine the morphology of fractured or sectioned surfaces. The SEM is most commonly used for generating three dimensional surface relief images derived from secondary electrons. The examination of the surface of polymeric drug delivery system can provide important information about the porosity and microstructure of the device.
- **Stability study:** the purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light, and labels recommended storage conditions and shelf-lives to be

  ICH specifies the length of study and storage conditions:-

  Long term testing 250±20c/75% RH±5% for 6 months.

  Accelerated testing 400c±20c/75% RH±5% for 6 months.

CONCLUSION

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. The introduction of fast dissolving dosage

forms has solved some of the problems encountered in administration of drugs to ODTs are to maximize the porous structure of the tablet matrix and incorporate super disintegrating agents in optimum concentration so as to achieve rapid disintegration and instantaneous dissolution of the tablet along with good taste masking properties and excellent mechanical strength.

REFERENCES

1. International Journal of PharmTech Research CODEN (USA): IJPRIF ISSN: 0974-4304 Vol.1, No.4, pp 1079-1091, Oct-Dec 2009.
2. Dr.Avani F. Amin Emerging Trends In the Development Of Orally Disintegrating Tablet Technology pharmainfo.net 01/26/2006.
3. Yajaman S, Ketousetuo K, Bandyopadhyay A, Buccal bioadhesive drug delivery-a promising option for orally efficient drugs Buccal Adhesive Research Laboratory, Division of Pharmaceutics, Department of Pharmaceutical Technology, Jadavpur University, Kolkata 700032, India, April 26 2006.
4. Acosta C., Tabare R. and Ouali A. US patent, 5: 807, 1998.
5. Bandari S, Mittapalli RK, Gannu R, Rao YM (2008). Orodispersible tablets: An overview. Asian J Pharm, 2(1): 2- 11.
6. O'Connor R, Schwartz J: "Extrusion and spheronization technology. In Pharmaceutical Pelletization Technology", Marcel Dekker Inc., New York, 1989; 37: 187.
7. Agarwal V, Kothari BH, Moe DV, Khankari RK. Drug delivery: Fast-dissolve systems. In: Swarbrick J, Encyclopedia of pharmaceutical technology. New York, USA: Informa Healthcare Inc, 2006; 1104 –1114.
8. Fini A, Valentina B, Gian CC, Celestino R, Carlos A, Fonseca de M (2008). Fast dispersible/slow releasing ibuprofen tablets. Eur. J. Pharm. Biopharm, 69: 335–341.
9. Masters K. Spray Drying Fundamentals: Process stages and Layouts. In: Spray Drying Handbook. USA: Longman Scientific and Technical, New York, 5th ed, 1991: 23–64.
10. Hughes L (2005). Selecting the right ion exchange resin. Pharma Quality, 1: 54–56.
11. Jeong SH, Park K (2008). Development of sustained release fast-disintegrating tablets using various polymercoated ion-exchange resin complexes. Int. J. Pharm, 353: 195–204.
12. Prasad N, Straus D, Reichart G (1999). Cyclodextrin flavor delivery systems. US Patent, 6,287,603.
13. Venkatesh DP, Geetha Rao CG (2008). Formulation of taste masked orodispersible tablets of ambroxol hydrochloride. Asian J. Pharm, 2: 261-264.

14. Ohwavworhu F., Adelakun T (2004). Phosphoric acidmediated depolymerization and decrystallization of α- Cellulose obtained from Corn Cob: Preparation of Low Crystallinity Cellulose and some Physicochemical Properties. Tropical J. Pharm. Res, 4(2): 509-516.
15. Venkateswarlu B.S, Chandira B.S , Talele A , Debjit B, Chiranjib (2010). Formulation and evaluation of fast dissolving tablets of Carvidilol. The Pharma Research (T. Ph.Res.) 3: 203-220.
16. Dobetti L. Fast-melting tablets: Development and technologies. Pharm. Technol. Drug Deliv, 2001; 44-45.
17. Virely P, Yarwood R (1990). Zydis – a novel, fast dissolving dosage form. Manuf. Chem. 36 37.
18. Seager H (1998). Drug delivery product and the Zydis fast-dissolving dosage form. J. Pharm. Pharmacol, 50: 375-382.
19. Shoukri R.A , Ahmed I.S , Shamma R.N (2009). In vitro and in vivo evaluation of nimesulide lyophilized orally disintegrating tablets. European Journal of Pharmaceutics and Biopharmaceutics, 73: 162–171
20. Bhoyar P.K , Baheti J.R, Naranje P.A, Bhandarkar S, Muraleedharan R, Deotale B.M (2012). Formulation design and optimization of taste masked rapid disintegrating tablets using freeze drying method. World J of Pharmaceutical Research, 1(2): 340-352
21. ishra DN, Bimodal M, Singh SK, Vijaya Kumar SG (2006) Spray dried excipient base: a novel technique for the formulation of orally disintegratinuhg tablets. Chem Pharm Bull, 54(1): 99-102.
22. Masareddy R, Kokate A, Shah V (2011). Development of orodispersible tizanidine HCl tablets using spray dried coprocessed exipient bases. Indian J Pharm Sci, 73: 392-6.
23. Koizumi K, Watanabe Y, Morita K, Utoguchi N, Matsumoto M (1997). New method of preparing highporosity rapidly saliva soluble compressed tablets using mannitol with camphor, a subliming material. Int. J of Pharm, 152(1): 127-31.
24. Kumar R., Patil M.B., Patil S.R., Paschpura M.S (2009). Development & characterization of melt-in-tablets of Haloperidol by sublimation technique. Int. J. of Pharmacy & P'ceutical Sci, 1(1): 65-73.
25. Shukla D, Chakraborty S, Singh S, Mishra B (2009). Mouth Dissolving Tablets I: An Overview of Formulation Technology. Sci Pharm, 77: 309–26.
26. Bhaskaran S, Narmada GV (2002). Rapid dissolving tablets a novel dosage form. Indian Pharmacist, 1: 9–12.

27. Mansing G. Patil, Suhas M. Kakade and Sandhya G. Pathade (2011). Formulation and evaluation oforally disintegrating tablet containing tramadol hydrochloride by mass extrusion technique. Journal of Applied Pharmaceutical Science, 01(06): 178-181.
28. Bhowmik D, Chiranjib B, Pankaj K, Chandira RM (2009). Fast Dissolving Tablet: An Overview. Journal of Chemical and Pharmaceutical Research, 1(1): 163-177.
29. Yoshio K, Masazumi K, Shuichi A, Hiroaki N (2005). Evaluation of rapidly disintegrating tablets manufactured by phase transition of sugar alcohols. J. Control. Release, 105(1- 2): 16-22.
30. Mishra DN, Bimodal M, Singh SK, Vijaya Kumar SG (2006). Spray dried excipient base: a novel technique for the formulation of orally disintegrating tablets. Chem Pharm Bull, 54(1): 99-102.
31. Rasheed SH, Arief M, Gajavalli SR, Vani PS, Rao KS, Kumar S, Rao T, Hussain SS (2011). A Comparison of different superdisintegrants in designing of fast dissolving tablets of salbutamol sulphate. Research Journal of Pharmaceutical, Biological and Chemical Sciences, 2(2): 155-163.
32. Mukesh, Ratnaparkhi P, Mohant GP, Upadhyay L (2009). Fast Dissolving Tablet. Journal of Pharmacy Research, 2(1): 5-12.