ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

A Recent Approach on Fast Dissolving Tablets

Anil Kumar[1], Vikas Kaushik[1], Kuldeep Malodia[1], Sunil Kumar[1] and Pankaj Rakha[2]

[1]Lord Shiva College of Pharmacy, Sirsa, India.
[2] Shri Baba Mast Nath Institute of Pharmaceutical Sciences and Research, Asthal Bohar, Rohtak.

ABSTRACT

The novel concept of fast dissolving drug delivery system emerged from the desire to provide patient with conventional mean of taking their medication. Oral routes of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, self-medication, pain avoidance and most importantly the patient compliance. The most popular solid dosage forms are being tablets and capsules. One important drawback of this dosage forms for some patients, is the difficulty to swallow. Fast-dissolving drug delivery systems offer a solution for these problems. Such FDTs can be administered anywhere and anytime, without the need of water and are thus quite suitable for children, elderly and mentally disabled patients.The excipients that are currently used as well as those that are expected to be used for the future development of improved FDTs are described in the review paper.

Keywords: Fast Dissolving Tablets, Drug Delivery System.

Corresponding author

ISSN: 0975-8585

INTRODUCTION

Oral administration is the most popular route for systemic effect due to its ease of ingestion, pain avoidance, versatility and most importantly, patient compliance [1]. Convenience of administration and patient compliance are gaining significant importance in the design of oral dosage forms. The Oral route of administration is considered as the most widely accepted route, but the most evident drawback of the commonly used oral dosage forms like tablets and capsules is difficulty in swallowing. Dysphagia this problem is most common for psdiatric and geriatric and bedridden patients. Recently more stress is laid down on the development of organoleptically elegant and patient friendly drug delivery system for pediatric and geriatric patients [2]. Thus, a new drug delivery system known as Fast Dissolving/Disintegrating (FDDDS) / melt-in-mouth tablets gaining importance by designing to be absorbed through the buccal and esophageal mucosa as the saliva passés into the stomach. In the latter case, the bioavailability of a drug from Fast Dissolving formulations may be even greater than that observed in conventional oral dosage forms [3].

Advantages of fast dissolving tablets [4-6]

- Ease of Administration to the patient who cannot swallow the solid dosage forms especially elderly, stroke victims, bedridden patients, patient affected by renal failure and patient who refuse to swallow such as pediatric, geriatric & psychiatric patients.
- No need of water to swallow the dosage form, which is highly convenient feature for patients who are traveling and do not have immediate access to water.
- Rapid dissolution and absorption of the drug, which will produce quick onset of action.
- Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases bioavailability of drug is increased.
- Pregastric absorption can result in improved bioavailability and improve clinical performance through a reduction of side effects.

Disadvantages of fast dissolving tablets

- Drugs with relatively larger doses are difficult to formulate in to FDTs [7]. Fast dissolving tablet is hygroscopic in nature so must be kept in dry place and requires special packaging for proper stability & safety of the products [8].
- Containdication in patients who concurrently take anticholinergic medicine, sometime it possesses unplesant mouth feeling and insufficient mechanical strength [9-10].

Suitable Drug Candidates for fast dissolving tablets

There are some examples of different category of drugs molecule that are suitable drug candidate for prepration of FDTs as shown in Table 1 [11-14]

ISSN: 0975-8585

Table 1: List of some suitable drugs for fast dissolving tablets

Sr No.	Name of category	Example
1	Anti emetics	Metoclopramide, Ondansetron, Metopmazine
2	Analgesic and anti inflammatory agent	Aloxiprin, Etodolac, Meclofenamic acid, Sulindac, Naproxen
3	Anti -bacterial agents	Ciprofloxacin HCL, Clarithromycin
4	Anti-diabetics	Acetohexamide, Chlorpropamide, Gliclazide
5	Anti-epileptics	Beclamide, Ethotoin, Methoin, Primidone
6	Anti- hypertensive agent	Amlodipine, Carvedilol, Isradipine,Reserpine
7	Anti-malarials	Amodiaquine, Chloroquine, Quinine sulphate
8	Anti-neoplastic agents and immunosupressants	Aminoglutethimide, Amsacrine, Busulphan, Etoposide, Lomustine
9	Anti-thyroid agents	Carbimazole, Propylthiouracil
10	Diuretics	Acetozolamideamiloride, Bendrofluazide, Cholorothiazide, Metolazone
11	Enzyme	All the Enzyme
12	Gastro-intestial agents	Bisacodyl, Cimetidine, Cisapride, Domperidone, Famotidine, Loperamide, Sulphasalazine
13	Histamine H_2 receptor antagonist	Acrivastine, Astemizole, Cyclizine, Dimenhydrinate, Loratidine
14	Opiod analgesic	Codien, Dextropropyoxyphene, Diaminophene
15	Stimulants	Amphetamine, Dexamphetamine, Dexfenfluramine

Manufactureing technique for FDTs

Direct compression

Direct compression represents the simplest and most cost effective tablet manufacturing technique. FDTs can be prepared by using this technique because of the good availability of improved excipients especially super-disintegrants and sugar based excipients [15]. The technique of direct compression is schematically represented in Fig. 1

Super-disintegrants

The rate of disintegration gets affected by the addition of superdisintegrants and hence the dissolution. Other ingredients like water-soluble excipients and effervescent agents also increase the disintegration [16-17].

Sugar based excipients

The sugar based excipients which are commonly used are especially bulking agents (like dextrose, fructose, lactilol, maltilol, maltose, mannitol, sorbitol, starch hydrolysate, polydextrose and xylitol) which display high aqueous solubility and sweetness, and hence impart taste masking property and provide pleasing mouth feel.

ISSN: 0975-8585

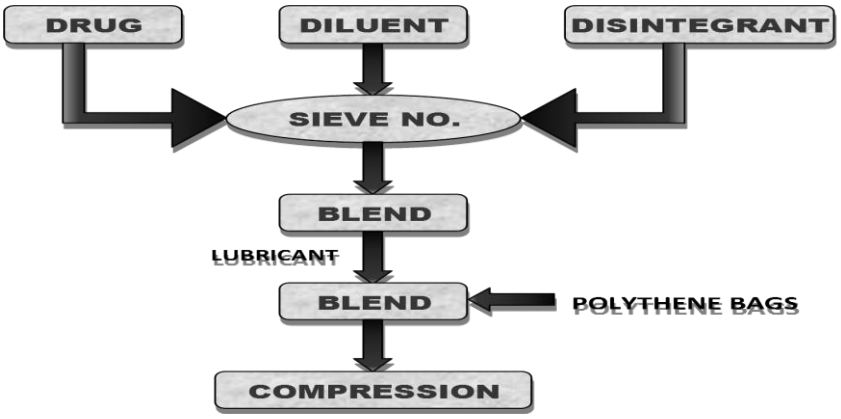

Fig. 1 Steps involved in direct compression

Freeze drying or lyoplilization

It is one of the first generation techniques for preparing FDTs, in which sublimation of water takes place from the product after freezing. The formulations show enhanced dissolution characteristics due to the appearance of glossy amorphous structure to bulking agents and sometimes to drug [18]. The advantage of using freeze-drying process is that pharmaceutical substances can be processed at non elevated temperature, thereby eliminating adverse thermal effects. High cost of equipment and processing limits the use of this process [19]. Other disadvantages include lack of resistance necessary for standard blister packs of the final dosage forms [20].

Tablet molding

There are two types of molding process 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). Below Air-drying is done to remove the solvent [21-22]. The tablets manufactured so formed are less compact than compressed tablets and posses a porous structure that hastens dissolution. In the heat molding process a suspension is prepared that contains a drug, agar and sugar (e.g. mannitol or lactose). This suspension is poured in the blister packaging wells, and then agar is solidified at the room temperature to form a jelly and dried at 30 ^{0}C under vacum. The main concern about these molded tablets is their mechanical strength, which can be achieved by using binding agents [23].

Cotton Candy Process

A matrix known as 'floss', with a combination of excipients, either alone or with drugs is prepared by using shear form technology.The floss is a fibrous material, simillar to cotton-candy fibers, commonly made of saccharides such as sucrose, dextrose, lactose and fructose at temperatures ranging between 180–266 °F [24-25]. However, other polysaccharides such as polymaltodextrins and poly-dextrose can be transformed into fibers at 30–40% lower

temperature than sucrose. Due to this modification thermolabile drugs can be safely incorporated into the formulation [26]. This process results in a highly porous product and offer very pleasant mouth feel due to fast solubilization of sugars in presence of saliva. The manufacturing process can be divided into four steps are [27]:

- Floss blend
- Floss processing
- Floss chopping and conditioning
- Blending and compression

Sprays-drying

Spray-Drying is used for the preparation of FDTs. The formulations contained hydrolyzed and non hydrolyzed gelatin as a supporting agent for the matrix, mannitol as a bulking agent and sodium starch glycolate or croscarmellose as a disintegrant. By adding an acid (e.g., citric acid) or an alkali (e.g., sodium bicarbonate) disintegration and dissolution were further enhanced. The porous powder was obtained by spray drying the above suspension which was compressed into tablets. Tablets manufactured by this method shows disintegration time < 20 sec in an aqueous medium [28].

Sublimatio

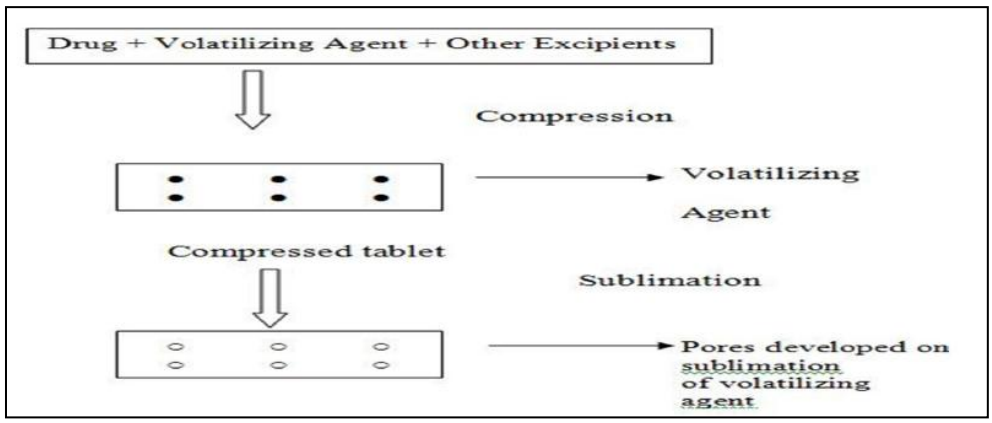

Fig. 2 Steps involve in sublimation

Sublimation is the technique which has been used to produce FDTs with high porosity, when volatile ingredients are compressed along with other excipients into tablets, a porous matrix is formed which are finally subjected to a process of sublimation. For this purpose inert solid ingredients with high volatility (e.g., ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, hexamethylene tetramine, naphthalene, urea and urethene) have been used. Solvents such as cyclohexane and benzene were also suggested for generating the porosity in the matrix [29-30]. A method using water as a pore-forming material. **Fig. 2** Shows the steps of Sublimation Process.

Mass-extrusion

This technology involves softening of the active blend using the solvent mixture of water soluble polyethylene glycol and methanol. This softened mass is extruded through the extruder or syringe and a cylindrical shaped extrude is obtained which are finally cut into even segments using heated blade to form tablets. Granules of bitter drugs can be coated Using this method to mask their taste [31].

Patented techniques for peparation of FDTs

Nanonization or Nanocrystal technology

Recently developed Nanomelt 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 into FDTs. This technique is mainly advantageous for poor water soluble drugs and also for a wide range of doses (up to 200 mg of drug per unit) [32].

Fast dissolving films

It is a newer developing front in FDDDS that provides a very convenient means of taking medications and supplements. In this technique, water soluble film forming polymer (Pullulan, CMC, HPMC, HPC, PVP etc.), drug and other taste masking ingredients are dissolved in non-aqueous solvent to prepare non-aqueous solution, which on evaporation of solvent forms a film. Resin adsorbate or coated micro particles of the drug can be incorporated into the film if the drug is bitter. This film when placed in mouth, melts or dissolves rapidly and release the drug in solution or suspension form. This system forms the thin films of size less than 2 X 2 inches which dissolves within 5 sec with instant drug delivery and flavoured taste [33].

Zydis technology

Zydis formulation is a unique freeze dried tablet in which drug is physically entrapped or dissolved within the matrix of fast-dissolving carrier material. When zydis units are put into the mouth, the freeze-dried structure disintegrates instantaneously and does not require water to aid swallowing. The zydis matrix is composed of many materials designed to achieve a number of objectives. To impart strength and resilience during handling, polymers such as gelatin, dextran or alginates are incorporated. These forms a glossy amorphous structure, which imparts strength. Zydis products are packed in blister packs to protect the formulation from moisture in the environment [34-35].

Orasolv technology

It is CIMA lab's first mouth dissolving formulation which involves taste masking of active drug. Effervescent disintegrating agent is also used. Conventional blenders and tablet

equipments are used for preparation of tablets. Less force of compaction is used for manufacturing so as to obtain soft and quickly disintegrating tablets. There is a limitation of this technology that soft and fragile tablets are formed, therefore needed to be packed in specially designed pick and place package system [39].

Wow Tab technology

WOW means "Without Water". In this process, combination of low mouldability saccharides and high mouldability saccharides is used to obtain a rapidly melting strong tablet. The active ingredient is mixed with a low mouldability saccharide and granulated with a high mouldability saccharide and compressed into tablet [40].

Lyoc

Oil in water emulsion is prepared and placed directly into blister pack followed by freeze drying. Nonhomogeneity during freeze drying is avoided by incorporating inert filler to increase the viscosity finally the sedimentation. High proportion of filler reduces porosity of tablets due to which disintegration is lowered [42].

Flash Tab technology

This technology includes granulation of excipients by wet or dry granulation method and followed by compressing into tablets. Excipients used in this technology are of two types. Disintegrating agents includes reticulated polyvinylpyrollidone or carboxymethyl cellulose. Swelling agents include Carboxymethylcellulose, starch, microcrystalline cellulose, carboxy methylated starch, etc. These tablets have satisfactory physical resistance. Disintegration time is within 1 min [43-44].

Durasolv technology

The tablets made by this technology consist of a drug, fillers and a lubricant. Tablets are prepared by using conventional tableting equipment and have good rigidity. These can be packaged into conventional packaging system like blisters. Durasolv is an appropriate technology for products requiring low amounts of active ingredients [45].

Oraquick technology

It utilizes taste masking microsphere technology called as micromask, which provides superior mouthfeel, significant mechanical strength, and quick disintegration of the product [32]. This process involves preparation of microparticles in the form of matrix that protects drug, which can be compressed with sufficient mechanical strength [47]. Low heat of production in this process makes it appropriate for heat sensitive drugs. Oraquick product dissolves within few seconds [48].

Ziplets/Advatabs

It utilizes water soluble ingredient combined with one or more effective disintegrants to produce FDTs with improved mechanical strength and optimal disintegration time at low compression force [26]. This technology handles high drug loading and coated drug partials and does not require special packaging, so they can be packed in push through blisters or bottles [38].

Flash dose

Flash dose tablets consist of self-binding shearform matrix termed as "floss". Shearform matrices are prepared by flash heat processing [29].
Some of examples of Patented FDTs are described in Table 2 with their Innovator name, active ingredients and advantages.

Table: 2 Example of Patented FDTs

Patented Technology	Technique Employed	Innovator Company	Active Ingredient & Brand Names	Advantages
Zydis	Lyophillization	R.P. Scherer, Corp.	Loratidine (Claritin, Reditab Pharmaceuticals)	Highly porous in nature, faster dissolution rate of tablets than conventional
Quicksolv	Lyophillization	Janssen Pharma	Cisapride monohydrate (Propulsid Quicksolv)	Short disintegration time, good mouthfeel property of tablets
Lyoc	Lyophillization	Farmalyoc	Phloroglucinol Hydrate (Spasfon Lyoc)	Accommodate high dose,disintegrates rapidly within a matter of seconds
Orasolv	Effervescent disintegrant compression	CIMA Labs, Inc.	Paracetamol (Tempra)	Unique taste masking, fast dissolution rate of tablets
Durasolv	Molding	CIMA Labs,	Hyoscyamine Sulfate(NuLev)	Good rigidity
Patented Technology	Technique Employed	Innovator Company	Active Ingredient & Brand Names	Advantages
Wowtab	Compression molded tablets	Yamanouchi Pharma	Famotidine (Gaster D)	Adequate dissolution rate and hardness in tablets
Flashdose	Cotton Candy Process	Fuisz Technology Ltd	Tramadol Hcl (Relivia Flash dose)	Highly porous in nature, and tablets shows pleasant mouthfeel property
Flashtab	Effervescent Disintegrant	Prographarm Group	Ibuprofen (Nurofen FlashTab)	Conventional tableting technology and faster dissolution rate

Ziplets	Molding	Eurand International	Ibuprofen (Cibalgina DueFast)	Sufficient mechanical strength
Oraquick	Micromask taste Masking	KV Pharm. Co., Inc	Hyoscyamine Sulfate ODT	Significant friability is present in tablets
Advatab	Microcaps	Eurand International	AdvaTab cetrizine,	High drug loading capacity is present in formulation

Superdisintegrants Used in FDTs

The basic approach in development of FDTs is use of disintegrant. Disintegrant play an important role in the disintegration and dissolution of FDTs. It is essential to choose a suitable disintegrant, in an optimum concentration so as to ensure quick disintegration and high dissolution rates. Superdisintegrant provide quick disintegration due to combined effect of swelling and water absorption by the formulation. Due to swelling of superdisintegrant, the wetted surface of the carrier increases this promotes the wetability and dispersibility of the system, thus enhancing the disintegration and dissolution. Superdisintegrante's are selected according to critical concentration of disintegrant. Below this concentration, the tablet disintegration time is inversely proportional to the concentration of the superdisintegrant, whereas if concentration of super disintegrant is above critical concentration, the disintegration time remains almost constant or even increases. Common disintegrants used in this formulation are croscarmellose sodium (Vivasol, Ac-Di-Sol), crospovidone (Polyplasdone), carmellose (NS-300), sodium starch glycolate etc [49]. Selection of Superdisintegrants primarily affect the rate of disintegration, but when used at high levels they can also affect mouth feel, tablet hardness and friability. Some of the superdisintegrants with mechanism of action are shown below in Table 3 [50-52]

Table 3: Superdisintegrants with mechanism of action

Superdisintegrants	Example	Mechanism of action	Comment
L-HPC	Low hydroxyl propyl cellulose	Both swelling and wicking	Promote disintegration
Croscarmellose Ac-Di-Sol	Crosslinked Cellulose	Swells 4-8 folds in < 10 seconds. Swelling	Swells in two Dimensions, Direct compression
Crospovidone Kollidon Polyplasdone	Crosslinked PVP	Swells very little	Water insoluble and spongy in nature
Sodium Alginate	Sodium salt of Alginic acid	Swelling	By wicking and swelling disintegrate the tablets rapidly
Sodium starch glycolate	Crosslinked Starch	-Swells 7-12 folds in < 30 seconds	Swells in three Dimensions
Acrylic acid	Poly		Capillary and wicking

Derivatives	(Acrylic acid) Superporous	Wicking action hydrogel	increase the disintegration
Alginic acid	Crosslinked alginic acid	Rapid swelling in aqueous medium	Promote disintegration
Calcium silicate		By Wicking	Highly porous
Soy polysaccharides	Natural Disintegrant	Swelling	EMCOSOY
Ion exchange Resin	Resins	By ion exchange mechanism	Amberlite (IPR 88)
Effervescent Mixture	Citric acid, tartaric acid and sodium bicarbonate	Effervescence	Promote disintegration

CONCLUSION

Fast dissolving tablets are formulated to improve patient compliance and convenience. They are a very good alternative for drug delivery to geriatric and pediatric patients. As a result of the variety of technologies for its formulation, several commercial products are available in the market. Thus, looking at the advances and advantages in this therapeutic approach, the pharmaceutical formulator need not restrict his choice in the development of conventional dosage forms but should also try to develop these fast dissolving drug delivery systems.

REFRENCES

[1] Siddiqui N, Garg G and Sharma P. Inter J Pharmaceu Sci Review and Res 2010; 4(20): 87-96.
[2] Shukla D, Chakraborty S and Mishra B. Scientia Pharmaceutica 2009; 77: 327-341.
[3] Council of Europe. European Pharmacopoeia 7thed.Vol.1.2008.p 749-750.
[4] Gavaskar B, Vijaya S, Sharan G, and Rao YM. Inter J Pharmaceu Sci Review and Res 2010; 1(8): 14-28.
[5] Manivannan R. Int J Pharm Res Development 2009; 1(10): 946-957.
[6] Swamivelmanickam M, Manvalan R and Valliappan K. Int J Pharmaceu Sci Review and Re 2010; 1 (1):43-55.
[7] Dutta S and Kumar P. Int J Drug Formulation and Res 2011; 2(1): 45-51.
[8] Kumari S, Vish S and Yadav RK. J Pharm Res 2010; 3(6): 1444-1449.
[9] Allen LV and Wang B. US Patent 5,595,761.1997.
[10] Chandan S, Varun D, Ashish G and Ajay A. Int J of Pharm sci 2010; 1(5): 250-256.
[11] Kumaresan C. Orally disintegrating tablet (Internet) 2008; 65. Available from Pharmainfo.net.
[12] Hirani JJ, Rathod DA and Vadalia KR. Tropical J Pharma Res 2009; 8(2): 161-172.
[13] Slowson M, Slowson S. Pharma Times 1985; 51: 90-96.
[14] Chang RK, Guo X, Burnside BA and Couch RA. Pharma Tech 2000; 24: 52-58.
[15] Lies MC, Atherton AD, Copping NM. US 5,188,825.1993.
[16] Sugihara M, Hidaka M, Saiton A. Jpn J Hosp Pharm 1986; 12: 322-328.
[17] Gupta A, Mishra AK, Gupta V and Singh AK. Int J Pharm Biol Arch 2010; 1(1): 1-10.

[18] Bhaskaran S, Narmada GV. Indian Pharmacist 2002; 1: 9-12.
[19] Mishra DN, Bimodal M, Singh SK and Vijaya SG. Chem Pharma Bull 2006; 54(1): 99-102.
[20] Myers GL, Battist GE and Fuisz R C.US Patent 5,567,439.1996.
[21] Myers GL,Battist GE,Fuisz RC. US Patent 5,871,781.1999.
[22] Kaur T, Gill B, Kumar S and Gupta GD. Int J Current Pharma Research 2011; 3(1):1-7.
[23] Gole DJ and Levinson RS. US Patent 5,215,756.1993.
[24] Sreenivas SA, Dandagi PM, Gaud AP and Bhagwati ST. Indian J Pharm Edu 2005; 39(4):177.
[25] Ratnaparkhi M, Mohanta GP and Upadhyay L. J Pharm Res 2009; 2(1): 5-12.
[26] Bhandari D, Agarwal A and Gupta H. Recent trends- Fast dissolving tablets (internet) 2008; 6(6). Available from: www. Pharmainfonet.
[27] Kuno Y and Kojima M. J Controlled Released 2005; 105(2): 16-22.
[28] Saroha K, Mathur P, Verma S and Kumar A. Der Pharmacia Sinica 2010; 1(1): 179-187.
[29] Sharma S and Gupta GD. Pharma buzz 2009; 4(1): 30-41.
[30] Gannu R and Mittapali R K. US Patent4, 616, 047.1986.
[31] Gole DJ, Levinson RS, Carbone J and Davies DJ. US 5,215,756.1993.
[32] Cousin G, Bruna E, Gendrot E. US Patent 5, 464, 632. 1995.
[33] Wehling F and Schuehle S. US Patent 5,503,846.1996.
[34] Wehling F, Schuele S and Madamala N. US Patent 5,178,878.1993.
[35] Amborn J and Tiger V. US Patent 6,311,462.2001.
[36] Khankari RK, Hontz J, Chastain SJ and Katzner L. US Patent 6,024,981.2000.
[37] Mizumoto T, Masuda Y and Fukai M. US Patent 5,576,041.1996.
[38] Mizumoto T and Nyshadham JR. US Patent 6,589,554.2003.
[39] Pahwa R, Piplani M and Kaushik D. Scholars Research Library 2010; 2(2): 35-58.
[40] Kumar M, Mattapalli RK, Gannu R and Rao YM. Asian J Pharm 2008; 2(1): 2-11.
[41] Panigrahi R and Bahera S. Web Med Central 2010; 1(9): 1-15.
[42] Bhowmik D, Krishankanth CB, and Chandira RM. J Chemical and Pharmaceutical Research 2009; 1(1): 163-177.
[43] Bagul SU. Current status of tablet disintegrants: A review (Internet). 2006. Available from www. Pharmainfonet.
[44] Rowe RC, Sheskey PJ and Owen SC. Handbook of Pharmaceutical Excepients.5th edition. Published by Pharmaceutical Press. Great Britain, 2006, pp.211-218,430-432,438-440,641-643,701-703,731-733,767-769.
[45] The Merck Index. 14thEdition.2006. Merck Research laboratories, USA, pp.1006.
[46] United States Pharmacopoeia/National Formulary. Volume 3. Twenty-Sixth Edition. 2008. Port-city Press, Baltimore, USA; pp.2607-2611.
[47] Martindale. Volume 1. Thirty-Fifth Edition.2007. Pharmaceutical Press, London; p-68.
[48] Indian Pharmacopoeia. Vol-1. Sixth-Edition. The Indian Pharmacopoeia Commission, Ghaziabad; 2010, pp-161.
[49] Indian Phamacopoeia Volume 3.Sixth-Edition. The Indian Pharmacopoeia Commission, Ghaziabad; 2010, pp-1646.
[50] Joshi A and Kumar G. Drug Development and Industrial Pharmacy 2011; 37(5): 1-5.
[51] Qbaidat A A and Rana M. Acta Pharmaceutica 2011; 61(1):83-91.