JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

"Review Study on Fast Dissolving Tablets Formulation of Antiemetic Medication"

Mr. Devendra S Lodhi[1]* Mr.Ganesh Prasad Patel[2]* Ms.Khushi Chouksey[2*]Dr.Pradeep Golani[1]*Dr.Megha Verma [1]*Dr. Aakash Singh Panwar 3***Mr.Sanjay Nagdev[1]**

1, 1 Gyan Ganga Institute of Technology & Sciences, Bargi hills Jabalpur M.P-482003 India

2, 2 Sagar Institute of Pharmacy & Technology (Siptec) Opposite International Airport Jaipur Road Gandhi Nagar Bhopal Madhya Pradesh India-462036.

3, 3 Institute of Pharmaceutical Sciences, SAGE University Kailod-Kartal Indore by Road Indore (MP) 452027

***Corresponding Author: Corresponding author. Devendra Singh Lodhi**

Email-devendralodhi86@gmail.com, Mo: 9907408992

Gyan Ganga Institute of Technology & Sciences, Bargi hills Jabalpur M.P-482003 India

ABSTRACT: - Fast dissolving tablets are those that, when placed on the tongue, instantly disintegrate/dissolve/disperse the medicine, which dissolves or disperses in the saliva. Their unique features, such as the ability to administer them without the need of water, anyplace, and at any time, make them ideal for geriatric and pediatric patients.Dolasetron mesylate is a phenothiazine antipsychotic that is primarily used to treat nausea, vomiting, and vertigo. It is more prone to develop extra pyramidal problems than chlorpromazine. An oral fast-dissolving or oral fast-dispersing dosage form is a solid dosage form that dissolves or disintegrates quickly in the oral cavity, resulting in a solution or suspension without the requirement for water administration. It is made of hydrophilic polymers that dissolve/disintegrate swiftly in the mouth within a few seconds after administration without water.

KEY WORDS:- Fast dissolving, Antiemetic drug, Dolasetron mesylate, Hydrophilic polymers,

INTRODUCTION:- The primary demand and need of today is the formulation of medications into a presentable form. The dosage form is a type of medication delivery method that is used to apply the medicine to a living body. There are several dosage forms available, including pills, syrups, suspensions, suppositories, injections, transdermal patches, and patches with various drug delivery systems. These traditional and current dose formulations both have merits and downsides. As a result, in the present situation, the pharmacist faces a

significant barrier in developing an optimum medicine delivery system. To accomplish the intended effect, the medicine should be delivered to its site of action at a pace and concentration that maximizes therapeutic impact while minimizing side effects. A comprehensive examination of the physicochemical principles that control a specific formulation of a medicine should be resorted to in order to establish an appropriate dosage form. [1]. Oral methods of medication delivery are widely accepted, accounting for 50-60% of total dose forms. Because of the convenience of administration, proper dose, self-medication, pain avoidance, and, most importantly, patient compliance, solid dosage forms are popular. Tablets and capsules are the most often used solid dose forms; nonetheless, one significant disadvantage of these dosage forms for some patients is their difficulty in swallowing. Drinking water is essential for the proper ingestion of oral dose forms. People frequently have difficulty swallowing conventional dose forms such as tablets when water is not available, in the event of motion sickness (kinetosis), and in the case of abrupt episodes of coughing during the common cold, allergic condition, and bronchitis. As a result, tablets that dissolve or disintegrate quickly in the oral cavity have received a lot of attention. [2] Swallowing difficulties are frequent in senior patients due to choking fears, hand tremors, dysphasia, and in young people due to undeveloped muscular and neurological systems, as well as in schizophrenia patients, resulting in poor patient compliance. Approximately one-third of the population (mostly children and the elderly) has swallowing problems, resulting in poor adherence to oral tablet medication therapy and lower overall therapeutic efficacy. As a result, tablets that dissolve or disintegrate quickly in the oral cavity have received a lot of attention. [3]

The United States Food and Drug Administration (USFDA) defines a fast dissolving tablet (FDT) as "a solid dosage form containing a medical drug or active component that disintegrates rapidly, generally within seconds, when put on the tongue." [4]

Fast dissolving drug delivery systems were first developed in the late 1970s as an alternative to conventional dosage forms for the pediatric and geriatric patient. These tablets are designed to dissolve or disintegrate rapidly in the saliva generally less than 60 seconds [5]. To fulfill these medical needs, pharmaceutical technologists have developed a novel oral dosage forms known as orally disintegrating (dispersible) tablets (ODTs) or Fast disintegrating (dissolving) tablets (FDTs) or mouth melting tablets (MMTs) or mouth dissolving tablets(MDTs), immediate release tablets which disintegrate rapidly in saliva, usually in a matter of seconds, without the need to take water. Recent market studies indicate that more than half of the patient population prefers FDTs to other dosage forms. Mouth dissolving tablets are formulated mainly by two techniques first use of super disintegrants like Croscarmellose sodium, sodium starch glycolate and crospovidone. Another method is maximising pore structure of the tablets by freeze drying and vacuum drying [5]. In all methods, direct compression is preferred because of its effortlessness, quick procedure and cost-effectiveness .The bioavailability of some drugs may be increased due to absorption of drugs in oral cavity and also due to pregastric absorption of saliva containing dispersed drugs that pass down into the stomach. Moreover, the amount of drug that is subjected to first pass metabolism is reduced as compared to standard tablets [5]. Fast dissolving tablets are innovative dosage forms

developed and specially designed to overcome some of the problems that seen in conventional solid dosage form i.e. difficulty in swallowing of the tablet in geriatric and pediatric patients. Fast dissolving tablets are designed to dissolve or disintegrate quickly in the saliva generally within less than 60 seconds (range of 5-60 seconds). Fast dissolving tablets have better patient compliance and acceptance may improve biopharmaceutical properties, bioavailability improved efficacy, convenience, and better safety compared with conventional oral dosage forms. The popularity of FDTs has increased fabulously over the last decade. FDTs need to be formulated for psychotic patients, bedridden, geriatric, pediatric patients, for those patients who may not have access to water, patients who are busy in traveling. FDTs formulations formulated by some of these convetional and patent technologies and FDTs have sufficient mechanical strength, quick disintegration/dissolution in the buccal cavity without water. The newer technologies utilized for the formulation of the FDTs that provide more effective dosage forms with more advantages and minimal disadvantages.

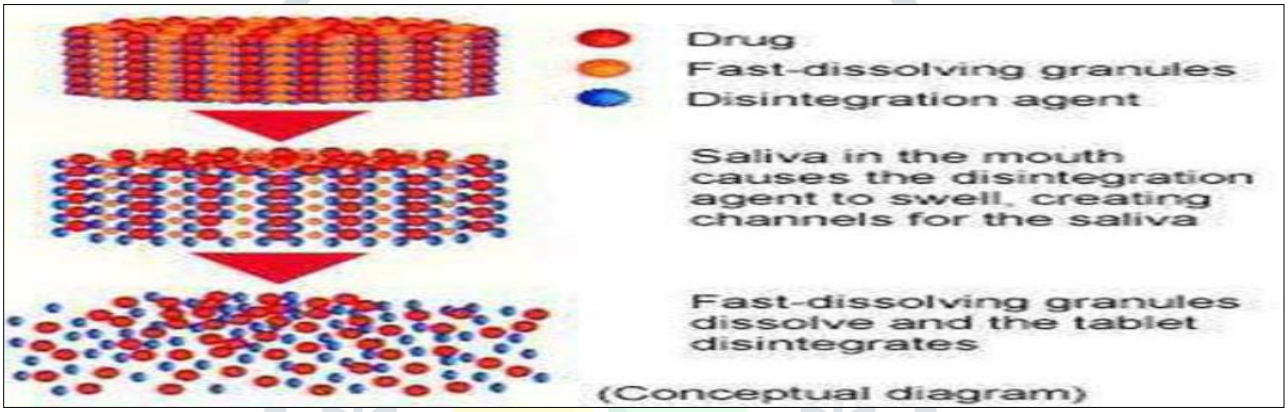

Figure 1: Conceptual mechanism of FDT Disintegration (By release of gases)

Requirements of fast dissolving tablets

Patient factors [3]

Fast dissolving dosage forms are suitable for those patients (particularly pediatric and geriatric patients) who are not able to swallow traditional tablets and capsules with an 8-oz glass of water.

These include the following:

• Patients who have difficulty in swallowing or chewing solid dosage forms.

• Patients in compliance due to fear of choking.

• Very elderly patients of depression who may not be able to swallow the solid dosage forms

• An eight-year-old patient with allergies desires a more convenient dosage form than antihistamine syrup.

• A middle-aged patient undergoing radiation therapy for breast cancer may be too nauseous to swallow her H2-blocker.

• A schizophrenic patient who may try to hide a conventional tablet under his or her tongue to avoid their daily dose of an atypical antipsychotic.

• A patient with persistent nausea, who may be a journey, or has little or no access to water.

Effectiveness factor [5]

Increased bioavailability and faster onset of action are a major claim of these formulations. Dispersion in saliva in oral cavity causes pre-gastric absorption from some formulates ions in those cases where drug dissolves quickly. Buccal, pharyngeal and gastric regions are all areas of absorption for many drugs. Any pre-gastric absorption avoids first pass metabolism and can be a great advantage in drugs that undergo hepatic metabolism. Furthermore, safety profiles may be improved for drugs that produce significant amounts of toxic metabolites mediated by first-pass liver metabolism and gastric metabolism, and for drugs that have a substantial fraction of absorption in the oral cavity and pre-gastric segments of GIT.

Manufacturing and marketing factors [7]

As a drug nears the end of its patent life, it is common for pharmaceutical manufacturers to develop a given drug entity in a new and improved dosage form. A new dosage form allows a manufacturer to extend market exclusivity, unique product differentiation and extend patent protection. For examples, Eisai Inc. launched Aricept FDT, a line extension of donepezil for Alzheimer's disease, in Japan in 2004 and in the U. S. in 2005 in response to a generic challenge filed in the U. S. by Ranbaxy.

Limitations of FDTs [4-5]

• The major disadvantages of FDTs is related to the mechanical strength of tablets.

• FDT are very porous and soft molded metrics or compressed in a tablet with low compression, which makes tablet friable and brittle which difficult to handle.

• Bad tastes drugs are difficult to formulate as FDT; special precaution should have to be taken before formulate such kind of drug.

• Several FDT are hygroscopic cannot maintain physical integrity under normal condition from humidity which requires specialized package.

• Dryness of the mouth due to decreased saliva production may not be good candidates for these tablet formulations.

• Rate of absorption from the saliva solution and overall bioavailability.

•Drug and dosage form stability.

Criteria for excipient used in formulation of FDTs [5-9]

• Their individual properties should not affect the FDTs.

• It must be able to disintegrate quickly.

• It should not have any interaction with drug and other excipients.

• When selecting binder (a single or combination of binders) care must be taken in the final integrity and stability of the product.

• The melting point of the excipients used should be in the range of 30-35 °C.

• It should not interfere in the efficacy and organoleptic properties of the product.

• The binder may be in liquid, semi-solid, solid or polymeric in nature

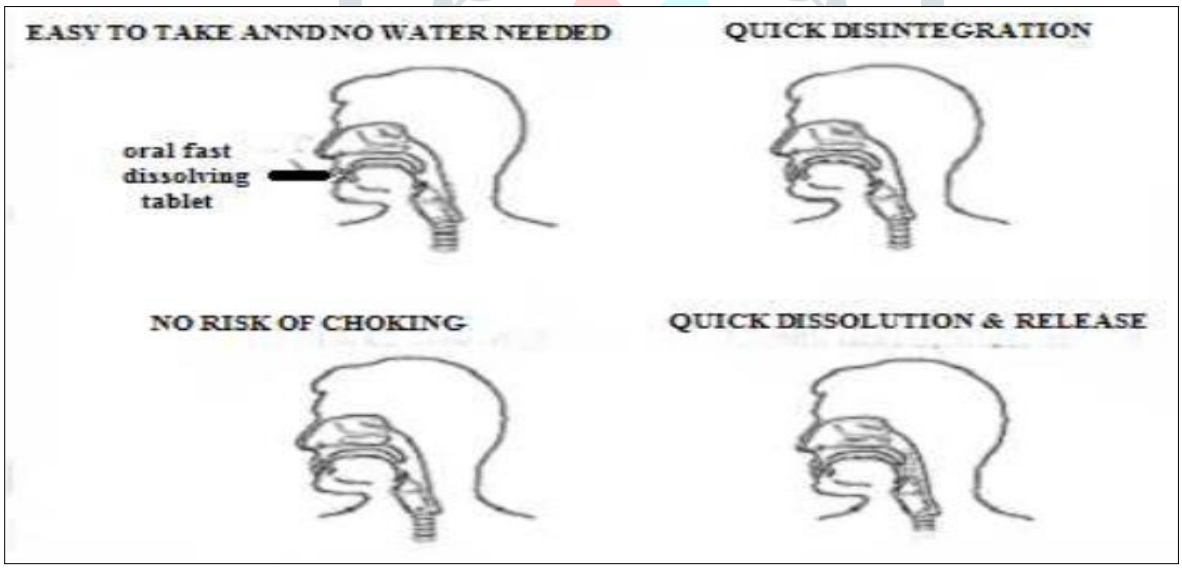

Figure 2: Advantages of oral fast dissolving tablets

Excipients used in FDT preparation [5, 9-16]

Excipients used in FDTs contain at least one super disintegrant, a diluent, a lubricant and optionally a swelling agent, a permeabilizing agent, sweeteners and flavouring agents.

Table 1: List of super disintegrants [5, 17]

S. No.	Superdisintegrant	Mechanism of action	Specific properties
1	Croscarmellose	Swells 4–8 folds in<10 s.	Effective in low

	Sodium	Swelling and wicking action	concentration (0.5–2.0%), high swelling capacity, cross-linking of the carboxyl ester groups.
2	Crospovidone	Combination of swelling and wicking action. Swells 7–12 folds in<30 s.	The effective concentration is 1–3%. Rapidly disperses and swells in water, available in micronized grades.
3	Cross-linked alginic acid	Hydrophilic colloidal substance which has high sorption capacity.	The combination of swelling and wicking action causes disintegration.
4	Gellan gum	Strong swelling properties upon contact withwater.	Anionic polysaccharide of linear tetrasaccharides, goodsuperdisintegrants property similar to the modified starch and celluloses.
5	Sodium starch glycolate	Strong swelling properties upon contact with water. Swells 7–12 folds in<30s.	Rapid absorption of water results in swelling up to 6%, highconcentration causes gelling.
6	Soy polysaccharide	Rapid dissolving	Does not contain starch or sugar so can be used in products meant for diabetics
7	Xanthan gum	Extensive swelling properties for faster disintegration	High hydrophilicity and low gelling tendency, low water solubility.

Drug delivery systems (DDS) are a strategic tool for expanding markets indications, extending product life cycles and generating opportunities. DDS has made a significant contribution to global pharmaceutical sales through market segmentation, and are moving rapidly. As there are various routes of drug delivery systems to the body, the oral delivery is considered as one of the golden standard in the pharmaceutical industry where it is regarded as the safe, convenient, and most economical method of drug delivery having the patient compliance from the elderly. Orodispersible tablets (ODT) are oral solid dosage forms that disintegrate in the oral cavity in easy swallow residue [18]. Over a decade, the demand for development of orally disintegrating tablets (ODTs) has enormously increased as it has significant impact on the patient compliance. Orally disintegrating tablets offer an advantage for populations who have difficulty in swallowing (Dysphagia). ODTs are useful among all age groups and more specific with paediatric, geriatric population along with institutionalized patients and patients with nausea, vomiting, and motion sickness complications [19-20]. Orally disintegrating tablets are also called as

orodispersible tablets, quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets, and rapid melts. However, of all the above terms, United States Pharmacopoeia (USP) approved these dosage forms as ODTs [21]. Recently ODT terminology has been approved by United States Pharmacopoeia, British Pharmacopoeia [22].Recently, European Pharmacopoeia has used the term orodispersible tablet for those tablets which disperses readily and within 3 min in mouth before swallowing. Such a tablet disintegrates into smaller granules or melts in the mouth from a hard solid to a gel-like structure, allowing easy swallowing by patients. The US food and drug administration centre for drug evaluation and research defines in the "orange book" ODTs as a solid dosage form containing medicinal substance which disintegrate rapidly, usually within a matter of seconds, when placed upon the tongue [23]. These tablets in contrast with conventional dosage forms (tablets and capsules) which takes several minutes to dissolve in mouth, ODTs disintegrates and dissolves in the mouth in less than 60 seconds and hence produce a rapid action. These tablets releases the medicament in the mouth for absorption through local oromucosal tissue and through pre-gastric (Oral cavity, Pharynx, and oesophagus), gastric (stomach) and post-gastric (small and large intestine) segments of Gastro Intestinal Tract (GIT) [24]. Along with the rapid market growth of ODT products, the technologies, too, have advanced considerably over the years. The newest generation of ODTs can produce more robust, versatile tablets that overcome some of the limitations of earlier ODTs [25]. Companies such as Eurand can produce pleasant tasting tablets, overcoming the common problem of poor drug taste compromising the benefits of an ODT. In addition, some companies is developing controlled release ODTs, significantly broadening the applications of this dosage form. A key reason that companies choose an ODT over other delivery technologies is that it is a relatively easy and often less risky delivery option to develop. Since the route of administration remains the same, ODTs that are formulated as bioequivalent line extensions or generic versions of an existing oral dosage form have minimal clinical requirements to gain approval.

Ideal Characteristics of ODT's:

- Exhibit low sensitivity to environmental conditions as humidity and temperature [26].
- Should dissolve or disintegrate in the mouth rapidly without aid of water in matter of seconds and without swallowing.
- Should maintain physical integrity and possess no friable loss with sufficient mechanical strength.
- Should have a pleasant mouth feel.
- Should leave minimum or no residue in the mouth after oral administration.
- Should exhibit low sensitive to environmental condition as temperature and humidity.
- Should allow high drug loading capacity.
- Should be adaptable and amenable to the existing processing and packaging machinery at low costs.
- Small to moderate molecular weight.

- Good solubility in water and saliva.
- Partially non-ionized at the oral cavity pH.
- Ability to diffuse and partition in to the epithelium of the upper GIT logp more than1 or preferably more than 2.
- Ability to permeate oral mucosal tissue
- The fast disintegration usually means disintegration of tablets in less than 1 minute, but it is preferred to have disintegration as soon as possible.
- The excipients should have high wettability, and the tablet structure should also have a highly porous network for fast dissolution.
- The disintegrated tablet should become a soft paste or liquid suspension, which can provide good mouth feel and smooth swallowing.
- A pleasant taste inside the mouth becomes critical for patient acceptance. Unless the drug is tasteless or does not have an undesirable taste, taste-masking techniques should be used. An ideal taste-maskingtechnology should provide drugs without grittiness and with good mouth feel.
- The amount of taste masking materials used in the ODTs formulation should be kept a slow as possible to avoid excessive increase in tablet size.
- Drug properties for example; the solubility, crystal morphology, particle size, hygroscopicity, compressibility, and bulk density should not affect the final ODT'sperformance and characteristics such as tablet strength and disintegration.

Significance of Oro-dispersible tablets:[27]

- As ODTs are unit solid dosage forms, they provide good stability, accurate dosing, easy manufacturing, small packaging size, and ease of handling by patients.
- No risk of obstruction of dosage form as rapidly dissolves in saliva.
- Administration without water, anywhere and anytime, hence beneficial for traveling patients who do not have access to water.
- Rapid disintegration of tablet results in quick dissolution and rapid absorption which provide rapid onset of action. Medication as "bitter pill" has changed by excellent mouth feel property produced by the use of flavors and sweeteners in ODTs.
- Suitable for delivering relatively low molecular weight and highly permeable drugs.
- Requires minimum number of ingredients and so it is cost effective dosage form.
- Solid oral delivery systems do not require sterile conditions, so less expensive to manufacture.
- Rapid dissolution and absorption of the drug, which will produce quick onset of action.
- Bioavailability of drug is increased as some drugs are absorbed from the mouth, pharynx and oesophagus as the saliva passes down into the stomach.

- Pre-gastric absorption of drugs avoids hepatic metabolism which can results in improved bioavailability which results of reduced dosage with improved clinical performance through the reduction of unwanted effects.
- The risk of chocking or suffocation during oral administration of conventional formulation due to physical obstruction is avoided and thus provided improved safety.
- Beneficial in cases such as motion sickness, sudden episodes of allergic attack or coughing, where an ultra-rapid onset of action is required.
- An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets.

Advantages of Oro-dispersible tablets: [28]

- ODTs have all the advantages of solid dosage forms; they provide good stability, accurate dosing, easy manufacturing, small packaging size, and easy to handle by patients.
- ODTs have the advantages of liquid formulations such as easy administration and no risk of suffocation resulting from physical obstruction by a dosage form.
- Ease of Administration to the patient who cannot swallow, such as the elderly, stroke victims, bedridden patients, patient affected by renal failure and patient who refuse to swallow such as paediatric, geriatric & psychiatric patients.
- No risk of obstruction of dosage form and 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 disintegration of tablet results in quick dissolution and rapid absorption which provide rapid onset of action.
- The tablets disintegrate inside the mouth; drugs may be absorbed in the buccal, pharyngeal, and gastric regions (pregastric absorption). Thus, rapid drug therapy intervention and increased bioavailability of drugs are possible.
- Hence drugs like anti-anginal, antiasthmatics, anti-allergics and NSAIDs and other emergency drugs can be administered.
- The pre-gastric drug absorption avoids the first-pass metabolism; the drug dose can be reduced if a significant amount of the drug is lost through the hepatic metabolism. Hence drugs which metabolised by first pass effect or metabolised by gastric enzymes, can also be administered.
- From the pharmaceutical industry's point of view, ODTs can provide new dosage for msas a life cycle management tool for drugs near the end of their patent life.

Challenges in development of ODTs:[29]

Palatability:

It is a formidable challenge for formulation scientists to mask the taste of bittertastingdrugs selected for ODT. As most drugs are unpalatable, orally disintegrating drugdelivery systems usually contain the medicament in a taste masked form. Hence, tastemasking of the drugs become critical to patient compliance.

Mechanical strength:

In order to allow ODTs to disintegrate in the oral cavity, they are made of either very porous or soft-moulded matrices or compressed in to tablets with very low compression force, which makes the tablets friable or brittle, and difficult to handle. Only few technologies can produce tablets that are sufficiently hard and durable to allow them to be packaged in multi dose bottles, such as Wowtab by Yamanouchi Shaklee, and Durasolv by CIMA labs.

Hygroscopicity/moisture sensitivity:

Several orally disintegrating dosage forms are hygroscopic and cannot maintain physical integrity under normal conditions of temperature and humidity. Hence, they need protection from humidity which calls for specialized product packaging.

Dose/Amount of drug:

The application of technologies used for ODTs is limited by the amount of drug that can be incorporated into each unit dose. Molecules requiring high doses present mainly three challenges to the development of fast dissolve dosage forms; a) taste masking of active ingredient, b) mouth feel or grittiness and c) tablet size. These challenges are not unrelated because most drugs require taste masking, the amount of taste masking materials used in different dosage forms will depend on the drugs degree of bitterness relative to its dose, which will in turn affect the final tablet size.

Aqueous solubility:

Water-soluble drugs pose various formulation difficulties because they form eutectic mixture, which result in freezing point depression and the formation of a glassy solid that may collapse upon drying because of loss of supporting structure during the sublimation process. Such collapse can be prevented by using matrix-forming excipients such as mannitol that can induce Crystallinity and hence, impart rigidity to the amorphous composite.

Size of tablet:

The degree of ease when taking a tablet depends on the size. It has been reported that the easiest size of tablet to swallow is 7-8 mm while the easiest size to handle was one larger than 8 mm. Therefore, the tablet size that is both easy to take and easy to handle is difficult to achieve.

Techniques for preparing ODTS

Freeze drying or Lyophilization

Freeze drying is the technique in which water is sublimed from the product when it is frozen. This technique creates an amorphous porous construction that can dissolve rapidly. A Typical process involved in the manufacturing of ODT using this technique. The active drug is dissolved/ dispersed in an aqueous solution of a carrier or polymer. The mixture is dosed through weight and poured in the wells of the preformed Blister packages. The trays holding the blister packs arepassed through liquid nitrogen freezing tunnel to freeze the drug Solution or dispersion. Then the frozen blister packs are placed in refrigerated cabinets to continue the freeze-drying. After Freeze-drying the aluminum foil backing is useful on a blister sealing Machine. Finally the blisters are packaged and shipped. Advantages of freeze drying the major advantage of using this technique is that the tablets Produced by this technology have a very low disintegration Time and have great mouth feel due to fast melting effect.

Sublimation

The slow dissolution of the compressed tablet having even highly water soluble components is due to the fact that the low Porosity of the drugs reduces water dispersion into the matrix. After inert volatile solid ingredients like ammonium Bicarbonate, ammonium carbonate, benzoic acid, camphor, hexamethylene tetra mine, naphthalene, phthalic anhydride, urea and urethane were additional too along with other tablet excipients and the blend were compressed into a tablet which is finally subjected to a process of sublimation resulting in exceedingly porosity. These compressed tablets exhibition Good mechanical strength and have high penetrability quickly Dissolved within 15 seconds in saliva.

Mass extrusion

This technology contains softening the active blend using the Solvent mixture of water soluble polyethylene glycol, using Methanol and expulsion of softened mass through the extruder or syringe to get a cylinder designed extrude which 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. This method used for preparing taste masked Granules. The tablet was prepared with different Super disintegrate. E.g. sodium starch glycolate, croscarmellose Sodium and crosspovidone etc.

Melt granulation

Melt granulation system is a process through which Pharmaceutical powders are efficiently agglomerated through a melt able binder. The benefit of this method associated to a Conventional granulation is that no water or organic solvents is necessary. For there is no drying step, the process is less time consuming and uses less energy than wet granulation. It is aUseful technique to enhance the dissolution rate of poorly water–soluble drugs such as griseofulvin. This methodology to prepare MDT with sufficient mechanical integrity, involves the use of a hydrophilic waxy binder (superpolystate, PEG-6Stearate). Superpolystate is a waxy material with a melting point of 33-37ºC and a HLB value of 9. So it determination not only act as a binder and increase the physical resistance of Tablets but will also help the disintegration of the tablets as it Melts in the mouth and solubilizes rapidly leaving no residues.

Spray drying

Spray dryers remain widely used in pharmaceuticals and Biochemical processes. Due to processing solvent is evaporated quickly; spray drying can produce highly porous, fine powder. Spray drying can be used to formulate quickly Disintegrating tablets. This technique is based on a particulate Support matrix, which is equipped by spray drying an aqueous Composition containing support matrix and other components to usage a highly porous and fine powder this is then mixed with active ingredients and compressed into tablets. The Tablets made from this technology are claimed to disintegrate within 20 seconds.

Molding

In this method, molded tablets are prepared by using water soluble Ingredients so that the tablets dissolve completely and rapidly. The powder blends is moistened with a hydro alcoholic Solvent and is molded into tablets under pressure Lower than that used in conventional tablet compression. The Solvent is then removed by air-drying. They are very less compact than compressed tablets. In this process porous Structure is formed and enhances the dissolution rate.

Nanonization

In this technology contains reduction in the particle size of drug to nano size by milling the drug using a patented wet milling technique. The nano-crystals of the drug are stabilized against agglomeration by surface absorption on selected Stabilizers which are then incorporated into mouth dissolving tablets. This system is suitable for poorly water soluble drugs.

Description: Dolasetron is an antinauseant and antiemetic agent indicated for the prevention of nausea and vomiting associated with moderately-emetogenic cancer chemotherapy and for the prevention of postoperative nausea and vomiting. Dolasetron is a highly specific and selective serotonin 5-HT3 receptor antagonist. This drug is not shown to have activity at other known serotonin receptors, and has low affinity for dopamine receptors.

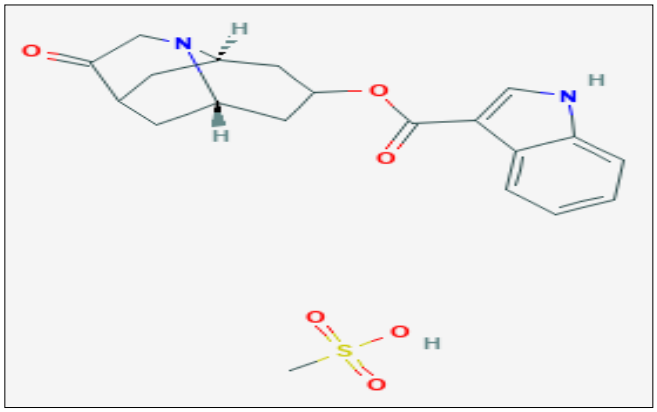

Figure 3: Structure ofDolasetron mesylate

Mol. weight: 324.38

Chemical Formula:$C_{19}H_{20}N_2O_3$

IUPAC Name:(1s, 3R, 5r, 7S)-10-oxo-8-azatricyclo [5.3.1.0] undecan-5-yl 1H-indole-3-carboxylate

Pharmacology

Indication: For the prevention of nausea and vomiting associated with emetogenic cancer chemotherapy, including initial and repeat courses of chemotherapy. Also used for the prevention of postoperative nausea and vomiting. This drug can be used intravenously for the treatment of postoperative nausea and vomiting.

Pharmacodynamics: Dolasetron is a highly specific and selective serotonin 5-HT_3 receptor antagonist, not shown to have activity at other known serotonin receptors and with low affinity for dopamine receptors. It is structurally and pharmacologically related to other 5-HT_3 receptor agonists. The serontonin 5-HT_3 receptors are located on the nerve terminals of the vagus in the periphery, and centrally in the chemoreceptor trigger zone of the area postrema. It is suggested that chemotherapeutic agents release serotonin from the enterochromaffin cells of the small intestine by causing degenerative changes in the GI tract. The serotonin then stimulates the vagal and splanchnic nerve receptors that project to the medullary vomiting center, as well as the 5-HT_3 receptors in the area postrema, thus initiating the vomiting reflex, causing nausea and vomiting.

Mechanism of action: Dolasetron is a selective serotonin 5-HT_3 receptor antagonist. In vivo, the drug is rapidly converted into its major active metabolite, hydrodolasetron, which seems to be largely responsible for the drug's pharmacological activity. The antiemetic activity of the drug is brought about through the inhibition of 5-HT_3 receptors present both centrally (medullary chemoreceptor zone) and peripherally (GI tract). This inhibition of 5-HT_3 receptors in turn inhibits the visceral afferent stimulation of the vomiting center, likely indirectly at the level of the area postrema, as well as through direct inhibition of serotonin activity within the area postrema and the chemoreceptor trigger zone.

Absorption: Orally-administered dolasetron is well absorbed.

Protein binding: 69-77%.

Metabolism: Hepatic.

Route of elimination: Hydrodolasetron is eliminated by multiple routes, including renal excretion and, after metabolism, mainly glucuronidation, and hydroxylation.

Half life: 8.1 hours.

Side effect

- headache
- diarrhea
- fever
- fatigue
- abdominal or stomach pain
- dizziness
- drowsiness
- chills
- shivering
- numbness or tingly feeling
- constipation
- anxiety, or
- Joint or muscle pain.

Uses

Used to prevent nausea and vomiting caused by cancer drug treatment (chemotherapy). Dolasetron works by blocking one of the body's natural substances (serotonin) that causes vomiting.

Model Excipient used

Sodium starch glycolate

Synonyms: Explotab,Primogel

Non proprietary Name: BP:Sodiumstarchglycolate,USPNF: Sodiumstarchglycolate.

Functionalcategory:Tabletandcapsuledisintegrant.

Chemical names:Sodiumcarboxymethylstarch.

CAS Registry Number:9063-38-1

Description:Sodiumstarchglycolateisawhitetooff-white, odour less,tasteless,free flowingpowder.Itconsistsofovalorspherical granules, 30-100μmindiameter withsome less sphericalgranulesrangingfrom10-35μmindiameter.

Structural formula:

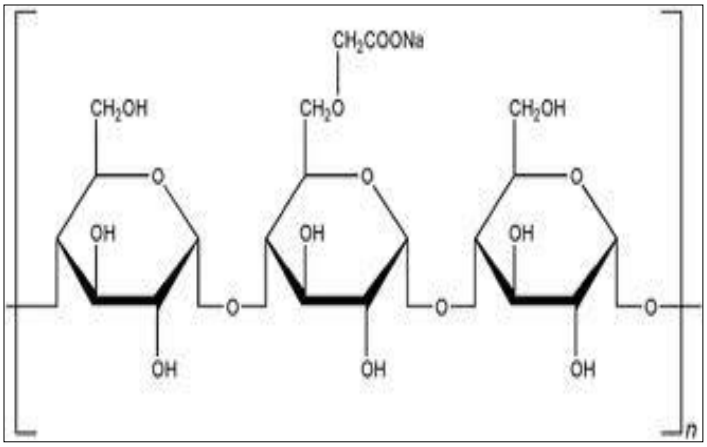

Figure 4: Structure of Sodium starch glycolate

Solubility: Practically insoluble in water; sparingly soluble in ethanol (95%).Inwaterit swells up to300 times its volume.

Stability and storage conditions: It is as table material. It should be stored in a well closed container to protect from wide variations in humidity and temperature that may cause cracking.

Incompatibilities: Incompatiblew it has corbicacid.

Safety:

It is generallyregardedas a non-toxicand non-irritantmaterial.However, oral ingestionof largequantitiesmaybeharmful.

Applications:

Asadisintegrantintablet(wetgranulationanddirectcompression)andcapsule formulationin2-8% concentration.

Crosscarmellose Sodium

Structural formula:

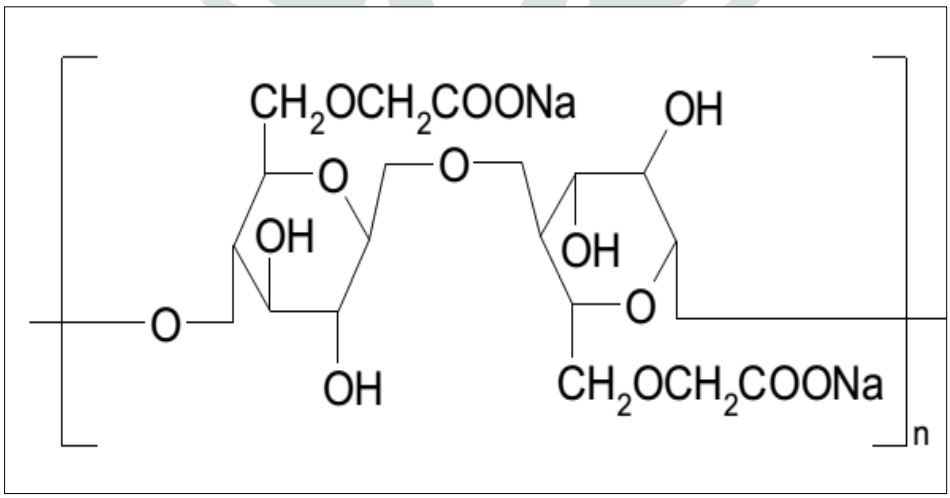

Figure 5: Structure of Sodium Starch Glycolate

Synonyms: Ac-Di-Sol, Cross-linked carboxymethylcellulose sodium.

Non-proprietary name: USPNF: Crosscarmellose sodium.

Functional category: Tablet and capsule disintegrant.

Chemical names: Cellulose, carboxymethyl ether, sodium salt, cross linked.

Molecular weight: 90000-700000.

pH (1% w/v dispersion) : 5.0-7.0.

Description: Crosscarmellose sodium occurs as an odourless, white coloured powder.

Solubility: Insoluble in water. Although crosscarmelose sodium rapidly swells to 4-8 times of its original volume on contact with water.

Storage condition: Crosscarmellose sodium is a stable though hygroscopic material. A model tablet formulation prepared by direct compression, with Crosscarmellose sodium as disintegrant, showed no significant difference in drug dissolution after storage at 300ºC for 14 months.

Incompatibilities: The efficacy of disintegrants, such as Crosscarmellose sodium, may be slightly reduced in tablet formulations prepared by wet granulation or direct compression process which contain which contain hygroscopic material such as sorbitol.

Safety: Crosscarmellose is mainly used as a disintegrant in oral pharmaceutical formulations and is generally regarded as an essentially non toxic and non irritant material.

Applications: As a disintegrant in tablet (wet granulation and direct compression) and capsule formulation in 2-8% concentration.

Crospovidone

Structural formula:

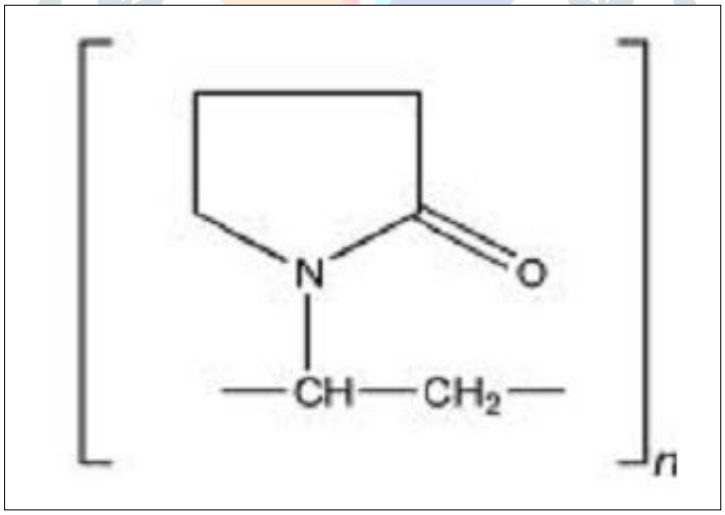

Figure 6: Structure of Crospovidone

Synonyms: Crosslinked povidone, E1202, Kollidon CL, Polyplasdone XL, Polyplasdone XL-10, PVPP and 1-vinyl-2-pyrrolidinone homopolymer.

Non-proprietary names: BP-Crospovidone, PhEur-Crospovidonum, USPNF: Crospovidone.

Chemical name: 1-Ethenyl-2-pyrrolidinone homopolymer.

Molecular weight: (C6H9NO)n >1 000 000.

Functional category: Tablet disintegrant.

Description: Crospovidone is a white to creamy-white, finely divided, free-flowing, practically tasteless, odourless and hygroscopic powder.

Stability and storage conditions: Since crospovidone is hygroscopic, it should be stored in an airtight container in a cool, dry place.

Applications in pharmaceutical formulation or technology: Crospovidone is a water-insoluble tablet disintegrant and dissolution agent used at 2–5% concentration in tablets prepared by direct-compression or wet- and dry-granulation methods. It rapidly exhibits high capillary activity and pronounced hydration capacity, with little tendency to form gels. Studies suggest that the particle size of crospovidone strongly influences disintegration of analgesic tablets.

Microcrystalline Cellulose

Structural formula:

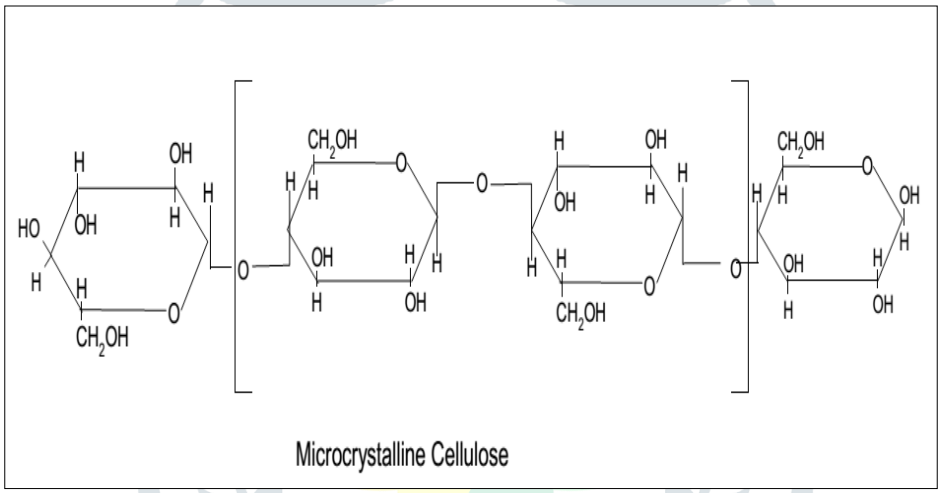

Figure 7: Structure of Microcrystalline Cellulose

Synonyms: Cellulose gel: Crystalline cellulose: Avicel PH101, 102.

Non-proprietary name: NF-Microcrystalline cellulose, USP- Microcrystalline cellulose.

Chemical names: Cellulose.

Empirical formula: $(C_6H_{10}O_5)_n = 220$.

Molecular weight: 36,000(approx).

Density: Apparent density - 0.28g/cm^3; Tap density - 0.43g/cm^3.

Functional category: Tablet and capsule diluent, tablet disintegrant, suspending and viscosity increasing agent.

Description: Purified, partially depolymerised cellulose occurs as a white, odourless, tasteless, crystalline powder composed of porous particles.

Solubility: Insoluble in water, dilute acids and most organic solvents, slightly soluble in 5% w/v NaOH solution.

Storage conditions: Stable, hygroscopic. Store in a well closed container.

Applications: Tablet binder/diluent, tablet disintegrant, tablet glidant.

Talc

Synonyms: Magsil Osmanthus, Magsil Star, Purtalc, Steatite.

Functional category: Glidant, tablet and capsule lubricant, anti- cackling agent.

Applications: It is used as a lubricant in solid dosage forms (1-10%), in topical preparations as dusting powder (90-99 %).

Stability: Talc is a stable material.

Solubility: Practically insoluble in dilute acids and alkalies, organic solvents and water.

Incompatibilities: Incompatible with quaternary ammonium compounds.

Description: It is a very fine, white to greyish-white coloured, odourless, impalpable, unctuous powder. It adheres to the skin, is soft to touch and free from grittiness.

Storage conditions: It should be stored in a well-closed container in a cool, dry, place.

Magnesium stearate

Synonyms: Metallic stearic; magnesium salt.

Non-proprietary name: NF- Magnesium stearate; BP/EP- Magnesium stearate.

Empirical formula: $C_{36}H_{70}MgO_4$.

Chemical names: Octadecanoic acid; magnesium salt; magnesium stearate

Molecular weight: 591.3.

Density (He): 1.03-1.08 g/cm^3

Bulk volume: 3.0-8.4 ml/g

Tapped volume: 2.5-6.2 ml/g

Functional category: Tablet and capsule lubricant.

Description: It is a fine, white, precipitated or milled, impalpable powder of low bulk density, having a faint characteristic odour and taste. The powder is greasy to touch and readily adheres to the skin.

Solubility: Practically insoluble in ethanol, ethanol (95%), ether and water, slightly soluble in benzene and warm ethanol (95%).

Stability and storage conditions: Stable, non-self polymerizable. Store in a cool, dry place in a well closed container.

Incompatibilities: Incompatible with strong acids, alkalies, iron salts and with strong oxidising materials.

Safety: Described as inert or nuisance dust. OSHA has adopted limits of 15mg/m3 for the total dust and 5mg/m3 for the respirable fraction. Dust clouds of magnesium stearate may be explosive. However, oral consumption of large quantities may result in some laxative effect or mucosal irritation.

Applications: Tablet and capsule lubricant, glidant and antiadherent in the concentration range of 0.25 to 2.0%.

CONCLUSION: - Dolasetron mesylate is an antiemetic medication. Dolasetron mesylate degrades slowly and remains in the body for a long period. One dosage generally lasts 4 to 9 hours and is taken once or twice daily. The liver and kidneys eliminate this medication from the body. The main symptoms of this condition include sudden acute vertigo, fluctuating hearing loss, ear fullness, tinnitus, nausea, and vomiting. It relieves symptoms within 3 hours of administration. It also has the benefit of having no sedative effect when compared to other anti-vertigo medications. All of the symptoms listed above must be alleviated as soon as possible.

REFRENCES:-

1. Hannan PA, Khan JA, Khan A, Safiullah S. Oral dispersible system: a new approach in drug delivery syste. Indian J Pharm Sci. 2016; 78:2-7.
2. Bhowmik D, Chiranjib B, Krishnakanth, Pankaj, Chandira RM. Fast dissolving tablet: an overview. J Chem Pharm Res. 2009; 1:163-77.
3. Siddiqui N, Garg G, Sharma PK. Fast dissolving tablets: preparation, characterization and evaluation: an overview. Int J Pharm Sci Rev Res. 2010; 2:87-96.
4. Gupta DK, Bajpai M, Chatterjee DP. Fast mouth is dissolving disintegrating tablet and patient counselling points for FDDTS: A review. Int J Res Dev Pharm L Sci. 2014; 3:949-58.
5. Nautiyal U, Singh S, Singh R, Gopal, Kakar S. Fast dissolving tablets as a novel boon: A review. J Pharm Chem Biol Sci. 2014; 2:5-26.
6. Pagar R, Ahirrao S, Yallatikar T, Wagh M. Review on orodispersible tablets. Int J Res Dev Pharm L Sci 2014; 3:949-58.
7. Mishra US, Prajapati SK, Bhardwaj P. A review on formulation and evaluation for mouth dissolving tablet. World J Pharm Pharm Sci 2014; 8:1778-810.
8. Kuchekar BS, Badha AC, Mahajan HS. Mouth dissolving tablets: a novel drug delivery system. Pharmatimes 2003; 35:7-9.
9. Sharma S. New generation of the tablet: fast dissolving tablet. Latest Rev Pharmainfo Net; 2008. p. 6.
10. Kumari S, Visht S, Sharma PK, Yadav RK. Fast dissolving drug delivery system: a review article. J Pharm Res 2010; 3:1444-9.
11. Mohanachandran PS, Sindhumol PG, Kiran TS. Superdisintegrants: an overview. Int J Pharm Sci Rev Res 2011;6:105-9.
12. Deshmukh VN. Mouth dissolving drug delivery system: a review. Int J Pharm Tech Res 2012; 4:412-21.
13. Kumaresan C. Orally disintegrating tablet-mouth dissolving, sweet taste and target release profile. Pharm Rev 2008; 6:1.
14. Parkash V, Maan S, Deepika, Yadav SK, Hemlata, Jogpal V. Fast disintegrating tablets: opportunity in drug delivery system. J Adv Pharm Technol Res 2011; 2:223-35.
15. Nagar P, Singh K, Chauhan I, Verma M, Yasir M, Khan A. Orally disintegrating tablets: formulation, preparation techniques and evaluation. J Appl Pharm Sci 2011; 4:35-45.
16. Velmurugan S, Vinushitha S. Oral disintegrating tablets: an overview. Int J Chem Pharm Sci 2010; 1:1-12.
17. Khan AB, Tripuraneni A. Fast dissolving tablets–a novel approach in drug delivery. Rguhs J Pharm Sci 2014; 1:7-16.
18. Sreenivas SA. Orodispersible tablets: New- fangled drug delivery system- A Review. Indian J.Pharm.Educ.Res, 2005; 39(4): 177-181.
19. Lindgren S, Janzon L. Dysphagia: Prevalence of swallowing complaints and clinical finding. Med Clin North Am, 1993; 77:3-5.

20. Sastry SV, Nyshadham JR, Fix JA. Recent technological advances in oral drug delivery: A review. Pharm Sci Technol Today, 2000; 3:138-145.
21. Ciper M, Bodmeier R. Modified conventional hard gelatin capsules as fast disintegrating dosage form in the oral cavity. Eur. J. Pharm. Biopharm, 2006; 62, 178–184.
22. Rakesh RK. Orally Disintegrating Tablets novel tablets novel approach to drug delivery. Pharma Review 2004; 2(12): 34-6.
23. Fu Y, Yang S, Jeong SH, Kimura S, Park K, Orally fast disintegrating tablets: Developments, technologies, taste-masking and clinical studies, Crit Rev Ther Drug Carr Sys, 2004; 21, 433-476.
24. Shyamala B, Narmada GY. Rapid dissolving tablets: A Novel Dosage Forms. The Indian Pharmacist (2002); 13(8): 09-12.
25. Harmon TM. Orally Disintegrating Tablets: A Valuable Life Cycle Management Strategy". Pharmaceutical Commerce, March (2007), available online www.pharmaceuticalcommerce.com.
26. Shukla D, Chakraborty S, Mouth Dissolving Tablets I: An Overview of Formulation Technology, Sci Pharm. (2009); 76; 309–326.
27. Patel P B, Fast Dissolving Drug Delivery Systems: Pharmainfo.net, (2006); 4 (4):1-7.
28. Nagar P, Singh K, Chauhan I, Verma M, Yasir M, Khan A, Sharma R, Gupta N. Orally disintegrating tablet: formulation, preparation techniques and evaluation. J Applied pharm sci, 2011; 1(4), 35-45.
29. Puttlingaiah L, Kavitha K, Mani TT. Fast disintegrating tablets: an overview of formulation techniques and evaluation. Res Jpharmaceu. Biolog, Chem Sci, 2011; 2(2), 589-601.
30. Ankur Sharma, Abhishek Jain, Anuj Purohit, Rakesh Jatav and R. V. Sheorey, Formulation and evaluation of aceclofenac fast dissolving tablets, Int. J. of Pharm. & Life Sci. (IJPLS), Vol . 2, Issue 4: April: 2011, 681-686
31. Kapil Chauhan, Bharat Parashar, Abhishek Chandel and Varun Thakur, Formulation and evaluation of fast dissolving tablets of telmisartan, IJPSR, 2013; Vol. 4(4): 1514-1520.
32. Narmada GY, Mohini K, Prakash Rao B, Gowrinath DXP, kumar KS, Formulation, Evaluation and Optimization of Fast Dissolving Tablets Containing Amlodipine Besylateby Sublimation Method, Ars Pharm,2009, Vol.50 no 3; 129-144.
33. Deepak Sharma, Gurmeet Singh, Dinesh Kumar and Mankaran Singh, Formulation Development and Evaluation of Fast DisintegratingTablets of Salbutamol Sulphate, Cetirizine Hydrochloride in Combined Pharmaceutical Dosage Form: A New Era in Novel Drug Delivery for Pediatrics and Geriatrics, Journal of Drug Delivery, Volume 2015,1-8
34. Deepak Sharma, Formulation Development and Evaluation of Fast Disintegrating Tablets of Salbutamol Sulphate for Respiratory Disorders, Hindawi Publishing Corporation, ISRN Pharmaceutics Volume 2013,
35. Priyanka Khokhar, Vikesh Shukla, Formulation and Evaluation of Fast Dissolving Tablets of Diclofenac Sodium Using PVP, International Journal of Pharma Research & Review, July 2014; 3(7):12-19

36. B. Shravani, N. G. Raghavendra Rao, Formulation and Evaluation of Fast Dissolving tablets of Montelukast, sodium using Co-Processed Super disintegrants, Int. J. Drug Dev. & Res., January - March 2014, 6 (1): 125-134
37. N. Damodharan, M. Mothilal, G. Vasundhara, Formulation and Optimization of Fast Dissolving Cinnarizine Tablets, nternational Journal of PharmTech Research, 2010, Vol.2, No.2, pp 1095-1100
38. Mangesh Machhindranath Satpute, Nagesh Shivaji Tour, Formulation and in vitro evaluation of fast dissolving tablets of metoprolol tartrate, Brazilian Journal of Pharmaceutical Sciences vol. 49, n. 4, oct./dec., 2013.
39. Sourabh Jain, SK Yadav and UK Patil, Preparation and Evaluation of Sustained Release Matrix Tablet of Furosemide using Natural Polymers, Research J. Pharm. and Tech. 1(4): Oct.-Dec. 2008, pp 374-376.
40. Aswani Macharla, Sellappan Velmurugan, Veerabhadra Rao P, Design and Evaluation of Torsemide Controlled Release Matrix Tablets, Asian J Pharm Clin Res, Vol 8, Issue 2, 2015, 159-163.
41. Jagdish Jadhav, Dharmendra Mundhada, Rajesh Mujoriya, Formulation Development and Evaluation of Gastro-Retentive Drug (Torsemide) Delivery System for Diuretic Drug, Asian J. Pharm. Res. 2015; Vol. 5: Issue 3, Pg 125-130

List of Table: - Table 1: List of super disintegrates

List of Figures:-