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FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF RIZATRIPTAN BENZOATE

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ABSTRACT

In the present investigate is an attempt towards developing a formulation of Anti-migraine drug. The patents for uses and dosage form of Rizatriptan Benzoate will expire in the future so our target was to develop a dosage form as that of innovator product to file an ANDA application . Innovations in the area of Oral Dispersible Tablets are aimed at both increasing the performance of the dosage form by decreasing the disintegration time and increasing the patient compliance by masking the objectionable taste of the ingredient by direct compression technique. It containing Rizatriptan Benzoate as model drug used for the treatment of migraine disease. Formulation were prepared by using different Super disintegrate and suggested nine formulation F01-F09 & prepared Oral Dispersible Tablets F01-F09 by direct compression techniques containing Croscarmellose sodium and Crospovidone as Super disintegrant in different concentration (10.5,13.0 and 15.5mg). Optimized F08 formulation containing concentration of Crospovidone 10.5mg, Pregelatinized Starch 20mg, Aspartame 5mg as sweetener and Peppermint 1mg as flavor, Mannitol 94.77mg, Microcrystalline cellulose Avicel pH 101 37.20mg &Avicel pH 102 5mg, and Mag Stearate 12mg were used and further evaluated. Which having shows good flow properties of powder and final blend, less weight variation, Thickness 2.70-3.20 mm, Hardness 2.7-3.0 N, less disintegration time 11-15 sec and maximum drug content 99.94%. From this study, it can be concluded that Direct Compression technique has low cost, more potential and applicability in future for formulation of Orodispersible Tablet of Rizatriptan benzoate than that of Lyophilization Technique.

KEYWORDS: Oral Dispersible Tablet, Rizatriptan Benzoate, Direct Compression, Superdisintegrant, Crospovidone, Croscarmellose Sodium.

1. INTRODUCTION[1,2,3]

The oral route of drug administration is the most popular and successfully used for conventional delivery of the drugs. It offers the advantages of convenience, ease of administration, greater flexibility in dosage form design, ease of production and low cost. The parenteral route of administration is important in case of emergencies, while the topical route of drug administration recently employed to deliver drug to the specific part of the body for systemic effect. It is probable that almost 90% of all the drugs are administered by oral route. The dosage form available for oral administrations are solutions, suspensions, powders, tablets and capsules. The physical state of most of the drugs being solid, they are administered in solid dosage form.

1.1 ORALLY DISINTEGRATING TABLETS[4]

Orally disintegrating tablets are also called as oral dispersible tablets, quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets, and rapimelts.

However, of all the above terms, USP approved these dosage forms as ODT's. Recently, European Pharmacopoeia has used the term orodispersible for tablets that disperse readily within 3 min. in mouth before swallowing. These tablets are distinguished from conventional sublingual tablets, lozenges and buccal tablets which require more than a minute to dissolve in the mouth.

Many patients found the difficult to swallow tablets and capsules, which results in a high incidence of ineffective therapy.[5] The difficulty is experienced in particular by pediatric and geriatric patients, but it also relates to people who are ill on bed and those patients who have no ease of access to water. With this huge problem, it was inevitable that science had to come up with a solution.[6] This can be decided by the creation of rapidly dispersing or dissolving oral forms, which do not require water to aid swallowing. Over the past three decades, orally disintegrating tablets (ODT's) have gained considerable attention as a preferred alternative to conventional tablets and capsules due to better patient compliance.

1.2 DEFINITION OF ODT[7]

"ODT's are solid dosage forms containing medicinal substances which disintegrate rapidly, usually in a matter of seconds, when placed on the tongue".

Table No. 1: Advantages and disadvantages of ODT's[8-13]

Advantages	Disadvantages
ODT can be administer to the patient who cannot swallow tablets, patients width esophageal problems & patient who refuse to swallow such as pediatric, geriatric& psychiatric patients.	ODT is hygroscopic in nature so must be keep in a dry place.
ODT is most convenient for disabled, bedridden patients, travelers and busy people, who do not always have access to water.	It possesses mouth feeling.
The risk of chocking of suffocation during oral administration of conventional formulations due to physical obstruction is avoided, thus providing improved safety.	It is also shows the fragile, effervescence granules property.
Good chemical stability as conventional oral solid dosage form.	ODT requires special packaging for properly stabilization & safety of stable product.

1.3 CHALLENGES IN FORMULATING ODT's[14]

1.3.1 Palatability

It is a difficult challenge for formulation scientists to the taste of bitter drugs selected for oral dispersible tablets. As most drugs are unpalatable, orally disintegrating drug delivery systems usually contain the medicament in a taste-masked form. Hence, taste-masking of the drugs becomes critical to patient compliance.

1.3.2 Mechanical strength

In order to allow ODT's to disintegrate in the oral cavity, they are made of either very porous or soft-molded matrices or compressed into tablets with very low compression force, which makes the tablets friable or brittle, and difficult to handle.

1.3.3 Hygroscopic/moisture sensitive

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.

1.3.4 Dose of drug

The application of technologies used for ODT's is inadequate by the amount of drug that can be incorporated into each unit dose. Molecules requiring high doses present mainly three challenges to development of fast dissolve dosage forms;

a] Taste masking of the active ingredient,

b] Mouth feel or grittiness and

c] tablet size

1.3.5 Aqueous solubility

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

1.3.6 Size of tablet

The degree of ease when taking a tablet depends on its 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.

1.3.7 The drug property

Many drug properties could potentially affect the performance of fast dissolving tablets. For example, the solubility, crystal morphology, particle size and bulk density of a drug can affect the final tablet characteristics, such as tablet strength and disintegration.

1.3.8 Month feel

The ODT should not disintegrate into larger particles in the oral cavity. The particles generated after disintegration of the ODT should be as small as possible. ODT should leave minimal or on residue in mouth after oral administration. Further addition of flavors and cooling agents like menthol improve the mouth feel.

1.3.9 Sensitivity to Environmental Conditions

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

1.4 Ideal Characteristics of ODT's[15-17]

ODT's should depict some ideal characteristics to distinguish them from traditional conventional dosage forms.

- ODT's have no requirement of water for swallowing purpose but it should dissolve or disintegrate in mouth within fraction of seconds.
- ODT's provide pleasant feeling in the mouth be compatible with taste masking.
- ODT's should leave negligible or no residue in the mouth after oral administration.
- ODT's exhibit low sensitivity to altered environmental conditions such as humidity and temperature.
- ODT's should be adaptable and amenable to conventional processing and packaging equipment at nominal expense.

1.5 Criteria for selection of drug candidate[18]

Several factors may be considered while section an appropriate drug candidate for development tablets. The ultimate characteristics of a drug for dissolution in mouth and pre-gastric absorption includes,

- ODT's should be free from bitter taste.
- ODT's has dose lower than 20mg.
- ODT's should have small to moderate molecular weight.
- ODT's should have good solubility in water and saliva.
- ODT's should be partially unionized at oral cavity pH.
- ODT's should have ability to diffuse and partition Into the epithelium of upper GIT (log>1, or preferably>2)
- ODT's should have ability to permeate oral mucosal tissue.

Investigators have formulated ODT's for various categories of drugs used for therapy in which rapid peak plasma concentration is required to achieve the desired pharmacological response. These include neuroleptics, cardiovascular agents, and analgesics, anti allergic, antiepileptic, anxiolytics, sedatives, hypnotics, diuretics, anti-parkinsonism agents, anti-bacterial agents and drugs used for erectile dysfunction.[15]

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

- Short half-life and frequent dosing.
- Very bitter or otherwise unacceptable taste because taste making cannot be successfully achieved.
- Combination with anticholinergic.

1.6 Patented Technologies

a. Zydis Technology[19]

A Zydis tablet is produced by lyophilizing or freeze-drying the drug in a matrix usually consisting of gelatin.

b. Orasolv Technology[19]

In this system active medicament is taste masked. It also contains effervescent disintegrating agent. Tablets are made by direct compression technique at low compression force in order to minimize oral dissolution time.

c. Durasolv technology[19]

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.

d. Wow Tab Technology[20]

It is patented by yamanouchi Wow means "without water". Wow tab is an intra buccally soluble, compressed tablets consisting of granules made with saccharine of low and high mould ability.

e. Oraquick[21]

This technology is patented by K.V.Pharmaceuticals. It utilizes taste masking microsphere technology is called as micro mask, which provides superior mouth feel, significant mechanical strength, and quick disintegration/dissolution of product.

f. Nano Crystal Technology[19]

Elan's proprietary Nano Crystal technology (NanomeltTM) can improve compound activity and final product characteristics. Decreasing particle size increases the surface area, which leads to an increase in dissolution rate.

g. Pharmaburst technology[19]

SPI Pharma, New castle, patent this technology. The Pharmaburst ODT uses a proprietary disintegrate (Pharmaburst) that is based on mannitol blended with conventional tableting aids.

h. Flash Tab[19]

Ethypharm, Saint Cloud, France has patented the Flash tab technology. This technology includes granulation of excipients by wet or dry granulation method and by compressing into tablets. (Change et al.,2000). This technology relays on the use of super disintegrates.

i.Frosta technology[22]

Akina patents this technology. The frosta technology is based on the compression of highly plastic granules at low pressure to prepare fast melting tablets.

j. Advantol^{TM}200[22]

Advantol^{TM} 200 is a directly compressible excipient system offering "Soft-Melt" functionality and specially formulated for nutraceuticalapplications. SPI Pharma's Advantol platform uses proprietary co-processing technology.

k. Advatab[22]

AdvaTab tablets disintegrate rapidly in less than 30 seconds. These are prepared using polymer-coated drugs particles that are uniformly dispersed in an ultra-fine, low-water content, rapidly disintegrating matrix with superior organoleptic properties.

- **Quicksolv technology**[21]

This technology is patented by Janssen Pharmaceuticals. It uses two solvents in formulating a matrix which disintegrates instantaneously. Methodology includes dissolving medium components in water and the solution or suspension is frozen. Then dry the matrix by removing water using an excess of alcohol (solvent extraction). Thus the product formed has uniform porosity and adequate strength for handling.

- **Ziplet technology**[23]

In ziplet technology water insoluble drugs or drugs as coated microparticles are used. The addition of a suitable amount of water-insoluble inorganic excipients combined with disintegrants imparted an excellent physical conflict to the oral dissolving tablets (ODT) and the simultaneously maintained optimal disintegration.

- **Oraquick**[24]

The oraquick fast-dissolving tablets preparation utilizes a patented taste masking technology. The taste masking method does not develop solvents of any kind, and consequently leads to faster and additional efficient production. Also, lower heat of manufacture than alternative fast-dissolving/ disintegrating technologies makes Oraquick suitable for heat-sensitive drugs.

1.7 Techniques for preparing mouth dissolving tablets

Techniques for preparing ODTs[21]

The various techniques are being utilized or adopted to Prepare ODTs

- Freeze drying or Lyophilization.
- Sublimation.
- Mass extrusion.
- Melt Granulation.
- Spray drying.
- Molding.
- Nanonization.
- Direct compression.
- Cotton candy process.
- Phase transition process.

- **Freeze drying or Lyophilization[24]**

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 dissolve rapidly. A Typical process involved in the manufacturing of ODT using this technique. The active drug is dissolve/disperse in an aqueous solution of a carrier or polymer. The mixture is dosed through weight and poured in the wells of the performed Blister packages. The trays holding the blister packs are passed 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.

Disadvantages of freeze drying

This technique is expensive and time consuming; fragility makes conventional packaging unsuitable for these products and poor stability under stressed condition.

- **Sublimation[25]**

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 insert 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**[21]

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 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 solvent is necessary. For there is no drying step, the process is less time consuming and uses less energy than wet granulation. It is a useful technique to enhance the dissolution rate of poorly water-soluble drugs such as griseofulvin 41. This methodology to prepare MDT with sufficient mechanical integrity, involves the use of a hydrophilic waxy binder(superpolystate, PEG-6-Stearate). Superpolystate is a waxy material with a melting point of 33-37^{0}C 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.[26]

- **Spray drying**[21]

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 particular Support matrix, which is equipped by spray drying an aqueous components 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**[18]

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 form and enhances the dissolution rate.

- **Advantage**

As the dispersion matrix is made from water-soluble sugars, molded tablets disintegrate more rapidly and offer improved Taste. These properties are enhanced when tablets with porous Structures are produced or when components that are physically modified by the molding process are used. In Comparison to Iyophilization process, tablets produced by molding technique are easier to adapt to the industrial scale.

- **Disadvantage**

The molded tablets have poor mechanical strength, they may Undergo erosion and breaking during handling. Through Hardening can increase the strength of tablets but it would be at the cost of their disintegration time.

- **Nanonization**[27]

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-crytals of the surface incorporated into mouth dissolving Tablets. This system is suitable for poorly water soluble drugs. Sahu et al., Novel Science International Journal of Pharmaceutical Science (2012),1(3):204-211208. Other advantages of this technology include fast Disintegration/ dissolution of nanoparticles leading to better Absorption and hence higher bioavailability and reduction in Dose, cost effective manufacturing process, conventional durability and wide range of Doses i.e.200 mg of drug per unit.

- **Direct compression**

This 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 pretreatment 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.[28]

Table No.2: Processing Steps Commonly Required In The Various Tablet Preparation Techniques (29)

Processing steps	Wet granulation	Dry granulation	Direct compression
Raw material	✓	✓	✓
Weight	✓	✓	✓
Screen	✓	✓	✓
Mix	✓	✓	
Compress (Slug)		✓	
Wet mass	✓		
Mill	✓		
Dry	✓		
Mill	✓	✓	
Mic	✓	✓	
Compress	✓	✓	

✓

- **Cotton candy process[30,31]**

It is also known as the “candy floss” method and forms the basis of the technologies such as flash dose (Fuisz Technology). It utilizes an inimitable spinning mechanism to Yield floss like crystalline structure which mimics cotton candy. ODT is formed using a candy floss or shear form Matrix; the matrix is formed from saccharides or Polysaccharides processed into amorphous floss by a simultaneous action of flash melting and centrifugal force. The matrix is then cured or partially recrystallized to provide a compound with good flow properties and compressibility. The candy floss can then be milled and blended with active ingredients and subsequently compressed into MDT. However the high processing temperature limits the use

of this technology. Characteristics: It can accommodate high doses of drugs and offers improved mechanical strength.

- **Phase transition process**

It is concluded that a combination of low and high melting point sugar alcohols, as well as a phase transition in the manufacturing process, are important for making MDTs without any special apparatus. MDT was produced by Compressing powder containing erythritol (melting point:122^{0}C) and xylitol (melting point:93^0,95^{0}C), and then heating at about 93^{0}C for 15 min. after heating, the median pore size of the tablets was increased and tablet hardness was also increased. The increase of the tablet hardness with heating and storage did not depend on the crystal state of the lower melting point sugar alcohol.[32]

Table No. 3: ODT's Products Available In The Market

Brand name	Active ingredient	Company
Dray MD	Domperidone	Ray Remidies
Olanex Instab	Olanzepine	Ranbaxy
Romilast	Montelukast	Ranbaxy
Torrox MT	Rofecoxib	Torrent
Zofex-25 MD	Rofecoxib	Zota Pharma
Nency MD	Nimesulide	Zenon Health care
Nexus MD	Nimesulide	Lexus
Nimez MD	Nimesulide	Zota pharma
Topmide	Nimesulide	Antigen Health Care
Zoming ZMT	Zolmitriptan	Astra Zeneca
Alavert	Loratidine	Wyeth health care
Cibalginadue FAST	Ibuprofen	Novartis Health care
NuLev	Hyoscyamine sulphate	Schwarz Pharma
Hyoscyamine sulphate ODT	Hyoscyamine sulphate	ETHEX corporation
Nurofen Flash Tab	Ibuprofen	Boots healthcare
Kemstro	Baclofen	Schwarz Pharma
Benadryl Fastmelt	Diphenhydramine	Pfizer
Zolpidem ODT	Zolpidem tratrate	Bioavail
Feldene Melt	Piroxicam	Pfizer
Maxalt MLT	Rizatriptan benzoate	Merck
Zofran ODT	Ondansetron	Glaxo Smith Kline
Fazalco	Clonzapine	Alamo Pharmaceuticals

1.8 Migraine

Migraine is a common neurological disorder, which is characterized by intense, unilateral, throbbing and pulsatile headache attacks, lasting for 4-72 hours and accompanied by anorexia, nausea, vomiting, photophobia and/or phonophobia.[33]

1.8.1 Trigger Factors

A tendency to get migraines can be inherited. Some people find certain things seem to trigger their migraines.

Common triggers include

- Stress or relaxing after stress.
- Hormone changes (e.g., menstruation, pregnancy)
- Glare, bright or flickering light.
- Strong smells or fumes.
- Weather, air pressure and altitude changes.
- Smoke, particularly from cigarettes.
- Dehydration.
- Alcohol.
- Caffeine withdrawal.
- Inadequate sleep.
- Delaying or missing meals.
- Certain foods and food additives (e.g., chocolate, citrus fruit, red wine, aged cheese, MSG).
- Certain medicines (e.g., oral contraceptives, overuse of pain relievers).
- Strenuous exercise, including sex.
- Back and neck problems.
- Eye strain.[34]

1.8.2 Types of Migraine (according HIS classification)

1.8.2.1 Migraine without aura, this is the most common type of migraine. Symptoms include the following:

- The headache is usually on one side of the head, typically at the front or side. Sometimes it is on both sides of the head. Sometimes it starts on one side, and then spreads all over the head. The pain is moderate or severe and is often described as ‘throbbing’ or ‘pulsating’. Movements of the head may make it worse. It often begins in the morning, but may begin at any time of day or night. Typically, it gradually gets worse and peaks after 2-12 hours, then gradually eases off. However, it can last from 4 to 72 hours.

- Other symptoms that are common include: feeling sick (nausea), vomiting, you may not like bright lights or loud noises, you may just want to lie in a dark room, being off food, blurred vision, poor concentration, stuffy nose, hunger, diarrhoea, abdominal pain, passing lots of urine, going pale, sweating, scalp tenderness, and sensations of heat or cold.

1.8.2.2 Migraine with aura, about 1 in 4 people with migraine have migraine with aura. The symptoms are the same as migraine without aura, but also include an aura (warning sign) before the headache begins.

- Visual aura is the most common type of aura. Examples of visual aura are: a temporary loss of part of vision, flashes of light, objects may seem to rotate, shake, or 'boil'. Numbness and 'pins and needles' are the second most common type of aura. Numbness usually starts in the hand, travels up the arm, then involves the face, lips, and tongue. The leg is sometimes involved.
- Problems with speech are the third most common type of aura.
- Other types of aura include: an odd smell, food cravings, a feeling of well-being, other odd sensations.

Rarer Types of Migraine with Aura

Basilar-type Migraine, include two or more of the following symptoms, visual disturbances, speaking difficulties, hearing problems, tingling in the hands and feet, dizziness, vertigo and ringing in the ears.

Familiar Hemiplegic Migraine (FHM), this condition linked with a genetic defect. Temporary paralysis on one side of the body, coma, confusion, and drowsiness. The headaches can go on for 5 to 10 days. The symptoms can be mistaken for epilepsy.

Sporadic Hemiplegic Migraine, this has the same symptoms as Familiar Hemiplegic Migraine but has no family link.

1.8.2.3 Childhood periodic syndromes, that are commonly precursors of migraine include cyclical vomiting (occasional intense periods of vomiting), abdominal migraine (abdominal pain, usually accompanied by nausea), and benign paroxysmal vertigo of childhood.

1.8.2.4 Retinal migraine, involves migraine headaches accompanied by visual disturbances (Acute head pain with blind sports) or even blindness in one eye.

1.8.2.5 Complications of migraine, describe migraine headaches and/or auras that are unusually long or unusually frequent, or associated with a seizure or brain lesion.

1.8.2.6 Probable migraine, describes conditions that have some characteristics of migraine but where there is not enough evidence to diagnose it as a migraine with certainty.[35]

1.8.3 Anti-migraines

An anti-migraine is a neurological medication used for alleviating acute migraine and prevention or prophylaxis migraine. Drug groups known as Natural ergot alkaloids and other semi-synthetic and synthetic derivatives and Triptans are particularly associated with the term. These medications are now among the drugs most commonly prescribed by physicians, and their effectiveness and adverse effects are the subject of many studies and competing claims.

Most anti-migraines have require rapid onset of action and are usually administered when symptom start like nausea, vomiting, throbbing, and sensitivity to light and noise etc.[36]

Oral delivery is currently the gold standard in pharmaceutical industry where it is regarded as the safest, most convenient and most economical. 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 patient, is the difficulty to swallow. Drinking water plays an important role in the swallowing of oral dosage forms.[37] Drug delivery systems become sophisticated as pharmaceutical scientist acquire a better understanding of the physicochemical and biochemical parameter patient to their performance.[38] Over the past three decades, orally disintegrating tablets have gained considerable attention as a preferred alternative to conventional tablets due to better patient compliance. This tablets will be formulated for regulated market. Such dosage forms might prove to be beneficial to the pediatric, geriatric, and bedridden patients and for active patients who are busy and traveling and may not have access to water. Such formulations provide an opportunity for product line extension in the many elderly person will have difficulties in the

taking conventional oral dosage forms(viz., solutions, suspension, tablet and capsules) because of hand tremors and dysphagia.[39] oral dispersible tablets are also called as fast dissolving tablet, mouth dissolving tablet, melt in mouth tablet, rapimelts, porous tablets, quick dissolving tablets etc.[40] orodispersible tablets are those when put on a tongue disintegrates instantaneously releasing the drug which dissolves or disperse in the saliva. The faster the drug into solutions quicker the absorption and onset of clinical effects.[41]

5. MATERIALS AND METHODS

DRUG PROFILE[4,42]

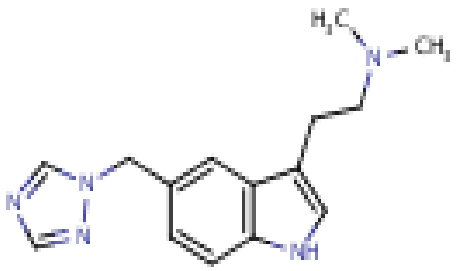
*** Name Of Drug : Rizatriptan Benzoate**.

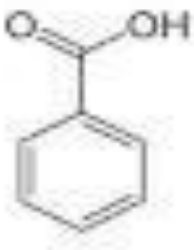
*** Molecular Formula :** $C_{15}H_{19}N_5C_7H_6O_2$

*** Molecular Weight :** 391.47

*** IUPAC Name :** 1H-Indole-3-ethanamine, N,N-dimethyl 5-(1H-1,2,4 triazole-1ylmethyl)-monobenzoate.

*** Molecular Structure :**





*** Melting Point :** 178-180^{0}c.

*** Category :** Anti-migraine.

*** Solubility :** Soluble in water, Sparingly soluble in methanol, Slightly soluble in methylene.

A. MATERIALS

The following drug, excipients and chemicals were used for the formulation and evaluation of orally disintegrating tablet.

Table N0. 4: Materials Used

Sr. No.	Name	Category	Suppliers of material
1	Rizatriptan Benzoate	Active	Alkem Lab Mumbai
2	Pearlitol 160C (Mannitol)	Diluent	Modern Science
3	Avicel pH 101 (MCC)	Diluent	Modern Science
4	Lycatab C (Pregelatinized starch)	Binder	Modern Science
5	Avicel pH 102 (MCC)	Diluent	Modern Science
6	Kollidon CL	Super disintegrant	Modern Science
7	Ac-di-sol(Croscarmellose sodium)	Super disintegrant	Modern Science
8	Polyplasdone XL10(Crospovidon)	Super disintegrant	Modern Science
9	Aspartame	Sweetener	Modern Science
10	Mag. Stearate	Glident, Lubricant	Modern Science
11.	Pappermint	Flavour	Modern Science

Table No. 5: Reagents Used

Sr. No.	Reagents	Suppliers of Material
1	Potassium Dihydrogen Phosphate	Modern Science

B. Equipments

Table No. 6: Equipments Used

Sr. No.	Equipment	Manufacturer & Model
1.	Electronic Weighing Balance	Citizon , CG 203
2.	UV-Visible Spectrophotometer	Shimadzu 2450
3.	Infra Red Spectrophotometer	Shimadzu 8400S
4.	Friability Tester	Roche Friabilator KI 91/01
5.	Differential Scanning Calorimeter	Shimadzu 60
6.	Melting Point Apparatus	KUMAR,VMP/D
7.	Digital pH meter	Toshniwan CL 54
8.	Dissolution Apparatus	Electrolab, EDP/08L_X
9.	Hot Air Oven	Biotecs, BT 10
10.	Stability Chamber	Thermolab, TH200H
11.	Tablet Disintegtation Tester	KUMAR Industries
12.	Tablet Compression Machine	Shivpharma Enginnering, Ahmedabad, ETBC 1974
13.	Ultrasonicator	SENEC, DTC 503

5.1 METHOD

Formulation Of Oral Dispersible Tablet By Direct Compression

1. Calculate and weigh Rizatriptan Benzoate (API) based on its potency.
2. Dispense and weigh accurately all other ingredients as per batch formula and then mix well Rizatriptan Benzoate and Pearlitol, magnesium stearate sift through # 60 mesh and other through # 40 mesh.
3. Transfer step material for 30 min. in Double Cone Blender.

4. Compressed above blend obtained in with their respective punch.

Process Flow Diagram

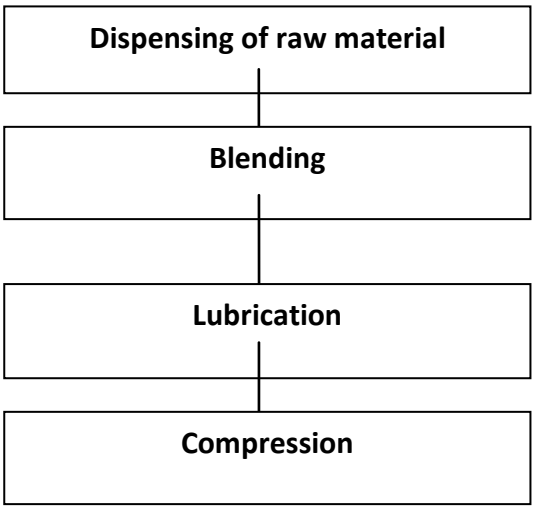


Fig: Process Flow Diagram

5.2 EXPERIMENTAL WORK [43,44]

5.2.1. Analysis Of Marketed Tablet (Maxalt – MLT 10 mg)

Analysis of the marketed product was carried out for various physical parameters and In-vitro dissolution profile. These tests are done according to the procedure described below in evaluation of tablet.

5.2.2 Preformulation Studies

Preformulation testing is the first step in the development of dosage forms of a drug substance. It can be defined as investigation of physical and chemical properties of a drug substance alone and when combined with excipients.The overall objective of preformulation studies is to generate information useful to the formulator in developing stable and bioavailable dosage forms, which can be mass-produce.

Preformulation study can devided into two subclasses:

A. API Characterization

B. Compatibility Study

A. API Characterization

Characteristics

White to off-white, Crystalline powder. It is odorless and has pungent bitter taste.

Melting Point Determination

Melting point of drug was determined by using laboratory melting point apparatus.

Loss On Drying

0.5gm of sample of Rizatriptan Benzoate was accurately weighed and the powder was kept in apparatus for 5 min. at 105^0c and the moisture content was calculated.

Bulk density

Bulk density of Rizatriptan Benzoate was determined by pouring gently 25gm of sample through a glass funnel into 100 ml graduated cylinder.

Bulk density = weight of sample in gram / volume occupied by the sample.

Tapped density = Wt. of sample in gram / Tapped volume.

Compressibility Index = Tapped Density - Bulk Density / Tapped Density x 100.

Housner's Ratio = Tapped Density / Bulk Density.

Angle of Repose

$\tan \theta = h / r$

$\theta = \tan^{-1} h / r$

Where, θ = angle of repose,

h = height,

r = radius.

Solubility Analysis

A semi quantitative determination of solubility can be made by adding a solute in small incremental amounts of fixed volume of solvents whose pH ranging from 1.2 to 7.4 including distilled water.

Compatibility Study

Compatibility studies were checked carefully for the best Excipients selection. One gram of each sample was filled in 10 ml clear glass vial and non leachable, impermeable closure was fitted to the vials. After mentioned storage time samples were analyzed as per schedule.

- Two vials (Drug + Excipients) in 40^0C/75 % RH along with the placebo.
- Two vials (Drug + Excipients) for initial analysis along with the placebo.

This is for to analyze the compatibility between Rizatriptan Benzoate and Excipients proposed to incorporate into the formulation.

5.3 EVALUATION OF TABLETS

5.3.1 Pre – compression Parameters

- Loss on drying (Dry mix and final blend)
- Density analysis
- Compressibility Index and Housner's Ratio
- Angle of repose

These parameters are determined using the same procedure as described previously in preformulation study.

5.3.2 Post – compression Parameters

1. Shape of tablets

Randomly picked tablets from each formulation were examined for the shape of the tablets.

2. Weight variation test

Twenty tablets were weighed and the average weight was calculated. The individual weight was compared with average weight. The tablets pass the test if not more than two tablets are outside the percentage limit and if no tablet differs by more than two times the percentage limit. The following percentage deviation in weight variation is allowed according to USP:

Table No. 7: Weight variation limit.

Average Weight Of Tablet	Percentage Weight Variation
The tablet of 130 mg or less	10 %
More than 130 mg and less than 324 mg	7.5 %
324 mg or more	5 %

In all the formulation the tablets weight is less than 324mg, hence 7.5% maximum difference allowed.

3. Thickness

Thickness was determined for twenty pre-weighed tablets of each batch using a vernier scale and the average thickness was determined in mm. the tablet thickness should be controlled within a ±5% variation of a standard.

4.Hardness

The crushing strength of the tablets was measured using a Monsanto hardness tester. Three tablets from each formulation batch were tested randomly and the average reading was noted.

5.Friability

The friability of a sample of 10 tablets was measured using a Roche Friabilator. Twenty preweighed tablets were rotated at 25 rpm for 4 minutes. The tablets were taken out, dedusted and reweighed. The percentage friability of the tablets was measured as per the following formula,

Percentage friability = (Initial weight – Final weight) / Initial weight × 100.

6.Disintegration Time

The disintegration test is carried out in an apparatus containing a basket rack assembly with six glass tubes of 7.75 cm in length and 2.15 mm in diameter, the bottom of which consists of a # 10 mesh sieve. The basket is raised and lowered 28-32 times per minute in a medium of 900 ml which is maintained at 37±20C. Six tablets were placed in each of the tubes and the time required for complete passage of tablet fragments through the mesh (#10) was considered as the disintegration time of the tablet. The disintegration time that patients can experience for oral disintegrating tablets ranges from 5 to 30 sec.

7. Drog Content Uniformity Test

Twenty tablets were weighed and powdered. An amount of the powder equivalent to 10 mg of Rizatriptan dissolved in 100 ml of 0.21 N HCL, filtered, diluted suitably and analyzed for drug content at 280 nm using UV-Visible spectrophotometer (UV grade – Shimadzu, 2450)

8. In- vitro dissolution test

Dissolution study of tablets preformed in USP II (paddle) dissolution test apparatus (Electrolab, EDP O8/L_X) using 900ml of water as a dissolution media. The tablets was loaded into an each basket of dissolution apparatus; the temperature of dissolution media was maintained at 37 ± 0.5^oC with stirring speed of 50 RPM throughout the study. Aliquots of dissolution media containing 5ml of sample were withdrawn at time interval of 0,5,10,15,20,30 minutes and 5ml of fresh dissolution media maintained at the same temperature was replaced after each withdrawal. The samples were analyzed spectrophotometrically at 280 nm using water as blank. The raw dissolution data was analyzed for calculating the amount of drugs released and percentage cumulative drug released at different time intervals.

Table No. 8: Dissolution Parameters

Drug Name	Dosage Form	USP Apparatus	Speed (RPM)	Medium	Volume (ml)	Sampling Times (Minutes)
Rizatriptan Benzoate	ODT	II (Paddle)	50	Water	900	5, 10, 15, 20 & 30

9. Stability Study[45]

Stability study was done by exposing the formulation to different conditions including stress conditions of temperature & pressure. Generally stability study was done at 40°C/75%RH (for 1, 2, 3, 6 months), 30°C/75%RH (for 1, 2, 3, 4, 6, 9, 12, 24 months), 2-8°C (1, 2, 3, 6, 9, 12, 24 months). After that study was over formulation was checked for its physical & chemical parameters, if all parameters were present within the specification limit then that formulation was selected.

FORMULATION AND DEVELOPMENT

Table No. 9: Materials Used

Sr. No.	Ingredient	F01	F02	F03	F04	F05	F06	F07	F08	F09
1.	Rizatriptan Benzoate	14.53	14.53	14.53	14.53	14.53	14.53	14.53	14.53	14.53
2.	Pearlitaol 160C(Mannitol)	94.77	94.77	94.77	94.77	94.77	94.77	94.77	94.77	94.77
3.	Avicel –pH101 (MCC)	37.20	37.20	37.20	37.20	37.20	37.20	37.20	37.20	37.20
4.	Lycatab C (Pregelatinized Starch)	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0
5.	Kollidone CL	15.5	10.5	13.0	-	-	-	-	-	-
6.	Ac-di-sol	-	-	-	15.5	10.5	13.0	-	-	-
7.	Polyplasdone XL10(Crosspovidone)	-	-	-	-	-	-	15.5	10.5	13.0
8.	Avicel pH 102	-	5.0	2.5	-	5.0	2.5	-	5.0	2.5
9.	Aspartame	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0
10.	Peppermint	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
11.	Mag. Stearate	12.0	12.0	12.0	12.0	12.0	12.0	12.0	12.0	12.0
	Total	200.0	200.0	200.0	200.0	200.0	200.0	200.0	200.0	200.0

6. RESULTS

The present investigation is carried out to develop Oral Dispersible Tablet dosage form of Rizatriptan Benzoate the Oral Dispersible Tablet was prepared by using different excipients.

6.1 PREFORMULATION STUDY OF DRUG

6.1.1. Characterization of drug

Melting Point

The M.P. of the drug was found to be in the range 178-180^{0}c which matches with the reported value(178-180^{0}c).

Table No. 10: pH Dependent Solubility Study

Medium	Solubility (mg/ml)
Purified Water	69.55
0.1N HCL	27.09
0.01N HCL	62.32
0.001N HCL	67.77
pH 4.5 Acetate Buffer	55.94
pH 5.5 Phosphate Buffer	55.20
pH 6.8 Phosphate Buffer	88.89
pH 7.4 Phosphate Buffer	44.95

Powder Flow Properties

Table No. 11: Powder Flow Properties

Parameters	Observations
Angle of repose	27
Bulk Density	0.54gm/ml
Tapped Density	0.64gm/ml
Housner's ratio	1.18
Compressibility Index	15.62
LOD	1.52%

Flow property of Rizatriptan Benzoate (API) was found to be **Fair**. Hence during dosage form developed excipients be incorporated to improve flow properties.

6.2 Compatibility Study

There is no any color change observed in the API and excipients. So, all components are compatible with each other. And they comply with compatibility study specifications of color.

IR SPECTRUM OF RIZATRIPTAN BENZOATE

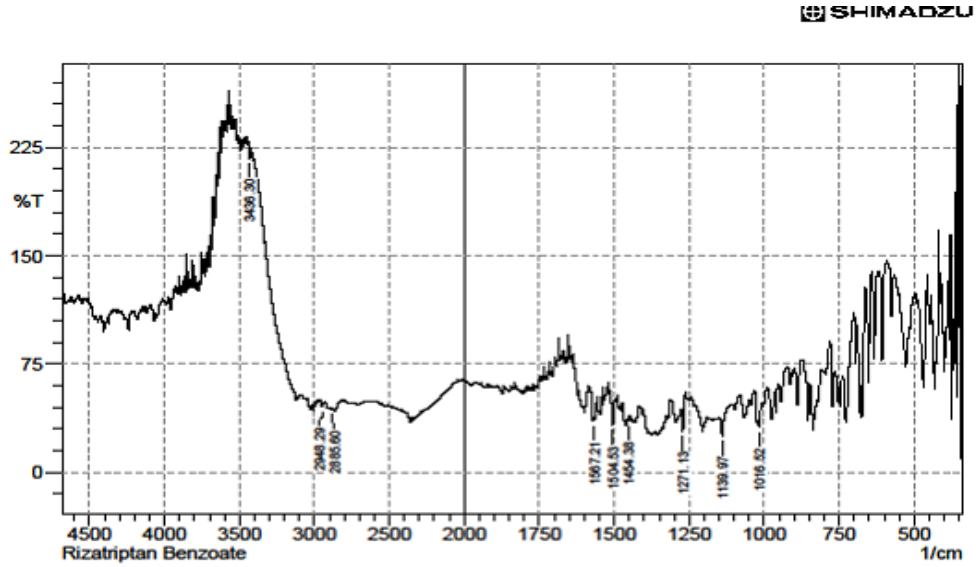


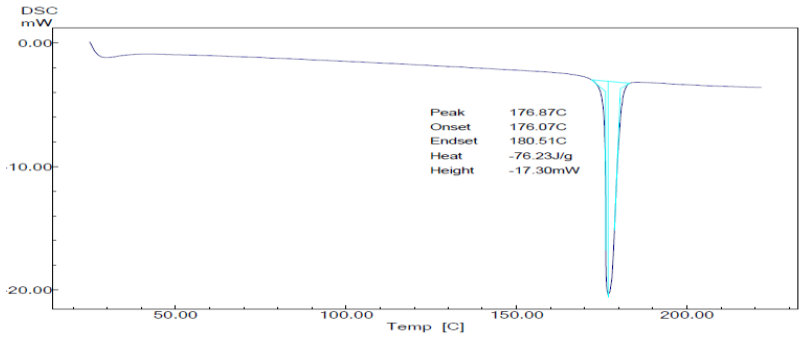
Fig: IR Spectrum of Rizatriptan Benzoate

Table No. 12: Vibrations and their respective frequencies for IR Spectrum of Rizatriptan Benzoate.

Sr. No.	Vibrations	Frequency cm^{-1}
1.	NH Stretch	3430
2.	CH_2 Stretch	2888
3.	C=N Stretch	1505
4.	NH Bend	1569
5.	CH_2 Bend	1446
6.	C-N Stretch	1271
7.	C-N Stretch	1140
8.	C-N Stretch	1016

Dsc Study

DSC thermogram of pure drug exhibited a sharp endothermic peak at 178-180^{0}C. In presence of the excipients neither peak nor a shift in DSC thermograms indicated absence of physical or chemical instabilities as shown in Figure.



a) DSC Of Rizatriptan Benzoate

6.3 Compatibility Study

Table No. 13 : Excipients Selected After Preformulation Study

Sr. No.	Name	Category	Remarks
1	Rizatriptan Benzoate	Active	-
2	Pearlitol 160C (Mannitol)	Diluent	Compatible
3	Avicel pH 101 (MCC)	Diluent	Compatible
4	Lycatab C (Pregelatinized starch)	Binder	Compatible
5	Avicel pH 102 (MCC)	Diluent	Compatible
6	Kollidon CL	Super disintegrant	Compatible
7	Ac-di-sol	Super disintegrant	Compatible
8	Polyplasdone XL10 (Crosspovidon)	Super disintegrant	Compatible
9	Aspartame	Sweetener	Compatible
10.	Peppermint	Flavour	Compatible
11.	Mag. Stearate	Glident, Lubricant	Compatible

6.4 Evaluation of Formulation Parameters

6.4.1 Table No. 14: Pre Compression Parameters of All Trials

Trial No.	Loss on Drying (%w/w)		Bulk Density (gm/ml)	Tap Density (gm/ml)	Carr's Index (%)	Housner's Ratio
	Pre-Lubricated Granules	Final Blend				
F01	1.19	2.46	0.62	0.68	8.8	1.18
F02	1.92	4.12	0.57	0.64	10.93	1.12
F03	1.19	3.18	0.58	0.66	12.12	1.13
F04	1.99	2.98	0.60	0.70	14.28	1.13
F05	1.83	2.73	0.62	0.70	11.42	1.12
F06	1.99	2.45	0.54	0.64	15.62	1.18
F07	1.92	2.49	0.60	0.70	14.28	1.16
F08	1.99	2.50	0.59	0.65	9.23	1.10
F09	1.19	3.00	0.62	0.70	11.42	1.12

6.4.2 Evaluation of tablet formulation

Table No. 15: Post Compression Parameters Of All Trials

Trial No.	Average wt.(mg)	Thickness (mm)	Hardness (N)	Friability (%)	Disintegration time (sec)	Assay (% w/w)
Marketed Product	66mg	3.70±0.04	Very Soft	0.30	5-9	98.15
F01	198-203	2.70-3.20	2.7-3.0	0.32	13-18	98.00
F02	196-204	2.80-3.10	2.7-3.0	0.34	15-19	97.89
F03	196-204	2.80-3.20	2.7-3.0	0.32	14-19	96.29
F04	197-203	2.70-3.20	2.7-3.0	0.47	13-17	96.58
F05	197-203	2.80-3.20	2.7-2.9	0.37	15-19	97.50
F06	197-203	2.70-3.10	2.7-3.0	0.30	14-19	99.15

F07	197-203	2.90-3.20	2.7-3.0	0.30	12-16	99.77
F08	198-203	2.70-3.20	2.7-3.0	0.30	11-15	99.94
F09	197-203	2.70-3.20	2.7-3.0	0.37	13-17	99.94

Table No. 16: Dissolution Data of Trials (F01 – F09) in 0.1 N HCL

Time Point	Formulation (% Drug Release)									
	Marketed Product	F01	F02	F03	F04	F05	F06	F07	F08	F09
2	82.93	84.87	74.32	78.17	86.13	74.83	79.83	91.12	94.42	85.27
5	94.08	85.15	76.91	79.45	88.69	79.01	82.38	92.91	95.43	89.53
10	94.49	91.21	77.76	81.96	89.55	83.63	84.90	95.01	95.85	91.61
15	95.73	94.52	80.28	86.58	95.41	84.08	85.76	95.43	98.37	92.49
20	97.79	97.12	84.90	88.70	96.70	88.62	88.63	95.84	98.75	65.83
25	99.93	97.54	89.11	89.55	97.96	93.31	84.98	96.26	99.65	97.50
30	100.41	98.80	90.38	91.64	99.64	94.48	92.00	99.21	100.00	97.51

Table No. 17: Dissolution Data of Trials (F01 – F09) in Phosphate Buffer pH 6.8 :

Time Point	Formulation (% Drug Release)									
	Marketed Product	F01	F02	F03	F04	F05	F06	F07	F08	F09
2	89.21	74.74	81.55	73.04	85.78	75.56	90.91	73.04	90.06	89.19
5	92.27	85.37	83.71	76.00	87.06	83.62	93.07	82.81	91.30	90.56
10	94.83	88.83	85.39	81.90	87.99	84.56	93.98	92.28	93.96	93.06
15	95.69	92.26	88.83	91.37	89.70	88.83	95.63	93.98	94.80	93.97
20	96.55	96.53	93.11	92.24	92.23	97.36	96.53	96.52	97.35	95.63
25	98.26	98.26	98.24	95.68	94.78	98.26	97.36	97.36	99.97	97.36
30	99.97	100.08	99.12	99.96	99.07	99.07	99.91	99.78	100.82	100.81

6.5 Exposure Study Of Final Formulation (F08)

Exposure studies were carried out for selected trial. In exposure study, our trial and innovator formulation was subjected to different environmental stress conditions like 800 for 2 days and in autoclave at 121^0C for 15 min. the result shows similar behavior between our trial and innovator in different conditions.

Table No. 18: Exposure Study Of Final Formulation (F08)

Storage Condition→	**Room Temperature**		**80^0C**		**Autoclave**	
Period→	**Initial**		**2 Days (open)**		**At 121^0C for 15 min.**	
Formulation→	Innovator	F08	Innovator	F08	Innovator	F08
Parameters↓	**Observations**					
Physical Appearance	Whitish yellow	White	Whitish yellow	White	Whitish Yellow	White

Hardness(N)	Very Soft	2.8-3.0	Very Soft	2.8-3.0	Not Applicable	
LOD (%)	NA	2.45	NA	1.88	NA	3.10
D.T. (sec)	2-5	11-15	2-5	14-16	Not Applicable	
Assay (%)	99.77	99.94	99.15	99.77	99.10	99.15
Dissolution (at 30 min.)	100.41	100.00	NA	NA	Not Applicable	

6.6 Stability Study

The stability studies of final trial was done for 3 months by packing in HDPE container in humidity chamber (40^0C/75%RH) The result given in table for 1 month, 2 months and 3 month show. All parameters of formulation including physical parameters, content uniformity or dissolution profile were within specification limit. So it indicates optimized formulation were stable.

Table No. 19: Stability Observations Of Trials F08

Storage Condition→	**Room Temperature**		**40^0C/75%RH**						**Specifications**
Period→	**Initial**		**1 Month**		**2 Month**		**3 Month**		
Formulations→	Innovator	F08	Innovator	F08	Innovator	F08	Innovator	F08	
Parameters	**Observations**								
Physical Appearance	Whitish yellow	White	Whitish yellow	White	Whitish yellow	White	Whitish yellow	White	No change should observe.
Hardness (N)	Very Soft	2.7-3.0	Very Soft	2.4-2.8	Very Soft	2.6-2.9	Very Soft	2.5-2.8	NMT 3.0 N
LOD(%)	NA	2.45	NA	2.55	NA	2.68	NA	2.77	NMT 4.0%
D.T.(sec)	2-5	11-15	2-5	11-16	2-5	13-16	2-5	13-17	NMT 60 sec.
Assay(%)	99.77	99.94	99.5	99.77	99.15	99.10	98.63	98.00	90-110%
Dissolution (at 15 min.)	95.73	98.37	-	97.35	-	95.85	-	94.80	NLT Q 80% in 15 min.

6.7 Analysis Of Marketed Tablet (Maxalt – MLT 10 mg)

Table No. 20: Marketed Product Details

Brand Name	Maxalt – MLT
Strengths	10 mg
Manufactured by	Merck & Company,INC
Dosage form	Orally Disintegrating Tablet
Composition	Gelatin, Mannitol, Glycine, Aspartame & Pappermint
Avg.wt.(mg)	66 mg
Description	White to Off-White, Round lyophilized Orally Disintegrating Tablet debossed with modified square on one side and plane on other side.
Thickness (mm)	3.70 ± 0.04

Dimensions (mm)	12.66-12.80 mm
Disintegration time (min)	1-2 sec
NDC No.	NDC 0006 – 3801-12
Storage	Store at room temperature,15-30^{0}C,Not remove from blister from the outer aluminum punch until the patient is ready to consume the ODT inside

Table No. 21: Marketed Product Characterization

Weight	63.5 mg
Thickness	4.08-4.20 mm
Hardness	Very soft
DT (min)	2-5 sec
Length x Width	4.20 mm x 12.25 mm
LOD at 1050C	1.88%
pH	5.503
Assay	99.15

DISCUSSION

Weight variation

The tablets weighing as 200 mg have the limit of ± 7.5% variation according to USP specification. The tablets evaluated showed the weight variation within limit and thus passes the test.

Dimension

The thickness of the formulation F01 to F06 ranged from 2.70 to 3.20 mm. The dimension of the tablets have to be specific, and they should not differ ± 5% of the average value. The thickness of the tablets evaluated was found to be within given limits.

Hardness and Friability

The hardness value of the tablets ranged from 2.7-3.0 N. However hardness alone cannot be considered as absolute indicator of the tablets strength. Hence, another parameter measured was the friability of the tablets. The friability of the tablets was found to be less than 0.5% which was considered within the limit [USP]. The measure of these two parameters gives the strength of tablets during handling, packaging, shipping etc.

Content uniformity of the tablets

The uniformity in drug is an important measures. It gives the percentage of drug present per unit dosage form. The content uniformity was found to be 99.94 % of the 200 mg of Rizatriptan Benzoate. Hence, the tablets prepared showed good content uniformity.

In-Vitro drug release profile

In-vitro drug release studies in water, 0.1 N HCL, pH 6.8 Phosphate buffer for 30 minutes. The drug release studies carried out in dissolution test apparatus using 900 ml of dissolution medium, maintained at 37 ± 0.5^0C. All formulation F01 to F09 was found to be in the range 94.42% to 100 % drug release in 0.1 N HCL and 90.06% to 100 % drug release in pH6.8 Phosphate buffer Among the formulation studied F08 was to be best, In 15 minute cumulative drug release 96.58% and after 30 min cumulative drug release 100%. The effect of faster disintegration into finer tablets fragments is shown, where the incorporation Ac-Di-Sol gives a very rapid dissolution but polyplasdone XL 10 (Crospovidone) give rapid dissolution with dispersion time and disintegrant time. Out of F01 to F09 batches trial F08 was selected on the basis of linearity and accuracy in performance characteristic (hardness, thickness, friability, assay) and dissolution.

CONCLUSION

Comparison of Evaluated Parameters of Marketed Formulation and Optimized Formulation

Sr. No.	Parameters	Marketed Formulation	Optimized Formulation
1	**Assay (%)**	99.15	99.94
2	**Disintegration Time (sec)**	5-9	11-15
3	**% Drug Release**	100	100
4	**Hardness (N)**	Very Soft	2.7-3.0
5	**Thickness (mm)**	3.70±0.4	2.70-3.20
6	**Weight Variation(mg)**	66	198-203

In the present study is an attempt towards developing a formulation of Anti-Migraine drugs, which has in-vitro dissolution profile similar to that of Innovator formulation. It is important for treatment regime to treat patients with Migraine, which also improve patient compliance and therapeutic action. Formulation were prepared by using different Super disintegrate and suggested nine formulation F01-F09 & prepared Oral Dispersible Tablets F01-F09 by Direct Compression Techniques containing and optimized F08 batch. F08 formulation containing concentration of Crospovidone 10.5mg, Pregelatinized Starch 20mg, Aspartame 5mg as sweetener, mannitol 94. 77mg, Microcrystalline cellulose Avicel pH101 37.20mg and Avicel pH102 5mg,and mag stearate 12mg were used and further evaluated. When optimize F8 batch were compare with innovator on the basis of evaluation and characterization of ODT. The Direct Compression Technique is found to be better than the Lyophilization Technique which was use by innovator because in process as well as results and having low cost. Which

having shows good flow properties of powder and final blend, less weight variation, Thickness 2.70 - 3.20 mm, Hardness 2.7-3.0 N, less disintegration time 11-15 sec and maximum drug content 99.94 %. From this study, it can be conclude that Direct Compression technique has more potential and applicability in future for formulation of orodispersible tablet of Rizatriptan benzoate than that of Lyophilization Technique.

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