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Separation Techniques 2020: Design, and in vitro evaluation of orodispersible tablets (ODTs) of rizatriptan- Mohammedi Iqra Mubeen - Arya College of Pharmacy

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Introduction:

Drug delivery systems are becoming increasingly popular as medical scientists gain a better understanding of the physicochemical and biochemical parameters associated with their performance. Thirty years ago, oral contraceptive pills (ODTs) received a lot of attention as an alternative
Access to standard tablets and tablets thanks to better patient compliance ODTs are dosage forms containing therapeutic substances that disperse rapidly, usually in seconds, when placed on the tongue. ODT technology products entered the market in the 1980s, grew in demand, and the pipeline for their production increased rapidly. The new ODT technology addresses a wide range of medical and patient needs, ranging from improved health cycle management to easier withdrawal of pediatric, obstetrics and psychiatric disorders with dementia. This has encouraged academics and industry to discover new ways of dispersing the word and techniques in the field. The purpose of this article is to review ODTs development, construction challenges, new ODT technologies and testing methods,
The suitability of drug representatives, and the prospects for the future
Drug delivery programs (DDS) are a strategic tool to increase markets / indicators, increase product life cycles and productive opportunities. DDS has made a significant contribution to global drug marketing by market segregation, and it is moving very fast. Breakfast tablets (ODT) are oral solid dosage forms that disintegrate in the oral cavity in easy swallow residue.
Orally disintegrating tablets are also known as “Mouth dissolving tablets”, “Or dispersible tablets”, “Melt- in-mouth Oral disintegrating drug delivery, Rap melts tablets, Porous tablets, Quick dissolving tablets” 2 etc.
Recently ODT terminology has been approved by United States Pharmacopoeia, British Pharmacopoeia, and Centre for Drug Evaluation and Research (CDER). US FDA defined ODT tablets as “A solid dosage form containing medicinal substances which disintegrates rapidly usually within a matter of seconds, when placed upon the tongue”. European pharmacopoeia also adopted the term Orally disintegrating tablet as a tablet that is to be placed in the mouth where it disperses, rapidly before swallowing despite various terminologies used. Recently, ODT have started gaining popularity and acceptance as new drug delivery systems, because they are easy to administer and lead to better patient compliance especially in elderly and children. In order to allow oral disintegrating tablets to dissolve in the mouth, 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 and/or brittle, which are difficult to handle, often requiring specialized peel-off blister packaging. 3-6
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. Companies such as Eurand can produce pleasant tasting tablets, overcoming the c 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. 7
Some of the common applications of ODTs are listed in table

MEDICATION TYPE INDICATIONS
Fast acting Pain, fever, migraine, diarrhea, heart burn, anxiety, insomnia Compliance-critical Parkinson’s disease, Alzheimer’s disease, Psychosis, Schizophrenia, Hypertension, Cholesterol, Transplantation
Pediatric Cough, cold, allergy, pain, fever

1.1 Requirements of ODTs: 8, 9, 10, 11

Ideal properties for ODTs:

The performance of ODTs depends on the manufacturing technology and the most necessary property of such a dosage form is the ability of rapidly

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Disintegrating and dispersing or dissolving in the saliva, thereby obviating the need for water intake. ODTs should depict some ideal characteristics to distinguish them from traditional conventional dosage forms. Important desirable characteristics of these dosage forms.

•Convenient and easy to administer as does not require water for oral

Administration for swallowing purpose, but it should dissolve or disintegrate in the

Mouth usually within few seconds.

•Allow high drug loading.

•Provide pleasant feeling in the mouth.

•Be compatible with taste masking and other excipients.

•Leave negligible or no residue in the mouth after oral administration.

•Have sufficient strength to withstand the rigors of the manufacturing process and post-manufacturing handling.

•Insensitive to environmental conditions such as humidity and temperature.

•Adaptable and amenable to conventional processing and packaging equipment's at nominal expense.

1.2. Advantages of orally disintegrating tablets: 8, 9, 10, 11

Improved compliance/added convenience

Ease administration for patients who are mentally ill, disabled and uncooperative

No water needed Can be designed to leave minimal or no residue in mouth after administration and also to provide a pleasant mouth feel.

No chewing needed, Better taste obtained by taste masking

Improved stability, low sensitivity to environmental condition

Suitable for controlled/sustained release actives Allows high drug loading.

Ability to provide advantages of liquid medication in the form of solid preparation.

Adaptable and amenable to existing processing and packaging high speed machinery.

Cost effective, lower production, packaging and distribution costs compared to current commercially available products.

The technology is versatile and suitable for the development of enhanced products for veterinary medicines, OTC, Rx medicines & line extensions.

The new proprietary method allows the incorporation of microencapsulated drugs for enhanced bioavailability, flexibility of dosing & immediate and/or controlled release. For superior therapeutic benefit.

1.3Mechanism of disintegrations by super disintegrates

The mechanism by which the tablets are broken into small pieces and then produce a homogeneous suspension is based on:

•Capillary action

•By swelling

•Air expansion

•Due to disintegrating particle

•Due to deformation

•Due to release of gases

•By enzymatic reaction.

Fig 1: Mechanism of disintegrations by super disintegrates By capillary action:

Disintegration by capillary action is always the first step. When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into fine particles. Water uptake by tablet depends upon hydrophobicity of the drug and on tableting conditions. For

These types of disintegrates maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particles.

By Swelling:

Perhaps the most widely accepted general mechanism of action for tablet disintegration is swelling tablets with high porosity show poor disintegration due to lack of adequate swelling force. On the other hand, sufficient swelling force is exerted in the tablet with low porosity. It is worthwhile to note that if the packing fraction is very high, fluid is unable to penetrate in the tablet and disintegration is again slows down.

Because of heat of wetting (air expansion)

When disintegrates with exothermic properties gets wetted, localized stress is generated due to capillary air expansion, which helps in disintegration of tablet. This explanation, however, is limited to only a few types of disintegrants and cannot describe the action of most modern disintegrating agents.

Due to disintegrating particle :

Another mechanism of disintegration attempts to explain the swelling of tablet made with, non-swellable disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that non swelling particle also cause disintegration of tablets. The electric repulsive forces

between particles are the mechanism of disintegraton and water is required for it. Researchers found that repulsion is secondary to wicking.

Due to deformation:

During tablet compression, disintegrated particles get deformed and these deformed particle set into their normal structure when they come in contact with aqueous media or water. Occasionally, the swelling capacity of starch was improved when granules were extensively deformed during compression. This increase in size of the deformed particles produces a breakup of the tablet.

Due to release of gases:

Carbon dioxide released within tablets on wetting due to interaction between bicarbonate and carbonate with citric acid. The tablet disintegrates due to generation of pressure within the tablet. As these disintegrants are highly sensitive to small changes in humidity level and temperature, strict control of environmentis required during manufacturing of the tablets.The effervescent blend is either added immediately prior to compression or can be added in to two separate fraction of formulation.

By enzymatic reaction: Here, enzymes presents in the body act as disintegrates. These enzymes destroy the binding action of binder and helps in disintegration. Superdisintegrants Example Mechanism of action Special Comment Croscarmellose Ac-Di-Sol Nymce Zymce ZSX Primellose Solutab Cross linked cellulose Swells 4-8 folds in <10 seconds Swelling and wicking both Swells in two dimensions Direct compression or granulation

Starch free Crosspovidone Crospovidone M Kollidon PolyplasdoneCrosslinked PVP Swells very little and returns to original size after compression but act by capillary action

Water insoluble and spongy in nature so get porous tablets

Sodium Starch glycolate Explotab Primogel

Crosslinked starch

Swells 7-12 folds

in <30 seconds Swells in three dimension and high level serve as sustain release matrix

SUPER DISINTEGRANTS :

Disintegrants are substances or mixture of substances added the drug to the

formulation that facilitates the breakup or disintegration of tablets or capsule content into smaller particles that dissolve more rapidly than in the absence of disintegrants. Examples of superdisintegrants are croscarmellose, crosspovidone, sodium starch glycolate which represent example of cross linked cellulose.

Disintegrating agents are substances routinely included in the tablet formulations to aid in the breakup of the compacted mass when it is put into a fluid environment. They promote moisture penetration and dispersion of the tablet matrix. In recent years, several newer agents have been developed known as"Superdisintegrants". These newer substances are more effective at lower concentratons with greater disintegrating efficiency and mechanical strength. On contact with water the superdisintegrants swell, hydrate, change volume or form and produce a disruptive change in the tablet. Some natural polymers provide the fast disintegration as synthetic superdisintegrants. Recently some gums and mucilage's have been investigated to improve the disintegration processes. 10, 11

1.4 Techniques for preparing Orally disintegrating Tablets

A. Freeze drying :

A process in which water is sublimated from the product after freezing. Lyophilisation is a pharmaceutical technology which allows drying of heat sensitive drugs and biologicals at low temperature under conditions that allow removal of water by sublimation. Lyophilisation results in preparations, which are

highly porous, with a very high specific surface area, and which dissolve rapidly and show improved absorption and bioavailability. Jaccard and Leyder used lyophilisation to create an oral pharmaceutical preparation that not only dissolves rapidly but also improved the bioavailability of several drugs such as Spironolactone and Trolendomycin. Corveleyn and Remon studied various formulation and process parameters by using hydrochlorothiazide as a model drug on the basis of which US Patent 6,010,719 was granted. Tablets prepared by lyophilisation, are fragile and possess low mechanical strength, which make them difficult to handle and they also exhibit poor stability on storage under stressed conditions. 16, 19

B. Molding:

Tablet produced by molding are solid dispersion. Molded tablets disintegrate more rapidly and offer improved taste because the dispersion matrix is generally made from water soluble sugars. The active ingredient in most cases is absorbed through the mucosal lining of the mouth. The manufacturing process of molding tablets involves moistening the powder blend with a hydro-alcoholic solvent followed by pressing into mold plates to form a wetted mass (compressing molding). The solvent is then removed by air drying. Thus the process is similar to what is used in the manufacture of tablet triturates. Such tablets are less compact than compressed tablets and possess a porous structure that hastens dissolution.
Molded forms are also prepared using a heat molding process that involves setting the molten mass that contains a dispersed drug. The heat

molding process uses an agar solution as a binder and a blister packaging well as a mold to manufacture a tablet. The process involves preparing a suspension that contains a drug, agar, and sugar (e.g., mannitol or lactose), pouring the suspension into the blister packaging well, solidifying the agar solution at room temperature to form a jelly, and drying at 3000 C under vacuum. Another process used is called no vacuum lyophilisation, which involves the evaporation of a solvent from a drug solution or suspension at standard pressure. Evaporated a frozen mixture containing a gum (e.g., acacia, carrageenan, guar, tragacanth, or xantham), a carbohydrate (e.g., dextrose, lactose, maltose, mannitol, or maltodextrin), and a solvent in a tablet shaped mould. Molded tablets typically do not possess great mechanical strength. Erosion and breakage of the molded tablet often occur during handling and opening of blister packs. 13, 16, 20

C. Spray drying:

Spray drying is a process by which highly porous, fine powders can be produced. Spray-dryers are invariably used in the pharmaceutical industry to produce highly porous powders. Applying this process to the production of oral disintegratingtablets. The formulations that were produced contained hydrolyzed and unhydrolyzed gelatin as a support agent for the matrix, mannitol as a bulking agent, and sodium starch glycolate or croscarmellose as a disintegrant. Disintegration and dissolution was further enhanced by adding an acid (e.g., citric acid) or an alkali (e.g., sodium bicarbonate). The formulation was spray dried to yield a porous powder. Tablets manufactured from this powder disintegrated in less than 20 second in an aqueous medium. 6, 21, 22

D. Sublimation:

The key to rapid disintegration for mouth dissolving tablets is the presence of a porous structure in the tablet matrix. Conventional compressed tablets that contain highly water soluble ingredients often fall to dissolve rapidly because of low porosity of the matrix. Hence, to generate porous matrix, volatile ingredients are used that are later subjected to a process of sublimation. Solid ingredients that displayed high volatility (e.g., ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, hexamethonium tetramine, naphthalene, phthalic anhydride, urea, and urethane) were compressed along with other excipients into a tablet. The volatile material was then removed by sublimation, leaving behind a porous matrix. Solvents such as cyclohexane and benzene were also suggested for the generation of porosity in the matrix.
Sublimation technology to manufacture tablets that rapidly dissolve in saliva. Mannitol is used as a matrix former, and camphor was used as a sublimating agent. The tablets dissolved in 10-20 seconds and displayed satisfactory handling properties. Makino et al.27 reported a method using water as pore forming material. A mixture of drug and a carbohydrate (e.g. erythritol, glucose, sucrose, xylitol). The water was then removed, yielding highly porous tablets with satisfactory mechanical strength and a high dissolution rate.

E. Direct compression:

It is the easiest way to manufacture tablets. Conventional equipment, commonly available excipients and a limited number of processing steps are

involved in direct compression. Also high doses can be accommodated and final weight of tablet can easily exceed that of other production methods. This technique can now be applied to oral disintegratingtablets because of the availability of improved tablet excipients, especially tablet disintegrants and sugar-based excipients. Addition of disintegrants in oral disintegratingtablets, leads to quick disintegration of tablets and hence improves dissolution. In many oral disintegratingtablet technologies based on direct compression, the disintegrants principally affect the rate of disintegration and hence the dissolution.
The introduction superdisintegrants and a better understanding of their properties have increased the popularity of this technology. Tablet disintegration time can be optimized by concentrating the disintegrants. Below critical concentration, tablet disintegration time is inversely proportional to disintegrants concentration. Above the critical concentration level, however, disintegration time remains approximately constant or even increases. 1, 6, 21
Microcrystalline cellulose, cross linked carboxymethyl cellulose sodium, cross linked polyvinyl pyrrolidone and partially substituted hydroxypropyl cellulose, though water insoluble, absorb water and swell due to capillary action and are considered as effective disintegrants in the preparation of oral disintegratingtablets. Bi et al. and Watanbe et al. used microcrystalline cellulose (MCC) and low substituted hydroxypropyl cellulose (HPC) to manufacture rapidly disintegrating tablets.
The ratios of MCC to HPC varied from 8:2 to 9:1. Ito and Sugihan investigated applying agar powder as a disintegrants because the powder

absorbs water and swells considerably without forming a gel at physiological temperatures. Fast disintegration of tablets can also be achieved by incorporating effervescent disintegrating agents, which generates carbon dioxide. This phenomenon also resulted in partial taste masking of unacceptable taste of the drug. The major drawback of effervescent excipients is their hygroscopicity (i.e., the ability to absorb atmospheric moisture). Hence, their manufacture requires control of humidity conditions and protection of the final product. This is reflected by the overall cost of the product. Another approach to oral disintegratingtablets by direct compression is the use of sugar-based excipients (e.g., dextrose, fructose, isomalt, maltitok, maltose, mannitol, sorbitol, starch hydrolyze, polydextrose, and xylitol), which display high aqueous solubility and sweetness, and hence, impart taste masking and a pleasing mouth feel.

F. Mass Extrusion:

This technology involves 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 of the product into even segments using heated blade to form tablets. The dried cylinder can also be used to coat granules of bitter tasting drugs and thereby making their bitter taste. 19

1.5 PATENTED TECHNOLOGY FOR THE ORALLY DISINTEGRATING TABLETS:

Each technology has a different mechanism, and each fast dissolving/

disintegrating dosage form varies regarding the following.

- Mechanical strength of final product;
- Drug and dosage form stability;
- Mouth feel;
- Taste;
- Rate of dissolution of drug formulation in saliva;
- Swallow ability;
- Rate of absorption from the saliva solution; and
- Overall bioavailability.

ZYDIS TECHNOLOGY:

Zydis, the best known of the fast-dissolving/ Disintegrating tablet preparations, and was the first marketed new technology tablet. The tablet dissolves in the mouth within seconds after placement on the tongue. Zydis tablet is produced by lyophilizing or freeze-drying the drug in a matrix usually consisting of gelatin. The product is very lightweight and fragile, and must be dispensed in a special blister pack. Patients should be advised not to push the tablets through the foil film, but instead peel the film back to release the tablet. The Zydis formulation is also self-preserving

because the final water concentration in the freeze-dried product is too low to allow for microbial growth. A major claim of the Zydis product is increased bioavailability compared to traditional tablets. Because of its dispersion and dissolution in saliva while still in the oral cavity, there can be a substantial amount of pre-gastric absorption from this formulation. Buckle, pharyngeal and gastric regions are all areas of absorption of the Zydis formulation. Any pre-gastric absorption avoids first-pass metabolism and can be an advantage in drugs that undergo a great deal of hepatic metabolism. However, if the amount of swallowed drug varies, there is the potential for inconsistent bioavailability. While the claimed increase in bioavailability is debatable, it is clear that the major advantage of the Zydis formulation is convenience. The amount of drug that could be incorporated should generally be less than 60 mg for soluble drugs. The particle size of the insoluble drugs should be less than 50mm and not more than 200mm to prevent sedimentation during processing. There are some disadvantages to the Zydis technology. The process of freeze-drying is a relatively expensive manufacturing process. As mentioned earlier, the Zydis formulation is very lightweight and fragile, and therefore should not be stored in backpacks or the bottom of purses. Finally, the Zydis formulation has poor stability at higher temperatures and humidity. It readily absorbs water, and is very sensitive to degradation at humidity greater than 65%.16, 17

ORASOLV TECHNOLOGY:

The OraSolv technology, unlike Zydis, disperses in the saliva with the aid of almost imperceptible effervescence. The OraSolv technology is best described as a fast-disintegrating tablet; the tablet matrix dissolves in less than one minute, leaving coated drug powder. The taste masking associated with the OraSolv formulation is twofold. The unpleasant flavor of a drug is not merely counter- acted by sweeteners or flavors, both coating the drug powder and effervescence are means of taste masking in OraSolv. This technology is frequently used to develop over the counter (OTC) formulations. The major disadvantage of the OraSolv formulations is its mechanical strength. The OraSolv tablet has the appearance of a traditional compressed tablet. However, the OraSolv tablets are only lightly compressed, yielding a weaker and more brittle tablet in comparison with conventional tablets. For that reason, Cima developed a special handling and packaging system for OraSolv. An advantage that goes along with the low degree of compaction of OraSolv is that the particle coating used for taste masking is not compromised by fracture during processing. Lyophilisation and high degrees of compression, as utilized in OraSolv's primary competitors, may disrupt such a taste masking approach. The OraSolv technology is utilized in six marketed products. These formulations can accommodate single or multiple active ingredients and tablets containing more than 1.0 g of drug have been developed. Their disintegration time is less than 30s.16, 18

DUROSOLV TECHNOLOGY:

DuraSolv is Cima's second-generation fast-dissolving/disintegrating tablet formulation. Produced in a fashion similar to OraSolv, DuraSolv has much higher mechanical strength than its predecessor due to the use of higher compaction pressures during tableting. DuraSolv tablets are prepared by using conventional

tableting equipment and have good rigidity (friability less than 2%). The DuraSolv product is thus produced in a faster and more cost-effective manner. DuraSolv is so durable that it can be packaged in traditional blister packaging, pouches or vials.17 One disadvantage of DuraSolv is that the technology is not compatible with larger doses of active ingredients, because the formulation is subjected to such high pressures on compaction. Unlike OraSolv, the structural integrity of any taste masking may be compromised with high drug doses. The drug powder coating in DuraSolv may become fractured during compaction, exposing the bitter-tasting drug to a patient's taste buds. Therefore, the DuraSolv technology is best suited for formulations including relatively small doses of active compound.
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FLASH DOSE TECHNOLOGY:

Fuisz Technologies has three oral drug delivery systems that are related to fast dissolution. The first two generations of quick dissolving tablets, Soft Chew and EZ Chew, require some chewing. However, these paved the way for Fuisz's most recent development, Flash Dose. The Flash Dose technology utilizes a unique spinning mechanism to produce floss like crystalline structure, much like cotton candy. This crystalline sugar can then incorporate the active drug and be compressed into a tablet. This procedure has been patented by Fuisz and is known as Shear form. The final product has a very high surface area for dissolution. It disperses and dissolves quickly once placed onto the tongue. Flash dose tablets consist of self-binding shear form matrix termed as “floss”. Shear-form matrices are prepared by flash heat processing and are of two types.

- Single floss or Unif loss, consisting of a carrier, and two or more sugar alcohols, of which one is xylitol.
- Dual floss consists of a first shear form carrier material (termed “base floss”, contains a carrier and at least one sugar alcohol generally sorbitol), and a second shear form binder matrix (“binder floss”, contains a carrier and xylitol).

Interestingly, by changing the temperature and other conditions during production, the characteristics of the product can be altered greatly. Instead of a floss-like material, small spheres of saccharides can be produced to carry the drug. The process of making microspheres has been patented by Fuisz, and is known as CEFORM and serves as an alternative method of taste masking. 18

Table 1: Some ODT technological patents

ODT Technologies Technological basi Patent owners
Zydis Lyophilisation R.P.Scherer Inc.
Quicksolv Lyophilisation Janseen Pharmaceutica
Flashtab Multiparticulate compressed tablets Prographarm
Lyoc Lyophilisation Cephalon Corporation
Orasolv Compressed tablets Cima Labs Inc.
DurasolvCompressed tablets Cima Labs Inc.
Wowtab Compressed molded tablets YamanouchiPharma Technologies, Inc
Flashdose Cotton candy process Fuisz Technologies, Ltd.
AdvaTab Microencapsulation Eurand Multiflash Multi-unit tablet Prographarm EFVDAS Effervescent system Elan Corporation

Table 2: Some of the marketed preparations of ODTs: Trade name Active drug Manufacturer Zontec MD Cetrizine Zosat pharma India Zofer MD Odansetron Sun pharma
Vomidon MD DomperidonOlcare lab Valus Valdecoxib Glen mark Ugesic Piroxicam Mayer organic Ltd.
Torrox MT Rofecoxib Torrent pharma
RomilastMoontelukast Ranbaxy Labs Ltd.
Rofixx MD Rofecoxib Cipla Ltd.

OBJECTIVES:

Need for the study:

Mouth Oral disintegrating Tablets (MFDT’s) have emerged as an alternative to conventional oral dosage forms to improve the patient compliance. Due to problem in swallowing ability with age, the pediatric and geriatric patients complain of difficulty to take conventional solid dosage forms. The MFDT’s are solid dosage forms that dissolve or disintegrate rapidly in the oral cavity, which results in solution or suspension without the need of water. The main objective of this work is to formulate and evaluate Rizatriptan MFDT’s using different concentrations of superdisintegrants like croscarmellose sodium (CCS), sodium starch glycolate (SSG) and their combinations in different ratios.Tablets were prepared by direct compression method and evaluated for hardness, friability, wetting time disintegration time and percent drug release. Stability studies of optimized formulation revealed that formulation is stable Rizatriptan hydrochloride (CTZ) is an orally active and selective H1-receptor antagonist used in seasonal allergic rhinitis, perennial allergic rhinitis and chronic urticaria.CTZ is a white, crystalline water soluble drug possessing bitter taste properties. Due to sore throat conditions, the patient experiences difficulty in swallowing a tablet type of dosage form. Thus, mouth oral disintegratingtablets would serve as an ideal dosage form for the patients as well as pediatric patients who find it difficult to swallow the tablet.

Objectives of the study:

The present research investigation was panned with the following objectives

1. To optimise the different concentrations of the disintegrants on release of the drug
2. To formulate orally disintegrating tablets of Rizatriptan hydrochloride by using different concentrations of disintegrates
3. To evaluate the formulations with respect to various physical parameters Plan of the study:

Reformulation studies.

Prepared mouth dissolving tablets of cetirizine will be subjected for the following evaluation parameters.

I. Pre-compression parameters:

1. Angle of repose
2. Bulk density
3. Carr’s consolidation index
4. Compatibility study

II. Post-compression parameters:

1. Uniformity of thickness.
2. Hardness test.

3. Friability test.

4. Weight variation test.

5. Wetting time.

6. Water absorption ratio.

7. In-vitrodisintegration time.

8. In-vitrodissolution studies.

9. Drug content uniformity REVIEW OF LITERATURE

The following are the research works carried out by various research scholars that strongly support to carry out the present dissertation work. 23

1. Mizumoto,T. et al., studied on "Formulation design of a novel fast- disintegrating tablet" They prepared fast disintegrating tablets which had sufficient hardness and could be manufactured by commonly used equipments. This was achieved by improving compressibility of low- compressibility saccharides and conducting process which made it possible to achieve sufficient hardness while maintain the fast disintegration time.

2. Schiermeier,S;Schmidt P.C. designed "Fast dispersible ibuprofen tablets" The work revealed fast dispersible tablets containing coated ibuprofen as a high dosed model drug with acceptable hardness and desirable taste, prepared by direct compression method. To develop an ODT, a tablet rotatable central composite design was applied to predict the effects of the quantitative factors mannitol and crospovidine as well as compression force on the characteristics of the tablet.

3. Mahajan, A; Sharma, R. reviewed "COX-2 selective Nonsteroidal Anti- inflammatory drugs: current status" They focused on the potentially lethal side effects associated with use of COX-2 specific inhibitors. However, it had been recommended that the choice of COX-2 selective inhibitor for a particular patient should be used upon their relative efficacy, toxicity, concomitant drug use, concurrent disease status, hepatic and renal function and relative cost.

4. Szepes, A. et al. investigated "Freeze-casting technique in the development of solid drug delivery system" The study reported that freeze- casting technique proved to be an appropriate alternate for the development of porous solid drug delivery system and the freeze-casted units **revealed a** highly porous nature and a remarkable difference in pore volume size distribution.

5. Fukami, J. et al. worked on "Evaluation of rapidly disintegrating tablets containing glycine and carboxymethylcellulose "They prepared rapidly disintegrating tablet using glycine as a disintegrant and evaluated the effect of disintegrant on the disintegration behaviour of the tablet. It was suggested that the tablet formulation containing NS-300 and glycine was highly applicable to water-insoluble drug, such as ethenzamide.

6. Amin, P. et al, investigated "Indion 414 as superdisintegrant in formulation of mouth dissolve tablets"The research paper introduced Indion 414, an ion exchange resin, as a new superdisintegrant for pharmaceutical dosage forms. Model drugs belonging to various classes were taste masked and formulated into palatable mouth dissolve tablets and compared with the conventional disintegrants to determine its relative efficacy.

7. S.A. Desai, et al. "Oro dissolving tablets of Promethazine Hcl" prepared orodissolving tablets of promethazine Hcl using superdisintegrants, sodium starch glycolate and croscarmellose sodium by direct compression method. They prepared tablets exhibited hardness between 2-4 k/cm.The tablets were disintegrating, in vitro and in vivo within 8 to 16 sec and 9 to 20 sec respectively and almost 100% of the drug was released from all formulations within 5 mins.

8. Mishra D.N, et al. 'Rapidly oral disintegrating tablets of valdecoxib" formulated rapidly disintegrating oral tablets of valdecoxib using superdisintegrants like croscarmellose sodium, crospovidone, L-HPC. The tablets showed improved disintegration and dissolution profile.

9. Omaima A. Sammour, et al. "Formulation and optimization of mouth dissolving tablets containing Rofecoxib solid dispersion" formulated and optimized mouth dissolving tablets containing Rofecoxib solid dispersion. The solid dispersions were prepared by using PVP (K30) by solvent evaporation method. The solid dispersion was found to have enhanced solubility and improved dissolution profile.

10. Chandrasekhar Patro et al. "Formulation and Evaluation of Rizatriptan Mouth Oral disintegratingTablets" The main objective of this work is to formulate and evaluate

DRUG AND EXCIPIENT PROFILE

A. Drug profile : Rizatripta
i. Chemical Name : dimethyl({2-[5-(1H-1,2,4-triazol-1-ylmethyl)-1H-indol- 3- yl]ethyl}) amine
ii. Molecular formula : C15H19N5

iii. Moleculare Weight : 269.3449

iv. Description : Solid
v. Melting point : 178-180 °C Indications: For treatment of acute migraine attacks Description: Rizatriptan Rizatriptan is a triptan drug used for the treatment of migraine headaches. It is a selective 5-hydroxytryptamine1 receptor subtype agonist. Pharmacodynamics: Rizatriptan is a selective agonist of serotonin (5- hydroxytryptamine; 5-HT) type 1B and 1D receptors. It is structurally and pharmacologically related to other selective 5-HT1B/1D receptor agonists and has only a weak affinity for 5-HT1A, 5-HT5A, and 5-HT7 receptors and no significant affinity or pharmacological activity at 5-HT2, 5-HT3 or 5-HT4 receptor subtypes or at alpha1-, alpha2-, or beta-adrenergic, dopamine1,; dopamine2; muscarinic, or benzodiazepine receptors. This action in humans correlates with the relief of migraine headache.Mechanism of action: Three distinct pharmacological actions have been implicated in the antimigraine effect of the triptans: (1) stimulation of presynaptic 5-HT1D receptors, which serves to inhibit both dural vasodilation and inflammation; (2) direct inhibition of trigeminal nuclei cell excitability via 5- HT1B/1D receptor agonism in the brainstem and (3) vasoconstriction of meningeal, dural, cerebral or pial vessels as a result of vascular 5-HT1B receptor agonism.
Absorption: Rapid following oral administration. Bioavailability is 45%. Food has no effect on the bioavailability of rizatriptan. However, administering rizatriptan with food will delay by 1 hour the time to reach peak plasma concentration. The rate of absorption is not affected by the presence of a migraine attack. Metabolism: Rizatriptan is metabolized by monoamine oxidase A isoenzyme (MAO-A) to an inactive indole acetic acid metabolite. In addition, several other inactive metabolites are formed. An active metabolite, N-monodesmethyl- rizatriptan, with pharmacological activity similar to that of the parent compound has been identified in small concentrations (14%) in the plasma. Route of elimination: Approximately 14% of an oral dose is excreted in urine as unchanged rizatriptan while 51% is excreted as indole acetic acid metabolite, indicating substantial first pass metabolism
Half-life: 2-3 hours.

B. Excipient Profile:

1. Sodium starch glycolate : 40

Synonyms: Explotab, primogel. Functional catergory : Tablet and capsule disintegrant. Chemical name : sodium carboxymethyl starch.
Description Sodium starch glycolate is the sodium salt of a carboxymethyl ether of starch.

It is a Very fine, white or off white, free flowing powder; odorless or almost odorless. Practically insoluble in water, insoluble in most organic solvents
It consists of oval or spherical granules, 30-100 µm in diameter with some less- spherical granules ranging from 10-35 µm in diameter.
Structural formula:
Solubility: Insoluble in cold water, hot water. Stability: The product is stable.
Storage: Keep container tightly closed. Keep container in a cool, well-ventilated area.
Incompatibilites : Incompatible with ascorbic acid. First Aid Measures
Eye Contact:
Check for and remove any contact lenses. In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Get medical attention if irritation occurs.
Skin Contact: Wash with soap and water. Cover the irritated skin with an emollient. Get medical attention if irritation develops.
Inhalation: If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention. Applications:
 Sodium starch glycolate is widely used in oral pharmaceutical as a disintegrant in capsule and tablet formulations. It is recommended to use in tablet prepared by either direct-compression or wet-granulation processes.
 The recommended concentration in a formulation is 2-8%, with the
optimum concentration about 4% although in many cases 2% is sufficient. Disintegration occurs by rapid uptake of water followed by rapid and enormous swelling.
 The disintegrant efficiency of sodium starch glycolate is unimpaired in the
presence of hydrophobic excipients, such as lubricants unlike many other disintegrants.
 increasing the tablet compression pressure also appears to have no effect

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on disintegration time. Sodium starch glycolate has also been investigated for use as a suspending vehicle.

2. CROSCARMELLOSE SODIUM: 41

Croscarmellose sodium is a cross linked polymer of carboxymethyl cellulose sodium. Cross linking makes it an insoluble, hydrophilic, highly absorbent material, resulting in excellent swelling properties and its unique fibrous nature gives it excellent water wicking capabilities. Croscarmellose sodium provides superior drug dissolution and disintegration characteristics, thus improving bioavailability of formulations.

Precautions:
Keep away from heat. Keep away from sources of ignition. Empty containers pose a fire risk; evaporate the residue under a fume hood. Ground all equipment containing material. Do not breathe dust.
Storage: Keep container tightly closed. Keep container in a cool, well-ventilated area. Hygroscopic
First Aid Measures Eye Contact:
Check for and remove any contact lenses. In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Cold water may be used. Get medical attention if irritation occurs.
Skin Contact:

Wash with soap and water. Cover the irritated skin with an emollient. Get medical attention if irritation develops. Cold water may be used.
Inhalation:

If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention. Application: Croscarmellose sodium is used in oral pharmaceutical formulations as a disintegrates for capsules, tablets and granules. When used in wet granulations the croscarmellose sodium is best added in both the wet and dry stages of the process (intra- and extra granularly) so that wicking and swelling ability of the disintegrant is best utilized.
Concentration of up to 5% w/w of croscarmellose sodium may be used as a tablet disintegrant although normally 2% w/w is used in tablets prepared by direct compression and 3% w/w in tablets prepared by a wet-granulation process.
Croscarmellose sodium is a stable though hygroscopic material. Croscarmellose sodium should be stored in a well-closed container in a cool, dry place.
3. MAGNESIUM STEARATE: 42 Synonyms: magnesium octadecanoate; stearic acid magnesium salt; octadecanoic acid, magnesium salt. Molecular formula C36H70MgO4 Molecular weight : 591.3 Functional category: tablet and capsule lubricant. Applications in pharmaceutical formulations and technology:
Magnesium stearate is widely used in cosmetics, foods, and

pharmaceutical formulations. It is primarily used as a lubricant in capsule and tablet manufacture at concentrations between 0.25-5%. It is also used in barrier creams.
Description:
Magnesium stearate is a fine, white, precipitated or milled, impalpable powder of low bulk density, having a faint odor of stearic acid and a characteristic taste. The powder is greasy to the touch and readily adheres to the skin.

4. COLLOIDAL SILICON DI-OXIDE:

Synonyms: Aerosol; light anhydrous silicic acid ; silicic anhydride. Chemical name : Silica
Structural formula : SiO2 Molecular weight : 60.08 Functional Category : Adsorbent ; anti caking agent ; emulsion stabilizer ; glidant ; suspending agent ; tablet disintegrate ; viscosity-increasing agent. Description: Colloidal silicon dioxide is a sub microscopic fumed silica with a particle size of about 15nm.It is a light, loose, bluish-white colored, odorless, tasteless, non-gritty amorphous powder.
Application in pharmaceutical formulation: Colloidal silicon dioxide is widely used in pharmaceutical, cosmetics, and food products. Its small particle size and large specific surface area give it desirable flow characteristics that are exploited to improve the flow properties of powder in a number of processes such as tableting.
Colloidal Silicon di oxide is also used to stabilize emulsion and as athixotropic thickening and suspending agent in gels and semisolid preparations.
5. LACTOSE MONOHYDRATE: 43
Chemical name: lactose monohydrate Synonyms: Milk sugar; Lactose standard; Lacto sum monohydric Molecular formula: C12H24O12 Molecular weight: 360.31
Melting Point: 214°C (417.2°F)
Solubility: soluble in water.
Description: Lactose is milk sugar. It is a disaccharide composed of one galactose and one glucose molecule. In pharmaceutical industry, lactose is used to help form tablets because it has excellent compressibility properties. It is also used to form a diluent powder for dry powder inhalations.
Precautions:
Keep away from heat. Keep away from sources of ignition. Empty containers pose a fire risk; evaporate the residue under a fume hood. Ground all equipment containing material. Do not ingest. Do not breathe dust. If ingested, seek medical

advice immediately and show the container or the label. Keep away from incompatibles such as oxidizing agents.
Storage: Keep container tightly closed. Keep container in a cool, well-ventilated area. Do not store above 23°C (73.4°F).
First Aid Measures Eye Contact:
Check for and remove any contact lenses. In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Cold water may be used. Get medical attention if irritation occurs.
Skin Contact:

Wash with soap and water. Cover the irritated skin with an emollient. Get medical attention if irritation develops. Cold water may be used.

Inhalation:

If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention.

MATERIALS AND METHODOLOGY

A. Procurement of Drug and Excipients:
The following materials and instruments used in the experiment are of laboratory grade.
Table 3: Details of materials used

Sl. No.	Materials
1	Cetrizine hydrochloride
2	Sodium starch glycolate
3	Croscarmellous sodium
4	Magnesium stearate
5	Colloidal silicon di-oxide
6	Lactose monohydrate

Table 4: Details of equipments used

Sl. No.	Instruments
1	UV Visible spectrophotometer
2	Multi station rotary punch tablet compression machine
3	Dissolution test apparatus
4	Friability Tester
5	Hardness Tester
6	Tablet disintegration tester
7	Vernier calliper

Formulation chart of Rizatriptan orally disintegrating tablets
Ingredients

(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Rizatriptan	10	1 0	10	10	10	10	10	10	10
Crospovidone (CP)		2	4	8	-	-	-	-	-
Cross caramel lose sodium (CCS)		-	-	-	-	-	2	4	8
Sodium starch glycol ate (SSG)		-	-	-	-	-	-	-	2
Silicon dioxide	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Magnesium stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Peppermint flavor	1	1	1	1	1	1	1	1	1
Avicel pH 102	84	82	78	84	82	78	84	82	78
Total tablet weight	100	100	100	100	100	100	100	100	100

Table 1: Formulation chart of Rizatriptan orally disintegrating tablets Total weight of each tablet – 100 mg
Punch size – 8 mm

Preparation of phosphate buffer pH 6.8

Dissolved 27.22 g of monobasic potassium phosphate in water and diluted to 1000 ml with water.
In 50 ml of above solution added 22.4 ml of 0.2 M sodium hydroxide solution and added water to make up 200 ml.
Procedure:

Or dispersible tablets (ODTs) were prepared by direct compression method according to formula given in Table 1. All the ingredients were passed through mesh # 30 except magnesium stearate. Magnesium stearate was passed through mesh # 40. Drug, and superdisintegrant were mixed by taking small portion of each in ascending order and blended to get a uniform mixture in a mortar. The other ingredients were weighed and mixed in geometrical order and tablets were compressed using 7mm round flat punches on a Cadmach single punch machine.
Tablet punching by direct compression method: Manufacturing steps for direct compression
Direct compression involves comparatively few steps:

1. Milling of drug and excipients.

2. Mixing of drug and excipients.

3. Tablet compression.

The Or dispersible tablets (ODTs) of batch 50 of formulations of A- series and F- series were prepared by direct compression process and the compositions are shown in tables --. .All the materials i.e., drug, Lactose monohydrate, colloidal silicon dioxide, super disintegrating agents were sifted through mesh no.40 and were collected in mortar and mixed well to get a uniform mixture. Magnesium stearate was sifted through mesh no.60 sieve, collected into the mortar containing other ingredients and mixed (added lastly as it is hydrophobic may affect dissolution and disintegration profile due to more time of mixing). The lubricated directly compressible blend was compressed by using direct compression machine to get hardness above 2.5 kg/ cm2.The tablets were sublimed at 40-50 0C in a vacuum oven for 24 hours to sublime subliming agent. End point of process is indicated by complete removal of subliming agent by sublimation.

Evaluation of Tablets:

Pre-compression Parameters:

A. Angle of Repose(θ):

Angle of repose (a) was determined using funnel method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. The radius of the heap (r) was measured and angle of repose was calculated.
Tan θ =h/r

Where θ is the angle of repose

Table 2: Relationship between Angle of Repose (θ) and flow properties.

Angel of Response (θ)	Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Method: A funnel was filled to the brim and the test sample was allowed to flow smoothly through the orifice under gravity. From the cone formed on the graph sheet was taken to measure the area of pile, thereby evaluating the flowability of the granules. Height of the pile was also measured.

B. Bulk Density:

Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. A suitable amount of powder from each formulation, previously lightly shaken to break agglomerates formed, was introduced into a 10 ml measuring cylinder. After initial volume was observed, the cylinder was allowed to fall under its own weight on to a hard surface from a height of 2.5cm at 2 seconds intervals (Bi et al, 1995.). The tapping was continued until no further change in volume was noted. LBD and TBD were calculated using following formula.
LBD= weight of the powder/ volume of the packing

TBD= weight of the powder/tapped volume of the packing

C. Carr's compressibility Index Compressibility index of the powder was determined by Carr's compressibility index.
Table 3: Grading of the powders for their flow properties according to Carr's Index

Compressibility Index (Carr's Ratio %)	Flow
5-15	Excellent
12-16	Good
18-21	Fair to passable
23-35	Poor
33-38	Very poor
>40	Very very poor

Post-compression Parameters:

Uniformity of weight:

The test was carried out according to the Indian pharmacopoeia. Twenty tablets, from each formulation were individually weighed and the mean of tablet weight was calculated. The percentage weight variation was calculated individually comparing to mean tablet weight.

Hardness:

The fracture strength, which is defined as the force required to break a tablet by radial compression, was measured with a tablet hardness tester (Monsanto hardness tester) (n=3).

Monsanto hardness tester Pfizer type hardness tester

Friability:

The pharmacopoeial limit of friability test for a tablet is not more than 1% using Tablet friability apparatus, carried out at 25 rpm for 4 min (100 rotations).
This test is again not applicable for lyophilized and flash dose tablets, but is always recommended for tablets prepared by direct compression and moulding techniques to ensure that they have enough mechanical strength to withstand the abrasion during shipping and shelf life.
Percentage friability = 100(initial weight-final weight)/initial weight (or)
% Friability = (Loss in weight / Initial weight) × 100

Wetting time:

The wetting time of the tablets was measured using a simple procedure.

For measurement of wetting time five circular tissue papers of 10 cm diameter are placed in a Petri dish with a 10 cm diameter. Ten millimeters of water- containing Eosin, a water-soluble dye, is added to Petri dish. A tablet is carefully placed on the surface of the tissue paper in the Petri dish at room temperature. The time required for water to reach upper surface of the tablet and completely wet them was noted as a wetting time30. To check for reproducibility the measurements were carried out (n=6) and the mean value was calculated.
Water absorption ratio:

The weight of the tablet before keeping in the Petri dish was noted (Wb) the wetted tablet from the Petri dish was taken and reweighed (Wa).the water absorption ratio, R was determined according to the following equation:
R=100(Wa- Wb)/Wb

Where Wb and Wa are the weight before and after absorption respectively.

Invitrodispersion time:

Invitrodispersion time was measured by using 10ml of phosphate buffer pH 6.8 in 25 ml beaker at 37± 0.5 ˚C temperature. Time required for dispersion of the tablets was noted. In each formulation three tablets were tested (n=3).

Invitrodissolution study:

ODTs were evaluated for dissolution behavior. Dissolution test was carried out using USP apparatus 2, paddle type. Dissolution was carried out with the rotation speed of 50 rpm using 900 ml of phosphate buffer pH 6.8 as the dissolution medium maintained at a temperature of 37 ± 0.5°C. Samples were withdrawn at predetermined time interval, diluted suitably and analyzed at 231nm for cumulative drug release using UV-Visible spectrophotometer.

RESULTS & DISCUSSION

Determination of λ max:

Rizatriptan was dissolved in distilled water and further diluted with 0.1N HCl. Then the solution was scanned for maximum absorbance in UV double beam spectrophotometer (Shimadzu 1700) in the range from 200 to 400 nm, using 0.1N HCl as blank. The λ max of the drug was found to be 226 nm.

Figure 1: Calibration curve of Rizatriptan at 226 nm Drug-Excipient Compatibility Studies
The results obtained with IR studies showed that there was no interaction between the drug and other excipients used in the formulation.

Figure 2: FTIR Spectra of Rizatriptan (Pure Drug) V/S FTIR Spectra of Rizatriptan FDT.
Results of pre-compression parameters for Rizatriptan tablets
Pre-compression parameters:
Powder ready for compression containing drug and various excipients were subjected for pre-compression parameters to study the flow properties of granules, to achieve uniformity of tablet weight. The results of all the reformulations parameters are given table

Angle of repose (θ):

The data obtained from angle of repose for all the formulations were found to be in the range of 24.19° and 28.56° which reveals good flow property. All formulations showing angle of repose within 30°, indicates a good flow property of the granules.
Bulk density:

Bulk density (BD) and tapped density (TD) for the blend was performed. The loose bulk density and tapped bulk density for the entire formulation blend varied from 0.508 gm/cc to 0.5438 gm/cc and 0.5941 to 0.6408 respectively.
Carr's compressibility index:

The results of Carr's consolidation index or compressibility index (%) for the entire formulation blend ranged from 14.30% to 17.53% had shown excellent compressibility index values up to 15% result in good to excellent flow properties. As shown in previous research work.

Table 4: Pre-compression parameters for Rizatriptan tablets

Form ulatio n code	Bulk density g/cc	Tapped density (g/cc)	Angle of repose	Carr's index (%)
F1	0.5434	0.6341	25.28	14.3037
F2	0.5212	0.6294	27.20	17.1909
F3	0.5937	0.6098	25.14	15.7592
F4	0.5098	0.5998	24.19	15.0050
F5	0.5438	0.6401	26.41	15.044
F6	0.5345	0.6296	28.56	16.296
F7	0.512	0.6210	25.71	17.5362
F8	0.5342	0.6408	26.38	16.6354
F9	0.5088	0.5941	26.01	14.3578

Results of post-compression parameters

Hardness: The hardness of all the tablets was maintained within the 2.00 kg/cm to 4.00 kg/cm. The mean hardness test results are tabulated in table.

Friability test: The friability was found in all designed formulations in the range

0.42 to 0.74% to be well within the approved range (<1%). The friability study results were tabulated in table.

Weight variation test:

The weight variation was found in all designed formulation in the range 97 to 100 mg. The mean weight variation test results are tabulated in table.

All the tablets passed weight variation test as the average percentage weight variation was within 7.5% i.e. in the pharmacopieal limits.

In-vitro disintegration time:

The in vitro disintegration time is measured by the time taken to undergo uniform disintegration. Rapid disintegration within several minutes was observed in all the formulations. The in vitro disintegration time of Rizatriptan prepared by direct compression method by super disintegrants were found to be in the range of 18 to 11sec fulfilling the official requirements.

Based on the in vitro disintegration time, formulation F3 were found to be promising and showed a disintegration time of 11 sec.

Disintegrating study showed that the disintegrating times of the tablets decreased with combination of both sodium starch glycolate and cross carmellose with different concentrations. It also showed least disintegration time in comparison with the all other formulation because of their lowest hardness and the porous structure is responsible for faster water uptake, hence it facilitates swelling action in bringing about fast disintegration.

Wetting time:

Wetting time closely related to the inner structure of the tablet. The results of wetting time are shown in table. The wetting time were found to be in the range of 11 to 18sec.

Water absorption ratio: Water absorption ratio for all the formulations found in

the range 11 to 16%. The results of water absorption ratio for tablets were shown in table.

Post-compression parameters of Rizatriptan tablets

Formulation	Hardness	Friability	Thickness	Weight variation
F1	3.5	0.69	3.21	100
F2	3.5	0.46	3.30	99
F3	4.0	0.72	3.12	101
F4	4.0	0.72	3.29	102
F5	3.6	0.68	3.34	99
F6	3..5	0.43	3.36	98
F7	4.0	0.42	3.29	99
F8	3.8	0.45	3.36	97
F9	3.7	0.54	3.30	100

Table 5: Post-compression parameters of Rizatriptan tablets

Post formulation studies

Formulation code	In-vitro dispersion time (sec)	Wetting time (sec)	Water absorption ratio (%)
F1	22	27	101
F2	18	25	102
F3	11	18	105
F4	50	33	90
F5	40	25	92
F6	30	21	102
F7	30	29	90
F8	26	26	102
F9	20	20	101

Table 6: Post formulation studies of Rizatriptan tablets In vitro dissolution studies:

Dissolution rate was studied by using USP type-2 apparatus using 900ml of phosphate buffer pH (6.8) as dissolution medium. Temperature of the dissolution medium was maintained at 37±0.5ºc, aliquot of dissolution medium withdrawn at every 15 sec interval and filtered. The absorbance of the filtered solution was measured by UV spectrophotometric method at 231nm and concentration of the drug was determined from the standard calibration curve. The dissolution of Cetrizine hydrochloride from the tablets is shown in the figures 1, 2 3, 4 (table no: 7) cumulative percentage drug release profiles.
Cumulative percentage drug release profiles

Table 7: In vitro dissolution studies of Rizatriptan tablets

Conclusion:

Rizatriptan oral disintegrating tablets were prepared using different concentrations of superdisintegrants like Croscarmellose sodium (CCS), Sodium starch glycolate (SSG). Tablets were prepared by direct compression method and evaluated for hardness, friability, wetting time, disintegration time and percent drug release. FT-IR studies revealed that there was no interaction between Rizatriptan and the excipients used in the study. The results indicated that formulation prepared with 8% crospovidone was found to be optimized (F3) which provides maximum drug release (95.6%) and minimum disintegration time (less than 20sec). Dissolution rate of tablets with croscarmellose sodium (CCS), sodium starch glycolate (SSG) improves when concentration increased from 2% to 4% and 4% to 8%. Dissolution rate of tablets with sodium starch glycolate (SSG) was significantly less when compared to the tablets with croscarmellose sodium (CCS), at initial time points. From the above results of the study it can be concluded that the best formulation is with 8 % of crospovidone (CP) showed faster disintegration time within 11sec when compared to the other formulations and it showed 95.6% drug release at the end of 30 min.

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