FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF ONDANSETRON HYDROCHLORIDE

Dissertation submitted to

The Tamilnadu Dr. M.G.R Medical University, Chennai

In partial fulfillment for the requirement of the degree of

MASTER OF PHARMACY
(Pharmaceutics)

MARCH-2012

DEPARTMENT OF PHARMACEUTICS

KMCH COLLEGE OF PHARMACY

KOVAI ESTATE, KALAPPATTI ROAD, COIMBATORE-641048

FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF ONDANSETRON HYDROCHLORIDE

Dissertation submitted to

The Tamilnadu Dr. M.G.R Medical University, Chennai

In partial fulfillment for the requirement of the degree of

MASTER OF PHARMACY
(Pharmaceutics)

MARCH-2012

Submitted by

Reg. No: 26107101

Under the Guidance of

Mrs. J. PADMAPREETHA, M. Pharm.,

DEPARTMENT OF PHARMACEUTICS

KMCH COLLEGE OF PHARMACY

KOVAI ESTATE, KALAPPATTI ROAD, COIMBATORE-641048

Dr. A. RAJASEKARAN, M. Pharm., Ph.D.,
PRINCIPAL,
KMCH COLLEGE OF PHARMACY,
KOVAI ESTATE, KALAPATTI ROAD,
COIMBATORE – 641048. (TN)

CERTIFICATE

This is to certify that this dissertation work entitled **"FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF ONDANSETRON HYDROCHLORIDE"** was carried out by **Reg.no:26107101.** The work mentioned in the dissertation was carried out at the Department of Pharmaceutics, Coimbatore - 641 048, under the guidance of **Mrs.J.PADMAPREETHA M.Pharm.** for the partial fulfillment for the Degree of Master of Pharmacy and is forward to The Tamil Nadu Dr.M.G.R. Medical University, Chennai.

DATE:

Dr.A.RAJASEKARAN, M.Pharm., Ph.D.,

Principal

Mrs.J.PADMAPREETHA, M. Pharm
ASST. PROFESSOR,
KMCH COLLEGE OF PHARMACY,
KOVAI ESTATE, KALAPATTI ROAD,
COIMBATORE-641048 (T.N)

CERTIFICATE

This is to certify that the dissertation work entitled **"FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF ONDANSETRON HYDROCHLORIDE"** submitted by **Reg.no:26107101** to the TamilNadu Dr.M.G.R.Medical University, Chennai, in partial fulfillment for the Degree of **Master of Pharmacy** in **Pharmaceutics** is a bonafide work carried out by the candidate under my guidance at the Department of Pharmaceutics, KMCH College of Pharmacy, Coimbatore, during the year 2011 – 2012.

Mrs.J.PADMAPREETHA, M.Pharm

Asst. Professor

EVALUATION CERTIFICATE

This is to certify that the dissertation work entitled **"FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF ONDANSETRON HYDROCHLORIDE "** Submitted by university **Reg.No:26107101** to the TamilNadu Dr.M.G.R.Medical University, Chennai, in partial fulfillment for the Degree of **Master of Pharmacy** in **Pharmaceutics** is a bonafide work carried out by the candidate at the Department of Pharmaceutics, KMCH College of Pharmacy, Coimbatore, and was evaluated by us during the academic year 2011 – 2012.

Examination Centre: KMCH College of Pharmacy, Coimbatore – 48.

Date:

Internal Examiner **External Examiner**

Convener of Examination

DECLARATION

I do hereby declare that this dissertation entitled **"FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF ONDANSETRON HYDROCHLORIDE"** submitted to the TamilNadu Dr.M.G.R.Medical University, Chennai, in partial fulfillment for the Degree of Master of Pharmacy in Pharmaceutics was done by me under the guidance of **Mrs.J.PADMAPREETHA,M.Pharm.,** Asst Professor, Department of Pharmaceutics, KMCH College of Pharmacy, Coimbatore, during the year 2011 – 2012.

(Reg.no:26107101)

ACKNOWLEDGEMENT

First and foremost it gives me great pleasure to record my deep sense of gratitude and indebtedness to my esteemed guide **Mrs.J.PADMAPREETHA,M.Pharm.,** Asst Professor, Department of Pharmaceutics, KMCH College of Pharmacy, for her constant insight, guidance, countless serenity, encouragement and pain taking efforts in my project work . I am indebted to her kindness and never failing co-operation.

I extend my gratitude to **Dr.A.RAJASEKARAN, M.Pharm., Ph.D.,** Principal, KMCH College of Pharmacy, Coimbatore, for his constant encouragement, support and facilities provided.

I extend thanks to our respected chairman **Dr.NALLA G.PALANISWAMI, MD, AB (USA)** and respected trustee madam **Dr.THAVAMANI D. PALANISWAMI, MD, AB (USA),** Kovai Medical Center Research and Education Trust, Coimbatore for the facilities provided by them to carry out this project in a nice manner.

I owe my heartfelt thanks to my esteemed and beloved staffs **Dr. K.S.G. Arulkumaran M.Pharm.,PhD., Dr.Arun Kumar M.Pharm.,PhD., Mr.J.Dharuman, M.Pharm.,(Ph.D), Dr.C.Sankar M.Pharm.,Ph.D** for their sensible help and suggestions.

My sincere thanks to all other staffs of KMCH College of Pharmacy, Coimbatore who directly or indirectly gave a helping hand to me while carrying out the study.

This project would not be a resplendent one without the timely help and continous support by ever-loving friends of the Dept of Pharmaceutics (Sandra joji Samuel , Lincy john, LincyVarghese, Christine Varghese Oomen, Sreejith , Dinesh raja, Mazin Mohammed, Kalgave sagar , Arun raj and Saranya.P.S).

I also express our heartfelt thanks to Ms.Thiruveni, Lab technician (Dept of Pharmaceutics) for her valuable support and timely help during the course of the entire work.

With immense pleasure I express my deep gratitude to computer lab technicians, library staff and other lab technicians of KMCH College of Pharmacy, and one all those who helped directly and indirectly in every aspect of constructing this work.

Above all I dedicate myself before the unfailing presence of GOD and constant love and encouragement given to me by my beloved ***Parents, husband and brothers*** who deserve the credit of success in whatever I did.

(Reg.no:26107101)

FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF ONDANSETRON HYDROCHLORIDE

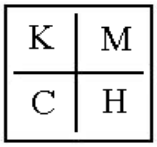
Dissertation submitted to

The Tamilnadu Dr. M.G.R Medical University, Chennai

In partial fulfillment for the requirement of the degree of

MASTER OF PHARMACY
(Pharmaceutics)

MARCH-2012



DEPARTMENT OF PHARMACEUTICS

KMCH COLLEGE OF PHARMACY

KOVAI ESTATE, KALAPPATTI ROAD, COIMBATORE-641048

FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF ONDANSETRON HYDROCHLORIDE

Dissertation submitted to

The Tamilnadu Dr. M.G.R Medical University, Chennai

In partial fulfillment for the requirement of the degree of

MASTER OF PHARMACY
(Pharmaceutics)

MARCH-2012

Submitted by

AMBIGA.M

(Reg. No: 26107101)

Under the Guidance of

Mrs. J. PADMAPREETHA, M. Pharm.,

DEPARTMENT OF PHARMACEUTICS

KMCH COLLEGE OF PHARMACY

KOVAI ESTATE, KALAPPATTI ROAD, COIMBATORE-641048

Dr. A. RAJASEKARAN, M. Pharm., Ph.D.,
PRINCIPAL,
KMCH COLLEGE OF PHARMACY,
KOVAI ESTATE, KALAPATTI ROAD,
COIMBATORE – 641048. (TN)

CERTIFICATE

This is to certify that this dissertation work entitled **"FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF ONDANSETRON HYDROCHLORIDE"** was carried out by **AMBIGA.M (Reg.no:26107101).** The work mentioned in the dissertation was carried out at the Department of Pharmaceutics, Coimbatore - 641 048, under the guidance of **Mrs.J.PADMAPREETHA M.Pharm.** for the partial fulfillment for the Degree of Master of Pharmacy and is forward to The Tamil Nadu Dr.M.G.R. Medical University, Chennai.

DATE:

Dr.A.RAJASEKARAN, M.Pharm., Ph.D.,

Principal

Mrs. J.PADMAPREETHA, M. Pharm
ASST. PROFESSOR,
KMCH COLLEGE OF PHARMACY,
KOVAI ESTATE, KALAPATTI ROAD,
COIMBATORE-641048 (T.N)

CERTIFICATE

This is to certify that the dissertation work entitled **"FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF ONDANSETRON HYDROCHLORIDE"** submitted by AMBIGA.M **(Reg.no:26107101)** to the TamilNadu Dr.M.G.R.Medical University, Chennai, in partial fulfillment for the Degree of **Master of Pharmacy** in **Pharmaceutics** is a bonafide work carried out by the candidate under my guidance at the Department of Pharmaceutics, KMCH College of Pharmacy, Coimbatore, during the year 2011 – 2012.

Mrs.J.PADMAPREETHA, M.Pharm

Asst. Professor

EVALUATION CERTIFICATE

This is to certify that the dissertation work entitled **"FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF ONDANSETRON HYDROCHLORIDE "** Submitted by **AMBIGA.M**, university **Reg.No:26107101** to the TamilNadu Dr.M.G.R.Medical University, Chennai, in partial fulfillment for the Degree of **Master of Pharmacy** in **Pharmaceutics** is a bonafide work carried out by the candidate at the Department of Pharmaceutics, KMCH College of Pharmacy, Coimbatore, and was evaluated by us during the academic year 2011 – 2012.

Examination Centre: KMCH College of Pharmacy, Coimbatore – 48.

Date:

Internal Examiner **External Examiner**

Convener of Examination

DECLARATION

I do hereby declare that this dissertation entitled **"FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF ONDANSETRON HYDROCHLORIDE"** submitted to the TamilNadu Dr.M.G.R.Medical University, Chennai, in partial fulfillment for the Degree of Master of Pharmacy in Pharmaceutics was done by me under the guidance of **Mrs.J.PADMAPREETHA,M.Pharm.,** Asst Professor, Department of Pharmaceutics, KMCH College of Pharmacy, Coimbatore, during the year 2011 – 2012.

AMBIGA.M

(Reg.no:26107101)

ACKNOWLEDGEMENT

First and foremost it gives me great pleasure to record my deep sense of gratitude and indebtedness to my esteemed guide **Mrs.J.PADMAPREETHA,M.Pharm.,** Asst Professor, Department of Pharmaceutics, KMCH College of Pharmacy, for her constant insight, guidance, countless serenity, encouragement and pain taking efforts in my project work . I am indebted to her kindness and never failing co-operation.

I extend my gratitude to **Dr.A.RAJASEKARAN, M.Pharm., Ph.D.,** Principal, KMCH College of Pharmacy, Coimbatore, for his constant encouragement, support and facilities provided.

I extend thanks to our respected chairman **Dr.NALLA G.PALANISWAMI, MD, AB (USA)** and respected trustee madam **Dr.THAVAMANI D. PALANISWAMI, MD, AB (USA),** Kovai Medical Center Research and Education Trust, Coimbatore for the facilities provided by them to carry out this project in a nice manner.

I owe my heartfelt thanks to my esteemed and beloved staffs **Dr. K.S.G. Arulkumaran M.Pharm.,PhD., Dr.Arun Kumar M.Pharm.,PhD., Mr.J.Dharuman, M.Pharm.,(Ph.D), Dr.C.Sankar M.Pharm.,Ph.D** for their sensible help and suggestions.

My sincere thanks to all other staffs of KMCH College of Pharmacy, Coimbatore who directly or indirectly gave a helping hand to me while carrying out the study.

This project would not be a resplendent one without the timely help and continous support by ever-loving friends of the Dept of Pharmaceutics (Sandra joji Samuel , Lincy john, LincyVarghese, Christine Varghese Oomen, Sreejith , Dinesh raja, Mazin Mohammed, Kalgave sagar , Arun raj and Saranya.P.S).

I also express our heartfelt thanks to Ms.Thiruveni, Lab technician (Dept of Pharmaceutics) for her valuable support and timely help during the course of the entire work.

With immense pleasure I express my deep gratitude to computer lab technicians, library staff and other lab technicians of KMCH College of Pharmacy, and one all those who helped directly and indirectly in every aspect of constructing this work.

Above all I dedicate myself before the unfailing presence of GOD and constant love and encouragement given to me by my beloved ***Parents, husband and brothers*** who deserve the credit of success in whatever I did.

AMBIGA.M

(Reg.no:26107101)

LIST OF ABBREVIATION

e.g	Example
Avg	Average
Bp	British Pharmacopoeia
IP	Indian Pharmacopoeia
i.e.	That is
%	Percentage
Kg	Kilogram
CR	Cumulative release
HPMC	Hydroxy propyl methyl cellulose
NMR	Nuclear Magnetic Resonance
mg	Milligram
ml	Milliliter
µg	Microgram
w/w	Weight by weights
v/v	Volume by volume
avg	Average
hrs	Hours

pH	Hydrogen ion concentration
°C	Degree centigrade
HCl	Hydrochloric acid
RPM	Revolution per minute
t	Time
MCC	Microcrystalline cellulose
Abs	Absorbance
Conc	Concentration
Fig	Figure
Tab	Table
UV- VIS	Ultra violet and visible spectroscopy
Mm	millimetre
C.I	Compressibility index

CONTENTS

1. INTRODUCTION

Tablets are solid preparations each containing a single dose of one or more active substances and usually obtained by compressing uniform volumes of particles. Tablets are intended for oral administration. Some are swallowed whole, some after being chewed, some are dissolved or dispersed in water before being administered and some are retained in the mouth where the active substance is liberated[1].

Several categories of tablets for oral use may be distinguished[1]

- Uncoated tablets
- Coated tablets
- Effervescent tablets
- Soluble tablets
- Dispersible tablets
- Orodispersible tablets
- Gastro-resistant tablets
- Modified-release tablets

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. One of the important drawbacks of this dosage forms for some patients, is the difficulty to swallow. Drinking water plays an important role in the swallowing of oral dosage forms. Often times people experience inconvenience in swallowing conventional dosage forms such as tablet when water is not available, in the case of the motion sickness and sudden episodes of coughing during the common cold, allergic condition and bronchitis. For these reason, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention. Orodispersible tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people.

ODTs are known by various names such as “fast-melting, fast-dissolving, oral disintegrating or orodisperse”. The European Pharmacopoeia defines the term “orodisperse” as a tablet that can be placed in the mouth where it disperses rapidly before swallowing. Fast

dissolving tablets are those when put on tongue disintegrate instantaneously releasing the drug which dissolve or disperses in the saliva. The faster the drug into solution, quicker the absorption and onset of clinical effect[2].

1.1. CRITERIA FOR FAST DISSOLVING DRUG DELIVERY SYSTEMS[2, 3]

The tablets should

- Not require water to swallow, but it should dissolve or disintegrate in the mouth in matter of seconds
- Be compatible with taste masking
- Be portable without fragility concern
- Have a pleasant mouth feel
- Leave minimum or no residue in the mouth after oral administration
- Exhibit low sensitive to environmental condition as temperature and humidity
- Allow the manufacture of the tablet using conventional processing and packaging equipments at low cost

1.2. SALIENT FEATURES OF ORODISPERSIBLE DRUG DELIVERY SYSTEM[2, 3]

- Convenience of administration and accurate dosing as compared to liquids.
- Ease of administration to patients who refuse to swallow a tablet, such as paediatric and geriatric patients and, psychiatric patients.
- No need of water to swallow the dosage from, which is highly convenient feature for patients who are traveling and do not have immediate access to water.
- Good mouth feels properly of ODDS helps to change the basic view of medication as “bitter pill”, particularly for paediatric patients.

- Some drugs are absorbed from the mouth pharynx and oesophagus as the saliva passes down into the stomach, in such cases bioavailability of drugs is increased.
- Rapid dissolution of drug and absorption which may produce rapid, onset of action.
- Pregastric absorption can result in improved bioavailability and as a result of reduced dosage, improved clinical performance through a reduction of unwanted effects.

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

1.3. ADVANTAGES OF ORODISPERSIBLE TABLETS[4,5]

- No water needed
- No chewing needed
- Better taste
- Improved stability
- Suitable for controlled/sustained release actives
- Allows high drug loading.
- Ability to provide advantages of liquid medication in the form of solid preparation.
- Cost- effective
- Rapid drug therapy intervention
- High drug loading is possible.
- Have acceptable taste and pleasant mouth feeling.
- Leave minimum residue.

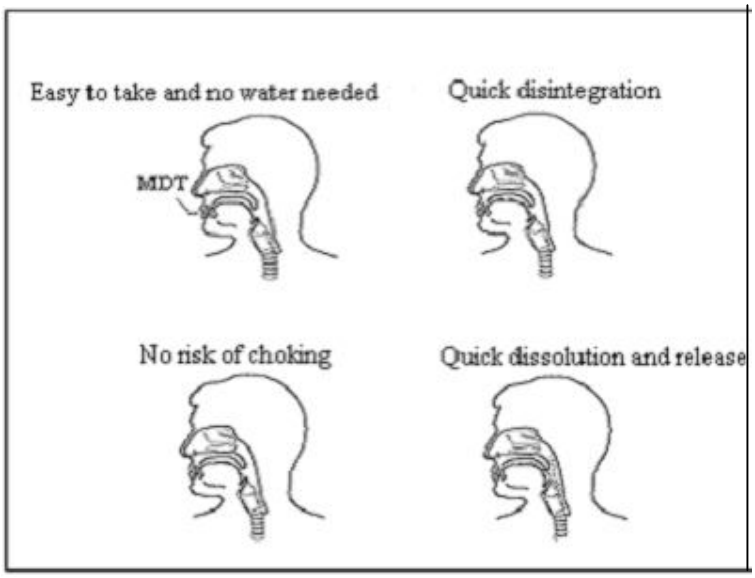


FIGURE – 1 STEPS INVOLVED IN MOUTH DISSOLVING TABLETS [5]

1.4. LIMITATIONS TO ORODISPERSIBLE TABLETS[5]

i) Drugs with relatively larger doses are difficult to formulate into ODTs e.g. antibiotics like ciprofloxacin with adult dose tablet containing about 500 mg of the drug.

ii) Patients who concurrently take anticholinergic medications may not be the best candidates for ODTS.

1.5. DRUG SELECTION CRITERIA

The ideal characteristics of a drug for oral dispersible tablet include:

- Ability to permeate the oral mucosa.
- At least partially non-ionized at the oral cavity pH.
- Have the ability to diffuse and partition into the epithelium of the upper GIT.
- Short half life and frequent dosing drugs are unsuitable for orodispersible tablets (ODT).
- Drug should have good stability in saliva and water.

- Very bitter or unacceptable taste and odor drugs are unsuitable for orodispersible tablets(ODT).

Excipients commonly used for ODT preparation[4]

Mainly seen excipients in FDT are as follows at least one disintegrant, a diluent, a lubricant, and, optionally, a swelling agent, a permeabilizing agent,sweeteners, and flavorings.

1.6. METHOD OF ADDITION OF DISINTEGRANTS[5]

Disintegrants are substances or mixture of substances added to the drug formulation that facilitates the breakup or disintegration of tablet or capsule content into smaller particles that dissolve more rapidly than in the absence of disintegrants. Superdisintegrants are generally used at a low level in the solid dosage form, typically 1-10% by weight relative to the total weight of the dosage unit. Examples of superdisintegrants are croscarmellose, crospovidone, sodium starch glycolate which represent example of a cross-linked cellulose, cross-linked polymer and a cross-linked starch respectively.

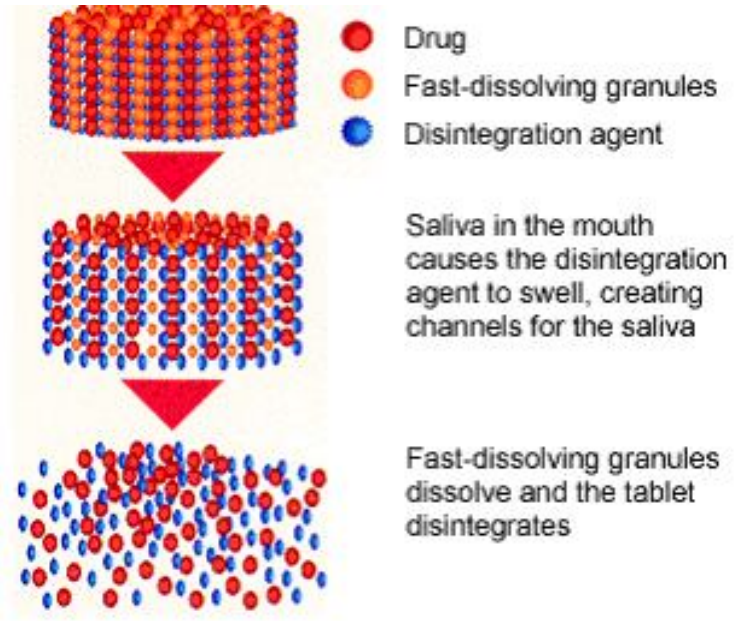


FIGURE -2: STAGES INVOLVED IN DISINTEGRATION

The ideal characteristics of a disintegrant has[3]

1. High solubility
2. Good gel formation
3. Good molding and flow properties
4. No tendency to form complexes with the drugs
5. Good hydration capacity

Disintegrants are essentially added to tablet granulation for causing the compressed tablet to break or disintegrate when placed in aqueous environment.

There are three methods of incorporating disintegrating agents into the tablet:

1. Internal addition (Intra granular)

2. External addition (Extra granular)

3. Partly Internal and External

In Internal addition method, the disintegrant is mixed with other powders before wetting the powder mixtures with the granulating fluid. Thus the disintegrant is incorporated within the granules. When these methods are used, part of disintegrant can be added internally and part externally. This provides immediate disintegrating agent within the granules produces further erosion of the granules to the original powder particles.

In External addition method, the disintegrant is added to the sized granulation with mixing prior to compression. The two-step method usually produces better and more complete disintegration than the usual method of adding the disintegrant to the granulation surface only[3].

TABLE NO: 1 NAME AND WEIGHT PERCENTAGE OF VARIOUS EXCIPIENTS

Name of the excipients	Percentage used
Disintegrant	1 to 15 %
Binder	5 to 10 %
Antistatic agent	0 to 10 %
Diluents	0 to 85%

1.7. MECHANISM INVOLVED IN ORODISPERSIBLE TABLET TECHNOLOGIES [6]:

Disintegrant is a substance or mixture of substances added to tablets to facilitate its break up or disintegration. The active constituents must be released from the tablet as efficiently as possible to allow its rapid action. The basic approaches used in fast dissolving tablet technologies are increasing the porous structure of the tablet matrix and incorporating disintegrating agents or highly water soluble excipients in the tablet formulation. The basic function of a disintegrant used in the formulations of tablets are to oppose the physical forces and efficacy of the tablet binder which act during the compression of tablet. The process involved in the production of a homogeneous suspension or solution of tablet where the tablet is broken down into smaller particles is based on:

a) By capillary action

b) By swelling

c) Because of heat of swelling

d) Due to release of gases

e) By enzymatic actions

f) Due to disintegrating particle/particle repulsive force

f) Due to deformation

MECHANISM OF ACTION:

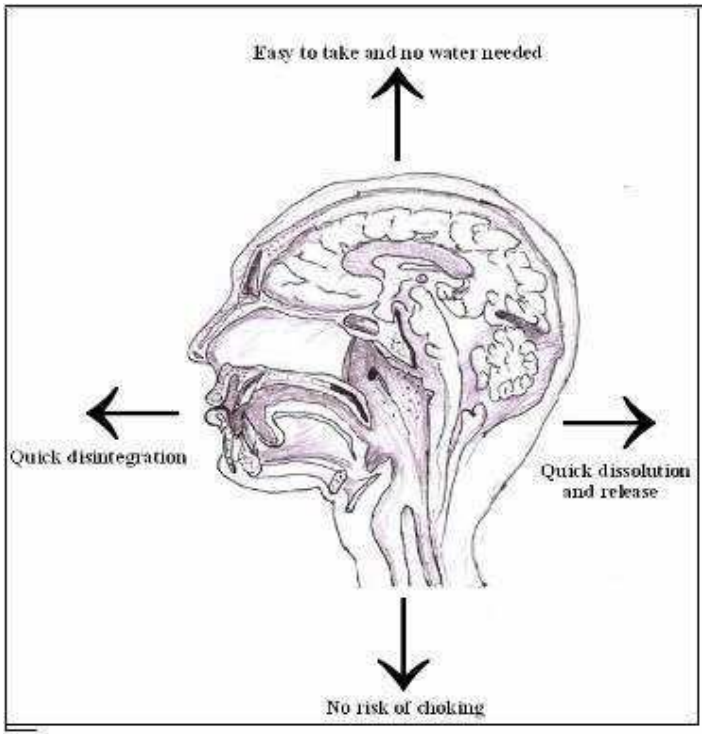


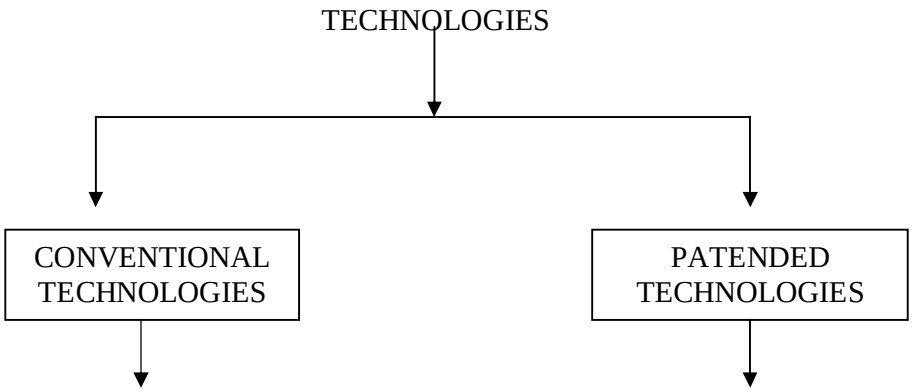
Figure 1

FIGURE-3: Mechanism of action of Orodispersible tablet

When such tablets are placed in oral cavity, saliva quickly penetrates into the pores to cause rapid tablet disintegration. Recent market studies indicate that more than half of the patient population prefers ODTs to other dosage forms. Most consumers would ask their doctors for ODTs (70%), purchase ODTs (70%), or prefer ODTs over regular tablets or liquids (>80%).The US Food and Drug Administration Center for Drug Evaluation and Research (CDER) defines, in the 'Orange Book', an ODT as "a solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue".

1.8. TECHNOLOGIES USED TO MANUFACTURE ORODISPERSIBLE TABLETS[6]

The technologies used to manufacture mouth dissolving tablets can be classified as:



1) Freeze drying
2) Direct compression
3) Spray drying
4) Tablet molding
5) Sublimation
6) Effervescent method
7) Phase transition process
8) Melt granulation

1) Zydis technology
2) Orasolv technology
3) Durasolv technology
4) Flash dose technology
5) Flash tab technology
6) Wow tab technology
7) Lyoc technology
8) Pharmaburst technology

1.8.1 CONVENTIONAL TECHNOLOGIES

1. Freeze Drying[6]

ZYDIS® (R.P. Scherer, Swindon, UK), using freeze drying processes is one of the first generations of fast disintegrating dosage forms. There are approximately 12 marketed

ZYDIS® products, including lorazepam, piroxicam, loperamide, loratidine, enalapril. A process in which water is sublimated from the product after freezing.

Lyophilization is a pharmaceutical technology which allows drying of heat sensitive drugs and biological at low temperature under conditions that allow removal of water by Sublimation. Lyophilization results in preparations, which are highly porous, with a very high specific surface area, which dissolve rapidly and show improved absorption and bioavailabity.

2. Direct Compression[8]

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 method.

a) Superdisintegrants[2]

The addition of superdisintegrants mainly affects the rate of disintegration in many ODT technologies based on direct compression and hence the dissolution is also affected by its action. The disintegration can be accelerated by the addition of ingredients like effervescent agents and water – soluble excipients

b) Sugar Based Excipients[2]

This is another method to manufacture ODT using direct compression. The addition of sugar based excipients like bulking agents e.g. dextrose, maltose, mannitol, isomalt, fructose, polydextrose and xylitol, which provide sweetness and high aqueous solubility thereby imparting a pleasant mouth feel and taste masking property. On the basis of moulding and dissolution rate, Mizumito et. Al, have classified sugar-based into two types.

Type 1 Saccharides (mannitol and lactose) which exhibit low mould ability but with high dissolution rate.

Type 2 Saccharides (maltilol and maltose) which exhibit high mould ability but with low dissolution rate.

Advantages of direct compression[8]

- Requires fewer unit operations compared with wet granulation (shorter processing time and lower energy consumption).
- Fewer stability issues for actives that are sensitive to heat or moisture.
- For certain compounds, faster dissolution rates may be generated from tablets prepared by direct compression compared with wet granulation. for example, norfloxacin.
- Fewer excipients may be needed in a direct compression formula.

Disadvantages of direct compression[8]

- Issues with segregation – these can be reduced by matching the particle size and density of the active drug substance with excipients.
- In general, the drug content is limited to approximately 30% or approximately 50 mg.
- Not suited for poorly flowing drug compounds.
- Static charges may develop on the drug particles or excipients during mixing, which may lead to agglomeration of particles producing poor mixing.

3. **Spray Drying[3,6]**

The formulations contained hydrolyzed and unhydrolyzed gelatin as a supporting agent for the matrix, mannitol as a bulking agent and sodium starch glycolate/croscarmellose as a disintegrant. Disintegration and dissolution were further enhanced by adding an acid (e.g., citric acid) or an alkali (e.g., sodium bicarbonate). The suspension of above excipients was spray-dried to yield a porous powder which was compressed into tablets. Tablets manufactured by this method disintegrated in < 20 secs in an aqueous medium.

4. **Tablet Molding[6]**

In this method, molded tablets are prepared by using water-soluble ingredients so that the tablets dissolve completely and rapidly. The powder blend 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. Molded tablets are very less compact than compressed tablets. These possess porous structure that enhances dissolution.

5. Sublimation[3,6]

Sublimation has been used to produce ODTs with high porosity. A porous matrix is formed by compressing the volatile ingredients along with other excipients into tablets, which are finally subjected to a process of sublimation. Inert solid ingredients with high volatility (e.g., ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, hexamethylene tetramine, naphthalene, phthalic anhydride, urea and urethane) have been used for this purpose. Solvents such as cyclohexane and benzene were also suggested for generating the porosity in the matrix.

6. Effervescent Method[7]

Orodispersible tablets are also prepared by effervescent method by using sodium bicarbonate and tartaric acid of concentration 12 % w/w along with super disintegrants like pregelatinised starch, crospovidone, croscarmellose, sodium starch glycolate. First, sodium bicarbonate and tartaric acid were preheated at a temperature of 80ºC to remove absorbed/residual moisture and thoroughly mixed in mortar. Finally, the blends are compressed in the punch.

7. **Phase Transition Process[7]**

In this process the combination of low and high melting point sugar alcohols, along with a transition of phase in the manufacturing process are important for formulating ODTs. For this transition, special equipments are not employed. ODTs were produced by compressing xylitol at melting point; 93.95º C and erythritol at melting point ; 122ºC and then heating at about 93º C for 15 min. The median pore size of the tablets along with hardness was increased after heating. The increased tablet hardness does not depend on the crystal state or the lowering melting point of sugar alcohol.

8. Melt Granulation[7]

This is a process in which with the help of a meltable binder, pharmaceutical powders are efficiently agglomerated. The advantage of the technique in comparison to the traditional granulation is that water or organic solvents are not needed as there is no drying step involved in it. Compared to wet granulation, the process is less time consuming and uses less energy. This technique can be applied for enhancing the dissolution rate of drugs which have poor

water solubility like grisiofulvin. To prepare ODT with sufficient mechanical integrity, the approach uses the hydrophilic waxy binder such as PEG-6-stearate and Superpolystate. Superpolystate is a waxy material which helps tablet disintegration as it melts in the mouth and acts as a binder. It also solubilizes rapidly without any residues.

1.8.2. PATENDED TECHNOLOGY

1. Zydis technology[9]

Zydis, the best known of the fast-dissolving/disintegrating tablet preparations was the first marketed new technology tablet. The tablet dissolves in the mouth within seconds after placement on the tongue. A Zydis tablet is produced by lyophilizing or freeze-drying the drug in a matrix usually consisting of gelatin. The product is very light weight 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 product is made to dissolve on the tongue in 2 to 3 seconds. 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.

Desired characteristics of zydis technology:

i. Drug should be chemically stable
ii. Particle size lesser than 50 μm
iii. Water insoluble
iv. Dose for water soluble drugs is limited (60 mg)

2. Flash dose technology[2, 9]

Flash dose technology has been patented by Fuisz. Nurofen melt let, a new form of ibuprofen as melt-in-mouth tablets, prepared using flash dose technology is the first commercial product launched by Biovail Corporation. Flash dose tablets consist of self binding shear form matrix termed as “floss”. Shear form matrices are prepared by flash heat processing.

3. Flash Tab Technology[9]

The technology is patented by Ethypharm France. This involves granulation of excipients by wet or dry granulation method followed by compression into tablets. Two types

of excipients are employed in this technology. Reticulated polyvinylpyrrolidine or carboxy methyl cellulose, starch, modified starch, microcrystalline cellulose, carboxy methylated starch, etc are some of the disintegrating agents included. Satisfactory physical resistance is present in these tablets.

4. Durasolv technology[9]

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

5. Orasolv technology[2]

CIMA labs have been developed orosolve technology. 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. Conventional blenders and tablet machine is used to produce the tablets. The tablets produced are soft and friable and packaged in specially designed pick and place system.

2. LITERATURE SURVEY

2.1. REVIEW OF ORODISPERSIBLE TABLET

Prakash Goudanavar et.al, (2011) The present study was aimed at developing and evaluating fast disintegrating tablets of Granisetron HCl using natural superdisintegrants like *Plantago ovata*, gum karaya and agar and synthetic superdisintegrants like Indion 234, croscaramellose sodium and crospovidone in different concentration. Fast disintegrating tablets were prepared by direct compression method. Effect of superdisintegrants on wetting, disintegration and dissolution parameters were studied. Fast disintegrating tablets were characterized by Fourier Transform Infrared (FTIR) spectroscopy and Differential Scanning Calorimetry (DSC) [10].

Metker Vishal et.al, (2011) The purpose of this investigation was to develop mouth dissolving tablets of Lornoxicam using KYRON T-314 (Polacrillin Potassium) as a novel Superdisintegrant. Mouth dissolving tablets of lornoxicam were prepared by wet granulation technique using KYRON T-314 as superdisintegrant and menthol as subliming agent. The present study demonstrated potentials for rapid absorption, improved bioavailability, effective therapy and patient compliance[11].

Abdul S.Althaf et.al, (2011) Mouth dissolving tablets of sildenafil citrate were prepared by wet granulation and direct compression method by superdisintegrant addition. Eight batches (B_1-B_8) of mouth dissolving tablets of sildenafil citrate were prepared by using crospovidone, ac-di-sol in different concentrations. All the formulations were evaluated for weight variation, hardness, friability, drug content, in-vitro disintegration time, wetting time, in-vitro dissolution etc., and batch B_8 shows the values within the limits. Formulation B_8 with 5% crospovidone, Ac-di-sol showed the less disintegration time (32 seconds) and less wetting time (41.5 seconds) [12].

C. Patil and S. Das et.al, (2011) The demand for orally disintegrating tablets of lamotrigine has been growing during the last decade especially for the geriatric and pediatric

patients. Lamotrigine is a recognized drug for epilepsy, so development of an ODT of lamotrigine and to evaluate the effect of various superdisintegrants on its disintegration time and release profile was the prime objective of this research work. Tablets were prepared by direct compression technique using 3 different superdisintegrants. Sodium starch glycolate, croscarmellose sodium and crospovidone XL-10 were used as superdisintegrants in combinations to achieve optimum release profile, disintegration time and hardness. Direct compression process was selected for this formulation of ODT tablets, because porous nature is more in direct compression blend than wet granulation blend, so it will give faster disintegration. Microcrystalline cellulose was used as diluent[13].

Prakash Goudanavar et.al, (2011) The present study aimed at preparing orodispersible tablets of lamotrigine by forming inclusion complex with hydroxypropyl β-cyclodextrin (HPβCD) employing kneading method. The complex was compressed into tablets along with superdisintegrants such as Kyron T-314, Sodium starch glycolate, Indion 414, croscarmellose sodium and crospovidone in different concentration. Bitter taste of drug is successfully masked by HPβCD complex and is also useful to enhance the solubility which was confirmed by phase solubility analysis. Orodispersible tablets were characterized by Fourier Transform Infrared (FTIR) Spectroscopy, Differential Scanning Calorimetry (DSC) and Powder X-ray Diffraction Analysis (PXRD). The Result revealed that F6 had shown short dispersion time with maximum drug release in 12 minutes. Formulation containing higher concentration of Indion 414 decreases disintegration time (22.71 sec) and optimize the drug release (99.09% in 12 minutes)[14].

Tejvir kaur et.al, (2011) Recent advances in Novel Drug Delivery Systems (NDDS) aim for designing dosage forms, convenient to be manufactured and administered, free of side effects, offering immediate release and enhanced bioavailability, so as to achieve better patient compliance. Though oral drug delivery systems, preferably, tablets are the most widely accepted dosage forms, for being compact, offering uniform dose and painless delivery. Yet, dysphagia is the most common disadvantage of conventional tablets. This is seen to afflict nearly 35% of the general population and associated with a number of conditions, like Parkinsonism, mental disability, motion sickness, unconsciousness, unavailability of water etc. To overcome such problems, certain innovative drug delivery systems, like ‘Mouth Dissolving Tablets’ (MDT) have been developed. These are novel

dosage forms which dissolve in saliva within a few seconds, when put on tongue. Such MDTs can be administered anywhere and anytime, without the need of water and are thus quite suitable for children, elderly and mentally disabled patients[5].

Dr. Lakshmi CSR et.al, (2011) Atenolol is a β1 selective antagonist without membrane stabilizing or intrinsic sympathomimetic activities. Administration of conventional tablets of atenolol has been reported to exhibit fluctuation in the plasma drug levels, resulting either in manifestation of side effects or reduction in drug concentration at the receptor site. In the present study an attempt has been made to prepare melt-in-mouth tablets (MMT) of atenolol with enhanced dissolution rate. The fast dissolving tablets of atenolol was prepared using various concentrations of subliming agents like ammonium bicarbonate, camphor, menthol, thymol, phthalic anhydride by direct compression method[15].

Sharma Shailesh et.al, (2010) The purpose of this research was to develop mouth dissolve tablets of domperidone. Tablet containing domperidone, camphor and crospovidone were prepared by direct compression technique. In the investigation, a 3^2 full factorial design was used to investigate the joint influence of 2 formulation variables amount of camphor and crospovidone. Camphor was sublimed from these tablets by exposure to vacuum. The tablets were evaluated for percent friability and disintegration time[16].

P. V. Swamy et.al, (2010) The aim of the present study was to develop orodispersible tablets of diethylcarbamazine citrate (anthelmintic).In the effervescent method mixture of sodium bicarbonate and tartaric acid along with treated agar were used as disintegrants. The present study clearly demonstrates that orodispersible tablets of diethylcarbamazine citrate could be successfully prepared by direct compression method in a cost effective manner employing treated agar. The use of effervescent mixture further assists in taste masking[17].

Mohanchandran P.S et.al (2010) This formulation has been made for the development of rapidly disintegrating oral tablets of amlodipine besylate by direct compression method. In this study, fast dissolving tablets of amlodipine besylate using different superdisintegrants were prepared by direct compression method. FDT's were evaluated for its physicochemical properties and in vitro dissolution. Effect of different superdisintegrants on disintegration behaviour of tablets was evaluated in phosphate buffer pH 7.2. All formulations were

evaluated for pre-compression and post- compression parameters. Wetting time of formulations containing croscarmellose sodium was least and tablets showed fastest disintegration. FT-IR studies revealed that there was no physico-chemical interaction between amlodipine besylate and other excipients. Of the twelve formulations studied, F10 showed short dispersion time with maximum drug release in 30 minutes[18].

A. Prameela rani et.al, (2010) In the present study an attempt has been made to prepare fast disintegrating tablets of Metformin.Hcl in the oral cavity with enhanced dissolution rate. The tablets were prepared with Isphagula husk, natural superdisintegrant and crospovidone, synthetic superdisintegrant. The pure drug and formulation blend was examined for angle of repose, bulk density, tapped density, compressibility index and hausner's ratio. The tablets were evaluated for hardness, tensile strength, drug content, friability and were found satisfactory. The disintegration time in the oral cavity was also tested and was found to be around 10sec. Based on dissolution rate the disintegrants can be rated as Isphagula husk > Crosspovidone. Hence Isphagula husk was recommended as suitable disintegrant for the preparation of direct compression melt-in-mouth tablets of Metformin.Hcl[19].

Kalpesh K. Mehta et.al, (2010) The purpose of this research was to develop fast dissolving tablets of nimesulide containing natural *Lepidium sativum* (family: Cruciferae) known as asaliyo and widely used as herbal medicine and pharmaceutical excipient as disintegrating agent. The mucilage was extracted from seeds of *Lepidium sativum* and was used to develop the fast dissolving tablet of nimesulide. The extracted mucilage was characterized for weight loss on drying, particle size, pH of solution, swelling ratio, bulk and tapped density, compressibility index, viscosity and Angle of repose. The disintegration property of extracted mucilage in FDTs was compared with widely used superdisintegrants like Sodium starch glycolate (SSG), Kyron T314, Ac Di Sol. The prepared FDTs were evaluated for uniformity of weight, hardness, tablet thickness, Percentage friability, Wetting time, *in vitro* disintegration time and *in vitro* dissolution[20].

Howida Kamal Ibrahim and Doaa A. El-Setouhy (2010) Valsartan orodispersible tablets have been developed at 40-mg dose, with the intention of facilitating administration to patients experiencing problems with swallowing and hopefully, improving its poor oral bioavailability. Work started with selecting drug compatible excipients depending on

differential scanning calorimetric analysis. A full factorial design was adopted for the optimization of the tablets prepared by freeze-drying technique. The effects of the filler type, the binder type, and the binder concentration were studied. The different tablet formulas were characterized for their physical properties, weight variation, disintegration time, surface properties, wetting properties, and *in vitro* dissolution. Amongst the prepared 27 tablet formulas, formula number 6 (consisting of 4:6 valsartan: mannitol and 2% pectin) was selected to be tested *in vivo*[21].

V.S. Mannur et.al, (2010) Prepared ranitidine dispersible tablets using a direct compression method was used to prepare these types of tablets using different super disintegrants viz. sodium carboxy methyl cellulose (SCMC), pregelatinised starch and sodium starch glycolate (SSG). Mannitol was employed to improve the mouth feel and aspartame to improve the taste. The formulations were evaluated for both precompression and post compression parameters. The tablets showed satisfactory hardness and the drug content were also found to within the IP range for all the formulations. The tablets disintegrated within 19 to 22 seconds and wetting time of the tablets was found to be between 17 to 20 seconds[22].

Jayashri G.Mahore et.al, (2010) In the present work, orodispersible tablets of metoclopramide HCl were designed by preparing tasteless complexes of metoclopramide HCl with weak cation ion exchange resins (Indion 234). The ion exchange complex were prepared by the batch process using activated Indion-234 with a drug: resin ratios 1:1,1:2 and 1:3 (% w/w) and IR analysis, assay content and decomplexation studies give evidence of complex formation. Drug shows maximum complexation with resin in pH range 4-6, while activation of ion exchange resin affects the percent drug loading. Drug release from drug: resin complex in salivary pH was in sufficient to impart bitter taste. A study on super-disintegrants i.e., croscarmellose sodium, sodium starch glycolate, crospovidone along with directly compressible mannitol to enhance mouth feel[23].

Niladri Shekhar Dey et.al, (2010) The present research work has been carried out for an optimized formulation of co-processed directly compressible vehicles in the preparation of the paracetamol mouth fast dissolving tablets (MFDTs). Paracetamol was chosen due to its poor compression properties. Co-processed direct compressible vehicles such as microcrystalline cellulose spray dried lactose and pearlitol were taken in different ratios such

as (10:90, 25:75, 50:50, 75:25 & 90:10) using crospovidone as superdisintegrant. The effects of other superdisintegrants were studied in the best formulation F15. Optimized formulation F15 B was found to be optimum compressibility characteristics hardness 4 kg/cm2 with fast disintegration (9 sec) compare to other formulations[24].

Pooja Mathur et.al, (2010) The desire of improved palatability in orally administered products has prompted the development of numerous formulations with improved performance and acceptability. Orally disintegrating tablets (ODTs) have received ever-increasing demand during the last few decades, and the field has become a rapidly growing area in the pharmaceutical industry. The unique property of mouth dissolving tablet is that they are rapidly disintegrating and/or dissolving and release the drug as soon as they come in contact with saliva, thus obviate the requirement of water during administration. This article reviews the earlier applications and methodologies of taste masking and also emphasize on the recent developments and approaches of bitterness reduction for orally used pharmaceuticals[25].

Suhas M. Kakade et.al, (2010) The present work, orodispersible tablets of losartan potassium were design with a view to enhance the patient compliance and provide a quick onset of action. Losartan potassium is an angiotension receptor antagonist, used in the management of hypertension. It has low bioavailability due to its first pass metabolism. Hence the main objective of the study was to formulate orodispersible tablets of losartan potassium to achieve a better dissolution rate and improve the bioavailability of the drug. The tablets are prepared by direct compression method by using the superdisintegrants such as polyplasdone XL 10 ,croscarmellose sodium and explotab in different concentration and evaluated for the pre-compressibility parameters[26].

Siraj sheikh (2010) Fast Disintegrating tablets have started gaining popularity and acceptance as new drug delivery systems, because they are easy to administered and lead to better patient compliance. Usually, elderly people experience difficulty in swallowing the conventional dosage forms such as tablets, capsules, solutions and suspensions because of tremors of extremities and dysphagia. Fast-dissolving drug delivery systems may offer a solution for these problems. Recent development in fast disintegrating technology mainly works to improve the disintegration quality of these delicate dosage forms without affecting their integrity. This article focuses on the patented technologies available and the advances

made so far in the field of fabrication of fast disintegrating tablets. Apart from the conventional methods of fabrication, this review also provides the detailed concept of some unique technologies like freeze drying, direct compression, spray drying, tablet molding, sublimation, fast dissolving films cotton candy process, along with their advantages and limitations[8].

Brahmeshwar Mishra et.al, (2009) This article focuses on the technologies available and the advances made so far in the field of fabrication of mouth dissolving tablets. Apart from the conventional methods of fabrication, this review also provides the detailed concept of some unique patented technologies like Zydis, Lyoc, Quicksolv, Orasolv, Durasolv, Flash tab, Oraquick, Wow tab and Zip let along with their advantages and limitations[27].

Galal El-Mahrouk et.al, (2009) Meloxicam is a non-steroidal anti-inflammatory drug with highly variable bioavailability due to its poor aqueous solubility and dissolution. This work aimed to improve meloxicam bioavailability by formulating it in orodispersible capsules containing a soluble complex of the drug with beta-cyclodextrin. Complexes were prepared by different methods and characterized by differential scanning calorimeter, X-ray diffraction, infrared spectroscopy and dissolution efficiency studies. Orodispersible capsule shells were prepared from conventional hard gelatin capsule shells by freeze-drying and evaluated by image analysis microscopy and moisture content estimation[28].

Debjit Bhowmik et.al, (**2009)** This tablet format is designed to allow administration of an oral solid dose form in the absence of water or fluid intake. Such tablets readily dissolve or disintegrate in the saliva generally within <60 seconds. Fast or mouth dissolving tablets have been formulated for 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 persons will have difficulties in taking conventional oral dosage forms (viz., solutions, suspensions, tablets, and capsules) because of hand tremors and dysphagia[2].

Radke R.S. et.al, (2009) The aim of this investigation was to prepare orodispersible tablets of baclofen using various concentrations of superdisintegrant agents like Ac-Di-Sol, crospovidone, sodium starch glycolate by direct compression method. Nine formulations having superdisintegrants at different concentration levels were prepared. These tablets were

evaluated for drug content, weight variation, friability, hardness, wetting time and *in vitro* disintegration time. Among the formulations tablets of batch F3 containing Ac-Di-Sol showed superior organoleptic properties along with excellent *in-vitro* disintegration time and drug release as compare to other formulations[29].

Ravi Kumar et.al, (2009) The purpose of this investigation was to develop fast dissolving tablets of haloperidol using camphor as a subliming agent. Orodispersible tablets of haloperidol were prepared by wet granulation technique using camphor as subliming agent and sodium starch glycolate together with croscarmellose sodium as superdisintegrants. Camphor was sublimed from the granules by exposing the granules to vacuum. The porous granules were then compressed in to tablets. Alternatively, tablets were first prepared and later exposed to vacuum. The formulations were evaluated for weight variation, hardness, friability, drug content, wetting time, *in vitro* and *in-vivo* dispersion, mouth feel and *in vitro* dissolution. All the formulations showed low weight variation with dispersion time less than 45 seconds and rapid *in vitro* dissolution[30].

Biraju patel et.al, (2009) In the present work, fast dissolving tablets of glipizide were prepared by direct compression method with a view to enhance patient compliance. Two superdisintegrants viz, crospovidone and croscarmellose sodium (4%, 5%, 6%) with different binders viz, pvp k-30 and pregelatinized starch (3%) were used. The prepared batches of tablets were evaluated for hardness, friability, and weight variation, disintegration, wetting time, drug content and *in vitro* dissolution studies. Based on evaluating parameters, formulation prepared by using 5% croscarmellose sodium with 3% PVPK30 was selected as optimized formulation. Finally, the optimized formulation was compared with marketed conventional formulation. Stability studies were carried out at 25ºC / 60% RH and 40ºC / 75% RH for optimized formulation for 2 months[31].

V.Balamuralidhara et.al, (2009) In present study an attempt was made to formulate orodispersible tablets of rabeprazole. Tablets were prepared by direct compression method using diluents and various disintegrants. Tablets were also prepared using treated agar (TAG) powder as one of the disintegrant. A total number of ten formulations were prepared and evaluated. Along with physicochemical parameters, the tablets were also evaluated for special parameters like wetting time, *in vitro* dispersion time, *in vitro* disintegration and *in*

vitro drug release. A better disintegration was observed in formulation OT_1, OT_2, OT_5 and OT_6 containing crospovidone and croscarmellose sodium[32].

Mukesh et.al, (2008) The ODT should disperse/disintegrate in less than three minutes. The basic approach used in development of MDT is the use of superdisintegrants like cross linked carboxymethylcellulose (croscarmeliose), sodium starch glycolate (Primo gel, Explotab), polyvinylpyrolidone (polyplasdone) etc. which provide instantaneous disintegration of tablet after putting on tongue, thereby releasing the drug in saliva. The bioavailability of some drugs may be increased due to absorption of drugs in oral cavity and also due to pregastric absorption of saliva containing dispersed drugs that pass down into the stomach[9].

S.R. Shahi et.al, (2008) Etoricoxib is a novel, selective second generation cyclo-oxygenase-2 inhibitor administered orally as an analgesic and anti-inflammatory drug that is used for the treatment of osteoarthritis, rheumatoid arthritis and gouty arthritis. The poor aqueous solubility of the drug leads to variable dissolution rates. In the present investigation an attempt has been made to prepare oro-dispersible tablets of etoricoxib with enhanced dissolution rate. The another purpose of the present investigation was to evaluate effect of superdisintegrants like crospovidone, (Polyplasdone XL), croscarmellose Sodium (Ac-Di-Sol) and sodium starch glycolate (Primojel) on dissolution of poorly soluble, selective COX-2 inhibitor in oro-dispersible tablets[33].

Vijay Sharma et.al, (2008) The purpose of this study was to develop a dosage form that was easy to administer and provides rapid release of the drug roxithromycin, using modified polysaccharides as rapidly disintegrating excipients. Modified polysaccharides co grinded treated agar (C-TAG) and co grinded treated guar gum (C-TGG) were prepared by subjecting pure polysaccharides namely agar and guar gum respectively to sequential processes of wetting, drying and co grinding with mannitol (1:1). The modified polysaccharides were characterized by scanning electron microscopy and diffuse reflectance spectroscopy and evaluated for particle size distribution, derived properties, swelling index and biodegradability[34].

2.2. REVIEW OF ONDANSETRON HYDROCHLORIDE

Prabakaran. L et.al, (2011) The purpose of this research was to introduce and evaluate natural excipient that has versatile property in the oral disintegrant and immediate release formulations. This natural excipient was used as disintegrant, binder, and diluent in the formulation of orodispersible tablets of some model drugs such as Ondansetron HCl (OND), Propranolol (PNL) and Gabapentin (GP).All the formulations are subjected for *in vitro* evaluations such as wetting time, water absorption ratio, *in vitro* dispersion time and disintegration time, etc. Therefore, we conclude that the natural excipient proposed can be used as binder, diluent and disintegrant in oral disintegrating tablets and immediate release dosage forms. Mainly the natural excipient used is biocompatible, cost effective and provides as nutrition supplements[35].

P. K. Lakshmi et.al, (2011) The main objective of this study was to formulate and evaluate the orodispersible tablets of ondansetron hydrochloride with synthetic and natural superdisintegrants. Various formulations were prepared by direct compression using different concentrations of natural superdisintegrant *i.e.* isolated mucilage of *Plantago ovata* and synthetic superdisintegrants namely Kyron T-314, crospovidone, and croscarmellose sodium ranging from 0.4% to 2%. The initial compatibility studies between the drug and excipients were carried out using FTIR spectroscopy. The blend was evaluated for additive properties. The tablets were evaluated for physical parameters and *in vitro* drug release. The disintegration time and *in vitro* drug release of optimized formulation (FK_5) was compared with that of marketed formulation. The disintegration time was found to be 32 sec as compared to 49 sec for marketed formulation[36].

Sunil H. Makwana et.al, (2010) The demand for mouth dissolving tablets has been growing, during the last decade especially for geriatric and pediatric patients because of swallowing difficulties. The purpose of this research was to mask the intensely bitter taste of ondansetron HCl and to formulate a orodispersible of the taste-masked drug. Taste masking was done by complexing ondansetron HCl with indion204 in different ratios by the solvent evaporation. Drug- resin complex were optimized by considering parameters such as optimization of resin concentration, optimization of swelling time, optimization of stirring time, optimization of pH and optimization of temperature on maximum drug loading. The

effects of variables were observed on maximum amount of the drug loading. During preparation of drug resin complex (resinate), the other variables were kept constant. The resinate was evaluated for taste masking, characterized by X-Ray diffraction and infra red spectrometer. In vitro drug release study of taste masked tablet showed that more than 90 % of the drug release within 20 minutes. Thus, results conclusively demonstrated successful masking of taste and rapid disintegration of the formulated tablets in the oral cavity[37].

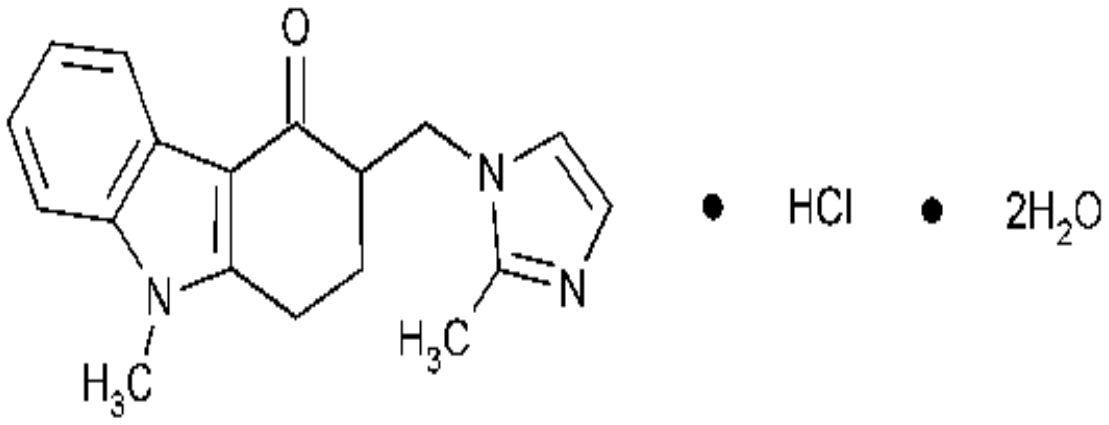
Prajapati R.H. et.al (2010) The purpose of this research was to mask the intensely bitter taste of ondansetron Hcl by complexing with indion204 resin by the solvent evaporation and to formulate a mouth dissolving tablets of the taste-masked drug. Tablets were formulated by direct compression method using different superdisintegrants like Polyplasdone XL-10 & sodium starch glycolate (SSG) in different concentration, diluents like mannitol, microcrystalline cellulose (MCC 112), sweetening agent aspartame, flavoring agents like peppermint and vanilla, lubricant magnesium Stearate & glidant aerosil. All formulations were evaluated for disintegration time, wetting time, percentage friability, Content uniformity and *in vitro* dissolution rate. Formulations with 7% Polyplasdone XL-10 showed the disintegration time 14 seconds and wetting time 25 seconds. In vitro drug release study of taste masked tablet showed complete drug release within 10 minutes & successful masking of taste and rapid disintegration of the formulated tablets in the oral cavity[38].

2.3. DRUG PROFILE[39, 40]

Drug : Ondansetron Hydrochloride

Molecular formula : C18H19N3O

Structure :



Chemical Name : 1, 2, 3, 9-Tetrahydro-9-methyl-3-[(2-methyl-1h-imidazole-1-yl)methyl]-4H-carbazol-4-one hydrochloride

Molecular Weight: 293.326 g/mol

Description : A white or whitish yellow crystal powder

Category : Histamine 5-HT_3 receptor antagonists

Dose : 4mg and 8 mg for oral dose

Solubility : Freely soluble in water

Mode Of Action : Ondansetron is a selective serotonin 5-HT_3 receptor antagonist. The antiemetic activity of the drug is brought about through the inhibition of 5-HT_3 receptors present both centrally (medullary chemoreceptor zone) and peripherally (GI tract). This inhibition of 5-HT_3 receptors in turn inhibits the visceral afferent stimulation of the vomiting center, likely indirectly at the level of the area postrema, as well as through direct inhibition of serotonin activity within the area postrema and the chemoreceptor trigger zone.

Pharmacodynamics: Ondansetron is a potent, chemotherapeutic agents and radiotherapy may cause release of 5HT in the small intestine initiating a vomiting reflex by activating vagal afferents via 5HT3 receptors.

Ondansetron blocks the initiation of this reflex. Activation of vagal afferents may also cause a release of 5HT in the area postrema, located on the floor of the fourth ventricle, and this may also promote emesis through a central mechanism. Thus, the effect of Ondansetron in the management of the nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy is probably due to antagonism of 5HT3 receptors on neurons located both in the peripheral and central nervous system. The mechanisms of action in post-operative nausea and vomiting are not known but there may be common pathways with cytotoxic induced nausea and vomiting. The role of Ondansetron in opiate-induced emesis is not yet established.

Pharmacokinetic data

Bioavailability : High

Protein binding : 70 – 76% (plasma protein binding)

Absorption : Ondansetron is well absorbed after oral administration and Undergoes limited first pass metabolism.

Metabolism : Metabolized in the liver by hydroxylation followed by Glucronide CYP 3A4.

Excretion : Renal and fecal

Half life : Males - 2.1 to 4.5 hr
Females - 1.9 to 6.24 hr

Clearance : 0.38 L/h/kg [Normal adult volunteers (19 – 40 yrs)]
0.32 L/h/kg [Normal adult volunteers (61 – 74 yrs)]
0.26 L/h/kg [Normal adult volunteers (> or = 75 yrs)]

Toxicity : Low blood pressure and fainting, sudden blindness, severe Constipation.

Contraindication : Hypersensitivity to any component of the tablets.

Storage : Do not store above 25ºC. Store in the original package.

Shelf life : 2 years

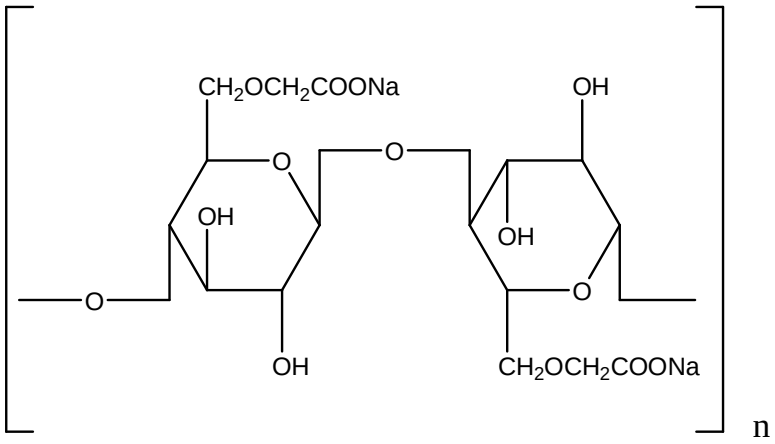
Uses : It is a $5HT_3$ receptor antagonist used mainly as the prevention of nausea and vomiting associated with emetogenic cancer chemotherapy, post operation, and radiation. Also used for the treatment of postoperative nausea and vomiting.

Commercial formulation: Zofran ODT- 4 mg (GlaxoSmithKline)

2.4. POLYMER PROFILE[41]

CROSCARMELLOSE SODIUM

Structure



Empirical formula : Cross linked polymer of carboxy methyl cellulose sodium.

Molecular weight : 90000 – 700000

Chemical name : Cellulose, Carboxy methyl ether, Sodium salt

Functional category : Tablet and capsule superdisintegrant

Description : CCS occurs as an odorless, white or grayish – white powder.

Melting point : Browns at approximately 227ºC and chars at approximately 252ºC.

Solubility : Insoluble in water, although Croscarmellos swells to 4-8 times its original volume on contact with water. Practically insoluble in acetone, ethanol and toluene.

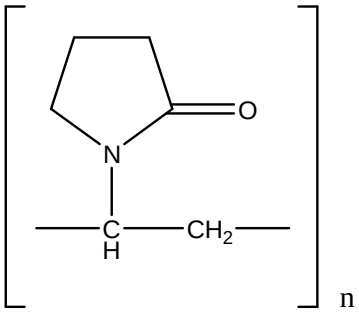
Density : 1.543g/cm^3

Chemical properties : Croscarmellose sodium is a cross linked polymer of carboxy methyl cellulose sodium. It is a stable though hygroscopic material. It is not compatible with strong acids or with soluble salts of iron and some other metals such as aluminium, mercury and zinc.

Uses : It is used in oral pharmaceuticals as disintegrant for capsules tablets and granules. In tablet formulations, croscarmellose sodium may be used in direct compression or wet granulation processes. croscarmellose sodium at concentrations up to 5% w/w 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 wet granulation process.

CROSPOVIDONE[41]

Structure



Molecular formula : $(C_6H_9NO)_n$

Molecular weight : >1000000

Chemical name : 1-Ethenyl-2-pyrollidone homopolymer

Functional category : Tablet superdisintegrant

Description : A white to creamy – white, finely divided, free flowing nearly odourless, hygroscopic powder.

Solubility : Practically insoluble in water, soluble in most organic Solvents.

Melting point : Softens at 150ºC

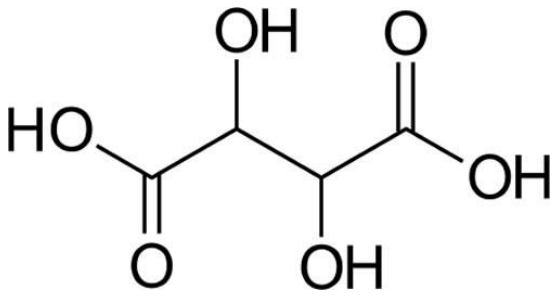
Density : 1.22g/cm^3

Chemical properties : Crospovidone is water – insoluble synthetic cross linked homopolymer of N- vinyl -2- pyrolidine. Crospovidone is compatible with wide range of inorganic salts, natural and synthetic resins, and other chemicals.

Pharmaceutical applications

1. It is water – insoluble tablet disintegrant and dissolution agent used at 2 – 5% concentration in tablets prepared by either direct compression or dry granulation method.
2. It can be used as a solubility enhancer with the technique of co-evaporation.
3. It can be used to enhance the solubility of poorly soluble drugs.
4. The drug is absorbed on to crospovidone in the presence of a suitable solvent and the solvent is then evaporated. This technique results in faster dissolution rate.
5. It rapidly exhibits high capillary activity and pronounced hydration capacity, with little tendency to form gels.

TARTARIC ACID[41]



Molecular weight : 150.1

Chemical name : Tartaric acid is (2R, 3R) - 2, 3 – dihydroxy butanedioic acid.

Molecular formula : It contains not less than 99.5% and not more than 101.0% of $C_4H_6O_6$, calculated on the dried basis.

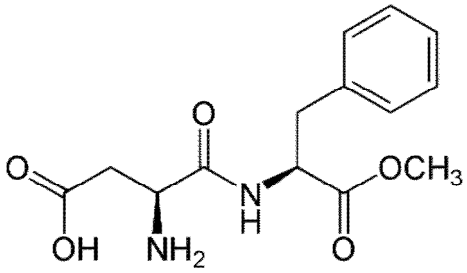
Description : Colourless crystals or White or almost White crystalline powder.

Application

1. Used in beverages, confectionery, food products and pharmaceutical formulations as an acidulant.
2. It is used as a combination with bicarbonates as the acid component of effervescent granules, powders and tablet.
3. It is also used as a sequestering agent and an antioxidant synergist.

ASPARTAME[41]

Structure



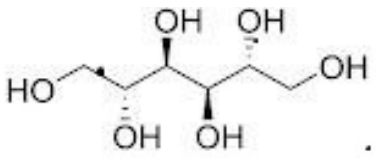
synonyms	: 3-Amino-N-(a carboxyphenethyl) succcinamic acid N-methyl ester, 3-Amino-N-(a- methoxycabonyl phenethyl) succinamic acid.
Chemical name	: N-a-L-Aspartyl-L-phenylalanine 1-methyl ester.
Empirical formula	: $C_{14}H_{18}N_2O_5$
Molecular weight	: 294.31
Description	: Aspartame occurs as an off white almost odourless crystalline powder with an intensely sweet taste.
Solubility	: Slightly soluble in ethanol (95%),sparingly soluble in water.
Functional category	: Sweetening agent

Pharmaceutical applications

1. Aspartame is used as an intense sweetening agent in beverage products, food products, table top sweeteners and in pharmaceutical preparations including tablets, powder mixes and vitamin preparations.
2. It enhances flavor systems and can be used to mask some unpleasant taste characteristics the approximate sweetening power is 180-200 times that of sucrose.
3. Therapeutically, aspartame is used in the treatment of sickle cell anemia.

MANNITOL[41]

Structure



Synonym : Cordycepic acid; E421; 1,2,3,4,5,6,- hexanehol; manita; mauna sugar; mannite; pearlitol.

Chemical name : D – Mannitol

Empirical formula : $C_6H_{14}O_6$

Molecular weight : 187.17

Solubility : Solubility at 20ºC.
Alkali- Soluble
Ethanol (95%) - 1 in 83
Ether - Practically insoluble
Water - 1 in 5.5

Stability : Mannitol is stable in dry state.

Storage : Stored in a well closed container in a cool, dry place.

Functional category : Sweetening agent, tablet and capsule diluent, tonicity agent, Vehicle (bulking agent) for hydrophilized preparations.

Pharmaceutical applications

1. In pharmaceutical preparations it is primarily used as a diluent (10 – 90 % w/w) in tablet formulations where it is of particular value since it is not hygroscopic and may thus be used with moisture sensitive active ingredients.
2. Mannitol may be used in direct compression tablet applications for which the granular and spray dried forms are available.
3. It is used in the manufacture of chewable tablet formulations because of its negative heat of solution, sweetness and mouth feel.
4. Therapeutically, mannitol administrated parenterally is used as an osmotic diuretic, diagnostic agent for kidney functioning, as an adjunct in the treatment of acute renal failure.
5. It is used as a plasticizer in soft gelatin capsules, as a component of sustained release tablet formulations, and as a carrier in dry powder inhalers.

TALC[41]

Synonym : Magsil Osmanthus, Magsil star, purtalc, steatite

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

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

Stability : Talc is stable material.

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

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

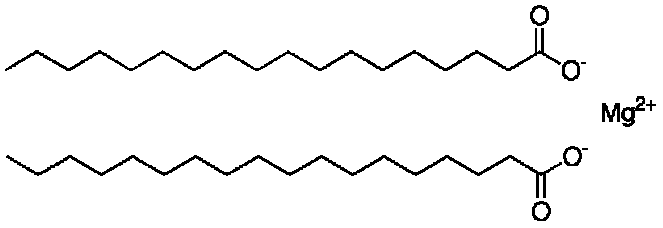
Functional category : Glidant, tablet and capsule lubricant, anti-cracking agent.

Incompatibilities : Incompatible with quaternary ammonium compounds.

Safety : Following oral ingestion talc is not absorbed systemically and may thus be regarded as an essentially non-toxic material. Intranasal or IV abuse of products containing talc.

MAGNESIUM STEARATE[41]

Structure



Synonym : Magnesium octadecanoate, octadecanoic acid, magnesium salt, stearic acid.

Chemical name : Octadecanoic acid magnesium salt

Emperical formula: $C_{36}H_{70}MgO_4$

Molecular formula: 591.34

Description : Magnesium stearate is a very fine, light white, precipitated or Milled, impalpable powder of low bulk density, having a faint odour of stearic acid and a characteristic taste. The powder is Greasy to touch and readily adheres to the skin.

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

Stability and Storage conditions: Magnesium stearate is stable and should be in a well Closed container in a cool, dry place.

Pharmaceutical applications

1. Magnesium stearate is widely used in cosmetics, foods and pharmaceutical formulations.
2. It is primarily used as a lubricant in capsule and tablet manufacture at concentrations between 0.25% and 5% w/w
3. It is also used in barrier creams.

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

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

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

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

Stability : Talc is stable material.

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

Incompatibilities : Incompatible with quaternary ammonium compounds.

Safety : Following oral ingestion talc is not absorbed systemically and may thus be regarded as an essentially non-toxic material. Intranasal or IV abuse of products containing talc.

3. RESEARCH ENVISAGED

3.1. AIM OF PRESENT STUDY

Difficulty in swallowing (dysphagia) is a common problem of all age groups, especially the elderly and pediatrics, because of physiological changes associated with those groups. Other categories that experience problems in using conventional oral dosage forms include the mentally ill, uncooperative and patients suffering from nausea, motion sickness, sudden episodes of allergic attack or coughing. Sometimes it may be difficult to swallow conventional products due to non-availability of water. These problems led to the development of a novel type of solid oral dosage form called orodispersible tablet, which disintegrates/dissolves rapidly in saliva without the need of drinking water.

The benefits in terms of patient compliance, rapid onset of action, increased bioavailability and good stability make these tablets popular as a dosage form of choice in the current market. Some drugs are in such cases bioavailability of drug is significantly greater than those observed from conventional tablet dosage form.

The basic approach used in the development of the ODTs is the use of superdisintegrants. Many approaches have been developed to manufacture ODTs. These include vacuum drying direct compression, lyophilization and molding. The direct compression method is inexpensive and convenient for producing tablets of sufficient mechanical strength.

Antiemetics are the agents which can block nausea and vomiting sensations, which are frequently encountered with chemotherapy, radiation therapy, and post operative inducing nausea and vomiting. Ondansetron hydrochloride is a selective serotonin 5-HT3 receptor antagonist indicated for the prevention of nausea and vomiting and reported to be well absorbed from the gastrointestinal tract.

In the present study, orodispersible tablets of ondansetron hydrochloride, are designed by using natural polymer (Treated agar) and synthetic polymers namely crospovidone and croscarmellose sodium. Effervescent substances like sodium bicarbonate and tartaric acid

accelerated the superdisintegrant action and mask the bitter taste of ondansetron hydrochloride. The designed tablets were evaluated for thickness, hardness, friability, weight variation, *in vitro* dispersion time, wetting time, water absorption ratio, disintegration time, drug content uniformity, *in vitro* dissolution rate (in pH 6.8 phosphate buffer), short term stability and drug excipient interactions (IR spectroscopy).

3.2. PLAN OF WORK

The present work was carried out to prepare and evaluate ondansetron hydrochloride orodispersible tablets using different polymers in various concentrations. This work was carried out as outlined below.

1. Precompression parameters

2. Preparation of orodispersible tablets

3. Physico-chemical evaluation
    a. Thickness
    b. Hardness
    c. Friability
    d. Weight variation
    e. *In vitro* dispersion time
    f. Wetting time
    g. Water absorption ratio
    h. Disintegration time
    i. Drug content uniformity

4. *In vitro* drug release studies

5. Stability studies

4. MATERIALS AND INSTRUMENTS

Table 2: Materials used

S.No	Materials	Resources
1.	Ondansetron hydrochloride	Madras Pharmaceuticals Chem Limited Chennai
2.	Sodium bicarbonate	SDFCL Fine Chem Limited , Mumbai
3.	Tartaric acid	SDFCL Fine Chem Limited , Mumbai
4.	Treated agar	Rea Chem Laboratory Chemical, Chennai
5.	Croscarmellose sodium	Mingatai Chemicals Co.Ltd, Taiwan
6.	Crospovidone	ISF Technologies, Chennai
7.	Aspartame	Nutra sweet company, Mumbai
8.	Orange 1208	Firminch Ltd., Mumbai
9.	DEC (corn starch : mannitol)	Rea Chem Laboratory Chemical, Chennai
10.	Magnesium stearate	Vijlak Pharma Ltd., Hyderabad
11.	Talc	SDFCL Fine Chem Limited , Mumbai

LIST OF INSTRUMENTS USED

Table 3: Instruments used

Sl.No	Instruments	Company name
1.	Electronic Weighing Balance	Shimadzu Corporation , Japan
2.	Sieves	Jayanth Test Sieves, Mumbai
3.	Bulk Density And Tapped Density Apparatus	Electro Lab, Mumbai
4.	FTIR (Fourier Trnsform Infrared Spectrometer)	Jasco Model, Japan
5.	RMG Mixer	Sreenex Machines Pvt. Limited, Hyderabad
6.	Rotary Tablet Compression Machine	Remek , Gujarat
7.	Monsanto Hardness Tester	TAB Machines, Mumbai
8.	Friability Tester	Thermonik Campbell Electronics, Mumbai
9.	Vernier Calliper	Eletro Lab, Mumbai
10.	Disintegration Test Apparatus	Electro Lab, Mumbai
11.	Dissolution Test Apparatus	Electro Lab TDT-08L, Mumbai

12.	Double Beam UV Spectrophotometer	Syntronics-pc based double beam spectrophotometer 2202,Mumbai
13.	Stability Chamber	Thermolab Scientific Equipments Pvt.Ltd.,Mumbai

5. EXPERIMENTAL INVESTIGATION

5.1. PREPARATION OF STANDARD CURVE FOR ONDANSETRON HYDROCHLORIDE

PREPARATION OF PH 6.8 BUFFER (phosphate buffer) [42]

27.218 gm of potassium dihydrogen orthophosphate was dissolved in 1000 ml of distilled water. And to prepare 0.1 N sodium hydroxide solution. Then from this Potassium dihydrogen orthophosphate solution 250 ml was taken and mixed with 112 ml of 0.1 N Sodium hydroxide solution. Finally to make up 1000 ml by using distilled water.

PREPARATION OF STANDARD CURVE FOR ONDANSETRON HYDROCHLORIDE

100 mg of ondensetron hydrochloride was accurately weighed and dissolved in small portion of phosphate buffer pH6.8 in a 100 ml of volumetric flask and the volume was made upto 100 ml with buffer. This is the primary stock solution. From the primary stock solution 10 ml was accurately pippetted out and transferred into a 100 ml volumetric flask. Then the volume was made upto 100 ml with buffer. From the secondary stock solution aliquots equivalent to 2-10 mcg (2ml,4ml,6ml,8ml, and 10 ml) were pippeted out into a series of 10 with buffer. The absorbance of above set solutions were against the phosphate buffer pH 6.8 as blank at 248nm[40]. Then calibration curve was plotted taking concentration on X-axis and absorbance on Y-axis.

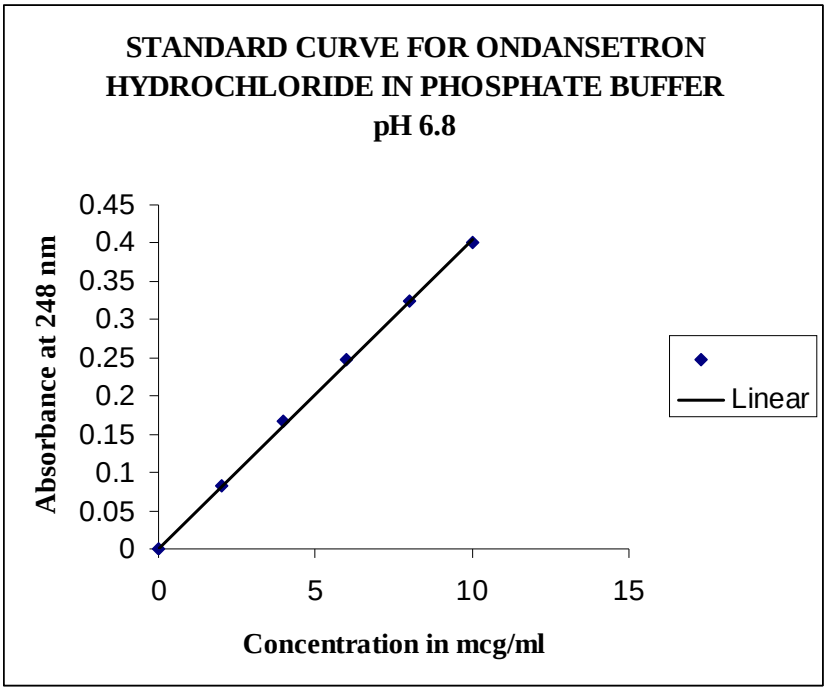
TABLE NO: 4

STANDARD CURVE FOR ONDANSETRON HYDROCHLORIDE IN PHOSPHATE BUFFER PH 6.8

Concentration in (µg/ml)	**Absorbance at 248 nm**
0	0
2	0.083
4	0.167
6	0.248
8	0.324
10	0.401
Slope	0.041
Correlation	0.9994

FIGURE – 4

STANDARD CURVE OF ONDANSETRON HYDROCHLORIDE IN PHOSPHATE BUFFER pH 6.8



5.2. PREFORMULATION STUDIES

Preformulation study relates to pharmaceutical and analytical investigation carried out proceeding and supporting formulation development efforts of the dosage form of the drug substance. Preformulation yields basic knowledge necessary to develop suitable formulation for the toxicological use. It gives information needed to define the nature of the drug substance and provide frame work for the drug combination with pharmaceutical excipients in the dosage form. Hence, the following preformulation studies were performed on the obtained sample of drug.

a) Bulk Density (D_b) [2]

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weighed powder into a measuring cylinder and initial weight was noted. This initial volume was called the bulk volume. From this the bulk density was calculated according to the formula mentioned below. It is expressed in gm/ml and is given by

$$\text{Bulk density } (D_b) = \text{Mass } (M) / \text{Bulk volume } (V_b)$$

Where, M is the mass of powder, V_b is the bulk volume of the powder.

b) Tapped density (D_t) [2]

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 750 times and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is continued for 1250 times and tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2 % (in a bulk density apparatus). It is expressed in gm/ml and is given by

$$\text{Tapped density } (D_t) = \text{Mass } (M) / \text{Tapped volume } (Vt)$$

Where, M is the mass of powder; Vt is the tapped volume of the powder.

C) Angle of repose[2]

The angle of repose of powder was determined by the funnel method. The accurately weighed powder was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of the powder. The powder was allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation.

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

Where, h and r are the height and radius of the powder cone, respectively

Table 5: Flow properties and corresponding angle of repose

ANGLE OF REPOSE	FLOW PROPERTY
25 – 30	Excellent
31 – 35	Good
36 – 40	Fair
41 – 45	Passable
46 – 55	Poor
56 – 65	Very poor
> 66	Extremely poor

d) Carr's Index or % compressibility[2]

It is indirectly related to the relative flow rate, cohesiveness and particle size. It is simple, popular and fast method of predicting powder flow characteristics. It is based on the apparent bulk density and the tapped density, the percentage compressibility of the the bulk drug was determined by the following formula.

$$\% \text{ compressibility index} = \frac{\text{Tapped bulk density} - \text{Initial bulk density}}{\text{Tapped bulk density}} \times 100$$

Table 6: Flowability based on compressibility index

Carr's index	Type of flow
5 – 15	Excellent
12 – 18	Good
18 – 23	Poor
35 – 38	Very poor
> 40	Extremely poor

e) Hausner's ratio[2]

The ratio of the tapped density to bulk density is called as hausner ratio. It is an indirect index of ease of powder flow. It is calculated by the following formula.

Hausner ratio = Tapped density (D_t) / Bulk density (D_b)

Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25)

Table 7: Scale of flowability based on Hausner's ratio

HAUSNER'S RATIO	TYPE OF FLOW
Less than 1.25	Good flow
1.25 – 1.5	Moderate
More than 1.5	Poor flow

TABLE NO – 8: PRECOMPRESSION EVALUATION

FORMULATIONS	PARAMETERS				
	Bulk density (gm/cm^3)	**Tapped density (gm/cm^3)**	**Angle of repose (θ)**	**Carr's index(%)**	**Hausner's ratio**
F1	0.463±0.003	0.543±0.002	34.96±0.051	14.81±0.015	1.18±0.010
F2	0.468±0.005	0.545±0.003	31.31±0.032	14.88±0.085	1.17±0.010
F3	0.471±0.013	0.569±0.006	31.08±0.091	14.30±0.135	1.18±0.010
F4	0.481±0.041	0.561±0.001	31.24±0.250	14.31±0.120	1.15±0.030
F5	0.540±0.010	0.613±0.009	30.25±0.230	11.61±0.162	1.23±0.105
F6	0.552±0.002	0.632±0.010	30.92±0.023	12.51±0.023	1.14±0.001
F7	0.568±0.001	0.663±0.001	29.51±0.022	14.53±0.250	1.12±0.038
F8	0.414±0.005	0.479±0.008	28.83±0.031	14.26±0.300	1.16±0.005
F9	0.395±0.040	0.444±0.005	28.25±0.054	13.17±0.100	1.15±0.015
F10	0.372±0.001	0.310±0.031	28.17±0.061	13.30±0.064	1.15±0.065

5.3. DRUG EXCIPIENT COMPATABILITY STUDY BY FTIR ANALYSIS

Compatibility of the drug with excipients was determined by FT-IR spectral analysis, this study was carried out to detect any changes on chemical constitution of the drug after combined it with the excipients.

Infrared spectra for pure ondansetron hydrochloride, drug with polymers, and best formulation that determined to check the intactness of the drug in the formulation.

The TABLE NO- 9 shows the wave number for the characteristic bands in the infrared spectra of pure ondansetron hydrochloride.

TABLE NO – 9

Characteristic peaks of Ondansetron hydrochloride

Wave number in cm-1	**Characteristic bands**
1622	C=O Stretching
2970,2850	CH Stretching of CH_3
1375	CH Bending vibration of CH_3
3498	NH Stretching

Infrared spectra for the pure drug, for the carriers and for the best formulations are shown in FIGURE – 5

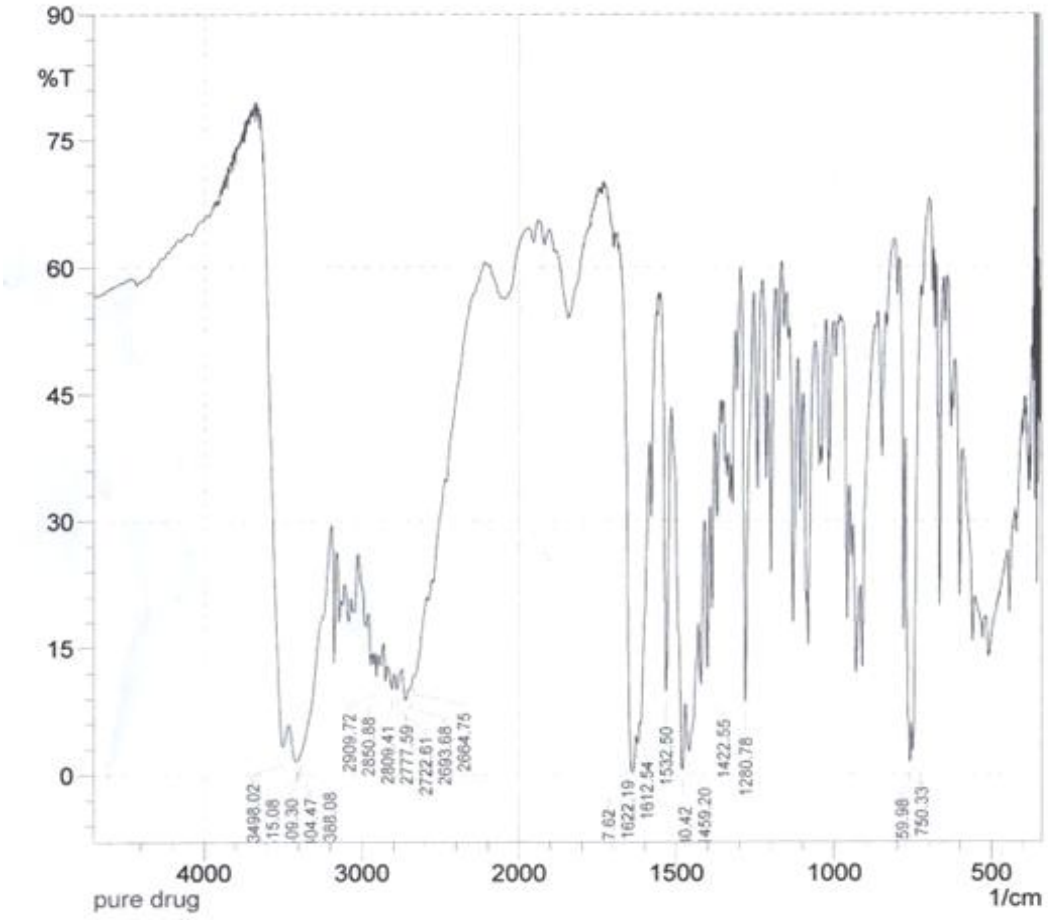


FIGURE-5

IR SPECTRA OF ONDANSETRON HYDROCHLORIDE

COMPATIBILITY STUDY OF DRUG WITH POLYMER

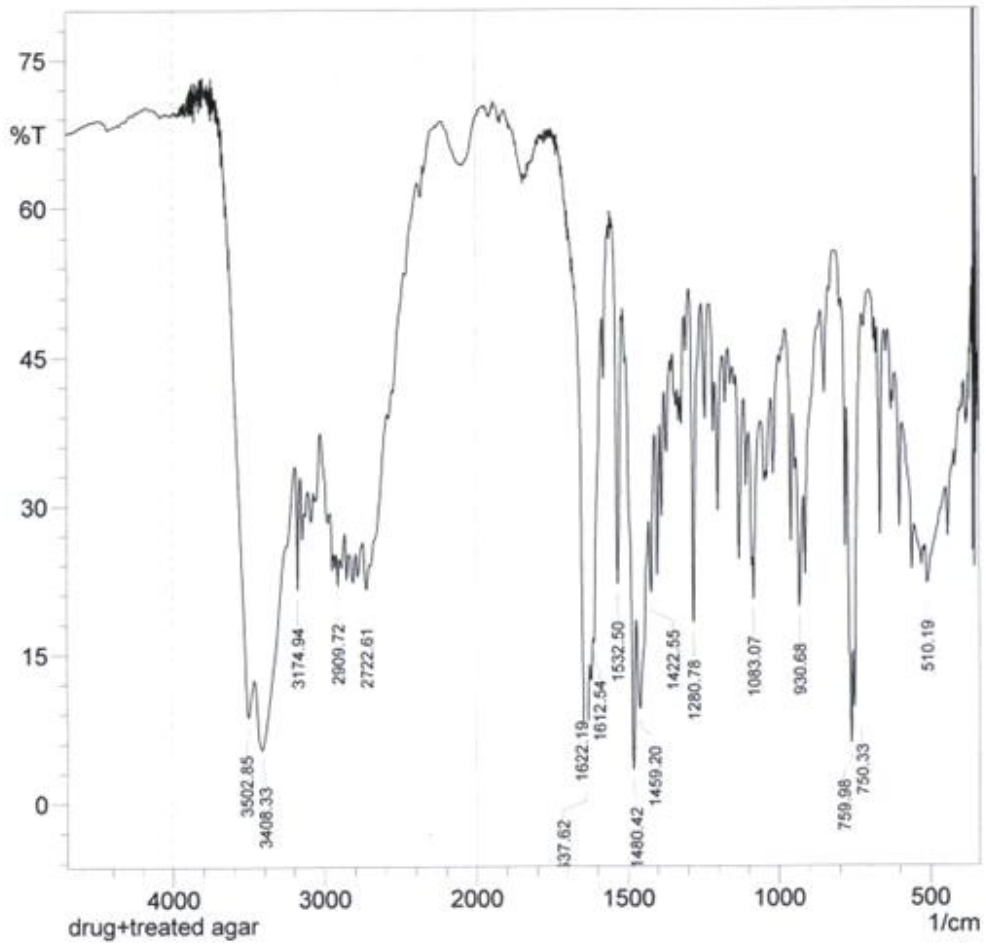


FIGURE-6

IR SPECTRA OF ONDANSETRON HYDROCHLORIDE+TREARED AGAR

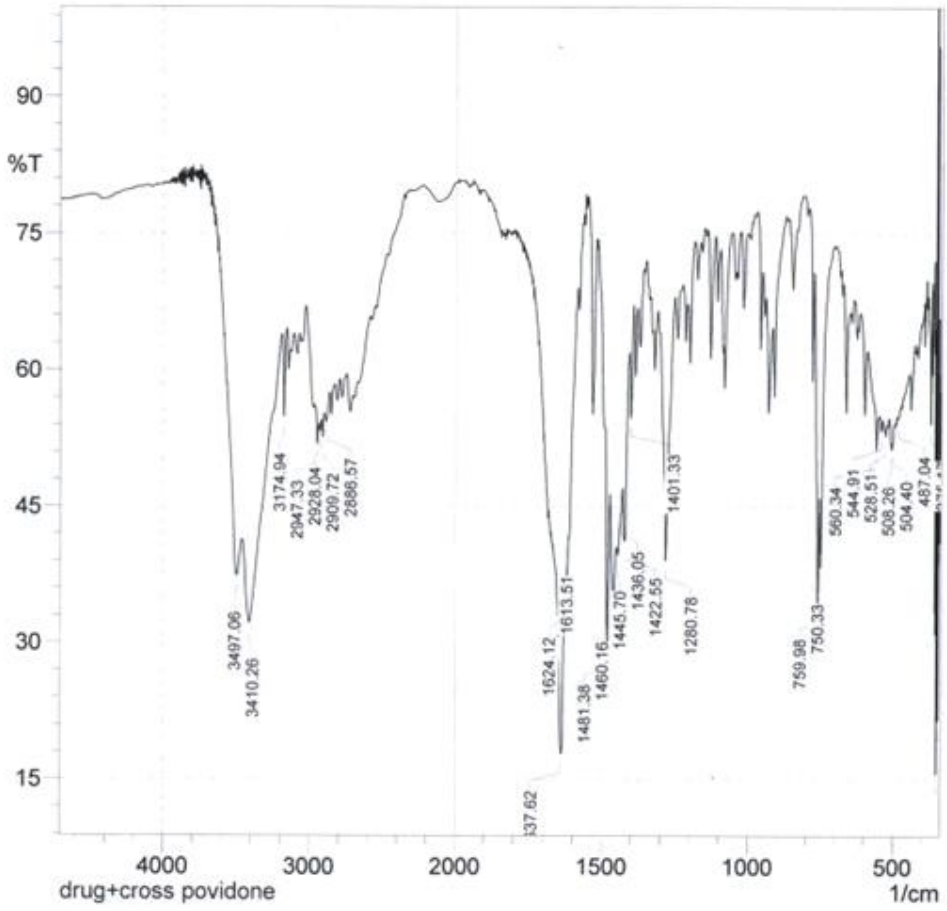


FIGURE-7

IR SPECTRA OF ONDANSETRON HYDROCHLORIDE +CROSPOVIDONE

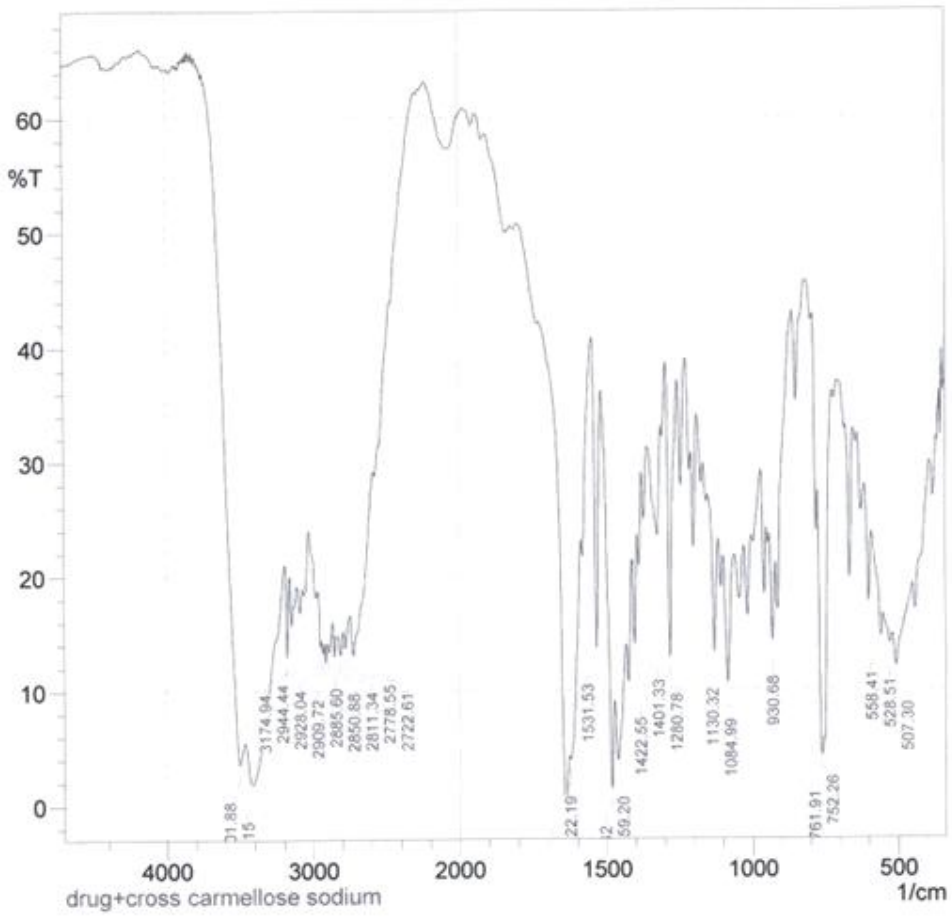


FIGURE-8

IR SPECTRA OF ONDANSETRON HYDROCHLORIDE+CROSCARMELLOSE SODIUM

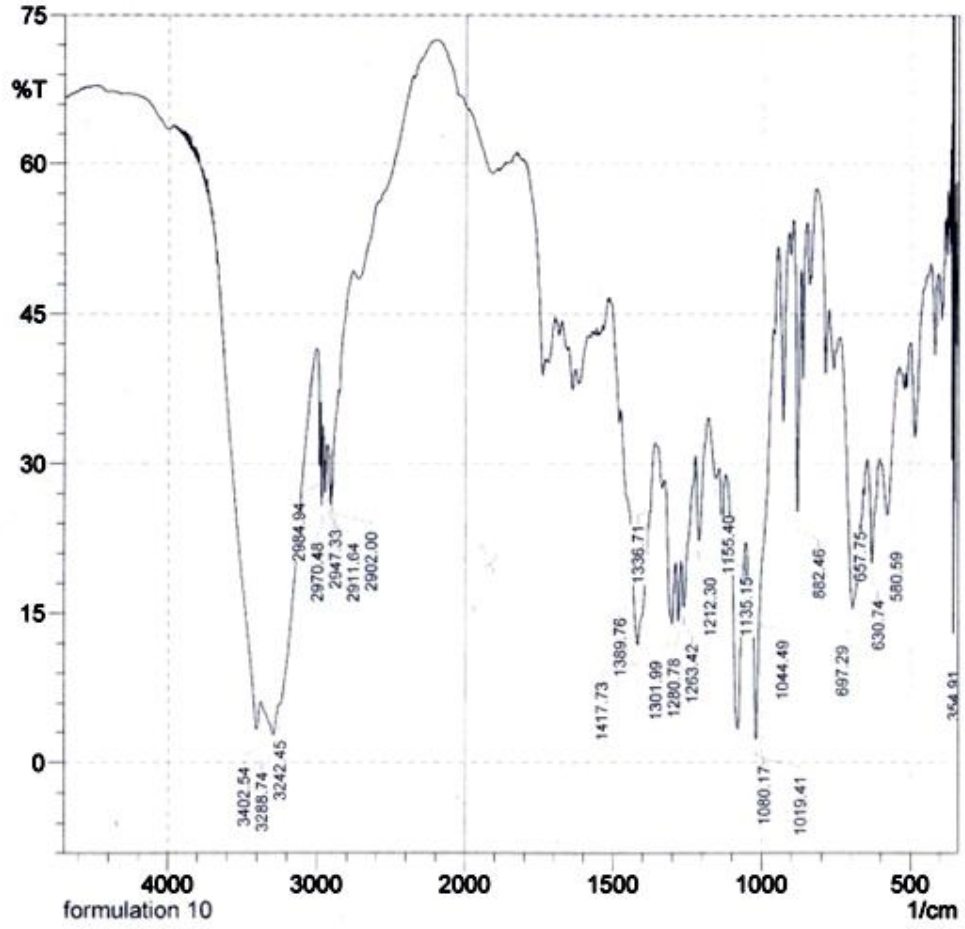


FIGURE-9

IR SPECTRA OF BEST FORMULATION (F10)

5.4. PREPARATION OF ONDANSETRON HYDROCHLORIDE ORODISPERSIBLE TABLETS

Preparation of Directly Compressible Excipient[17]

The directly compressible excipient (DCE) was prepared using a local variety of food grade corn starch along with mannitol in 1:1 ratio using 10% w/w starch paste for granulation.

Method

All the ingredients were powdered separately in a dry, clean porcelain mortar and passed through # 60 mesh sieve and mixed well in geometrical ratio. Granulating fluid, starch paste (10% w/w) is added to the powder mixture in small quantities, while mixing thoroughly after each addition until a coherent mass was formed. Then it was passed through # 44 mesh sieve and the wet granules were spread on a paper and dried in hot air oven at 55-60ºC. The dried granules were then passed through # 36 mesh sieve.

Preparation of treated agar[17]

Treated agar (TAG) powders were prepared by taking 10 gm agar powder in distilled water (100 ml) and stirring at 50 rpm with a three- bladed mechanical stirrer for one day. This causes water absorption and swelling. Then the liquid was poured in a large petri-dish and allowed for drying up to three days in incubator at 37±1ºC and then the mass was pulverized and sifted through # 80 mesh sieve .

PREPARATION OF ORODISPERSIBLE TABLET [17]

Orodispersible tablets of Ondansetron hydrochloride were prepared by effervescent method according to the formula. All the ingredients were passed through # 60 mesh sieves separately. The drug and directly compressible excipient were mixed by adding small portion of each at a time and blending it to get a uniform mixture and kept aside. Sodium bicarbonate and tartaric acid were pre-heated at a temperature of 80ºC for 2 h to remove absorbed/residual moisture and thoroughly mixed in a mortar to get a uniform powder and then added to the above blend. Then the other ingredients were mixed in geometrical order but magnesium stearate and purified talc were added at the last and mixed for further two minutes. The blend was compressed using 9 mm flat round punches to get tablets of 200 mg weight on 10-station rotary tablet machine. A batch of 60 tablets was prepared for all the designed formulations.

TABLE NO: 10

FORMULATION DESIGN FOR ONDANSETRON HYDROCHLORIDE TABLETS

Ingredients (mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**
Drug	4	4	4	4	4	4	4	4	4	4
NaHCO3	18	18	18	18	18	18	18	18	18	18
Tartaric acid	18	18	18	18	18	18	18	18	18	18
Treated agar	_	10	15	20	_	_	_	_	_	_
Crospovidone	_	_	_	_	10	15	20	_	_	_
Croscarmellose sodium	_	_	_	_	_	_	_	10	15	20
Aspartame	8	8	8	8	8	8	8	8	8	8
Orange 12809	3	3	3	3	3	3	3	3	3	3
Magnesium stearate	2	2	2	2	2	2	2	2	2	2
Talc	1	1	1	1	1	1	1	1	1	1
DCE	146	136	131	126	136	131	126	136	131	126
Total weight	200	200	200	200	200	200	200	200	200	200

5.5. PHYSICO CHEMICAL EVALUATION

A. Weight variation [26]

Twenty tablets were taken and their weights were determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. Average weight was compared with the individual weight and the percentage deviation of individual tablet was calculated.

Table 11 : Weight variation limit as per IP

Average weight of Tablet	Percentage Deviation
80 mg or less	± 10%
More than 80 mg but less than 250 mg	± 7.5%
250 mg or more	± 5%

B. Thickness [4]

The thickness of the tablets was determined by using vernier caliper of Electro lab model. Five tablets are randomly selected from each batch. It is expressed from mm and the average values were calculated.

C. Hardness [4]

Hardness was determined by taking five tablets from each formulation and was measured by using Monsanto hardness tester. The hardness was measured in terms of kg/cm^3.

D. Friability [43]

The friability of the tablet was measured using an Roche friabillator (Electro lab, India).Twenty reweighed tablets were rotated at 25 rpm for 4 rpm and dropping the tablets at a height of 6 inches at each revolution and the tablets were subjected to 100 revolutions. The tablets were then dedusted using soft muslin cloth and reweighed and the percentage of weight loss was calculated. The percentage friability of the tablets were measured as per the following formula.

$$\text{Percentage friability} = (\text{Initial weight} - \text{final weight}/\ \text{Initial weight}) \times 100$$

TABLE NO: 12

PHYSICOCHEMICAL EVALUATION OF ONDANSETRON HYDROCHOLORIDE

Formulation code	Weight variation (mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)
F1	200.4±0.84	2.35±0.03	2.20±0.10	0.831±0.01
F2	200.2±1.35	2.34±0.01	2.13±0.20	0.781±0.03
F3	200.1±0.06	2.34±0.03	2.13±0.21	0.836±0.07
F4	200.3±0.94	2.32±0.01	2.30±0.17	0.747±0.08
F5	200.1±0.05	2.31±0.01	2.33±0.11	0.814±0.04
F6	200.3±0.94	2.34±0.01	2.40±0.26	0.832±0.01
F7	200.2±0.05	2.32±0.00	2.02±0.15	0.780±0.10
F8	199.9±1.10	2.33±0.01	2.16±0.11	0.907±0.08
F9	200.2±1.30	2.34±0.00	2.20±0.10	0.941±0.04
F10	199.8±1.34	2.32±0.01	2.26±0.05	0.922±0.01

E. *In vitro* dispersion time [33]

In vitro dispersion time was measured by dropping a tablet in a measuring cylinder containing 10ml of simulated saliva fluid of pH 6.8. After dropping a tablet in the simulated saliva fluid, the tablet started to swell quickly, broke and followed by dispersed. Five tablets from each formulation were randomly selected and *in vitro* dispersion time was performed and it was expressed in seconds.

F. Wetting time[25]

Wetting time is closely related to the inner structure of the tablets and to the hydrophilicity of the excipient. A linear relationship exists between wetting time and disintegration time. Thus wetting is the important step for disintegration process to take place.

A piece of tissue paper folded double was placed in a petri plate (internal diameter is 6.5cm) containing 6ml of purified water. A tablet having a small amount of Eosine dye powder on the upper surface was placed on the tissue paper. The time required to develop a red color on the upper surface of the tablet was recorded as the wetting time.

G. Disintegration time[31]

Disintegration time was measured using disintegration test apparatus. A tablet was placed in each six tube of the basket. The basket with the bottom surface is made up of stainless – steel screen (mesh no. 10) was immersed in water maintained at 37°C as the disintegration fluid and the paddle at 100rpm as stirring element was used. The time taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds.

H. Water absorption ratio [25]

A piece of double folded tissue paper was kept in a petri dish (internal diameter 5.5 cm) containing 6 ml of purified water. The weight of tablet before keeping in petri-dish was noted as (W_b) and after completely wetted tablet in petriplate was noted as (Wa). The wetted tablet was removed and reweighed. Water absorption ratio, R was determined according to the following equation.

$$R = 100 (W_a – W_b) / W_b$$

Where, W_b and W_a are before and after water absorption, respectively.

I. Drug content [19]

Ten tablets from each batch were weighed and powdered. The required amount of the powder equivalent to 4 mg of ondansetron hydrochloride was dissolved in 100 ml of phosphate buffer pH6.8. From this solution 1 ml was taken and made up to 100 ml by using phosphate buffer pH6.8 and the solution was filtered by using whatmann filter paper. The solution was analysed for drug content at 248nm using UV visible spectrophotometer.

TABLE NO: 13 PHYSICOCHEMICAL EVALUATION OF ONDANSETRON HYDROCHOLORIDE

Formulation code	*In vitro* Dispersion time(sec)	Wetting time(sec)	Disintegration time(sec)	Water absorption ratio	Assay (%)
F1	60.37±0.40	41.03±0.05	50.73±0.64	39.30±0.81	90.44±0.50
F2	49.16±0.15	35.83±0.73	42.26±0.35	33.06±0.51	96.54±0.48
F3	43.36±0.40	32.66±0.57	40.56±0.45	43.66±0.41	97.37±0.57
F4	40.52±0.44	30.23±0.32	36.13±0.20	33.56±0.58	100.85±0.16
F5	38.56±0.77	33.23±0.25	34.40±0.60	33.70±0.34	99.52±0.17
F6	35.26±0.28	31.63±0.30	32.18±0.23	27.96±0.95	100.48±0.22
F7	32.41±0.17	28.46±0.30	29.63±0.40	32.76±0.68	101.29±0.34
F8	30.37±0.22	30.40±0.36	25.26±0.17	31.36±0.32	102.55±0.48
F9	28.44±0.50	28.30±0.40	22.15±0.17	30.50±0.50	100.15±0.27
F10	26.45±0.41	26.26±0.30	20.27±0.40	29.50±0.30	99.96±0.06

5.6 IN VITRO DRUG RELEASE STUDY [17]

In vitro dissolution of the orodispersible tablets was studied in USP XXIII type-II dissolution test apparatus (Electro lab, model: TDT-06N) employing a paddle stirrer at 50 rpm using 900 ml of pH 6.8 phosphate buffer at 37±0.5^{o} C as dissolution medium. One tablet was used in each test. Aliquots of dissolution medium were withdrawn at specified intervals of time and analyzed for drug content by measuring the absorbance at 248 nm. The volume withdrawn at each time interval was replaced with fresh quantity of dissolution medium. Cumulative percent of the drug released was calculated and plotted against time. The results obtained are given in TABLE NO: 14.

Dissolution Condition:

Apparatus	: USP XX111 paddle apparatus 2.
RPM	: 50
Medium	: phosphate buffer (pH 6.8)
Sampling Interval	: Every 5 minute.
Sampling Volume	: 5 ml.
Study Period	: 30 min

TABLE NO: 14

***IN VITRO* DRUG RELEASE DATA (F1-F10)**

Formulation code	% Cumulative release					
	5 min	10 min	15 min	20 min	25 min	30 min
F1	56.15	62.08	62.95	64.37	65.80	66.69
F2	66.14	80.60	82.66	84.19	85.18	85.63
F3	66.98	82.94	83.92	85.46	86.45	87.45
F4	72.19	84.63	86.71	88.80	89.27	90.28
F5	67.80	81.78	84.94	87.57	88.03	90.67
F6	77.15	80.07	89.63	92.28	93.85	94.89
F7	74.47	90.26	92.26	94.50	95.00	96.59
F8	74.98	84.21	87.93	84.48	91.04	92.61
F9	76.65	89.74	91.31	92.88	94.46	95.50
F10	77.78	91.45	95.20	96.79	98.39	99.49

FIGURE 10

***IN VITRO* DRUG RELEASE FOR F1,F2,F3 AND F4**

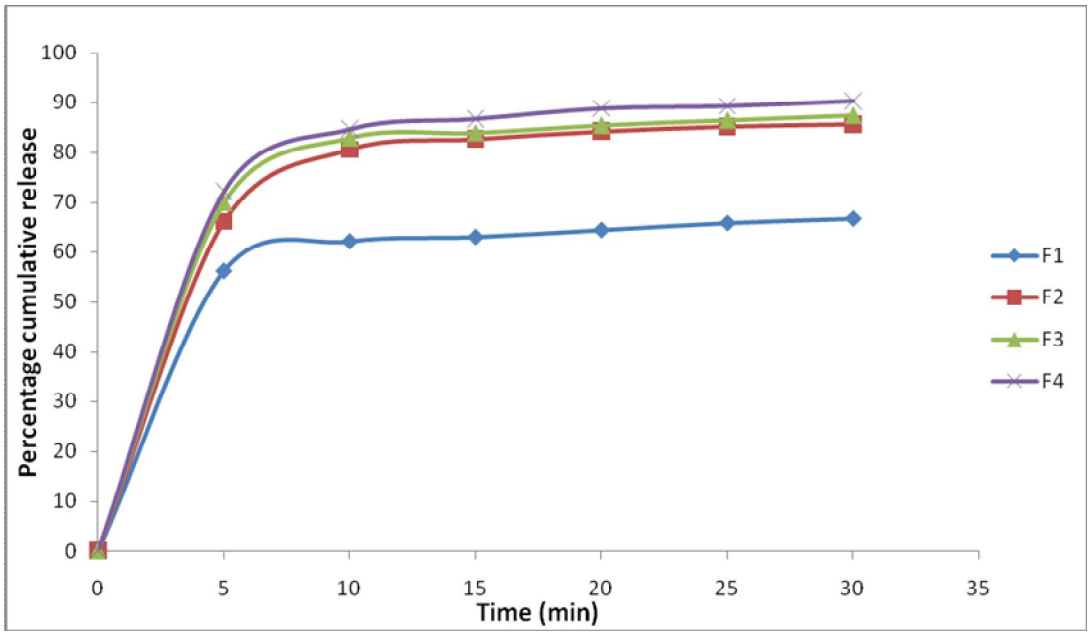


FIGURE 11: *IN VITRO* DRUG RELEASE FOR F5,F6 AND F7

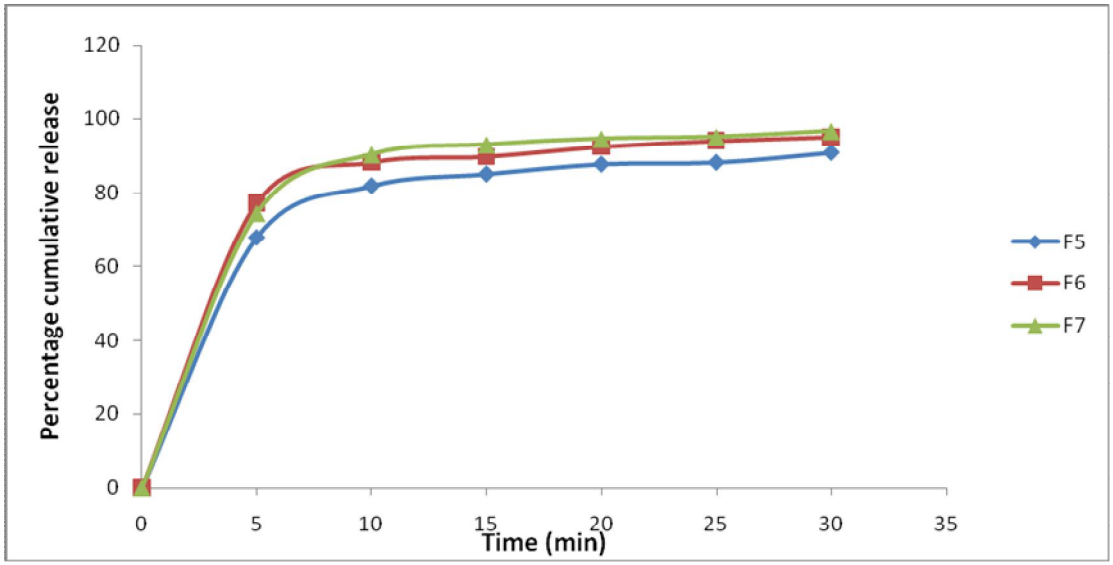
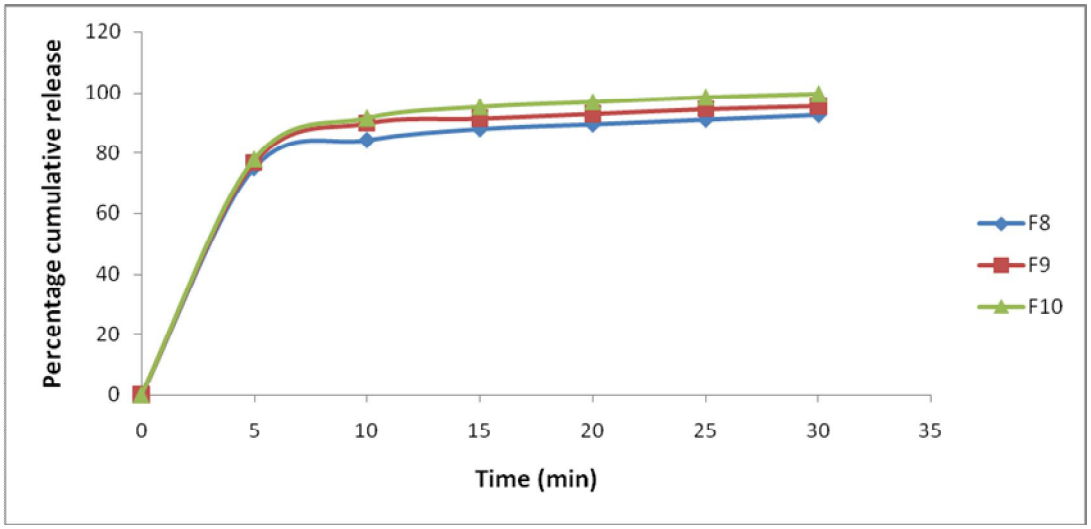


FIGURE 12: *IN VITRO* DRUG RELEASE FOR F8,F9 AND F10



5.7. Accelerated stability studies .[23]

The goal of a stability program is not uniquely defined, but depends on the stage of development of the product in question. At the very onset of development, it is desired to know what the inherent stability of the drug substance is and what interactions with the excipients can be expected. On the analytical side, it is usually supported by an assay procedure, which helps in developing the stability program.

The stability program varies from one dosage form to another and formulation to formulation. Accelerated stability studies are of great interest and are attractive as which can document satisfactory results under stressed conditions time saving can be achieved.
The stability of this optimized formulation was known by performing stability studies for three months at accelerated conditions of 40°C±75 % RH on optimized formulation.

The formulation was found to be stable, with insignificant change in the hardness, disintegration time, and *in vitro* drug release pattern. The results are presented in TABLE NO: 15.

TABLE NO: 15

STABILITY DATA FOR FORMULATION F10

Parameters	Time in months			
	0 (Initial)	**1st month**	**2nd month**	**3rd month**
Hardness (kg/cm^2)	2.93±0.02	2.92±0.01	2.89±0.01	2.86±0.01
Disintegration time (sec)	23.63±1.46	23.45±1.01	23.38±0.05	24.30±0.17
Drug content (%)	100.10±0.13	99.92±0.05	99.88±0.08	99.58±0.36
In vitro drug release (%)	99.41±0.17	99.69±0.16	99.44±0.11	99.89±0.08

6. RESULTS AND DISCUSSION

WEIGHT VARIATION

The weight variation in all the ten formulation was found to be 199.8±1.34 to 200.4±0.84 mg. Formulations were with in pharmacopoeial limits with free flow of the powder blend and demonstrating the efficiency of compression of particles into tablets.

HARDNESS

The Hardness was maintained to be within 2.02±0.15 to 2.40±0.26 kg/cm^2 as these tablets are rapidly disintegrating. No variation in the hardness was found which clearly indicates that the proper blending of the mixture for the preparation of orodispersible tablets. The prepared tablets in all the formulation possess good mechanical strength with sufficient hardness.

THICKNESS

Thickness of all tablets prepared in the range of 2.31±0.01 to 2.35±0.03 mm was acceptable without much variation.

PERCENTAGE FRIABILITY

Percentage Friability is below 1% in all the formulation and values obtained lies between 0.747±0.08 to 0.941±0.04%. It indicated that of good mechanical resistance of the tablets.

WETTING TIME

The Wetting time was rapid in croscarmellose sodium followed by crospovidone, treated agar. The value lies between 26.26±0.30 to 41.03±0.05 sec. Fig. 13 depicts the relation between the concentration of superdisintegrants and wetting time. It indicated that as concentration of disintegrant increases the time taken for wetting was reduced. Wetting time is used a parameter to correlate with disintegration time in oral cavity. This is an important criterion for understanding the capacity of disintegrants to swell in the presence of little amount of water.

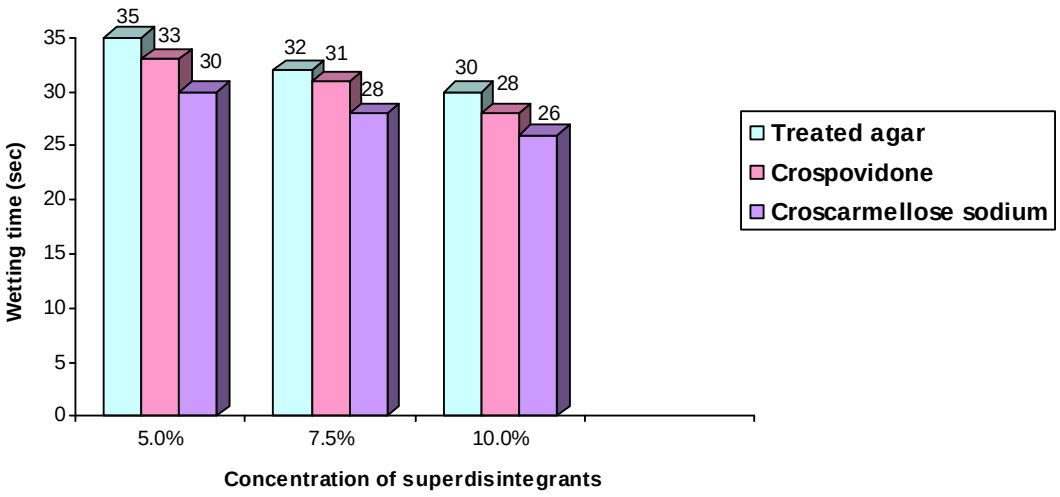


FIGURE 13: WETTING TIME OF DIFFERENT SUPERDISINTEGRANTS WITH DIFFERENT CONCENTRATION

DISPERSION TIME

Further the tablets were subjected *in vitro* dispersion in which the time taken by the tablet to produce complete dispersion is measured. The values for all the ten formulations lie between 26.45±0.41 to 60.37±0.40 sec. The in *vitro* dispersion time was rapid in croscarmellose sodium followed by crospovidone and treated agar. The comparative results are shown in the following figure 14.

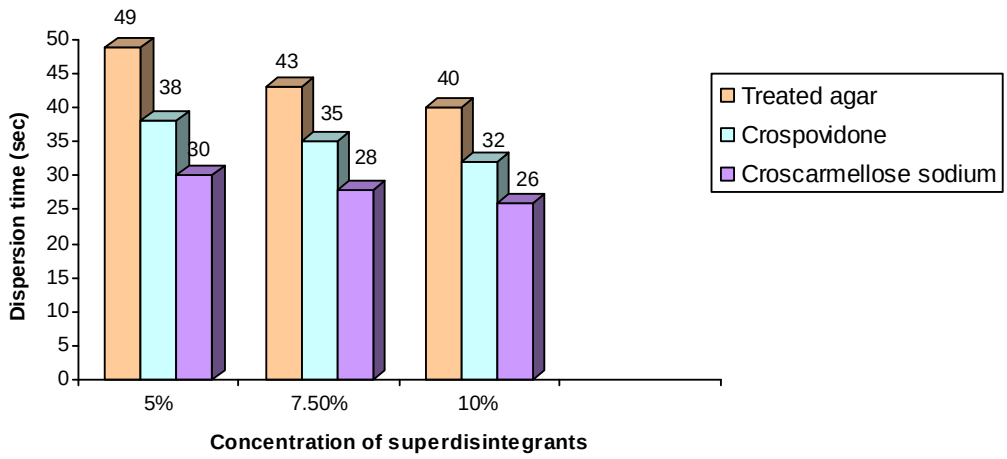


FIGURE 14: DISPERSION TIME OF DIFFERENT SUPERDISINTEGRANTS WITH DIFFERENT CONCENTRATION

DISINTEGRATION TIME

The disintegration time for all the formulations lie between 20.276±0.402 to 50.73±0.646 sec. Fig.15 depicts the disintegration behavior of the tablets in water. This rapid disintegration of the oral dispersible tablets were due to penetration of saliva into the pores of the tablets, which leads to the swelling of super disintegrants to create enough hydrodynamic pressure for quick and complete disintegration of the tablet. Batch F10 was selected as best formulation containing croscarmellose sodium as superdisintegrant in 10% concentration. It was observed that less disintegration time of 20 sec was observed when croscarmellose sodium was used as superdisintegrant, may be due to swelling at faster rate upon contact with water and elimination of lump formation after disintegration when compared with crospovidone and treated agar.

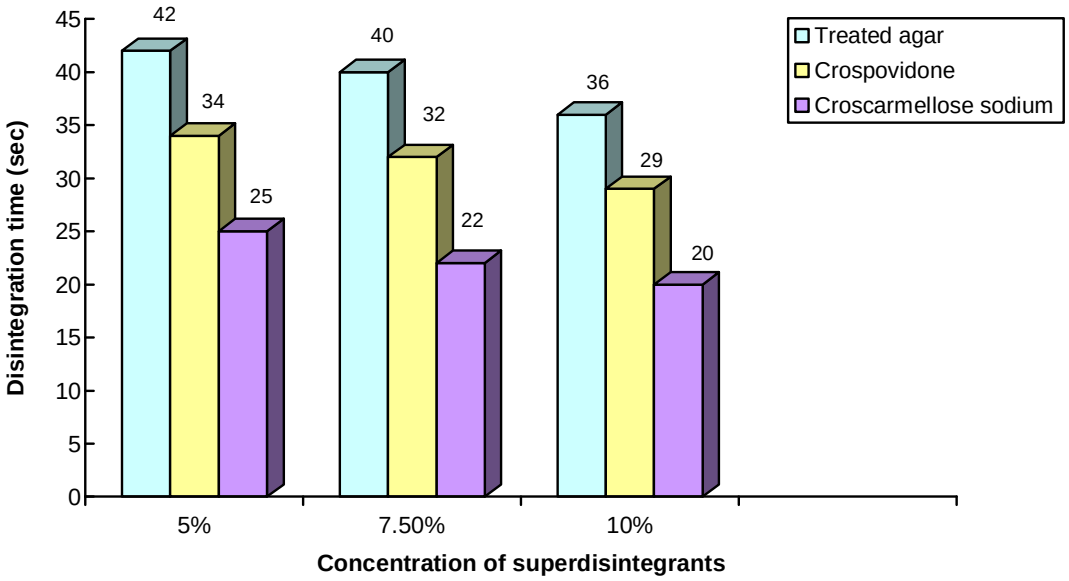
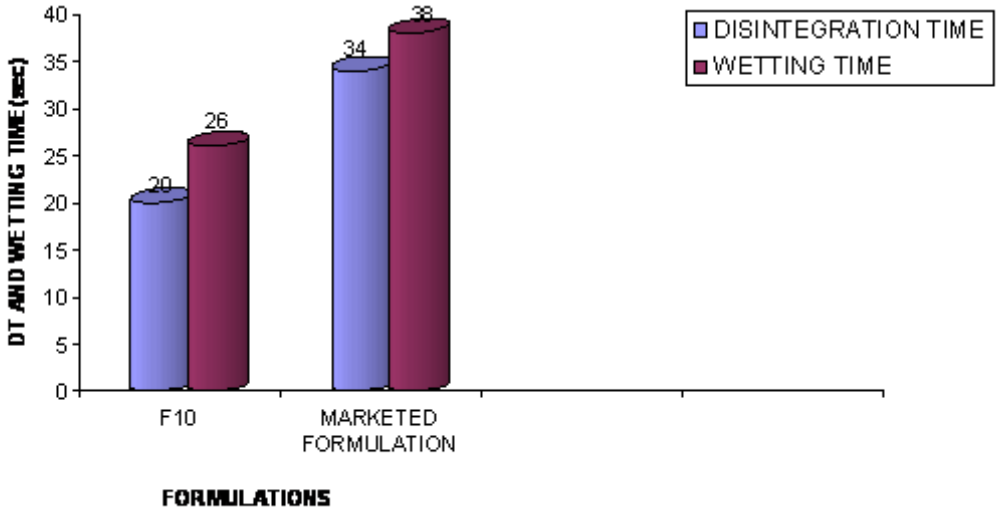


FIGURE 15: DISINTEGRATION TIME OF DIFFERENT SUPERDISINTEGRANTS WITH DIFFERENT CONCENTRATION

FIGURE 16: COMPARISON OF DISINTEGRATION TIME AND WETTING TIME OF BEST FORMULATED TABLET WITH MARKETED TABLET.



Finally the disintegration time of best formulation was compared with marketed formulation the results showed that formulated tablet disintegrated in 20 sec as compared to 34 sec for marketed Ondansetron tablet (ZOFER ODT). The formulation F10 was found to be the best, as this formulation showed less disintegration time and possessing good tableting properties.

The rapid drug dissolution might be due to easy breakdown of particles and rapid absorption of drug into the dissolution medium. This signifies that disintegrant concentration in 10% is suitable for the formulation of orodispersible tablets of ondansetron hydrochlorie.

The various dissolution parameter values viz., percent drug dissolved in 4 min (D_4), $t_{50\%}$ and $t_{70\%}$ for promising formulations of 10% concentration of all the three different polymers (i.e) F4, F7,F10 were compared with the control shown in Table-16 and the dissolution profile depicted in fig 17. This data reveals that the F10 formulation shows faster drug release compared to the commercial formulation (CF) based on $t_{50\%}$ and $t_{70\%}$ values in pH 6.8 Phosphate buffer. The best formulation F10 compared with marketed formulation.

TABLE 16: *IN VITRO* DISSOLUTION PARAMETERS IN pH 6.8 PHOSPHATE BUFFER

Formulation code	$t_{50\%}$ (min)	$t_{70\%}$(min)	D_4(%)
F1	7.49	10.49	55.30%
F4	5.53	7.75	68.54%
F7	5.17	7.23	75.705
F10	5.02	7.03	74.16%
CF	5.72	8.01	65.77%

The Control formulation of (F1),10% concentration of superdisintegrants for (F4,F7,F10) and commercial formulation of *in vitro* cumulative drug release was shown in the fig 17.

The best and marketed formulation is depicted as shown in fig 18.

FIGURE:17 PERCENTAGE CUMULATIVE DRUG RELEASE FOR F1,F4,F7,F10 AND COMMERCIAL FORMULATION

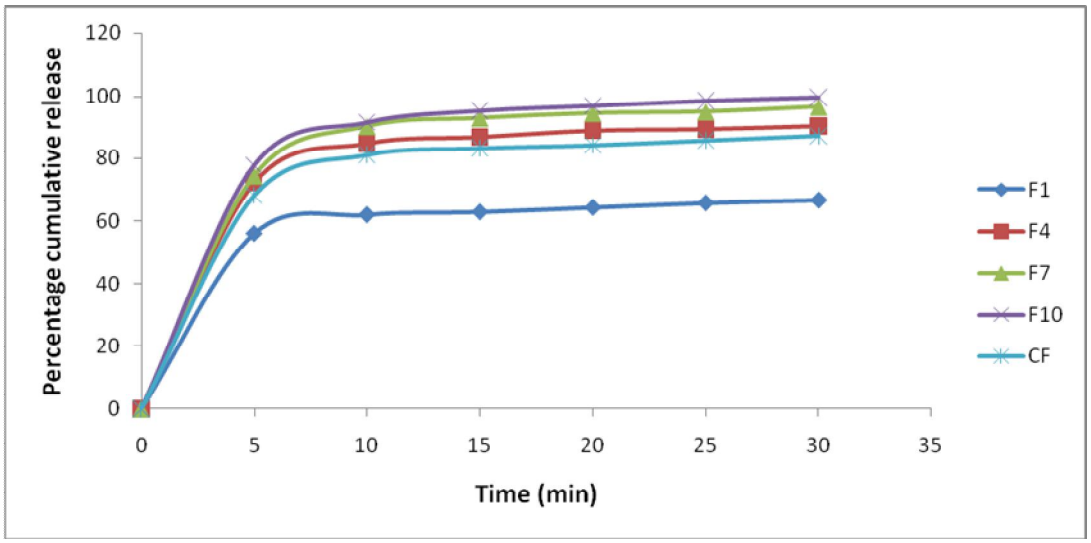
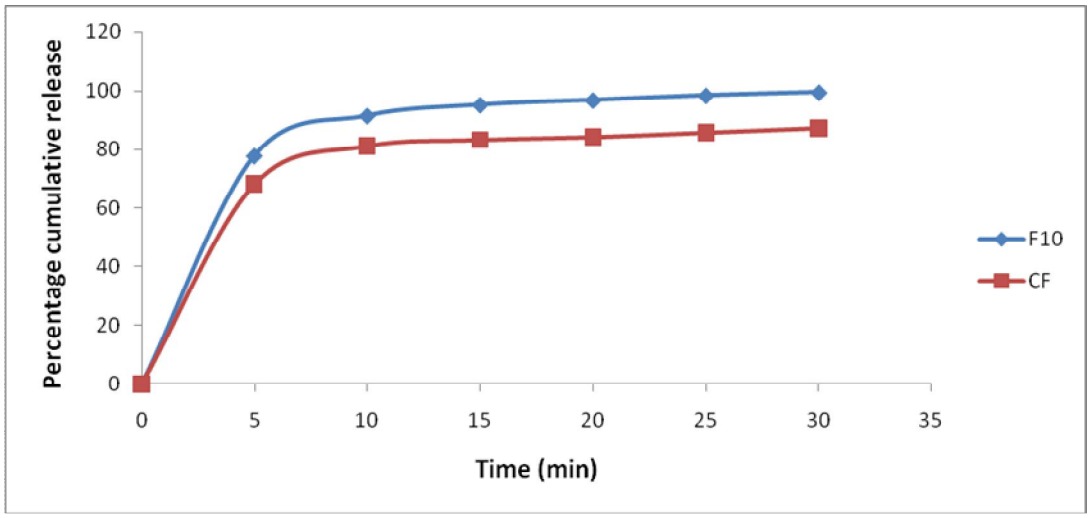


FIGURE 18: PERCENTAGE CUMULATIVE DRUG RELEASE FOR F10 AND MARKETED FORMULATION



7. CONCLUSION

Orodispersible tablets of ondansetron hydrochloride is prepared by Direct compression method. The formulation F10 containing 10% of superdisintegrant (i.e) Croscarmellose sodium has shown best release with 99.46% at the end of 30 min. The effervescent mixture further assists in taste masking of Ondansetron hydrochloride.

According to IR studies there is no incompatibility shown in F10. The formulation F10 was stable at 40°C±2ºC and 75%RH±5%RH.

In conclusion formulation F10 achieved the targets of the present study such as,

i) Not require water to swallow, but it should dissolve or disintegrate in the mouth in matter of seconds.
ii) To mask the bitter taste.
iii) Have a pleasant mouth feel.
iv) Rapid dissolution of drug and absorption which may produce rapid, onset of action.
v) Improved bioavailability.

BIBILIOGRAPHY

1. http:// www.nuaire.com
2. Debjit Bhowmik, Chiranjib.B, Krishnakanth, Pankaj, Margret Chandra.R. Fast dissolving tablets. Journal of Chemical & Pharmaceuticeutical Research, 2009; 1(1): 163-177.
3. Dali shukla, Subhashis Chakraborty, Sanjay Singh, Brahmeshwarn Mishra.Mouth dissolving tablets I: an overview of formulation technology.2009, 77:309- 326.
4. Tapan kumar, Dulal Krishna,, Rana.Formulation aspects in the development of Orodispersible tablets: an overview. International journal of pharmacy and Pharmaceutical sciences, 2010: May 07:2(3).
5. Tejvir, Bhavandeep , Sandeep ,Gupta GD. Mouth dissolving tablets; A novel approach to drug delivery. International journal of current pharmaceutical research.2011:July 17:3(1).
6. Deshpandi KB.Orodispersible tablets: An overview of formulation and technology.International journal of pharma and biosciences.2012 March;2(1)
7. Paramita dey, Sabyasadi maiti. Orodispersible tablets: A new trend in drug Delivery. Journal of natural science. Biology and medicine.2010: July: 1(1).www.jnsbm.org.
8. Siraj sheikh, Khirsagar RV, Aamer quazi. Fast disintegrating tablets an overview of formulation and technology. International journal of pharmacy and pharmaceutical sciences**.** International journal of pharmacy and pharmaceutical sciences.2010,2(3).
9. Mukesh P, Mohanta GP, Lokesh Upadhyay. Review on : Fast dissolving tablet.Journal of pharmacy research. 2009; Jan 2(1).
10. Prakash Goudanavar, Doddayya Hiremath, Spandana D, Reddy SR. Development and evaluation of fast disintegrating tablets of Granisetron Hydrochloride with natural and synthetic polymers. Asian J. Pharm. Res. 2011; Sep,1(3):72-77.
11. Metker Vishal, Kumar Anuj, Pathak Naveen, Padhee Kumud, Sahoo Sangram**.** Formulation and evaluation of orodispersible tablet of Loranoxicam. International Journal of drug development and research.2011, March; 3(1).
12. Sivakranth M, Athaf S, Rajasekhar S.Formulation and evaluation of oral fast dissolving tablets of Sildenafil citrate. International Journal of Pharmacy and Pharmaceutical Sciences.2011, Feb; 3.

13. Patil C, Das S. Effect of various superdisintegrants on the drug release profile and disintegration time of Lamotrigine orally disintegrating tablets. African Journal of Pharmacy and Pharmacology.2011, January; 5(1):76-82.
14. Prakash goudanavar, Shivam H, Doddayya hire math. Development and characterization of lamotrigine orodispersible tablets. International journal of pharmacy and pharmaceutical sciences.2011; 3(3).
15. Lakshmi CSR, Sagar Pravin Akul, Anup Vijay Totala, Jitesh Jagdish Chaudhary,Nitesh Jagdishbhai Patel, Vedhavati SV. Development and characterization of melt- in mouth tablets of Atenolol by sublimation technique. International journal Of Pharmaceutical research and development.2011; May, 3(3); 27-36.
16. Sharma Shailesh , Singh Gurjeet , Gupta GD. Formulation design of mouth dissolving tablets of Domperidone using sublimation technique.An international journal of pharmaceutical sciences.2010;1(1).
17. Swamy PV, Gada SN, Shirsand SB, Kinagi B, Shilpa H. Design and evaluation of cost effective orodispersible tablets of Diethylcarbamazine citrate by effervescent method. International journal of pharma sciences and research. 2010,1(6):258-264.
18. Mohanchandran PS, Krishna PR, Saju, Bini KB, Beenu. Formulation and Evaluation of mouth dispersible tablets of Amlodipine besilate. International Journal of applied pharmaceutics.2010, March 20,2(3).
19. Prameela rani A, Archana.N, Siva teja P, Mohan vikast P,Sudheer kumar M, Bala sekaran C. Formulation and evaluation of orodispersible Metformin tablets: A comparative study of Ispaghula husk and Crospovidone as superdisintegrants. International journal of applied pharmaceutics.2010; 2(3).
20. Kalpesh K, Hetul H,Nitin D,Chintan N,Patel NJ.Comparative evaluation of natural and superdisintegrant for promoting Nimisulide dissolution for fast dissolving technology. International journal of pharmacy and pharmaceutical sciences.2010; 2(3).
21. Howida Kamal Ibrahim, Doaa A. El-Setouhy. Valsartan Orodispersible Tablets: Formulation, In vitro/In vivo Characterization. AAPS PharmSciTech.2010, March; 11(1).
22. Mannur VS, Karki SS, Ketan B. Ramani.Formulation and characterization of Ranitidine hydrochloride fast disintegrating tablets. International Journal of ChemTech Research.2010,June; 2(2): 1163-1169.

23. Jayashri G, Kamlesh J, Milind J. Formulation and *in vitro* evaluation of taste Masked Orodispersible tablet of metclopramide hydrochloride. International journal of pharm tech research. 2010; 2(3).
24. Niladri Shekhar Dey, Bibhu Prasad Panda, Bhanoji Rao ME.Effect of co-processed direct compressible vehicles on fast dissolving tablets. International journal of pharm tech research.2010,March;2(1):771-783.
25. Pooja mathur, Navneet syan, Kamal saroha, Surender verma, Jagmohan oberoi. Formulation, evaluation and optimization of fast dissolving tablets of Losartan by central composite design. International journal of pharmacy and pharmaceutical sciences.2011; 3 (5).
26. Kakade M, Mannur S, Ramani B, Dhada A, Naval V, Bhagwat. Formulation and Evaluation of mouth dissolving tablets of losartan potassium by direct compression techniques. International Journal of Research & Pharmaceutical Sciences. 2010; 1(3): 290- 295.
27. Brahmeshwar mishra, Dali shukla, Subhashis chakraborty, Sanjay singh. Mouth dissolving tablets I: An overview of formulation technology.Scientia pharmaceutica. 2009, March 6; 309-326.
28. Galal El-Mahrouk, Mona Hassan Aboul-Einien, Nermeen Adel Elkasabgy. Formulation and evaluation of Meloxicam orally dispersible capsules. Asian Journal of Pharmaceutical Sciences. 2009, 4 (1): 8-22.
29. Radke RS, Jadhav JK, Chajeed MR.Formulation and evaluation of orodispersible tablets of Baclofen. International Journal of Chem Tech Research. 2009,July-Sep 1(3):517-521.
30. Ravikumar, Patil MB,Sachin R, Mahesh S. Development and characterization of melt in mouth tablets of Haloperidol by sublimation technique. International journal of pharmacy and pharmaceutical sciences.2009;Sep,1(1).
31. Biraju patel, Dhaval patel, Ramesh parmar,Chirag patel,Tejas serasiya, Sanja SD. Development and in-vitro evaluation of fast dissolving tablets of Glipizide. International journal of pharmacy and pharmaceutical sciences.2009;Dec,1(1).
32. Balamuralidharan V, Sreenivas SA, Gangadharappa HV, Pramodkumar TM. Investigation on the effect of different disintegrants on the orodispersible tablets of Rabeprazole. Asian Journal of Scientific Research. 2009.
33. Shahi SR, Agrawal R, Shinde NV, Shaikh SA, Shaikh SS, Somani VG,Shamkuvarand B. Formulation and *in vitro* evaluation of Oro-

dispersibletablets of Etoricoxibe with emphasis on comparative functionality evaluation of three classes of superdisintegrants. Rasayan J. Chem.2008, 1(2) : 292-300.

34. Vijay Sharma, Philip Anil K, Kamla Pathak. Modified Polysaccharides as fast disintegrating excipients for orodispersible tablets of Roxithromycin. Journal of 2008, March ; 9(1).
35. Prabakaran L, Senthil D.Formulation development of patient friendly dosage form all in one natural excipient as binder,diluent and disintegrant.International journal of pharmacy and pharmaceutical sciences.2011; 3(2).
36. Makwana H, Patel LD, Tejas B, Timir B , Tushar R. Formulation and Evaluation of Taste Masked Orodispersible Tablets of Ondansetron Hydrochloride.Journal of pharmaceutical sciences and research.2010, 2(4): 232-239.
37. Prajapati RH, Raval SB, Seth AK, Ghelani TK, Shah NV, Chauhan SP, Aundia CJ, Sainy V.Formulation and evaluation of taste masked mouth dissolving tablets of Ondansetron hydrochloride.
38. Gattu Jyothi , Lakshmi PK. Comparative evaluation of natural and synthetic Superdisintegrants with newer superdisintegrant Kyron T-314. Acta Pharmaceutica Sciencia.2011,53: 35-44.
39. Reddy`s.Newseland data sheet,newzeland limited level 6,Po box 911-267.Aukland,2010:July 17.3(1).
40. Structure of Ondansetron hydrochloride (Internet):Available on online:www.newdrug info.com/Pharmacopoeia.
41. Hand book of pharmaceutical excipient fifth edition. Available on online
42. Indian pharmacopoeia (1996), pp-A147.
43. Swamy PV, Divate SP, Shirsanel SB, Rajendra P. Orodispersible tablets of pheniramine maleate : Indian Journal of Pharmaceutical sciences. 2009, March- April.
44. Patil C, Das S. Effect of various superdisintegrants on the drug release profile and disintegration time of Lamotrigine orally disintegrating tablets. Africa Journal of Pharmacy and Pharmacology. 2011, January; 5(1): 76-82.
45. Prabhu K, Shaista, Rajanna S, Pranesh K. Formulation and Evaluation of mouth disintegrating tablets of Famotidine by using Hibiscus Rosa- Mucilage and treated Agar. International Journal of Research in Ayurveda & Pharmacy. 2010, Nov – Dec; 1(2): 497- 505.

46. Swamy PV, Patil AN, Shirsand SB, Amitkumar T, Laeeq Farhana. Design and Eval42. uation of low cost directly compressible excipients. International Journal of Research in Ayurveda & Pharmacy. 2010, Nov – Dec; 1(1): 424-432.
47. Mohan, Margret R. Recent advances in orodispersible tablets : A Review. International Journal of Drug Discovery and Herbal Research. 2011, April - June; 1(2): 78-83.
48. Puttewar TY, Kshirsagar MD, Chandewar AV, Chikhale RV. Formulation and evaluation of orodispersible tablets of masked doxylamine succinate using ion exchange resin. Journal of King Saud University. 2010, May; 22 : 229-240.
49. Kiran N, Palanichamy S, Rajesh M, Rajadas T, Anusha V, Parasakthi N, Thirupathi A. Formulation and evaluation of orodispersible Piroxican tablets. Journal of Pharmaceutical Sciences & Research. 2010; 2(10): 615- 621.
50. Mahamuni B, Shahi R, Shinde V, Agrawal R. Formulation and Evaluation of fast dissolving tablets of Promethazine HCL with masked bitter taste. International Journal of Pharmaceutical Research and Development. 2009, Sep; 7.
51. Nagendrakumar D, Raju SA, Shirsand SB, Para MS. Design of fast dissolving Granisetron HCL tablets using Novel Co- processed superdisintegrants. Journal of Bioscience & Technology. 2009; 1(1): 8-14.
52. Ramesh Veeraveni, Kamaeswara Rao CH, Shreedhar Nampalli, Ganesh Kumar Y, Krishna PC, Shiva Prasad MS. Design and evaluation of orodispersible taste masked valdecoxib tablets. Journal of Chemical and Pharmaceutical Research.2011; 3(4): 882-892.
53. Jaykar B, Margret Chandira R, Chakrabarty BL. Formulation and evaluation of Orodispersible tablets of terbutaline sulphate. Drug Invention Today. 2010; 2(1):31-33.
54. Omaima A, Sammour, Mohammed A, Hammad, Nagia A, Megrab, Ahmed S, Zidan. Formulation and Optimization of Mouth Dissolve Tablets Containing Rofecoxib Solid Dispersion. AAPS PharmSciTech. 2006, July; 7 (2).
55. Jashanjit Singh, Philip K, Kamla Pathak. Optimization Studies on Design and Evaluation of Orodispersible Pediatric Formulation of Indomethacin. AAPS Pharm Sci Tech.2008,March; 9 (1).
56. Prameela rani A, Archana.N, Siva teja P, Mohan vikast P,Sudheer kumar M, Bala sekaran C. Formulation and evaluation of orodispersible Metformin tablets: A

comparative study of Ispaghula husk and Crospovidone as superdisintegrants. International journal of applied pharmaceutics.2010; 2(3).

57. Jayashri G, Kamlesh J, Milind J. Formulation and *in vitro* evaluation of taste masked Orodispersible tablet of metclopramide hydrochloride. International journal of pharmtech research. 2010; 2(3).
58. Poojamathur, Navneetsyan, Kamalsaroha, Surenderverma, Jagmohan oberoi. Formulation,evaluation and optimization of fast dissolving tablets of Losartan by central composite design. International journal of pharmacy and pharmaceutical sciences.2011; 3 (5).
59. Mukesh P, Mohanta GP, Lokesh Upadhyay. Review on : Fast dissolving tablet. Journal of pharmacy research. 2009;Jan 2(1).
60. http://www. ijprd.com
61. http://www.mpa.se
62. Ahmed IS,Nafadi MM ,Fatatahala FA. Formulation of fast dissolving Ketoprofen tablet using freeze drying in blister technique. Drug develop IND pharm 2006:32:437-442.
63. Remon JP and Correleyen S.Freeze dried rapidly disintegrating tablets.US patent 6010719,20000.

ABSTRACT

The purpose of this research work is to formulate and evaluate the Orodispersible drug delivery system of already used therapeutic molecule to enhance bioavailability and effectiveness of the drug. Among ODT drugs, the most promising antiemetic is Ondansetron hydrochloride & it was selected for the present study. Thus the objectives of the drug work were to formulate and evaluate Orodispersible tablets of Ondansetron hydrochloride, having adequate mechanical strength, rapid disintegration and fast action. Pre compression parameters like angle of repose, bulk density, tapped density, compressibility index & post compression parameters like wetting time, water absorption ratio, *in-vitro* disintegration and *in-vitro* dispersion time were studied. The hardness, friability and drug content of all the formulations were found to be with in the limits. The best formulation F10 have shown good disintegration time, dissolution time and dispersion time. The best promising formulation were also be found to be stable at 40°C±75 % . Finally the *in-vitro* drug released characteristics of best formulation was compared to commercial formulation.