FORMULATION DEVELOPMENT AND *INVITRO* EVALUATION OF MOUTH DISSOLVING TABLETS OF SERTRALINE HCL BY DIRECT COMPRESSION METHOD

A Dissertation submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY,

CHENNAI- 600 032

In partial fulfilment of the award of the degree of

MASTER OF PHARMACY

IN

Branch-I -- PHARMACEUTICS

Submitted by

Name: SRUTHI S

REG.No. 261810264

Under the Guidance of

Mr. C. KANNAN, M.Pharm.,

ASSOCIATE PROFESSOR

DEPARTMENT OF PHARMACEUTICS

J.K.K.NATTARAJA COLLEGE OF PHARMACY
KUMARAPALAYAM – 638183
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CERTIFICATES

EVALUATION CERTIFICATE

This is to certify that the dissertation work entitled **"FORMULATION DEVELOPMENT AND *INVITRO* EVALUATION OF MOUTH DISSOLVING TABLETS OF SERTRALINE HCL BY DIRECT COMPRESSION METHOD",** submitted by the student bearing **Reg. No: 261810264** to "**The Tamil Nadu Dr. M.G.R. Medical University – Chennai**", in partial fulfilment for the award of Degree of **Master of Pharmacy** in **Pharmaceutics** was evaluated by us during the examination held on……

Internal Examiner **External Examiner**

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Mr. C. KANNAN, M.Pharm.,
Associate Professor
Department of Pharmaceutics

Dr. S. Bhama, M. Pharm., PhD.,
Professor & HOD,
Department of Pharmaceutics

Dr. R. Sambathkumar, M. Pharm., PhD.,
Professor & Principal,

CERTIFICATE

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Place: Kumarapalayam
Date:

Mr. C. KANNAN, M.Pharm.,
Associate Professor
Department of Pharmaceutics

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Place: Kumarapalayam
Date:

Dr. R. Sambathkumar, M. Pharm., PhD.,
Professor & Principal,
J.K.K.Nattraja College of Pharmacy,
Kumarapalayam.

DECLARATON

I do hereby declared that the dissertation **"FORMULATION DEVELOPMENT AND *INVITRO* EVALUATION OF MOUTH DISSOLVING TABLETS OF SERTRALINE HCL BY DIRECT COMPRESSION METHOD"** submitted to "**The Tamil Nadu Dr. M.G.R Medical University - Chennai",** for the partial fulfilment of the degree of **Master of Pharmacy** in **Pharmaceutics,** is a bonafide research work has been carried out by me during the academic year 2019-2020, under the guidance and supervision of **Mr. C. KANNAN, M.Pharm.,** Associate Professor, Department of Pharmaceutics, J.K.K.Nattraja College of Pharmacy, Kumarapalayam.

I further declare that this work is original and this dissertation has not been submitted previously for the award of any other degree, diploma, associate ship and fellowship or any other similar title. The information furnished in this dissertation is genuine to the best of my knowledge.

Place: Kumarapalayam **SRUTHI S**

Date: **Reg.no. 261810264**

Dedicated to

Parents,

Teachers &

My Family

ACKNOWLEDGEMENT

ACKNOWLEDGEMENT

I am proud to dedicate my deep sense of gratitude to the founder, (Late) Thiru **J.K.K. Nattaraja Chettiar,** providing the historical institution to study.

My sincere thanks and respectful regards to our reverent Chairperson **Smt. N. Sendamaraai, B.Com.,** and Director **Mr. S. Omm Sharravana, B.Com., LLB.,** J.K.K. Nattraja Educational Institutions, Kumarapalayam for their blessings, encouragement and support at all times.

It is most pleasant duty to thank for our beloved **Dr. R. Sambathkumar, M.Pharm., Ph.D.,** Principal & Professor, Department of Pharmaceutics, J.K.K. Nattraja College of Pharmacy, Kumarapalayam for ensuring all the facilities were made available to me for the smooth running of this project and tremendous encouragement at each and every step of this dissertation work. Without his critical advice and deep-rooted knowledge, this work would not have been a reality.

It is my privilege to express deepest sense of gratitude toward **Mr. C. Kannan, M.Pharm.,** Associate Professor, Department of Pharmaceutics, for their valuable suggestions and inspiration.

Our glorious acknowledgement to our administrative officer **Dr. K. Sengodan, M.B.B.S.**, for encouraging using kind and generous manner to complete this work.

My sincere thanks to **Dr. S. Bhama, M. Pharm., Ph.D.,** Professor & Head, Department of Pharmaceutics, **Mr. R. Kanagasabai, B.Pharm, M.Tech.,** Associate Professor, **Dr. V. Kamalakannan M. Pharm., Ph.D.,** Associate Professor, **Mr. K. Jaganathan, M.Pharm.,** Associate Professor, **Ms. S. Manodhini Elakkiya, M.Pharm.,** Assistant Professor, **Mr. M. Subramani, M.Pharm.,** Assistant Professor, **Dr. Rosmi**

Jose, Pharm.D., Lecturer, **Mr. R. Neelamegarajan,** Lecturer, **Dr. Sathya Priya. K, Pharm.D.,** Lecturer and Department of pharmaceutics for the in valuable help during my project.

My sincere thanks to **Dr. N. Venkateswaramurthy, M.Pharm., Ph.D.,** Professor and Head, Department of Pharmacy Practice, **Dr. K. Krishna Veni, M.Pharm., Ph.D.,** Associate Professor, **Dr. R. Kameswaran, M.Pharm., Ph.D.,** Assistant Professor, **Dr. Mebin Alias, Pharm.D.,** Assistant Professor, **Dr. Cindy Jose, Pharm.D.,** Lecturer, **Dr. Krishna Ravi, Pharm.D.,** Lecturer, **Dr. S.K.Sumitha, Pharm.D.,** Lecturer, and **Mr. A. Mohammed Thafiq Ilahi, M.Pharm.,** lecturer, Department of Pharmacy Practice, for their help during my project.

It is my privilege to express deepest sense of gratitude toward **Dr. M. Vijayabaskaran**, **M.Pharm., Ph.D.,** Professor & Head, Department of Pharmaceutical chemistry, **Dr. P. Senthilkumar, M.Pharm., Ph.D.,** Professor, **Mrs. B. Jeyalakshmi M.Pharm.,** Associate Professor, **Mrs. B. Vasuki, M.Pharm.,** Assistant Professor and **Ms. P. Lekha,** Lecturer for their valuable suggestions and inspiration.

My sincere thanks to **Dr. V. Sekar, M.Pharm., Ph.D.,** Professor and Head, Department of Analysis, **Dr. Ananda Thangadurai, M.Pharm., Ph.D.,** Professor, **Dr. I. Caolin Nimila, M.Pharm., Ph.D.,** Associate Professor, **Mr. D. Kamalakannan,** Assistant Professor, **Mrs. P. Devi, M.Pharm.,** Assistant Professor and **Ms. V. Devi, M.Pharm.,** Lecturer, Department of Pharmaceutical Analysis for their valuable suggestions.

My sincere thanks to **Dr. Senthilraja, M.Pharm., Ph.D.,** Associate Professor and Head, Department of Pharmacognosy, **Dr. V. Kishorkumar, M.Pharm., Ph.D.,** Professor, **Mrs. P. Meena Prabha, M.Pharm.,** Associate Professor, Department

of Pharmacognosy and **Mr. Nikhil.P.S, M.Pharm.,** Lecturer, Department of Pharmacognosy for their valuable suggestions during my project work.

My sincere thanks to **Dr. R. Shanmugasundaram, M.Pharm., Ph.D.,** Vice Principal & HOD, Department of Pharmacology, **Dr. B. Rajkapoor, M.Pharm., Ph.D.,** Professor, **Dr. C. Kalaiyarasi, M.Pharm., Ph.D.,** Associate Professor, **Mr. V. Venkateswaran, M.Pharm.,** Assistant Professor, **Mrs. M. Sudha M.Pharm.,** Assistant Professor, **Mr. T. Thiyagarajan, M.Pharm.,** Assistant Professor, **Mrs. R. Elavarasi, M.Pharm.,** Assistant Professor , **Mrs. M. Babykala, M.Pharm.,** Lecturer, and **Mrs. P.J. Sujitha, M.Pharm.,** Lecturer, Department of Pharmacology for their valuable suggestions during my project work.

I greatly acknowledge the help rendered by **Mrs. K. Rani,** Office Superintendent, **Miss. M. Venkateswari, M.C.A.,** Assistant Professor**, Miss. S. Sudhalakshmi,** Typist, **Mrs. V. Gandhimathi, M.A., M.L.I.S.,** Librarian, **Mrs. S. Jayakala B.A., B.L.I.S.,** and Asst. Librarian for their co-operation. I owe my thanks to all the technical and non-technical staff members of the institute for their precious assistance and help.

Last, but nevertheless, I am thankful to my lovable parents and all my friends for their co-operation, encouragement and help extended to me throughout my project work.

SRUTHI S

Reg.no. 261810264

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FORMULATION DEVELOPMENT AND *INVITRO* EVALUATION OF MOUTH DISSOLVING TABLETS OF SERTRALINE BY DIRECT COMPRESSION METHOD

CHAPTER 1

INTRODUCTION

1. INTRODUCTION

1.1. ORAL DRUG DELIVERY SYSTEM

Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drug via various pharmaceutical products of different dosage forms. The reason that the oral route achieved such popularity may be attributed to its ease of administration as well as the traditional belief that by oral administration the drug is well absorbed as the food staffs ingested daily. In fact the development of pharmaceutical products for oral delivery, irrespective of physical form involves varying extents of optimization of dosage form within the inherent constraints of GI physiology. Therefore a fundamental understanding of various disciplines, including GI physiology Pharmacokinetics, pharmacodynamics and formulation design are essential to achieve a systemic approach to the successful development of an oral dosage form. The more sophisticated a delivery system the greater is the complexity of these various disciplines involved in the design and optimization of the system. In any case the scientific development of oral drug delivery system consists of a basic understanding of the following there aspects[1].

a) Physicochemical, pharmacokinetic and pharmacodynamic characteristics of the drug.
b) The anatomic and physiologic characteristic of the GIT.
c) Physicochemical characteristic and the drug delivery mode of the dosage form to be designed.

Oral route of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, self-medication, pain avoidance and most importantly the patient compliance. The most popular solid dosage forms are being tablets and capsules. Drinking water plays an important role in the swallowing of oral dosage forms. One important

drawback of these dosage forms for some patients however is difficult to swallow. Often times people experience inconvenience in swallowing conventional tablets and capsules when water is not available in case of motion sickness and sudden episodes of coughing during the common cold, allergic conditions and bronchitis.

Many patients have difficulty swallowing tablets and hard gelatin capsules and consequently do not take medications as prescribed. It is estimated that 50% of the population is affected by this problem which results in a high incidence of non-compliance and in effective therapy. It has been reported that dysphagia (difficulty in swallowing) is common among all age groups and more specific with pediatric, geriatric population along with institutionalized patients and patients with nausea. Because of the increase in the average human life span and the decline, with age, in swallowing ability, oral tablet administration to patients is a significant problem and has become the object of public attention. The problem can be resolved by the creation of rapidly dispersing or dissolving oral forms, which do not require water to aid swallowing. The dosage forms are placed in the mouth, allowed to disperse or dissolve in the saliva, and then are swallowed in the normal way.

The orally disintegrating tablets are also caused as oro dispersible tablet, quick disintegrating tablets, fast disintegrating tablets, porous tablets rapimelts. However of all the above terms, United States pharmacopeia (USP) approved these dosage forms as ODTs. Recently, European pharmacopeia has used the term “orodispersible tablet” for tablets that disperse readily and within three minutes before swallowing. United States food and drug administration (FDA) defined ODT as “A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue”. The disintegration times for ODTs generally range from several seconds to about a minute.

Mouth dissolving tablets are most widely used dosage form because of it's convenience in terms of self-administration, compactness and ease in manufacturing. Fast disintegrating tablets rapidly gaining acceptance as an important new drug technology. These dosage forms dissolve or disintegrate in oral cavity within a minute even without the need of water or chewing.

1.1.1 MOUTH

The mouth also referred to as the oral (or) buccal cavity is formed by the cheeks, hard and soft palates and tongue. The cheek from the lateral walls of the oral cavity. They are covered externally by skin and internally by a mucous membrane ,which consist of nonkeratinized stratified squamous epithelium buccinators muscles and connective tissue lie cheeks. The anterior portions of the cheeks end at the lips. The lips (or) labia are freshly folds surrounding the opening of the mouth. They contain the orbicularisoris muscle and are covered externally by skin and internally by a mucous membrane. The inner surface of each lip is attached to this corresponding gum. By a midline fold of mucous membrane called the labial frenulum. During chewing contraction of the buccinators muscles in the cheeks and orbicularisoris muscle in the lips helps keep food between the upper and lower teeth. These muscles also consist in speech.

The oral vestibule of the oral cavity is a space bounded externally by the cheeks and lips and internally by the gums and teeth. The oral cavity proper is a space that extends from the gums and teeth to the opening between the oral cavity and the oropharynx. The palate is a wall (or) septum that separates the oral cavity from the nasal cavity, forming the loof of the mouth. This important structure makes it possible to chew and breath at the same time. The hard palate the anterior portion of the loof of the mouth is formed by maxillae and palatine bones and is covered by a mucous membrane it forms a bony partition between the oral and nasal cavity. The soft palate, which forms the posterior

portion of loof of the mouth is an arch-shaped muscular partition between the oropharynx and nasopharynx that is lined with mucous memberane.

1.2. DESIRED CRITERIA FOR MOUTH DISSOLVING DRUG DELIVERY SYSTEM

The tablet should:

- Not require water to swallow, but is should dissolve (or) disintegrate in the mouth in matter of seconds.
- Be compatible with taste masking.
- Be portable with taste masking.
- Have a pleasing mouth feel.
- Leave minimal (or) no residue in the mouth after oral administration.
- Exhibit low sensitivity to environmental conditions as humidity and temperature.
- Allow the manufacture of tablet using conventional processing and packaging equipment at low cost,
- Allow the manufacture of tablet using conventional processing and packaging equipment at low cost.

1.3. SALIENT FEATURES OF MOUTH DISSOLVING TABLET

- Ease of administration to patient who refuses to swallow tablets, such as pediatric, geriatric and psychiatric patients.
- No need of water to swallow the dosage form, which is highly convenient feature for patients who are travelling and do not have immediate access to water.
- Rapid dissolution and absorption of drug which will produce quick onset of action.
- Some drugs are absorbed from the mouth, pharynx, and esophagus as the saliva passes down into the stomach in such cases bio-availability of drugs in increased.

- Pre-gastric absorption can result in improved bio-availability and as a result of reduced dosage. Improve clinical performance through a reduction of unwanted effects.

1.4. ADVANTAGES OF MOUTH DISSOLVING TABLETS

- Improved patient compliance.
- Rapid onset of action and may offer an improved bio-availability.
- Patient having difficulty in swallowing tablet can easily administer this type of dosage form.
- Useful fro-pediatric, geriatric and psychiatric patients.
- Suitable during travelling where water is may not be available.
- Gives accurate dosing as compared to liquids.
- Good chemical stability.
- Free of need of measuring, an essential drawback in liquids.

1.5. LIMITATION OF MOUTH DISSOLVING TABLETS

- The tablets usually have insufficient mechanical strength. Hence careful handling is required.
- The tablets may leave unpleasant taste and for grittiness in mouth if not formulated properly.
- These tablets usually have low hardness, so they are friable or brittle. They are difficult to handle.
- And require specialized packaging.

1.6. SIGNIFICANCE OF DISSOLVING TABLETS

- They provide good stability, accurate dosing, easy manufacturing small packaging size and easy to handle by patients.
- No risk of obstruction of dosage from, which is beneficial for travelling patients who do not have access to water.
- Easy to administer for pediatric, geriatric and institutionalized patients. (especially for mentally retarded and psychiatric patients)
- Rapid disintegration of the tablet results in quick dissolution and rapid absorption which provide rapid onset of action.

- Medications as "bitter pill" has changed by excellent mouth feel property produced by the use of flavors and sweeteners in mouth dissolving tablets.
- Bioavailability of drugs that are absorbed from mouth, pharynx and oesophagus is increased.
- Pregastric absorption of drugs avoids hepatic metabolism, which reduces the dose and increase the bioavailability.
- Improved taste and not produce any residue in the mouth.
- Insensitive to environmental conditions.

1.7. FORMULATION ASPECTS IN DEVELOPING MDT

Mouth disintegrating tablets are formulated by utilizing several process, which differ in their methodologies and the MDTs formed vary in various properties such as,

- Mechanical strength of tablets
- Taste and mouth feel
- Swallowability
- Drug dissolution in saliva.
- Bioavailability
- Stability

1.7.1. VARIOUS APPROACHES FOR MOUTH DISSOLVING TABLETS

The property of mouth dissolving tablets is attributable to a quick intake of water in to the tablet matrix resulting rapid disintegration and instantaneous dissolution of the tablets.

- Maximizing the pore structure of tablet matrix.
- Using highly water soluble excipients in the formulation.
- Incorporating appropriate disintegrating agents.

Disintegrates act by any one of the following mechanisms,

- Capillary action
- High swell ability
- Release of gas by chemical reaction.

1.7.2.METHODS FOR THE FORMULATION OF MOUTH DISSOLVING TABLETS

Various processes employed in formulating MDTs are described below.

A.PATENTED TECHNOLOGIES

1. ZYDUS TECHNOLOGY

This technology involves physical trapping of drug in a matrix composed of a saccharide and a polymer .The polymer generally used are partially hydrolyzed gelatin, hydrolyzed dextran, dextrin, alginate, polyvinyl alcohol, polyvinyl pyrrolidone, acacia and these mixtures. The methodology involves solution or dispersion of components is prepared and filled in to blister cavities, which are frozen in a liquid nitrogen environment. The frozen solvent is removed or sublimed to produce porous wafers. Peelable backing is used to pack zydis units. These formulations are sensitive to moisture and may degrade at humidity greater than 65% zydis is patented by R.P. Scherer.

2. LYOC

Oil in water emulsion is prepared and placed directly in to blister cavities followed by freeze drying. Non homogeneity during freeze drying is avoided by incorporating inert filler to increase the viscosity finally the sedimentation. The methodology is patented by pharmalyoc.

3. QUICK SOLV

Methodology includes dissolving matrix components in water and the solution or dispersion is frozen. Then dry the matrix by removing water using an excess alcohol (solvent extraction). The product formed has uniform porosity and adequate strength for handling. This technology patented by Jassen Pharmaceuticals.

4. NANOCRYSTAL TECHNOLOGY

Nano crystal technology includes lyophilization of colloidal dispersion of drug and water soluble ingredients filled into blister pockets. This method avoid manufacturing process such as granulation,

blending and tableting. This method is advantageous for highly potent and hazards drugs, manufacturing losses are negligible and the process is small quantities of drugs. This methodology is patented by Elanking of Prussia.

5. FLASH TAB TECHNOLOGY

This technology includes granulation of excipients by wet granulation method and follow by compressing in to tablets excipients used in this technology are of two types. Disintegrating agents include reticulated polyvinyl pyrolidone or carboxy methyl cellulose, starch, modified starch, microcrystalline cellulose, carboxy methylated starch, etc. tablets formed have satisfactory physical resistance. Disintegration time is within 1 minute. This methodology patented by Ethypharm, France.

6. ORASOLV TECNOLOGY

This includes use of effervescent disintegrating agents compressed with low pressure to produce MDTs. The evaluation of carbon dioxide from the tablet produces fizzing sensation, which is a positive organoleptic properties. Concentration of effervescent mixed usually employed is 20-25%of tablet weight .as the tablets prepared at low compression force, they are soft and fragile in nature. This is initiated to develop paksolv, a special packaging to protect tablets during storage and transport. Paksolv is dome-shaped blister package, which prevents vertical movements of tablets in the depression. This offers moisture, light and child resistance packing.

7. DURASOLV TECNOLOGY

This methodology utilized conventional tableting equipment and tablets are formulated by using drug non-direct compression fillers and lubricants. Non direct compression fillers are dextrose mannitol, sorbitol, lactose, and sucrose which have advantages of quick dissolution avoid gritty structure (which is generally present in direct compressible sugar)The tablets formed are strong and can be packed in conventional

packing in bottles and blisters. Nondirect compressible fillers generally used in the range of 60-95%,lubricants in 1-2.5%.this technology patented by CIMA labs. Durasolv products include Nulev (hyoscyaminesulphate),Zoming ZMT(Zolmitraptan).

8. WOW TAB TECNOLOGY

This technology utilizes conventional granulation and tableting methods to produce MDTs employing low-and high moldability saccharides. WOW means with out water. Low moldabilty saccharides are lactose, mannitol, glucose, sucrose and xylitol. High moldability saccharides are maltose, maltitol, sorbitol and oligosaccharides. When these two type saccharides used alone tablets obtained do not have desired properties of rapid disintegration and hardness, so combination are used. This technology involves granulation of low-moldable saccharieds as a binder and compressing in to tablets followed by moisture treatment. So the tablets formed showed adequate hardness and rapid disintegration .this technology patented by Yamanouchi. WOW tab product include Benadryl allergy and sinus fast melt (OTC).

9. DISPERSIBLE TABLET TECNOLOGY

It offers development of MDT improved dissolution rate by incorporating 8-10% of organic acid and disintegrating agents. disintegrating agents facilitates rapid swelling and good wetting results in quick disintegration. Disintagrants include starch, modified starches, microcrystalline cellulose, alginic acid, cross linked sodium carboxy methyl cellulose and cyclodextrines. Combilnation of disintegarants improved disintegration usally less than 1 minutes. The methodology patented lek, Yugoslavia.

10. PHARMA BURST TECNOLOGY

It utilize co proceed exicipients to develop MDT which dissolves within 30-40 seconds. The technology involves dry blending of drugs, flavor and lubricant followed by compression in to tablets. The tablets

obtained have sufficient strenghth so they can be packed in blister packs and bottles. This technology patened by SPI pharma, new castle.

11. FROSTA TECHNOLOGY

It utilizes the concept of formulating plastic granules and compressing at low pressure to produce strong tablets with high porosity. Plastic granules composed of porous and plastics material, water penetration enhancer and binder. The process involves mixing the porous plastic material with water penetration enhancer and followed by granulating with binder. The product showed excellent hardness and rapid disintegration within 15-30 seconds. This methodology patented by Akina.

12. ORAQUICK

It utilize taste masking microspheres technology called as micro mask, which provides superior mouth feel, significant mechanical strength and quick disintegration and dissolution of the products. This process involves preparation of micro particles in the form of matrix that protects the drug which can be compressed with sufficient mechanical strength. Low heat of production in this process make it suitable for heat sensitive drug. The products formed dissolves within few seconds. The methodology patented by K.V Pharmaceuticals.

13. ZIPLETS OR ADVATAB

It utilize water insoluble gradients combined one are more effective disintegrants to produce MDT s with improved mechanical strength and optimum disintegration time at low compression force. Advantage of the method include high drug loading, formation of coated particles and does not require special packaging. This technology patented by pessano con Bornago.

14. FLASHDOSE

The flash dose tablets consists of self binding shear form matrix termed as floss. Shear form matrices are prepared by flash heat

processing. This technology patented by Fluzisz. Egibuprofen melt in mouth tablets.

B.CONVENTIONAL METHODS

1. LYOPHILIZATION OR FREEZE-DRYING

Lyophilization is a process which includes removal of a solvent from a frozen suspension of drug with structure forming additives. Freeze drying of a drug along with additives imparts glossy amorphous structure resulting in highly porous and light weight product. The resulting tablet has rapid disintegration and dissolution when placed on a tongue and the freeze dried leutin dissolves instantly to release the drug. MDT s formed by lyophilization have some demerits like low mechanical strength, poor stability at higher temperature and humidity. Use of expensive equipment for freeze drying is another demerits of the process.

2. MOULDING

Molding process include moistening, dissolving or dispersing the drug with a solvent then molding the moist mixer in to tablets(compression molding with a low pressure than conventional tablet compression)evaporating the solvent from drug solution, or suspension at ambient pressure respectively. The molded tablets formed by compression molding are air dried. As the compression force employed is lower than conventional tablet, the molded tablet results in highly porous structure, which increase the disintegration and dissolution of the product. To further improve the dissolution rate of the product powder mixer should be sieved through very fine screen. This process is applied usually with soluble ingredients (saccharides) which offer improved mouth feel and disintegration of tablets. Some of the demerits observed are the tablet formed by this process shows low mechanical strength, which results in erosion and breakage during handling.

3. COTTON CANDY PROCESS

Cotton candy process involves formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to have improved flow properties and compressability. This candy floss matrix is then milled and blended with active ingredients and excipients and subsequently compressed to MDTs. This process is so named because it utilizes a unique spinning mechanism to produce floss-like crystalline structure, which mimic cotton candy. The main merits of this method are the process can accommodate high doses of drug and offers improved mechanical strength. The main demerit is the use of high process temperature.

4. SPRAY DRYING

In this method MDTs formulated by using hydrolyzed / unhydrolyzed gelatin as supporting agent for matrix, mannitol as bulking agent and sodium starch glycolate or croscarmellose sodium as disintegrating agent. Disintegration and dissolution were further improved by adding effervescent components.ie citric acid (an acid) and sodium bicarbonate (an alkali). The formulation was spray dried to yield a porous powder. The products formed are highly porous fine powders and are disintegrated in<20 seconds. Allen et al utilized this method for preparing MDTs.

5. MASS EXTRUSION

It involves softening the active blend using the solvent mixture of water soluble polyethylene glycol and methanol and subsequent expulsion of softened mass through the extruder or syringe to get a cylinder of the product in to even segments using heated blade to forms tablets**. (yadav A.V et al,2010)**

6. COMPACTION MELT GRANULATION

The method involves incorporation of hydrophilic waxy binder (super poly state.) PEG -6-sterate. Super poly state is a waxy material

with an M.P of 33-37c. and an hydrophilic lipophilic balance of 9. It act as binder, increase the physical resistance of tablets and it helps the disintegration of tablets as it melt in the mouth and solubilizes rapidly leaving no residue. Super poly state incorporated in the formula by melt granulation method, where granules are formed by the molten form of the material. eg crystallized paracetamol was used as model drug and in addition mannitol added as water soluble excipient and cross carmellose sodium as disintegrating agents. Abdlbary *et al* prepared MDT by this method.

7. PHASE TRANSITION PROCESS

Kuno *et al* investigated disintegration of MDTs are formulated by sugar alcohols using erythriol (M.P 122C), xylitol (m.p 93-95), trehalose (97c) and mannitol (166c). This method involves compressing a powder containing two sugar alcohols with high and low-melting points and subsequent heating at temperature between their melting points. Before heating process the tablet do not have sufficient hardness because of low compatibility. The tablet hardness was increased after heating process, due to the increase of interparticular bonds or bonding surface area in tablets induced by phase transition of low melting point sugar alcohols.

8. SUBLIMATION

The method involves addition of volatile salt to the tableting components, mixing and volatilizing the volatile salt creates pores in the tablets come in contact with saliva. Camphor, naphthalene, urea, ammonium bi carbonate etc., can be used to prepare porous tablets of good mechanical strength. The tablets were subjected to vaccum at 80 c for 30 minutes to eliminate camphor. The tablet formed have highly porous matrix which is the key factor for rapid disintegration.

C. OTHER METHODS

Other methods includes dry granulation, wet granulation and direct compression methods. The important components used in these methods are super disintegrants.

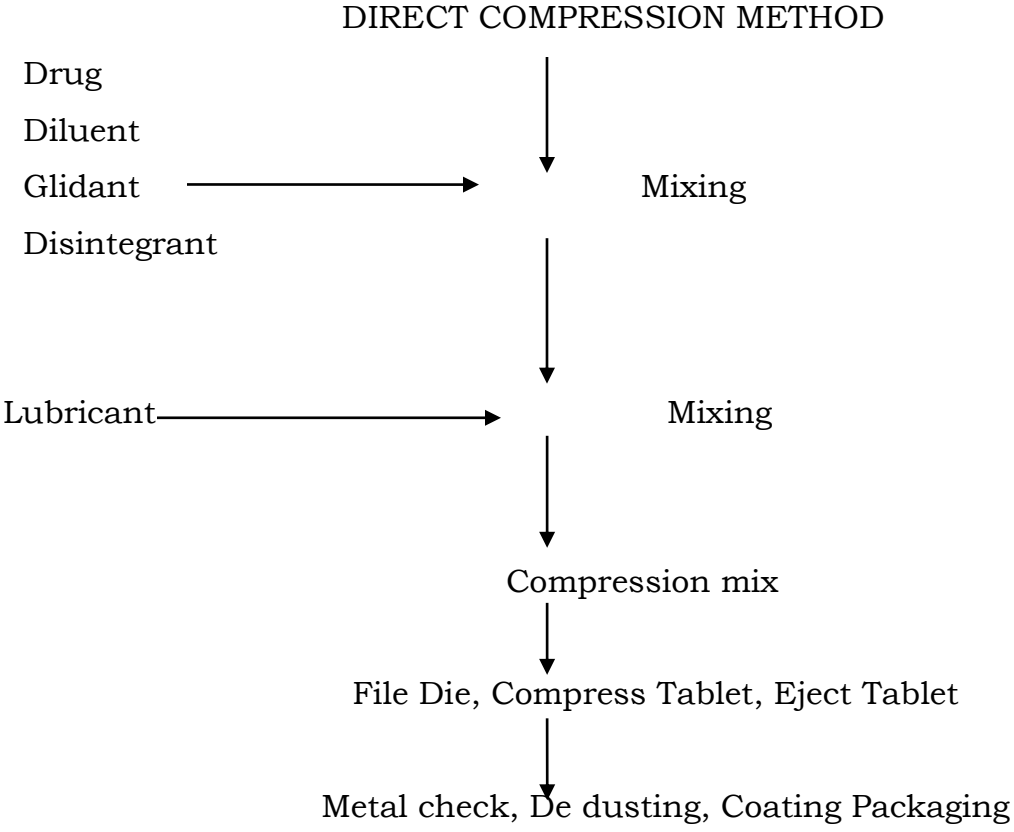
1. DRY GRANULATION

In this technique there is no use of liquids. The process involves the formation of slugs. Then slugs are screened are milled to produce granules. The granules formed are then compressed to form tablet.

2. WET GRANULATION

The process involves addition of liquids to a powder in a vessel equipped with any type of agitation that will produce agglomeration or granules. These granules after drying are compressed to form tablets. This method have more operational manipulation and is more time consuming than other methods. this method is not suitable for drugs which ass thermo labile or hydrolysable by presence of water in the liquid binder.

Figure 1: Flow sheet of direct compression



3. DIRECT COMPRESSION

In direct compression method, of powder blends of active ingredients and suitable excipients, which will flow uniformly in the die

cavity and formed a film compact (**Banker G.S et al 1987**).direct compression method are very popular because it reduse the number of steps involved and the materials required.

Advantages

1. Easiest method to manufacture fast dissolving tablets.
2. Low manufacturing cost.
3. Use of conventional equipment and commonly available excipients.
4. High quality finished product.

1.8: Types of Excipients used in Tablets:

Conventional oral tablets for ingestion usually contain some classes of components in addition to active ingredients. They are:-

(a) Diluents
(b) Binders
(c) Antiadherents
(d) Disintegrants
(e) Fillers and diluents
(f) Flavours
(g) Colours
(h) Lubricants
(i) Glidants
(j) Preservatives
(k) Sorbents
(l) Sweeteners

(a) Diluents:

Diluents are fillers designed to makeup the required bulk of the tablet when the drug dosage itself is inadequate to produce this bulk. The dose of some drugs is sufficiently high that no filler is required.

Example: Lactose, Starch, Dextrose, Mannitol, Sorbitol, Sucrose, Microcrystalline cellulose(Avicel).

(b) Binders:

Binders hold the ingredients in a tablet together. Binders ensure that tablets and granules can be formed with required mechanical strength, and give volume to low active dose tablets. These material are added either dry or in liquid form during wet granulation to form granules or to promote cohesive compacts for directly compressed tablets.

Example: Starch, Cellulose, Micro Crystalline Cellulose, Gelatin, Tragacanth, etc.

(c) Antiadherents

Antiadherents are used to reduce the adhesion between the powder (granules) and the punch faces and thus prevent sticking to tablet punches. They are also used to help protect tablets from sticking. Most commonly used is magnesium stearate.

(d) Disintegrants

Disintegrants expand and dissolve when wet causing the tablet to break apart in the digestive tract, releasing the active ingredients for absorption. Disintegrants may function by drawing water into the tablet, swelling, and causing the tablet to burst apart such as tablet fragmentation may be critical to the subsequent dissolution of the drug and to the attainment of satisfactory drug bioavailability.

Examples: carboxymethyl cellulose (croscarmellose sodium), polyvinyl pyrrolidone, Starch, Veegum, Bentonite.

(e) Fillers and diluents

Fillers fill out the size of a tablet or capsule, making it practical to produce and convenient for the consumer to use. By increasing the bulk volume, the fillers make it possible for the final product to have the proper volume for patient handling.

Examples: lactose, sucrose, glucose, mannitol, sorbitol, calcium carbonate, magnesium stearate etc.

(f) Flavours

Flavours can be used to mask unpleasant tasting active ingredients and improve the likelihood that the patient will complete a course of medication. Flavours are usually limited to chewable tablets or other tablets intended to dissolve in the mouth.

Examples: mint, cherry, anise, vanilla, raspberry, peach, apricot, liquorice., etc.

(g) Colours

The use of colors and dyes in tablet making has three purposes over the years, distinguishing of off-colors drugs, product identification, and production of a more elegant decertification of many synthetic dyes. The availability of natural vegetable colors is limited, and these colors are often unstable. Two forms of colors have typically been used in tablet preparation. These are the FD&C and D&C dyes.

(h) Lubricants

Lubricants prevent ingredients from clumping together and from sticking to the tablet punches or capsule filling machine i.e., Lubricants are intended to reduce the friction during tablet ejection between the walls of the tablet and the walls of the die cavity on which the tablet are formed.

Examples: talc, silica, magnesium stearate, stearic acid etc.

(i) Glidants

Glidants are used to promote powder flow by reducing interparticle friction and cohesion. These are used in combination with lubricants as they have no ability to reduce die wall friction.

Examples : fumed silica, talc, and magnesium carbonate.

(j) Preservatives

Some typical preservatives used in pharmaceutical formulations are:

- Antioxidants like vitamin A, vitamin E, vitamin C, retinylpalmitate, and selenium
- The amino acids cysteine and methionine.
- Citric acid and sodium citrate.
- Synthetic preservatives like the parabens: methyl paraben and propyl paraben.

(k) Sorbents

Sorbents are used for tablet/capsule moisture-proofing by limited fluid sorbing (taking up of a liquid or a gas either by adsorption or by absorption) in a dry state.

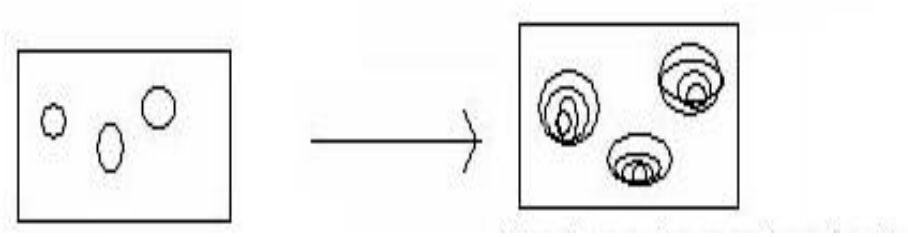
(l) Sweeteners

Sweeteners are added to make the ingredients more palatable, especially in chewable tablets such as antacid or liquids like cough syrup. Therefore, tooth decay is sometimes associated with cough syrup abuse. Sugar can be used to disguise unpleasant tastes or smells.

(m) Super Disintegrants in Immediate Release Tablets

Super-disintegrants are effective at low concentration and have greater disintegrating efficiency and they are effective intra-granularly as well as extra-granularly. But have one drawback that it is hygroscopic therefore not used with moisture sensitive drugs. These super-disintegrants act by swelling and due to swelling pressure exerted in the outer direction or radial direction, it causes tablet to burst or accelerate the absorption of water leading to an enormous increase in the volume of granules to promote disintegration is shown in Fig 2.

Fig 2: Mechanisms of Super-disintegrant swelling



Granules with super disintegrant granules in aqueous medium

Swelling of granules due to super-disintegrant

Table 1: LIST OF SUPERDISINTEGRANTS

SUPERDISINTEGRANTS	TYPE	MECHANISM OF ACTION	SPECIAL COMMENTS
Croscarmellose Ac-Di-Sol Nymce ZSX Primellose Solutab Vivasol	Crosslinked Cellulose	Swells 4-8 folds in < 10 seconds Swelling and wicking both.	Swells in two dimensions. Direct compression or Granulation Starch free
Crospovidone Crospovidon M Kollidon Polyplasdone	Crosslinked PVP	Swells very little and returns to original size after compression but act by capillary action	Water insoluble and spongy in nature so get porous tablet

Sodium starch glycolate Explotab Primogel	Crosslinked Starch	Swells 7-12 folds in <30 seconds	Swells in three dimensions and high level serve as sustain release matrix
Alginic acid NF Satialgine	Crosslinked alginic acid	Rapid swelling in aqueous medium or wicking action	Promote disintegration in both dry or wet granulation

Table 2: PARAMETERS INFLUENCING THE SWELLING BEHAVIOUR OF SUPERDISINTEGRANTS [6-8]

PARAMETERS	EFFECTS
Amount of superdisintegrant	A minimum amount of superdisintegrant is necessary for the development of sufficient swelling to outer membrane
Additives (binders)	Polymeric binders can reduce swelling pressure by spacial separation of superdisintegrant particles or competition for free water
Ionic strength of the medium	Competition of the ions for free water
pH values	Swelling can be influenced for the superdisintegrants with ionizable groups(e.g:carboxylic groups in croscarmellose)

EFFECT OF EXCIPIENTS USED IN THE FORMULATION:

a) Effect of fillers:

The solubility and compression characteristics of fillers affect both rate and mechanism of disintegration of tablet. If soluble fillers are used then it may cause increase in viscosity of the penetrating fluid which tends to reduce effectiveness of strongly swelling disintegrating agents and as they are water soluble, they are likely to dissolve rather than disintegrate. Insoluble diluents produce rapid disintegration with adequate amount of disintegrants. Tablets made with spray dried lactose (water soluble filler) disintegrate more slowly due to its amorphous character and has no solid planes on which the disintegrating forces can be exerted than the tablet made with crystalline lactose monohydrate.

b) Effect of binder:

As binding capacity of the binder increases, disintegrating time of tablet increases and this counteract the rapid disintegration. Even the concentration of the binder can also affect the disintegration time of tablet.

c) Effect of lubricants:

Mostly lubricants are hydrophobic and they are usually used in smaller size than any other ingredient in the tablet formulation. When the mixture is mixed, lubricant particles may adhere to the surface of the other particles. This hydrophobic coating inhibits the wetting and consequently tablet disintegration. Lubricant has a strong negative effect on the water uptake if tablet contains no disintegrants or even high concentration of slightly swelling disintegrants. On the contrary, the disintegration time is hardly affected if there is some strongly swelling disintegrant present in the tablet.

Methods of addition of Disintegrants:

Disintegrating agent can be added either prior to granulation (intragranular) or prior to compression (after granulation i.e. extragranular) or at both processing steps.

Extragranular fraction of disintegrant (usually, 50% of total disintegrant requires) facilitates breakup of tablets to granules and the intragranular addition of disintegrants produces further erosion of the granules to fine particles.

CHAPTER 2

LITERATURE REVIEW

2. LITERATURE REVIEW

J. Dwivedi., ***et. al,*** studied to develop Rosuvastatin calcium into immediate release tablets. Pre-formulation study and drug excipients compatibility study was done initially and the results obtained direct the way and method of formulation. Preformulation and drug excipients compatibility study, prototype formulation carried out for the dose of Rosuvastatin calcium 10 mg and optimized to get the final formula. Rosuvastatin calcium is prone to degradation so compaction and direct compression method is used. Granules were evaluated for tests such as bulk density, tapped density, compressibility index and Hauser's ratio and sieve analysis before compression. Tablets were tested for weight variation, thickness, hardness, friability and dissolution. In vitro dissolutions were performed and values were calculated.

Nyol Sandeep., ***et. al,*** studied of all dosage forms tablet is the most popular dosage form existing today because of its convenience of self administration, compactness and easy manufacturing, sometimes immediate onset of action is required than conventional therapy in many cases. So that to overcome these drawbacks, immediate release dosage form has emerged as alternative oral dosage forms. Immediate drug release dosage forms disintegrate rapidly after administration with enhanced rate of dissolution. The basic approach used in development tablets is the use of superdisintegrants like Cross linked Polyvinylpyrrolidone or crospovidone (Polyplasdone), Sodium starch glycolate (Primogel, Explotab), carboxymethylcellulose (Croscarmellose) etc. The development of immediate release therapy also provides an opportunity for a line extension in the marketplace, a wide range of drugs e.g., neuroleptics, cardiovascular drugs, analgesics, antihistamines and other drugs can be considered candidates for this dosage form.

Alpana, P.and kulkarni, et. al, had developed oral disintegrating tablet of rizatriptan benzoate with inhibited bitter taste. ODTs of Rizatriptan benzoate were prepared by using super disintegrants namely, sodium starch glycolate, crospovidone and croscaramellose sodium using the direct compression method. The evaluated formulations showed successful taste masking and rapid disintegration in the oral cavity with adequate dissolution.

C. F .Lourence, *et. al,* had studied on formulation and evaluation of rizatriptan benzoate mouth dissolving tablets. Mouth disintegration tablets of rizatriptan benzoate were prepared using super disintegrants crospovidone, carboxy methyl celluse calcium, indion 414 and 234 using the direct compression method.the tablets disintegrated invitro and *invivo* within 4to 7 seconds and 6 to 9 seconds, respectively. Almost 90% of drug was released from all formulation within 20 minutes.

BK Garg., *et. al,* has carried the study to develop and evaluate a pulsatile drug delivery system consisting of cores coated with two layers of swelling and rupturable coatings was prepared and evaluated as pulsatile drug delivery system. Cores containing Rosuvastatin calcium as model drug were prepared by direct compression of different ratios of spray-dried lactose and microcrystalline cellulose and were then coated sequentially with an inner swelling layer containing a superdisintegrant (croscarmellose sodium) and an outer rupturable layer of ethylcellulose. The effect of level of swelling layer was investigated. Rupture and dissolution tests were performed using the USP XXIV paddle method at 50 rpm in 0.1 N HCl. The lag time of the pulsatile release tablets decreased with increasing levels of swelling layer. Increasing levels of the ethylcellulose coating retarded the water uptake and thus prolonged the lag time.

Jigar A Patel., *et. al,* studied on developing immediate release tablet is accomplished by using a suitable diluents and super-disintegrants. Faster disintegration of the tablet administrated orally minimizes absorption time and improves its bioavailability in less time. Immediate Release tablet of Antibiotic drug is formulated using dry granulation using super disintegrant croscarmellose sodium. One of the important studies included in the present investigation is of study on process parameter effect on performance of the Immediate Release tablets. The effect of selected process parameters on critical properties of immediate release (IR) tablets were studied, like effect of disintegration time, friability, dissolution profile.

Ujwala R. Bagmar., *et. al,* carried a research work is to develop immediate release tablets of Fexofenadine hydrochloride. The rate of dissolution and bioavailability of the Fexofenadine HCL may be increased by using superdisintegrant in its immediate release tablets. Direct compression method was adapted to prepare the tablets by using lactose, microcrystalline cellulose as filler, crospovidone and sodium starch glycolate as superdisintegrant in different concentration (2-8%). Disintegration time decreased with increase in the level of crospovidone. Whereas, disintegration time increased with increase in the level of sodium starch glycolate. The results indicate that the selected batch of tablet formulation containing crospovidone provides DT between 3-6 minutes with sufficient crushing strength and accepted friability. It was concluded that immediate release tablet for Fexofenadine hydrochloride can be formulated for fast treatment of allergic rhinitis.

Mayank Bansal., *et. al,* studied on an immediate release tablet of Zaltoprofen for the treatment of pain and inflammation, by using superdisintgrant such as Croscarmellose sodium and different grades of microcrystalline cellulose. Immediate release tablets of Zaltoprofen were prepared by direct compression method using superdisintgrant such as

Croscarmellose sodium and different grades of microcrystalline cellulose in different ratios. Sodium starch glycolate was added to aid disintegration. Tablets were found to be satisfactory when evaluated for thickness, hardness, friability, weight uniformity, drug content, disintegration time and in vitro drug release. The tablet disintegration time was less than one minute for all the tablet formulations. The in vitro drug release in optimized formulation F14 was found to be 98.89 % in 45 min.

Rohit Vaishnani., ***et. al,*** studied on an various formulations of immediate release tablet of Paroxetine using different superdisintegrants (Sodium Starch Glycolate, Croscarmellose, Crospovidone) and different grades of dicalcium phosphate by wet granulation method. The granules and tablets of Paroxetine were evaluated for various pre and post compression parameters like Angle of repose, Compressibility index, Hausner's ratio, Tablet hardness, Friability, Weight variation, Drug content and in vitro dissolution. Their results were found satisfactory. The in vitro dissolution studies show the release is in the following order of superdisintegrants: Sodium Starch Glycolate > Croscarmellose > Crospovidone. These results suggest that, as determined by f2 factor (similarity factor) and maximum in vitro dissolution was found to be with Formulation F-7 and it clearly shows due to Sodium Starch Glycolate (4%)

Hitesh P. Patel., ***et al*** studied on The aim of this study was to compare the disintegrants efficiency of the three superdisintegrants (Ac-Di-Sol, Crospovidone, Sodium starch glycolate) by formulating Zolpidem Tartrate immediate release tablets by direct compression method. Disintegration efficiency of powder disintegrants compared by swelling & hydration capacity of disintegrants. While efficiency of disintegrants in tablets compared by various test like disintegration time, dissolution test, wetting time & maximal water uptake study of Zolpidem Tartrate

immediate release tablets. The rapid disintegration observed for the Ac-Di-Sol containing tablets, comparing three classes of superdisintegrants represented by Ac-Di-Sol, Crospovidone, Sodium starch glycolate (SSG). The disintegration efficiency was found in following decreasing order Ac-Di-Sol, Crospovidone and Sodium starch glycolate.

Sravani Shilpa. K., *et al* investigated is undertaken with an aim to develop pharmaceutically equivalent, stable, cost effective and quality improved formulation of clopidogrel bisulfate immediate release tablets The current study involves preparation and evaluation of clopidogrel bisulfate tablets, comparison of dissolution rate of optimized formula with innovator's product and estimation of similarity and difference factors.The similarity and dissimilarity factor obtained for clopidogrel bisulfate was found to be within the standards.The formulation F-6 exhibited similar release profile to that of innovators product at each time point. Hence, F-6 was considered as the best formulation.

Rajesh., *et al* carried a research work to develop a stable formulation of antibiotic drug clarithromycin as an immediate- release tablet. The task of developing immediate release tablet is accomplished by using suitable diluents and superdisintegrants. The formulation development work was initiated with wet granulation method and a total of 8 formulations (F1-F8) were made. The formulation F8 showed satisfactory physical parameters, and it was found to be stable among other formulations. Formulation F8 was subjected to 32 randomized full factorial optimization studies and 9 formulations (OF1-OF9) were developed and evaluated for various precompression and post compression parameters. The drug release of clarithromycin IR tablet (OF7) was found to be 101.62±0.48 at the end of 30 min.The tablets of OF7 optimized batch was subjected to accelerated stability studies as per ICH guidelines and the results showed that there were no significant changes in the physical and chemical parameters studied. From this study, it was concluded that

optimized clarithromycin tablet (OF7) containing croscarmellose sodium (3.029%) and Pregelatinized starch (6.029%) showed better characteristics of immediate release tablets.

Mansoor A. Khan., *et al* carried a research work to investigate correlation between disintegration and dissolution for immediate release tablets containing a high solubility drug and to identify formulations where disintegration test, instead of the dissolution test, may be used as the acceptance criteria based on International Conference on Harmonization Q6A guidelines. A statistical design of experiments was used to study the effect of filler, binder, disintegrating agent, and tablet hardness on the disintegration and dissolution of verapamil hydrochloride tablets. Slower dissolution was observed with increasing disintegration time when either the filler or the disintegrating agent was kept constant. However, no direct corelationship was observed between the disintegration and dissolution across all formulations due to the interactions between different formulation components. Although all tablets containing sodium carboxymethyl cellulose as the disintegrating agent, disintegrated in less than 3 min, half of them failed to meet the US Pharmacopeia 30 dissolution criteria for the verapamil hydrochloride tablets highlighting the dependence of dissolution process on the formulation components other than the disintegrating agent. The results identified only one formulation as suitable for using the disintegration test, instead of the dissolution test, as drug product acceptance criteria and highlight the need for systematic studies before using the disintegration test, instead of the dissolution test as the drug acceptance criteria.

Sanil Kumar Ramachandra Nair., *et al* studied to develop a pharmaceutically equivalent, stable, cost effective and quality improved formulation of immediate release tablets of Escitalopram Oxalate using different concentration of disintegrants. The tablets were compressed

using microcrystalline cellulose, colloidal anhydrous silica, croscarmellose sodium, talc, magnesium stearate and opadry white was used for coating the tablets. Croscarmellose sodium was used as the disintegrant in the formulation of immediate release tablets of Escitalopram Oxalate. The stability studies were carried out for the optimized batch for six months. The results of the present study showed that among all the formulations, F4 was better in all terms of preformulation and post compression parameters and showed comparably a good dissolution profile like that of the marketed product.

CHAPTER 3

AIM AND OBJECTIVE

3. AIM AND OBJECTIVES

- The present study is planned to develop sertraline into immediate release tablets by direct compression Method.
- Sertraline is a popular antidepressant medication commonly known as a selective serotonin reuptake inhibitor (SSRI), and is similar to drugs such as Citalopram and Fluoxetine. Despite marked structural differences between compounds in this drug class, SSRIs exert similar pharmacological effects.
- Sertraline It is used to treat major depressive disorder, obsessive–compulsive disorder, panic disorder, post-traumatic stress disorder, premenstrual dysphoric disorder, and social anxiety disorder. Sertraline is taken by mouth.
- Sertaline exhibits only 44% of oral bioavailability because of extensive first pass metabolism and has low solubility. In view of all the above reasons, this study will be an attempt to optimize the therapeutic effect of sertraline by formulating as mouth dissolving tablets by using various types of super disintegrants, glidants, and lubricants.
- To improve the oral bioavailability and onset of action Sertraline is prepared in the form of mouth dissolving tablets by direct compression method.

CHAPTER 4

PLAN OF WORK

4. PLAN OF WORK

- Literature Survey.
- Selection of drug and excipients
- Procurement of Drugs and Excipients/adjuvants.
- Preformulation Studies
    - Solubility
    - Drug and excipient compatibility studies by FTIR
    - Bulk density
    - True density
    - Carr's index
    - Hausner's ratio
    - Angle of repose
- Formulation development
- Evaluation Studies
    - Hardness
    - Friability
    - Thickness
    - Weight variation
    - Content uniformity
    - Assay
    - Wetting time
    - Uniformity of dispersion
    - Water absorption ratio
    - *Invitro* Dissolution study
    - Stability Studies

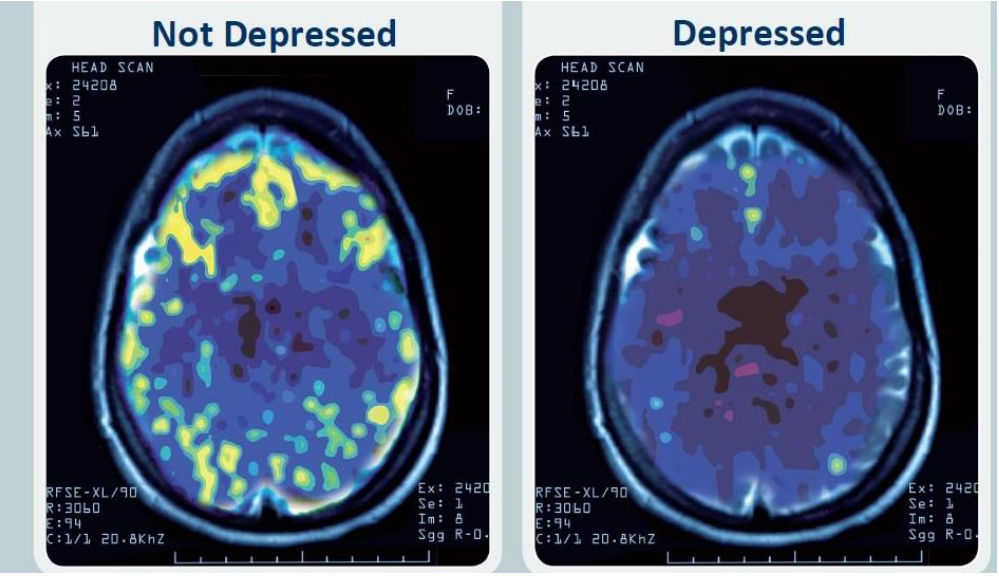
CHAPTER 5

DISEASE PROFILE

5. DISEASE PROFILE

Depression is a mood disorder that causes a persistent feeling of sadness and loss of interest. Also called major depressive disorder or clinical depression, it affects how the person feel, think and behave and can lead to a variety of emotional and physical problems.

Figure No-3 – BRAIN METABOLISM IN BRAIN.



Sometimes physical problems can cause depression. But other times, symptoms of depression are part of a more complex psychiatric problem. There are several different types or subtypes of depression, including:

Major depressive disorder

Dysthymia and chronic depression (now called persistent depressive disorder)

Seasonal affective disorder

Psychotic depression

Bipolar depression

5.1. MAJOR DEPRESSION[39]

An individual with major depression, or major depressive disorder, feels a profound and constant sense of hopelessness and despair.

Major depression is marked by a combination of symptoms that interfere with the person's ability to work, study, sleep, eat, and enjoy

once pleasurable activities. Major depression may occur only once but more commonly occurs several times in a lifetime.

5.2. WHAT ARE THE SYMPTOMS OF MAJOR DEPRESSION[40]

Symptoms of depression include:

A. Sadness
B. Irritability
C. Loss of interest in activities once enjoyed
D. Withdrawal from social activities
E. Inability to concentrate
F. Disrupted sleep
G. Fatigue or loss of energy
H. Appetite changes
I. Thoughts of suicide

5.3. CAUSES[39,40,41]

It's not known exactly what causes depression. As with many mental disorders, a variety of factors may be involved, such as:

- **Biological differences.** People with depression appear to have physical changes in their brains. The significance of these changes is still uncertain, but may eventually help pinpoint causes.
- **Brain chemistry.** Neurotransmitters are naturally occurring brain chemicals that likely play a role in depression. Recent research indicates that changes in the function and effect of these neurotransmitters and how they interact with neurocircuits involved in maintaining mood stability may play a significant role in depression and its treatment.
- **Hormones.** Changes in the body's balance of hormones may be involved in causing or triggering depression. Hormone changes can result with pregnancy and during the weeks or months after delivery (postpartum) and from thyroid problems, menopause or a number of other conditions.

- **Inherited traits.** Depression is more common in people whose blood relatives also have this condition. Researchers are trying to find genes that may be involved in causing depression.

5.4. DYSTHYMIA[41]

- Dysthymia, sometimes referred to as a form of chronic depression, is a less severe form of depression but the depression symptoms linger for a long period of time, typically years. Those who suffer from dysthymia are usually able to function normally, but seem consistently unhappy.
- It is common for a person with dysthymia to also develop superimposed periods of depression, which then lessen without fully going away. This is called "double depression."

5.5. TYPES OF DEPRESSION[41]

Symptoms caused by major depression can vary from person to person. To clarify the type of depression you have, your doctor may add one or more specifiers. A specifier means that you have depression with specific features, such as:

- **Anxious distress —** depression with unusual restlessness or worry about possible events or loss of control
- **Mixed features —** simultaneous depression and mania, which includes elevated self-esteem, talking too much and increased energy
- **Melancholic features —** severe depression with lack of response to something that used to bring pleasure and associated with early morning awakening, worsened mood in the morning, major changes in appetite, and feelings of guilt, agitation or sluggishness
- **Atypical features —** depression that includes the ability to be cheered by happy events, increased appetite, excessive need for sleep, sensitivity to rejection, and a heavy feeling in arms or legs

- **Psychotic features —** depression accompanied by delusions or hallucinations, which may involve personal inadequacy or other negative themes
- **Catatonia —** depression that includes motor activity that involves either uncontrollable and purposeless movement or fixed and inflexible posture
- **Peripartum onset —** depression that occurs during pregnancy or in the weeks or months after delivery (postpartum)
- **Seasonal pattern —** depression related to changes in seasons and reduced exposure to sunlight

5.6. OTHER DISORDERS THAT CAUSE DEPRESSION SYMPTOMS[40,41]

Several other disorders, such as those below, include depression as a symptom. It's important to get an accurate diagnosis, so you can get appropriate treatment.

- **Bipolar I and II disorders.** These mood disorders include mood swings that range from highs to lows. It's sometimes difficult to distinguish between bipolar disorder and depression.
- **Cyclothymic disorder.** Cyclothymic (sy-kloe-THIE-mik) disorder involves highs and lows that are milder than those of bipolar disorder.
- **Disruptive mood dysregulation disorder.** This mood disorder in children includes chronic and severe irritability and anger with frequent extreme temper outbursts. This disorder typically develops into depressive disorder or anxiety disorder during the teen years or adulthood.
- **Persistent depressive disorder.** Sometimes called dysthymia (dis-THIE-me-uh), this is a less severe but more chronic form of depression. While it's usually not disabling, persistent depressive disorder can prevent you from functioning normally in your daily routine and from living life to its fullest.
- **Premenstrual dysphoric disorder.** This involves depression symptoms associated with hormone changes that begin a week

before and improve within a few days after the onset of your period, and are minimal or gone after completion of your period.

- **Other depression disorders.** This includes depression that's caused by the use of recreational drugs, some prescribed medications or another medical condition.

5.7. TREATMENTS AND DRUGS[42]

Medications and psychological counseling (psychotherapy) are very effective for most people with depression. Your primary care doctor or psychiatrist can prescribe medications to relieve symptoms. However, many people with depression also benefit from seeing a psychologist or other mental health professional.

5.8. CLASSES OF ANTI-DEPRESSANT DRUGS[42]:

Table No: 3 CLASSES OF ANTI-DEPRESSANT DRUGS

S.No	Antidepressant type	Examples
1.	**SSRIs (selective serotonin reuptake inhibitors)**	Citalopram Escitalopram Fluoxetine Fluvoxamine Paroxetine **Sertraline**
2.	**SNRIs (serotonin and norepinephrine reuptake inhibitors)**	Duloxetine Venlafaxine Desvenlafaxine
3.	**Noradrenaline reuptake inhibitor**	Reboxetine
4.	**TCAs (tricyclic antidepressants)**	Amitriptyline Nortriptyline Clomipramine Dothiepin Doxepin Imipramine Trimipramine
5.	**RIMA (reversible inhibitor of monoamine oxidase)**	Moclobemide
6.	**Tetracyclic antidepressant**	Mianserin
7.	**Tetracyclic analogue of mianserin (sometimes called noradrenergic and specific serotonergic antidepressant [NaSSA])**	Mirtazapine
8.	**MAOIs (monoamine oxidase inhibitors)**	Phenelzine Tranylcypromine
9.	**Melatonergic antidepressant**	Agomelatine

5.9. SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)[42]:

SSRIs are one of the first choices when someone is first prescribed an antidepressant. This is because they are as effective as other types of antidepressant, but tend to have fewer side effects than some older types, such as tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs).

The following SSRIs are approved to treat depression, anxiety, and other mood disorders:

- Citalopram (Celexa)
- Escitalopram (Lexapro)
- Fluoxetine (Prozac)
- Fluvoxamine (Luvox, Luvox CR)
- Paroxetine (Paxil, Paxil CR)
- Sertraline (Zoloft)

5.9.1. HOW DO SSRIs WORK?

SSRIs work by enhancing the function of nerve cells in the brain that regulate emotion. Information is communicated between your brain cells with signals. The chemical messengers that deliver these signals are called neurotransmitters. Serotonin is one type of neurotransmitter.

When these brain cells (called neurons) send signals to one another, they release a little bit of a neurotransmitter so that the message can be delivered. They then have to take back the neurotransmitter they released so they can send the next message. This process of replacing the neurotransmitter is called “reuptake.”

If you’re struggling with depression, the areas of your brain that regulate mood and send messages using serotonin might not function properly. SSRIs help make more serotonin available by blocking the reuptake process. This allows serotonin to build up between neurons so messages can be sent correctly. They’re called “selective” serotonin reuptake inhibitors because they specifically target serotonin.

5.9.2. Mechanism of action[41]:

As their name indicates, SSRIs reduce the amount of serotonin that is reabsorbed by the presynaptic neuron. As a result, more of this neurotransmitter remains in the synaptic gap for a longer time, compensating for the lower levels of serotonin in some depressed people.

SSRIs are different from tricyclics, because they block only the reuptake pumps for serotonin, and not those for norepinephrine.
They do, however, affect norepinephrine indirectly, because the levels of this neurotransmitter are closely linked with those of serotonin; raising the level of serotonin automatically raises the level of norepinephrine as well.

5.9.3.SIDE EFFECTS:

Antidepressants are not addictive. However, you may experience some withdrawal effects on stopping your antidepressant. Reactions vary between medications and between people. All SSRIs have been reported to produce some withdrawal effects - physical discomfort, restlessness and flu-like symptoms - if suddenly stopped. These symptoms are reduced by stopping the medication gradually (over 2 weeks from higher doses).

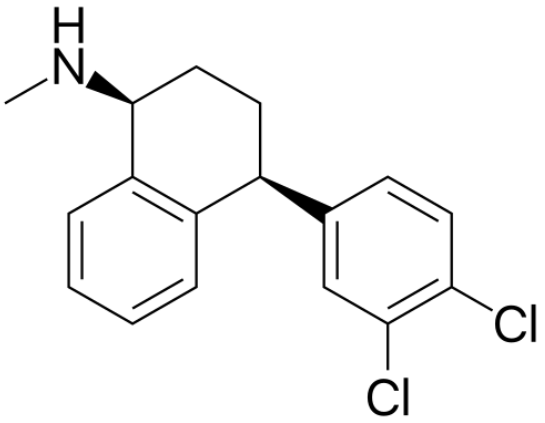
CHAPTER 6

DRUG PROFILE

6. DRUG PROFILE- SERTRALINE HCL

6.1. Description

Sertraline, is an antidepressant of the selective serotonin reuptake inhibitor (SSRI) class. It is used to treat major depressive disorder, obsessive–compulsive disorder, panic disorder, post-traumatic stress disorder, premenstrual dysphoric disorder, and social anxiety disorder. Sertraline is taken by mouth.



Chemical Structure of Sertraline

5.2. CHEMICAL DATA

- Empirical formula - $C_{17}H_{17}Cl_2N$
- Molecular weight - 342.69 g/mol
- CAS Registry No. - 79617-96-2

6.2.1. Systemic (IUPAC) Name:

(1S,4S)-4-(3,4-dichlorophenyl)-N-methyl-1,2,3,4-tetrahydronaphthalen-1-amine.

6.3. Pharmacology:

6.3.1 Indication

Sertraline is indicated for the management of major depressive disorder (MDD), post-traumatic stress disorder (PTSD), obsessive-

compulsive disorder (OCD), panic disorder (PD), premenstrual dysphoric disorder (PMDD), and social anxiety disorder (SAD). Common off-label uses for sertraline include the prevention of post stroke depression, generalized anxiety disorder (GAD), fibromyalgia, premature ejaculation, migraine prophylaxis, diabetic neuropathy, and neurocardiogenic syncope.

6.3.2. Pharmacodynamics

Sertraline improves or relieves the symptoms of depression, OCD, post-traumatic stress disorder, obsessive-compulsive disorder, panic disorder, and premenstrual dysphoric disorder via the inhibition of serotonin reuptake. Clinical studies have shown that it improves cognition in depressed patients. It has less sedative, anticholinergic, and cardiovascular effects than the tricyclic antidepressant drugs because it does not exert significant anticholinergic, antihistamine, or adrenergic (alpha1, alpha2, beta) blocking activity. The onset of action and beneficial effects are usually noticed after 4-6 weeks, for reasons that are not fully understood and currently under investigation.

6.3.3. Mechanism of action

Sertraline selectively inhibits the reuptake of serotonin (5-HT) at the presynaptic neuronal membrane, thereby increasing serotonergic activity. This results in an increased synaptic concentration of serotonin in the CNS, which leads to numerous functional changes associated with enhanced serotonergic neurotransmission. These changes are believed to be responsible for the antidepressant action and beneficial effects in obsessive-compulsive (and other anxiety related disorders). It has been hypothesized that obsessive-compulsive disorder, like depression, is also caused by the disregulation of serotonin.

In animal studies, chronic administration of sertraline results in down-regulation of brain norepinephrine receptors. Sertraline displays affinity for sigma-1 and 2 receptor binding sites, but binds with stronger affinity to sigma-1 binding sites. In vitro, sertraline shows little to no

affinity for GABA, dopaminergic, serotonergic (5HT1A, 5HT1B, 5HT2), or benzodiazepine receptors. It exerts weak inhibitory actions on the neuronal uptake of norepinephrine and dopamine and exhibits no inhibitory effects on the monoamine oxidase enzyme.

6.3. Pharmacokinetics:

Absorption:

Following once-daily administration of 50 to 200 mg for two weeks, the mean peak plasma concentrations (Cmax) of sertraline occurred between 4.5 to 8.4 hours after administration, and measured at 20 to 55 µg/L. Steady-state concentrations are reached after 1 week following once-daily administration, and vary greatly depending on the patient. Bioavailability has been estimated to be above 44%. The area under the curve in healthy volunteers after a 100mg dose of sertraline was 456 µg × h/mL in one study.

Effects of food on absorption

The effects of food on the bioavailability of the sertraline tablet and oral concentrate were studied in subjects given a single dose with and without food. For the tablet, AUC was slightly increased when sertraline was administered with food, the Cmax was 25% greater, and the time to peak plasma concentration was shortened by about 2.5 hours. For the oral concentrate preparation of sertraline, peak concentration was prolonged by approximately 1 hour with the ingestion of food

Distribution:

Sertraline is widely distributed, and its volume of distribution is estimated to be more than 20L/kg. Post-mortem studies in humans have measured liver tissue concentrations of 3.9–20 mg/kg for sertraline and between 1.4 to 11 mg/kg for its active metabolite, N-desmethyl-sertraline (DMS). Studies have also determined sertraline distributes into the brain, plasma, and serum. Sertraline is highly bound to serum proteins, at about 98%-99%.

Metabolism:

Sertraline is heavily metabolized in the liver and has one major active metabolite. It undergoes N-demethylation to form N-desmethylsertraline, which is much less potent in its pharmacological activity than sertraline. In addition to N-demethylation, sertraline metabolism involves N-hydroxylation, oxidative deamination, and finally, glucuronidation. The metabolism of sertraline is mainly catalyzed by CYP3A4 and CYP2B6, with some activity accounted for by CYP2C19 and CYP2D6.

Excretion:

Since sertraline is extensively metabolized, excretion of unchanged drug in the urine is a minor route of elimination, with 12-14% of unchanged sertraline excreted in the feces.

In pharmacokinetic studies, the clearance of a 200mg dose of sertraline in studies of both young and elderly patients ranged between 1.09 ± 0.38 L/h/kg - 1.35 ± 0.67 L/h/kg.

6.3.4. Pharmacokinetic Parameters:

- Bio-availability – 44%.
- Half life – 26 hours.
- Metabolism – Metabolized in the liver.
- Protein binding- ~98%.

6.4. Medical uses:

Sertraline is used to treat depression, panic attacks, obsessive compulsive disorder, post-traumatic stress disorder, social anxiety disorder (social phobia), and a severe form of premenstrual syndrome (premenstrual dysphoric disorder).This medication may improve mood, sleep, appetite, and energy level and may help restore interest in daily living. It may decrease fear, anxiety, unwanted thoughts, and the number of panic attacks. It may also reduce the urge to perform repeated tasks (compulsions such as hand-washing, counting, and checking) that

interfere with daily living. Sertraline is known as a selective serotonin reuptake inhibitor (SSRI). It works by helping to restore the balance of a certain natural substance (serotonin) in the brain.

6.4.1. Side Effects:

Commonly reported side effects of sertraline include: diarrhea, dizziness, drowsiness, dyspepsia, fatigue, insomnia, loose stools, nausea, tremor, headache, paresthesia, anorexia, decreased libido, delayed ejaculation, diaphoresis, ejaculation failure, and xerostomia. Other side effects include: abdominal pain, agitation, pain, vomiting, anxiety, hypouricemia, and malaise.

6.4.2. Dose:

Adult Dose for Depression & Obsessive Compulsive Disorder:

Initial dose: 50 mg orally once a day
Maintenance Dose: 50 to 200 mg orally once a day

Adult Dose for Panic Disorder, Social Anxiety Disorder & Post Traumatic Stress Disorder:

Initial dose: 25 mg orally once a day, increased after one week to 50 mg orally once a day
Maintenance dose: 50 to 200 mg orally once a day

Usual Adult Dose for Premenstrual Dysphoric Disorder:

Initial dose: 50 mg orally once a day during the menstrual cycle
Maintenance dose: 50 to 150 mg orally once a day during the menstrual cycle

Usual Pediatric Dose for Obsessive Compulsive Disorder:

6 to 12 years:

Initial dose: 25 mg orally once a day

Maintenance dose: 25 to 200 mg orally once a day

13 to 17 years:

Initial dose: 50 mg orally once a day

Maintenance dose: 50 to 200 mg orally once a day

CHAPTER 7

EXCIPIENT PROFILE

7. EXCIPIENTS PROFILE

7.1. Cellulose, Microcrystalline

Nonproprietary Names

BP: Microcrystalline Cellulose

JP: Microcrystalline Cellulose

PhEur: Cellulose, Microcrystalline

USP-NF: Microcrystalline Cellulose

Synonyms: Avicel PH

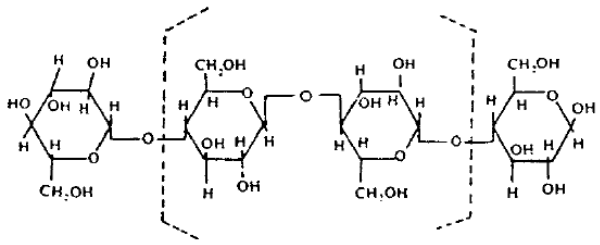
Chemical Name and CAS Registry Number: Cellulose [9004-34-6]

Empirical Formula and Molecular Weight:

$(C_6H_{10}O_5)n \approx 36\,000$

where n ≈ 220.

Structural Formula



Functional Category

Adsorbent, suspending agent, tablet and capsule diluents, tablet disintegrant.

Description

Microcrystalline cellulose is purified, partially depolymerized cellulose that occurs as a white, odorless, tasteless, crystalline powder composed of porous particles. It is commercially available in different particle sizes and moisture grades that have different properties and application.

The different commercial grades are available based on particle size distribution (μm)

Solubility:

Slightly soluble in 5% w/v sodium hydroxide solution, practically insoluble in water, dilute acids, and most organic solvents. They partly dissolve in dilute alkali and swell in it.

Table No 4: Uses of microcrystalline cellulose

Uses	Concentration %
Adsorbent	20-90
Antiadherent	5-20
Capsule binder/diluents	20-90
Tablet disintegrant	5-15
Tablet binder/diluents	20-90

7.2. Croscarmellose Sodium

Nonproprietary Names

BP: Croscarmellose Sodium

JP: Croscarmellose Sodium

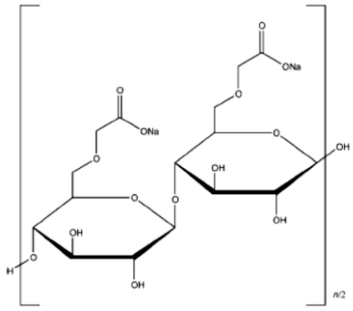
PhEur: Croscarmellose Sodium

USP-NF: Croscarmellose Sodium

Synonyms: Ac-Di-Sol, crosslinked carboxy methyl cellulose sodium, Explocel, modified cellulose gum, Nymcel, ZSX Pharmacel XL, Primellose, Solutab, Vivasol.

Chemical Name and CAS Registry Number:

Cellulose, carboxymethyl ether, sodium salt, crosslinked [74811-65-7]



Empirical Formula and Molecular Weight :

The USP 32 describes carboxymethylcellulose sodium as the sodium salt of a polycarboxymethyl ether of cellulose.

Structural Formula

Functional Category: Tablet and capsule disintegrant.

Description: Croscarmellose sodium occurs as an odorless, white or grayish white powder.

Solubility: Insoluble in water, croscarmellose sodium rapidly swells to 4–8 times its original volume on contact with water. Practically insoluble in acetone, ethanol and toluene.

Applications in Pharmaceutical Formulation or Technology

- Croscarmellose sodium is used in oral pharmaceutical formulations as a disintegrant for capsules, tablets, and granules.
- In tablet formulations, croscarmellose sodium may be used in both direct-compression and 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 a wet-granulation process.

7.3. Crospovidone

Nonproprietary Names

BP: Crospovidone

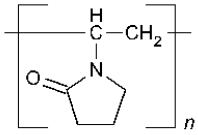
PhEur: Crospovidone

USP-NF: Crospovidone

Synonyms: Crospovidonum; E1202;Kollidon CL;Kollidon CL-M;

Chemical Name and CAS Registry Number: 1-Ethenyl-2-pyrrolidinone homo polymer [9003-39-8]

Empirical Formula and Molecular Weight :$(C_6H_9NO)n>1$ 000 000



Structural Formula

Functional Category: Crospovidone as tablet super disintegrant.

Description: Crospovidone is a white to creamy-white, finely divided, free flowing, practically tasteless, odorless or nearly odorless, hygroscopic powder.

The different commercial grades are available based on particle size distribution (μm)

Solubility

Practically insoluble in water and most common organic solvents.

Applications in Pharmaceutical Formulation or Technology

- Crospovidone is a water-insoluble tablet disintegrant and dissolution agent used at 2–5% concentration in tablets prepared by direct compression or wet- and dry-granulation methods.
- It rapidly exhibits high capillary activity and pronounced hydration capacity, with little tendency to form gels.
- Studies suggest that the particle size of crospovidone strongly influences disintegration of analgesic tablets. Larger particles provide a faster disintegration than smaller particles.
- Crospovidone can also be used as a solubility enhancer. With the technique of co-evaporation, crospovidone can be used to enhance the solubility of poorly soluble drugs.

7.4. Sodium Starch Glycolate

Nonproprietary Names

BP: Sodium Starch Glycolate

PhEur: Sodium Starch Glycolate

USP-NF: Sodium Starch Glycolate

Synonyms: Carboxymethyl starch, sodium salt, carboxymethylamylum natricum, Explosol, Explotab, starch carboxymethyl ether, sodium salt, Tablo,Vivastar P.

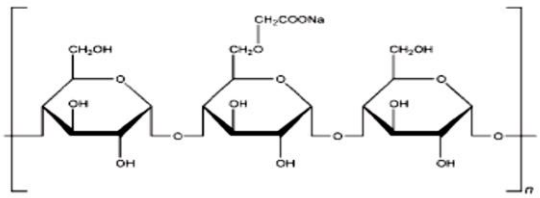
Chemical Name and CAS Registry Number:

Sodium carboxymethyl starch [9063-38-1]

Empirical Formula and Molecular Weight :

The molecular weight is typically $5X10^5$–110^6.

Structural Formula



Functional Category: Tablet and capsule disintegrant.

Description: Sodium starch glycolate is a white or almost white free-flowing very hygroscopic powder. When examined under a microscope it is seen to consist of granules, irregularly shaped, ovoid or pear-shaped, 30–100 mm in size, or rounded, 10–35 mm in size, compound granules consisting of 2–4 components occur occasionally. The granules show considerable swelling in contact with water.

Solubility

In water, sodium starch glycolate swells to up to 300 times its volume.

Applications in Pharmaceutical Formulation or Technology

- Sodium starch glycolate is widely used in oral pharmaceuticals as a disintegrant in capsuleand tablet formulations.
- It is commonly used in tablets prepared by either direct-compression or wet-granulation processes.
- The usual concentration employed in a formulation is between 2% and 8%, with the optimum concentration about 4%, although in many cases 2% is sufficient.
- Disintegration occurs by rapid uptake of water followed by rapid and enormous swelling. Although the effectiveness of many disintegrants is affected by the presence of hydrophobic excipients such as lubricants.
- Increasing the tablet compression pressure also appears to have no effect on disintegration time.

7.5. Mannitol

Nonproprietary Names

BP : Mannitol

JP : D-Mannitol

PhEur : Mannitol

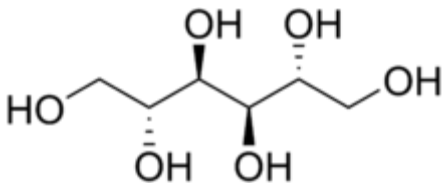
USP : Mannitol

Synonyms: Cordycepic acid, C Pharm Mannidex, E421, Emprove, manna sugar.

Chemical Name and CAS Registry Number: D-Mannitol [69-65-8]

Empirical Formula and Molecular Weight: $C_6H_{14}O_6$ and 182.17

Structural Formula



Functional Category

Diluent, plasticizer, sweetening agent, tablet and capsule diluents, therapeutic agent, tonicity agent.

Description

Mannitol is D-mannitol. It is a hexahydric alcohol related to mannose and isomeric with sorbitol. Mannitol occurs as a white, odorless, crystalline powder, or free flowing granules. It has a sweet taste, approximately as sweet as glucose and half as sweet as sucrose, and imparts a cooling sensation in the mouth. Microscopically, it appears as orthorhombic needles when crystallized from alcohol. Mannitol shows polymorphism.

Applications in Pharmaceutical Formulation or Technology

- Mannitol is widely used in pharmaceutical formulations and food products. In pharmaceutical preparations it is primarily used as a diluent (10–90% w/w) in tablet formulations.
- Mannitol may be used in direct-compression tablet applications for which the granular and spray-dried forms are available.

- Mannitol is commonly used as an excipient in the manufacture of chewable tablet.
- In lyophilized preparations, mannitol (20–90% w/w) has been included as a carrier to produce a stiff, homogeneous cake that improves the appearance of the lyophilized plug in a vial. A pyrogen-free form is available specifically for this use.
- Mannitol has also been used to prevent thickening in aqueous antacid suspensions of aluminum hydroxide (<7% w/v).

7.6. Magnesium Stearate

Nonproprietary Names

BP: Magnesium Stearate

JP: Magnesium Stearate

PhEur: Magnesium Stearate

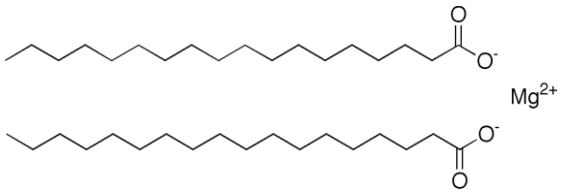
USP-NF: Magnesium Stearate

Synonyms: Dibasic magnesium stearate, magnesium distearate, magnesia stearas.

Chemical Name and CAS Registry Number: Octa decanoic acid magnesium salt and [557-04-0]

Empirical Formula and Molecular Weight: $C_{36}H_{70}MgO_4$ and591.24

Structural Formula: $[CH_3(CH2)_{16}COO]_2Mg$



Functional Category: Tablet and capsule lubricant

Description:

Magnesium stearate as a compound of magnesium with a mixture of solid organic acids that consists chiefly of variable proportions of magnesium stearate and magnesium palmitate. ($C_{32}H_{62}MgO_4$).

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

Applications in Pharmaceutical Formulation or Technology

Magnesium stearate is widely used in cosmetics, foods, and pharmaceutical formulations. It is primarily used as a lubricant in capsule and tablet manufacture at concentrations between 0.25% and 5.0% w/w. It is also used in barrier creams.

7.7. Aspartame

Nonproprietary Names

BP: Aspartame

PhEur: Aspartame

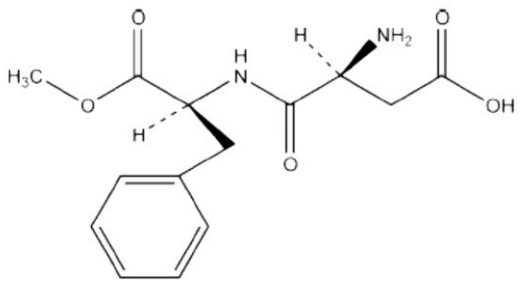
USP-NF: Aspartame

Synonyms: 3-amino-N-(a-methoxycarbonylphenethyl)-succinamic acid, APM, aspartamum, aspartyl phenylamine methyl ester, Canderel, E951, Equal, methyl N-L-a-aspartyl-L-phenylalaninate, NatraTaste, NutraSweet, Pal Sweet, Pal Sweet Diet.

Chemical Name and CAS Registry Number: N-L-a-Aspartyl-L-phenylalanine 1-methyl ester [22839-47-0]

Empirical Formula and Molecular Weight: C14H18N2O5 294.30

Structural Formula:



Functional Category: Sweetening agent.

Description: Aspartame occurs as an off white, almost odorless crystalline powder with an intensely sweet taste.

Applications in Pharmaceutical Formulation or Technology

Aspartame is used as an intense sweetening agent in beverage products, food products, and table-top sweeteners, and in pharmaceutical preparations including tablets, powder mixes, and vitamin preparations. 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.

Unlike some other intense sweeteners, aspartame is metabolized in the body and consequently has some nutritive value: 1 g provides approximately 17 kJ (4 kcal).

CHAPTER 8

MATERIALS AND EQUIPMENTS

8. MATERIALS AND EQUIPEMENTS

8.1. MATERIALS USED:

Table No 5: Materials Used

S.No	Materials	Suppliers / Manufacturer
1	Sertraline HCL	Apex Pharmaceuticals.
2	MCC PH 102 (Avicel 102)	Loba Chem
3	Polyplasdone XL (Crospovidone XL-10)	Loba Chem
4	Croscarmellose sodium (CCS)	Nice
5	Sodium Starch Glycolate (SSG)	Nice
6	Magnesium stearate	Loba Chem
7	Mannitol SD-200	Nice
8	Aspartame	Loba Chem

8.2. INSTRUMENTS USED

Table No 6: Instruments Used

S.No	Equipment	Manufacturer
1	Digital Balance	Wensar PGB - 300
2	Sieves	Indicot (India)
3	Tapped Density Tester	Electrolab
4	Mechanical Stirrer	Remi Motors Bombay
5	UV-Visible Spectrophotometer	LAB INDIA UV 3000+
6	Dissolution Test Apparatus	Labindia Analytical Instruments Pvt Ltd. Mumbai , Model-DISSO 2000
7	Temperature controller(hot air oven)	GABAKS
8	FTIR	BRUKER HTS-XT
9	Compression machine	Proton Mini press
10	Vernier Calipers	Mitutoyo
11	Disintegration Test Apparatus, USP.	ROLEX

CHAPTER 9

PREFORMULATION

9. PREFORMULATION

Preformulation testing is first step in the rational development of dosage forms of a drug substance. It can be defined as – " as investigation of physical and chemical properties of a drug substance alone and when combined with excipients". The overall objective of preformulation testing is to generate information useful to the formulation in developing stable and bioavailable dosage forms that can be mass produced. The preformulation should start at the point after biological screening, when a decision is made for further development of compound in clinical trials. The Preformulation studies should consider the following before going through the formal program which includes:

- Available physicochemical data (including chemical structure and different salts available).
- Anticipated dose
- Supply situation and development schedule.
- Availability of stability , assay.
- Nature of information the formulator should have or would like to have.

The following preformulation studies were performed for the obtained sample of drug.

9.1. Organoleptic properties

9.1.1. Color and nature

Transferred small quantity of the sample on a white piece of paper, spreaded the powder and examined visually.

Sertraline white fine powder.

9.1.2. Taste and odour

Very less quantity of Sertraline was used to get taste with the help of tongue as well as smelled to get the odor

9.1.3. Particle Size , Shape and Surface Area

Various physical and chemical properties of drug substances are affected by their particle size distribution and shapes. Size also plays a role inthe homogeneity of final tablet. When large differences in size exist between the API and excipientsm mutual sieving (demixing) effects can occur making through mixing difficult on, it attained, difficult to maintain during the subsequent processing steps.

If the material become too fine, then undesirable properties such as electrostatin force effects and other surface active properties causing undue stickiness and lack of flowability manifest. It is probably safest to grind most drugs having particles that are approx 100μm in diameter.

Table No: 7. General Techniques For Determining Particle Size

Techniques	Particle size(μm)
Microscopic	1-100
Sieve	>50
Sedimentation	>1
Eutriation	1-50
Centrifugal	<50
Permeability	>1
Light Scattering	0.5-50

9.2. Physical characteristics:

9.2.1. Flow properties:

The flow properties of powders are critical for an efficient tableting operation. A good flow of powder or granulation to be compressed is necessary to assure efficient missing and acceptable weight uniformity for the compressed tablets. If a drug is identified at the pre formulation stage to be “poorly flowable”, the problem can be solved by selecting appropriate excipients. In some cases, drug powders may have to be pre-compressed or granulated to improve their flow properties. During pre

formulation evaluation of drug substance, therefore, its flowability characteristic should be studied, especially when the anticipated dose of the drug is large.

9.2.2.Angle of Repose:

Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and the horizontal plane.

Procedure:

A funnel was kept vertically in a stand at a specified height above a graph paper placed on a horizontal surface. The funnel bottom is closed and 10 gm of sample powder is filled in funnel. Then funnel was opened to release the powder on the paper to form a smooth conical heap, is found by measuring in different direction. The height of the heap was measured by using scale. The values of angle of repose are calculated by using the following formula:

$$\tan\theta = h/r$$

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

Where, θ – angle of repose

h- Height of the heap

r - Radius of the heap

Table No: 8. Angle of repose limits.

Angel of repose	**Flowability**
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

The results shown in results and discussion.

9.2.3.Bulk density

Bulk density is the ratio of mass of powder to the bulk volume. Bulk density largely depends on particle shape, as the particles become more spherical in shape, bulk density is increase. In addition as granules size increase, bulk density decrease.

Bulk density is determined by measuring the volume of a known mass of powder sample that has been passed through a screen into a graduated cylinder.

Procedure:

A known quantity of powder was poured into the measuring cylinder carefully level the powder with out compacting, if necessary and read the unsettled apparent volume. Calculate the bulk density, in gm per ml, by the formula

$$(\rho_b) = m / V_b.$$

Where, ρ_b =Bulk Density
m = mass of powder
V_b = initial / bulk volume

The results shown in results and discussion

Tapped density:

Tapped density is the ratio of mass of powder to the tapped volume.

Procedure:

A quantity of 5g of the powder (W) from each formula was introduced into a 25 ml measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2 sec intervals. The tapping was continued until no further change in volume was noted. Calculate the tapped density, in gm per ml, by the formula:

$$(\rho_t) = m/V_t$$

Where, ρ_t =Tapped Density
m = mass of powder
V_t= final / tapped volume

9.2.4.Measurement of Powder Compressibility:

The compressibility Index are measures of the propensity of a powder to be compressed. As such, they are measures of the relative importance of inter particulate interactions. In a free flowing powder, such interactions are generally less and tapped densities will be closer in value. For poorer flowing materials, there are frequently greater inter particle interactions, and a greater difference between bulk and tapped densities will be observed. These differences are reflected in the compressibility Index Calculated by the formula,

$$\% \text{ Compressibility (Carr's index)} = \frac{\text{Tapped density - Initial bulk density}}{\text{Tapped density}} \times 100$$

Table No: 9. Flow properties and corresponding Carr's Index values

Excellent	<10
Good	11 – 15
Fair	16 – 20
Possible	21 – 25
Poor	26 – 31
Very poor	32 – 37
Very very poor	>38

The results are shown in results and discussion

9.2.5.Hausner Ratio:

It is the ratio of volume of tapped volume or tapped density to bulk density. **Hausner Ratio = Vb/Vt or ρ_t / ρ_b.**

Table No: 10. Flow Properties and Corresponding Hausner's ratio

Excellent	1.00 – 1.11
Good	1.1 – 1.18
Fair	1.19 – 1.25
Possible	1.26 -1.34
Very poor	1.35 -1.45
Very very poor	>1.60

9.2.6. Melting point:

It is one of the parameters to judge the purity of crude drugs. In case of pure chemicals, melting points are very sharp and constant.

Procedure:

A small quantity of powder was placed into a fusion tube. That tube is placed in the melting point apparatus containing castor oil. The temperature of the castor oil was gradual increased automatically and read the temperature at which powder started to melt and the temperature when all the powder gets melted. The results shown in results and discussion.

9.2.7. Solution properties:

9.2.7 a) p^H of the solution

Weighed and transferred accurately about 1.0 g of sample in a 200 ml clean and dried beaker, dissolved in carbon dioxide free water and made up the volume to 100 ml with same solvent, mixed. Read the pH of freshly prepared solution by using precalibrated pH meter. The results are shown in results and Discussion.

9.2.7 b) Solubility:

A semi quantitative determination of the solubility was made by adding solvent in small incremental amount to a test tube containing fixed quantity of solute or vice versa. After each addition, the system is vigorously shaken and examined visually for any undissolved solute

particles. The solubility are expressed in terms of ratio of solute and solvent. The results are shown in results and discussion.

9.2.8 Identification of drug and compatibility study:

9.2.8 a) Identification of drug By FT-IR:

The drug can be identified by using FT-IR.

9.2.8 b) By Physical observation

It was determined as per procedure given in method section. The following table illustrated the result.

Table No:11. Physical Compatibility Studies

Test	Observations	Inference
Physical compatibility	No change of color	These materials are compatible for formulations.

9.2.8 c) Procedure By FT-IR Studies

The IR spectrums of the Sertraline with excipients were taken by preparing dispersion in dry potassium bromide under dry condition. Superimposed these spectra. The transmission minima (absorption maxima) in the spectra obtained with the sample corresponded in position and relative size to those in the spectrum obtained with the standards.

9.3. UV SPECTROSCOPIC METHOD FOR ANALYSIS OF SERTRALINE

9.3.1. CALIBRATION CURVE OF SERTRALINE:

Measured the absorbance of the above prepared standard solutions by using phosphate saline buffer (PBS 7.4) at λmax 235 nm. Plotted a graph of concentration (in μg/ml) on X axis and absorbance (in nm) on Y axis

CHAPTER 10

FORMULATION

10. FORMULATION AND DEVELOPMENT OF SERTRALINE HCL IMMEDIATE RELEASE TABLETS

Table No: 13. FORMULATION

INGREDIENTS(in mg)	FORMULATION BATCHES											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Sertraline HCL	50	50	50	50	50	50	50	50	50	50	50	50
MCC PH 102 (Avicel 102)	200	200	200	200	200	200	200	200	200	200	200	200
Polyplasdone XL (Crospovidone XL-10)									4	8	12	16
Croscarmellose sodium (CCS)	4	8	12	16								
Sodium Starch Glycolate (SSG)					4	8	12	16				
Mannitol	87	83	79	75	87	83	79	75	87	83	79	75
Magnesium Stearate	2	2	2	2	2	2	2	2	2	2	2	2
Aspartamate	7	7	7	7	7	7	7	7	7	7	7	7
Average Weight	350	350	350	350	350	350	350	350	350	350	350	350

Procedure:

All the ingredients were weighed and mixed well. Then it is tableted by direct compression method (proton Mini Press 9mm Punch).

CHAPTER 11

EVALUATION

11. EVALUATION

11.1. PRE-COMPRESSION PARAMETERS:

A) Angle of repose:

Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and the horizontal plane.

5 grams of the sample was taken in a funnel fixed in a holder (6 cm) above the surface at an appropriate height and a graph of sheet was placed below the funnel. The sample was passed through the funnel slowly. The height of the powder heap formed was measured. The circumference of the heap formed was drawn with a pencil on the graph paper. The radius was measured and the angle of repose was determined using the above formula. This was repeated five times for a sample.

Table No: 14. Flow properties and corresponding Angle of Repose

Flow property	Angle of Repose (Degree)
Excellent	25-30
Good	31-35
Fair-aid not needed	36-40
Passable- may hang up	41-45
Poor- must agitate, vibrate	46-55
Very poor	56-65
Very, very poor	> 66

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

Where,

h = height,

r = radius,

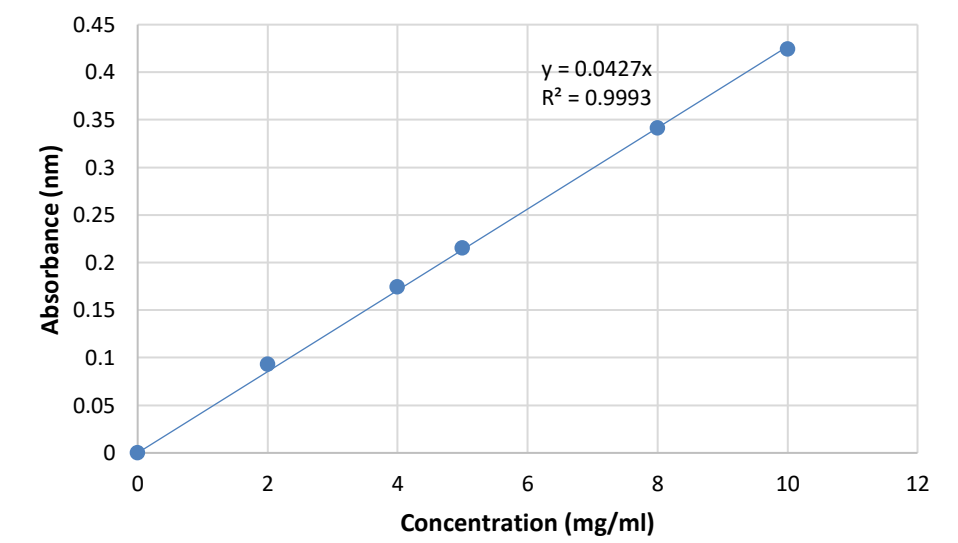
θ = Angle of repose.

The results are given in results and discussion.

TableNo: 12. Calibration curve for Sertraline

S. No.	Concentration (µg/ml)	Absorbance (nm)
1	0	0
2	2	0.093
3	4	0.174
4	5	0.215
5	8	0.341
6	10	0.424
Slope	**0.0427**	
R^2	**0.9993**	

Figure No: 4 : Caliberation Curve of Sertraline



B) Determination of bulk density and tapped density:

A quantity of 5g of the powder (W) from each formula was introduced into a 25 ml measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2 sec intervals. The tapping was continued until no further change in volume was noted. The bulk density, and tapped density were calculated using the following formulas

$$\text{Bulk density}(\rho_b) = m / V_b$$

$$\text{Tapped density}(\rho_t) = m/V_t$$

Where,

m = mass of the powder,

V_b = initial or bulk volume,

V_t = final or tapped volume.

The results are shown in results and discussion.

C)Measurement of Hausner ratio and Carr's Index

C1).Hausner's Ration:

Hausner's ratio indicates the flow properties of powder and measured by the ratio of tapped density to bulk density. Hausner's ratio was determined by the given formula:

Hausner Ratio = Vb/Vt

Where,

V_b = initial or bulk volume

V_t = final or tapped volume

The results are shown in results and discussion.

Table No: 15. Scale of flowability

Compressibility index (%)	Flow character	Hausner Ratio
≤ 10	Excellent	1.10-1.11
11-15	Good	1.12-1.18
16-20	Fair	1.19-1.25
21-25	Passable	1.26-1.34

26-31	Poor	1.35-1.45
32-37	Very poor	1.46-1.59
>38	Very, very poor	>1.60

C2).Carr's Index/Compressibility Index:

Compressibility is the ability of powder to decrease in volume under pressure using bulk density and tapped density the percentage compressibility of powder were determined, which is given as carr's compressibility index. It is indirectly related to the relative flow rate. Carr's compressibility index was determined by the given formula

$$\text{\% Compressibility (Carr's index)} = \frac{\text{Tapped density - Initial bulk density}}{\text{Tapped density}} \times 100$$

The results shown in results and discussion.

11.2.EVALUATION OF SERTRALINE:

A)Weight Variation Test:

The tablet of one particular batch should have uniformity in weight. If any weight variation is found, it should fall within the prescribed limits. According to USP maximum % deviation allowed are as follows :-

Table No: 16.Weight Variation Test.

Average weight of tablets(mg)	Maximum % difference allowed
130mg or less	±10%
130-324mg	±7.5%
Above 324mg	±5%

A sample of 20 tablets is selected randomly from a particular batch and weighed individually and collectively. The average weight of the tablets is calculated. The individual weights are then compared with average weight. The weights of not more than two of the tablets should not differ and calculate the average weight by more than the prescribed limit and no tablet should differ by more than the double the limits.

$$\% \text{ Deviation} = \frac{\text{Tablet weight-Average weight}}{\text{Tablet weight}} \times 100$$

The results shown in results and discussion

B) Friability Test:

20 tablets were weighed and subjected to rotate on friability test apparatus. The drum rotated at a speed of 25 rpm for 4 minutes, then dedusted and reweighed the tablets. Percentage friability was calculated by the following formula.

$$\text{Percentage of Friability (\%F)} = 100\ (1 - w/w_0)$$

Where,

Wo = Initial weight,

W = Final weight.

Percentage friability of tablets less than 1% is considered acceptable. The results shown in results and discussion.

C) Hardness Test:

Hardness of a tablet determines its tensile strength. It must be such that the tablets withstand the shock of handling, packing, and shipping. It is measured in terms of load/pressure required to crush it when placed on its edge. Generally, two types of hardness testers are used to determine the hardness.

C1) Monsanto Hardness Tester:

It consists of a barrel containing a compressible spring held between two plungers. The spring can be compressed by moving the knob forward. The tablet to be tested held between a fixed and moving plunger and reading of the indicator is adjusted to zero. The force applied to the edge of the tablet is gradually increased by moving the screw know forward until the breaks. The reading is noted from the scale which indicates the pressure required in kg or lb/$cm^2$to break the tablet. Hardness of 4kg/cm^2 is considered to be minimum requirement.

C2) Pfizer Tablet Hardness Tester:

This is slightly improved instrument used for determing the hardness of tablet. It works on the principle of plier. Pressure gauze is fitted on one arm of the tester. The tablet to be tested is put vertically in between the jaws which are pressed with hand until the tablet breaks. The reading can be noted from the indicator of the pressure gauze in terms of kg or lbs.

The hardness of a sample batch of Sertraline tablets was carried out by using Monsanto type hardness tester. The hardness of the tablet kg / cm^2 was measured.

The results are shown in results and discussion.

D) Thickness Test:

Control of physical dimension of the tablets such as sizes and thickness is essential for consumer acceptance and to maintain tablet to tablet uniformity. Manufacturers set the limits on the thickness of the tablets of their products in order to avoid any problems during automatic counting and packing. If the thickness of the tablet goes beyond a certain limit, it may block the channels of the machines. Hence there should be in-process control to maintain the thickness of the tablets. The dimensional specifications were measured using Vernier calipers.

Six tablets from each batch were tested and average values were calculated. The thickness of the tablet is mostly related to the tablet hardness can be uses as initial control parameter.

The results are shown in results and discussion.

D1) Diameter and Shape:

The diameter and shape of the tablets are determined by the dies and punches used for the compression. Less concave the punches, the more flat will be the tablets. Conversely, the more concave the punches, more convex would be the resulting tablets. Similarly, punches having raised impressions will produce recessed impressions on the tablets. Whereas punches having recessed impression, will produce raised impressions on the tablet surface. Therefore, proper selection of punches and dies should be done so as to produce tablets will desired diameter and shape.

D2) Drug content:

Weigh and powdered 10 tablets in a mortar. From this powder equivalent to 100mg of Sertraline was taken in a 100ml volumetric flask to this water was added and then the solution was subjected to sonication for about 10min's for complete solubilization of drug and the solution was made up to the mark with water filtered the drug content was estimated by measuring the absorbance at 244 nm by using UV-Visible spectrophotometer.

E) Disintegration Time:

The test is performed *invitro* to determine the time in which a tablet disintegrates in the water at the 37±2°C. The apparatus which is used to simulate all the conditions of mouth, for the determination of disintegration time is called as Disintegration Time.

It consist of two hot plates with housing for beakers, thermostatically controlled heaters to maintain the temperature, two baskets each having provision for fixing 6 glass or plastic tubes provided

with guided discs and stainless wire mesh. Each unit is suitable for performing two tests at a time.

The glass or plastic tubes are open at one end and fitted with sieve No. 10 mesh at the other end. The tubes are suspended in bath containing water or suitable liquid which is maintained through a distance of 75mm, the volume of the liquid and the distance of movement is adjusted in such a way that the highest point, the sieve should break the surface of the liquid.

six tablets are placed in each of the six tubes along with a guided plastic disc over the tablets tube and the assembly was suspended into the 1000ml beaker containing Water maintained at 37±2˚C and operated the apparatus for 15 minutes. The tubes are allowed to move up and down as per the specification discussed above and the disintegration time is noted when all the tablets particles have passed through the sieve. The disintegration time should comply with official time unless otherwise in the monographs. The assembly was removed from the liquid and the tablets were observed. If one or two tablets fail to disintegrate completely, repeat the test on 12 additional tablets. The requirement is met if not less than 16 of the total of 18 tablets tested are disintegrated.

E) Wetting time and water absorption ratio:

Wetting time of dosage form is related to with the contact angle. Lower wetting time implies a quicker disintegration of the tablet.

E1) Wetting time:

It is closely related to the inner structure of the tablets and to the hydrophilicity of the excipients. To measure wetting time, five circular tissue papers of 10cm diameter are placed in a petridish with a 10cm diameter. 10ml of water containing eosin, a water soluble dye, is added to petridish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time.

E2) Water absorption ratio:

A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of water. A tablet was put on the paper & the time required for complete wetting was measured. The wetted tablet was then weighed. The water absorption ratio, *R* can be the determined according to the following equation;

$$R = 100 (Wa-Wb) / Wb$$

Where,

Wb; The weight of the tablet before keeping in the petridish.

Wa; The wetted tablet from the petridish is taken and reweighed.

F) Dissolution:

F1) Dissolution Rate:

Dissolution rate is defined as the amount of solute dissolved in a given solvent per unit time under standard conditions of temperature, pH, solvent composition and constant solid surface area. The developed dissolution test can serve also a routine control mechanism to assure the proper dissolution characteristics, as well as the uniformity of regular production.

F2) Measurement of the Intrinsic Dissolution Rate:

- This measurement is extremely important input factor during the initial drug screening and formulation development programs.
- Measurement over the entire physiological pH range can be very useful in predicting whether the absorption of moderately or poorly soluble drugs is dissolution rate limited.
- Such information is essential in order to develop a suitable dosage form that is free from bioavailability problems.
- The information also is very useful for improving existing formulations that have demonstrated bioavailability problems.
- It is important to point out while the intrinsic dissolution rate data is very useful in characterizing the solubility behavior of drug

substance, it is of little value in describing the characteristics of the pharmaceutical forms.

F3) Dissolution Apparatus of Immediate Release Sertraline tablets:

invitro dissolution of Sertraline was studied in USP dissolution apparatus (Electrolab) employing a Basket stirrer. 900 ml Water phosphate saline buffer (PBS 7.4) was used as dissolution medium at 50 rpm. The temperature of 37 ± 0.5 °C was maintained throughout the experiment. Complex equivalent to mg of Sertraline was used in each test. 5 ml of sample of dissolution medium were withdrawn by means of syringe fitted with pre-filter at known intervals of time and analyzed for drug release by measuring the absorbance at 235 nm after suitable dilution with phosphate buffer. The volume withdrawn at each time interval was replaced with fresh quantity of dissolution medium. The amount of Sertraline released was calculated and plotted against time and compared with marketed drug was studied.

F4) Dissolution Study

***In-vitro* release profile:**

Medium : phosphate saline buffer (PBS 7.4).
Apparatus : USP II (Paddle)
Speed : 50 rpm
Time : 45 minutes
Temperature : 37 ^{0}C ± 0.5 ^{0}C
λ Max : 235 nm

Perform the test on six tablets place one tablet in each dissolution vessel containing 900 ml of phosphate saline buffer (PBS 7.4) maintained at 37 ^{0}C ± 0.5 ^{0}C. At specified time withdrawn required amount of sample and replace the same amount with (maintain sink condition), then absorbance was taken and calculate percentage release.

$$\% \text{ Purity} = \frac{\text{Absorbance X 900 X Dilution}}{\text{Slope X 1000 X label claim}} \times 100$$

The results are given in results & discussion.

G) Stability studies:

The optimized tablets were packed in amber-colored bottle, which was tightly plugged with cotton and capped. It was then stored at 40°C / 75% RH for 12 weeks. The tablets were evaluated for hardness, drug content and dissolution study and compared with tablets evaluated immediately after manufacturing.

CHAPTER 12

RESULTS AND DISCUSSION

12. RESULT AND DISCUSSION

12.1.Pre formulation Studies:

Organoleptic properties:

These tests were performed as per procedure. The results are illustrated in following table.

Table No. 17: Organoleptic Properties

Test	Specification / limits	Observations
Color	White color Crystalline	white powder
Odour	Odourless	Odourless

The result complies as per specification.

Angle of repose :

It was determined as per procedure given in material and method part. The results are,

Table No.18: Flow properties

Material	Angle of repose
Sertraline	34°.36”

The result shows that drug having poor flow.

Bulk density and tapped density:

It was determined as per procedure given in material and method part. The results are,

Table No.19: Density

Material	Bulk Density (gm/ml)	Tapped density (gm/ml)
Sertraline	0.45	0.51

Powder compressibility:

It was determined as per procedure given in material and method part. The results are,

Table No.20: Powder Compressibility

Materials	Compressibility index	Hausner ratio
Sertraline	32.41%	1.44

Melting point:

It was determined as per procedure given in material and method part. The results are,

Table No. 21: Melting point

Material	Melting point range	Result
Sertraline	245-246^0 C	Complies

The result indicates that the Sertraline drug was pure one.

SOLUTION PROPERTIES:

pH of the solutions

pH of the solution was determined as per procedure given in material and method part.

Table No.22: pH

Material	Test	Specification	Observation
Sertraline	pH	5.3	Complies

The result complies as per specification

Solubility:

It was determined as per procedure given in 9.4.2 in material and method part. The following table 17 illustrated the result.

Table No.23: Solubility

Test	Specification	Result
Solubility	It is soluble in water and slightly soluble in isopropyl alcohol.	Complies

The result complies as per specification.

Drug - Excipient Compatibility Studies

A) Physical Observation:

There are no such changes in the physical observation after mixing of ingredients.

B) Drug Identification by FTIR:

The graph is compared with the standard FTIR graph given in pharmacopoeia or prescribed standards and confirmed through the corresponding peaks.

Table No. 24: Peak of functional groups of Sertraline Oxalate observed in IR spectra of compatibility studies:

Value of Peaks (cm^{-1})	Indicating Bond
3010	Ar-CH- Str
1582, 1468	-C≡C Stretch
2960	Aliphatic –CH Str. of CH_3
789	C-Cl Str.
2810	CH Str of Tetrahydro napthaline
3430	C-NH str.
1428	CH Bending of Tetrahydro napthaline

- In order to check the integrity of the drug in the formulation, FTIR spectra of pure drug (Sertraline Oxalate) and mixture of drug excipients were taken and compared. The FTIR spectrum of Sertraline oxalate reveal the presence of peaks at 1506.48 due to the presence of C-C stretching, 1708.99 due to the presence of C=O stretching, 2231.71 due to the presence of C≡C or C≡N stretching, 3030.27 due to the presence of O-H stretching, 3624.37 due to the presence of O-H stretching.
- Major frequencies of functional groups of pure drug remain intact in powder containing mixture of excipients. Hence there is no major interaction between the drug and polymers used in the study.

PRECOMPRESSION PARAMETERS:

Table. No. 25: EVALUATIONS OF GRANULES

Batch . N0.	Angle of Repose(^{0})	Bulk Density(g/ ml)	Tapped bulk density(g/ ml)	Carr's index (%)	Hausner's Ratio
F1	27°46'	0.453	0.512	11.40	1.24
F2	26°27'	0.489	0.532	11.81	1.26
F3	27°32'	0.412	0.554	13.63	1.21
F4	24°17'	0.409	0.512	14.96	1.26
F5	24°.52'	0.467	0.568	12.13	1.19
F6	24°.26'	0.449	0.587	11.12	1.11
F7	25°.33'	0.456	0.501	11.33	1.23
F8	27°.68'	0.467	0.569	12.28	1.22
F9	23°.91'	0.471	0.547	13.88	1.17
F10	23°.28'	0.413	0.534	12.52	1.24
F11	26°.11'	0.464	0.561	11.14	1.23
F12	26°.58'	0.491	0.545	12.39	1.26

Discussion:

The angle of repose for the formulated blend F1-F12 was found to be in the range 24^0.17' to 27^0.68' shows good flow property.

Compressibility index for the formulations F1-F12 found between 11.12% to 13.88% indicating the powder blend has the required flow property for compression.

Hausner's Ratio for the formulations F1-F12 found between 1.11 to 1.26 indicating the powder blend has the required flow property for compression.

EVALUATION OF SERTRALINE TABLETS:

Table. No: 26.WEIGHT VARIATION AND FRIABILITY:

Batch. No	Weight Variation (%)	Friability (%)
F1	350±1.52	0.41
F2	350±2.37	0.34
F3	348±1.44	0.30
F4	351±1.86	0.48
F5	351±2.56	0.48
F6	351±2.13	0.48
F7	350±1.52	0.39
F8	351±1.49	0.40
F9	351±2.37	0.39
F10	350±1.91	0.51
F11	350±1.34	0.46
F12	351±2.03	0.59

Discussion:

The weight variation of the tablet in the range of ± 1.44 % to ± 2.56 % (below 5%) complying with pharmacopoeial specification.

The friability of the tablet in the range of 0.23 % to 0.59% **(**below 1%) complying with pharmacopoeial specifications.

Table. No: 27. Thickness, Hardness and Disintegration Time:

Batch. No	Thickness (mm)	Hardness (Kg/cm^2)
F1	2.12±0.2	2.13
F2	2.02±0.2	2.61
F3	2.23±0.1	2.12
F4	2.12±0.1	2.34
F5	2.23±0.1	2.62
F6	2.10±0.1	2.78
F7	2.05±0.2	2.51
F8	2.08±0.3	2.59
F9	2.22±0.2	2.54
F10	2.16±0.1	2.38
F11	2.09±0.2	2.42
F12	2.23±0.2	2.53

Discussion:

The thickness of the formulations from F1- F12 was found to be in the range of 2.02±0.2 to 2.23±0.2 and hardness of the formulated tablets was found to 2.13 to 2.78 indicating a satisfactory mechanical strength.

Table. No: 28. Wetting Time and Disintegration Time:

Batch. No	Wetting Time (Sec)	DISINTEGRATION TIME (seconds)
F1	130	135
F2	104	108
F3	76	80
F4	63	66
F5	118	122
F6	81	84
F7	53	56
F8	45	48
F9	104	107
F10	65	69
F11	45	51
F12	18	21

Discussion:

The Wetting time of the formulations from F1- F12 was found to be in the range of 18-130 seconds. Lower wetting time implies a quicker disintegration of the tablet. F12 shows very lower wetting time it reflects in faster DT.

Water absorption ration is around 67% shows for the formulation F12.

Table. No:29. CUMULATIVE % RELEASE OF SERTRALINE Mouth Dssolving Tablets F1-F4

Time (mts)	% Drug Release of Formulations			
	F1	F2	F3	F4
0	0	0	0	0
1	24.21	28.21	31.47	34.71
2	40.39	46.45	50.39	54.07
4	53.91	59.62	61.22	64.73
6	66.26	68.71	71.46	78.38
8	75.54	76.63	81.92	86.42
10	89.19	85.22	89.75	92.53
12	93.65	91.38	93.71	97.34
15	96.78	98.76	99.27	99.81
17	98.37	---	---	---

Discussion:

From the *invitro* dissolution study of all formulations (F1-F12), formulation F12 release around 98% of drug at the end of 8 min's for a immediate release tablets of Sertraline. Therefore the F12 formulation chosen as the best formulation from all 12 batches.

Table. No:30. CUMULATIVE % RELEASE OF SERTRALINE Mouth Dissolving

Tablets F5-F8

Time (mts)	% Drug Release of Formulations			
	F5	F6	F7	F8
0	0	0	0	0
1	15.62	21.23	24.02	29.63
2	29.65	30.43	35.31	38.21
4	42.32	42.86	43.17	45.73
6	54.43	56.33	58.45	61.72
8	67.09	68.90	70.51	72.08
10	75.34	76.58	79.14	85.74
12	81.26	87.10	89.91	97.19
15	91.47	94.39	96.24	99.74
17	97.38	98.12	98.69	---

Table. No:31. CUMULATIVE % RELEASE OF SERTRALINE Mouth Dissolving Tablets F9-F12

Time (mts)	% Drug Release of Formulations			
	F9	F10	F11	F12
0	0	0	0	0
1	22.13	30.12	34.23	40.41
2	38.39	46.43	51.17	56.43
4	53.12	64.64	69.17	76.73
6	69.46	77.31	82.45	89.27
8	82.31	89.37	90.90	98.14
10	97.18	99.33	98.92	---
12	97.25	---	---	---
15	---	---	---	---
17	---	---	---	---

Fig.No.7: Graph of Cumulative % Release of Sertraline Mouth Dissolving Tablets F1-F4

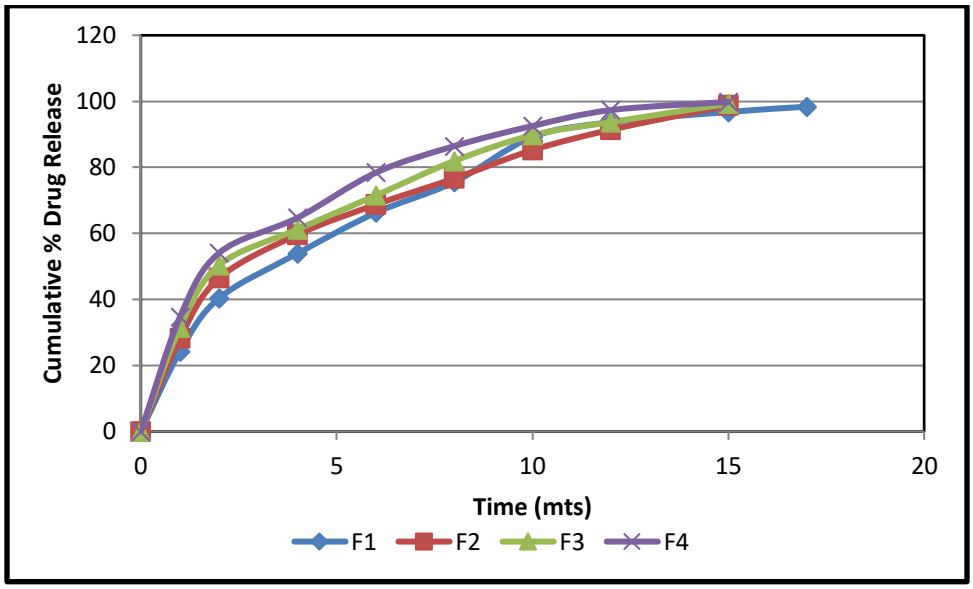


Fig.No.8: Graph of Cumulative % Release of Sertraline Mouth Dissolving Tablets F5-F8

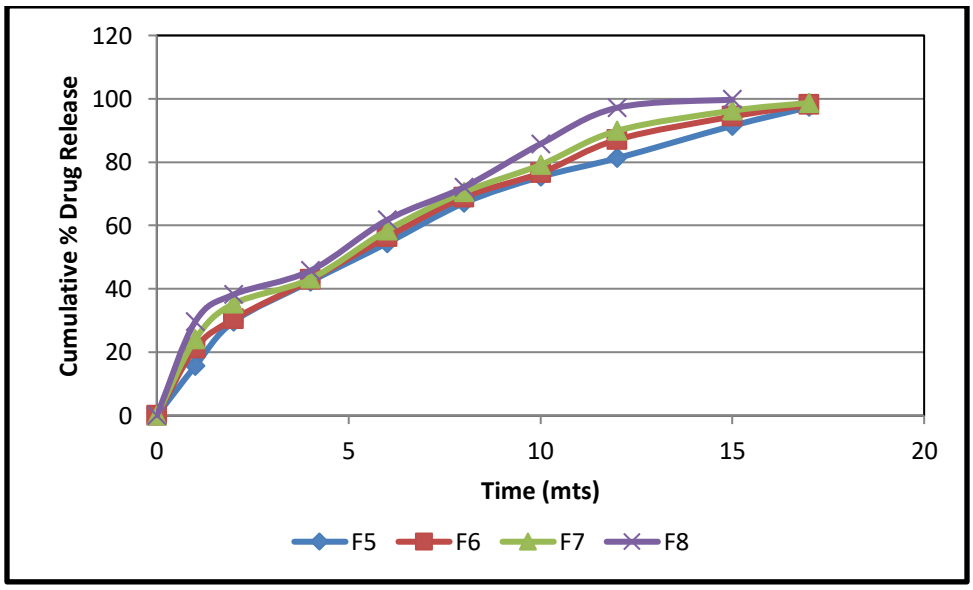


Fig.No.9: Graph of Cumulative % Release of Sertraline Mouth Dissolving Tablets F9-F12

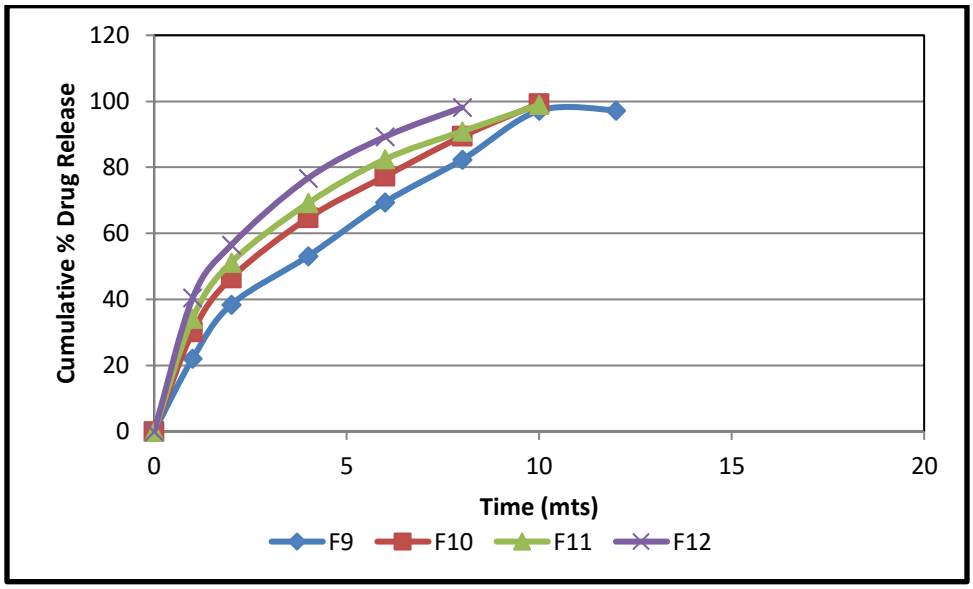
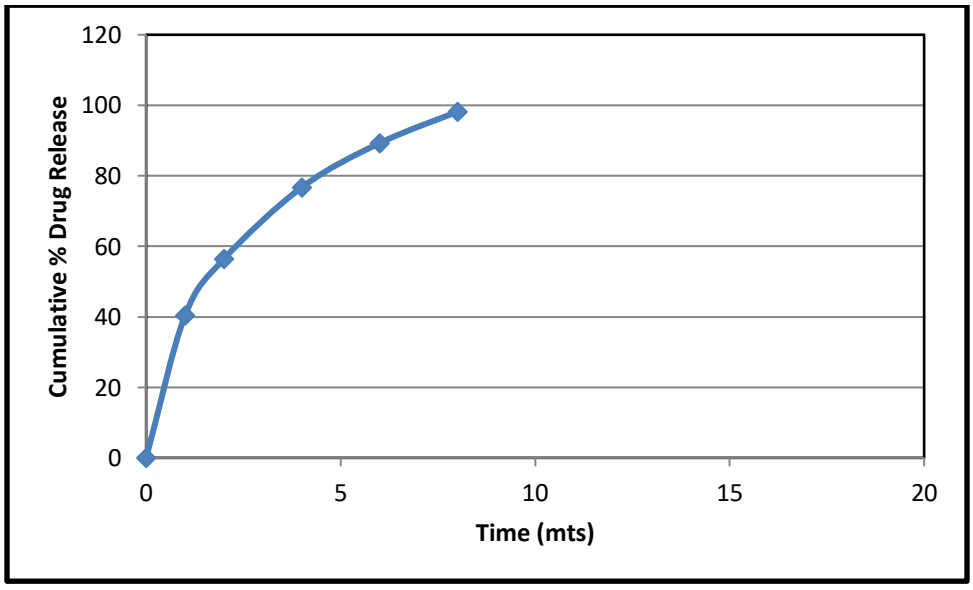


Fig.No.10: Graph: Cumulative % Release of Sertraline Mouth Dissolving Tablets F12



DISINTEGRATION FIGURE

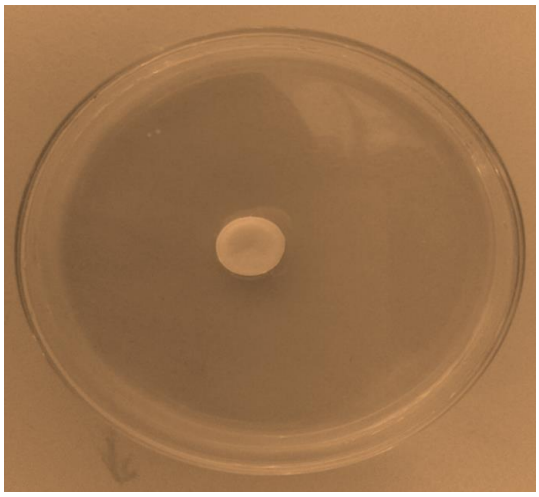


Figure 11: 7 sec

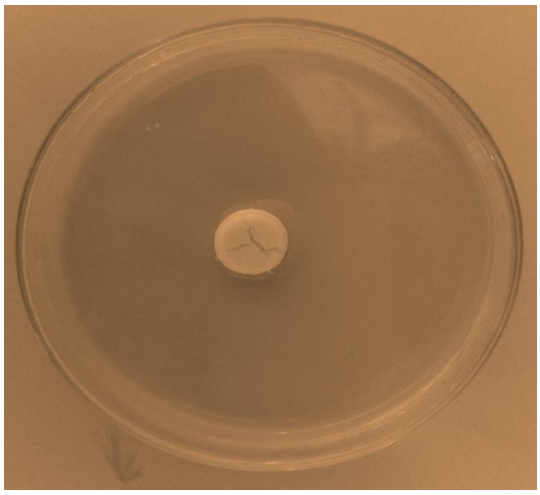


Figure 12: 15 sec

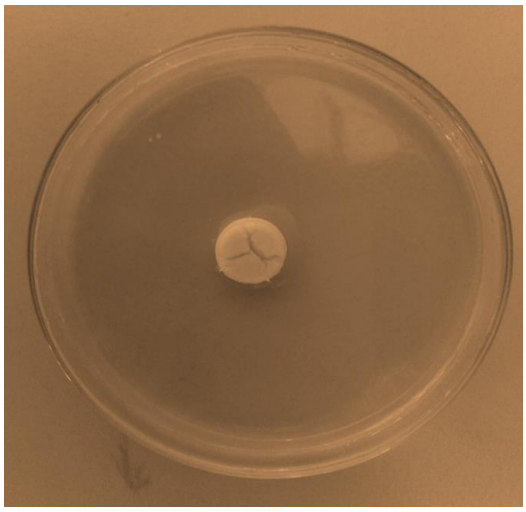


Figure 13: 25 sec

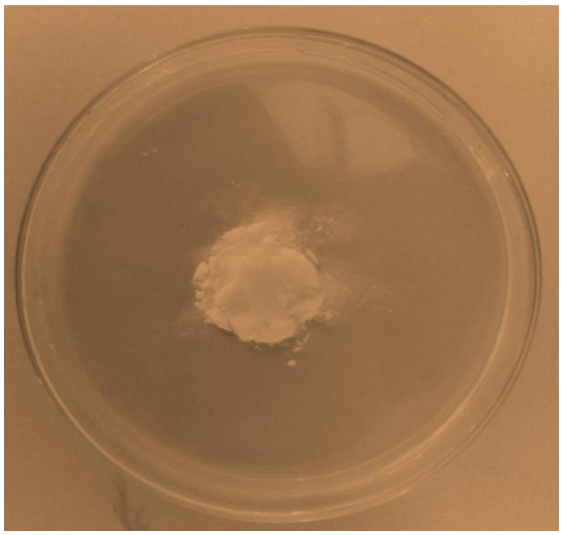


Figure 14: 40 sec

DISINTAGERATION FIGURE

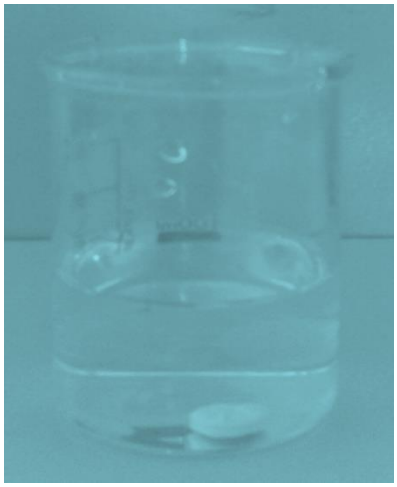
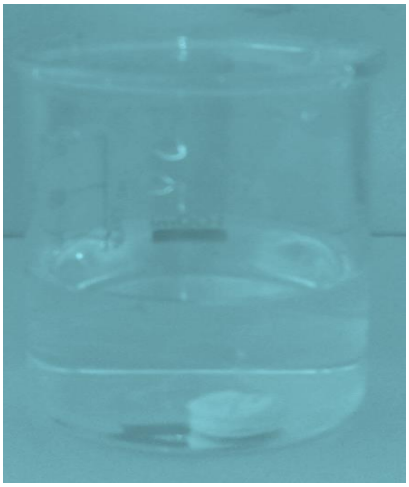


Figure 15: 5 sec



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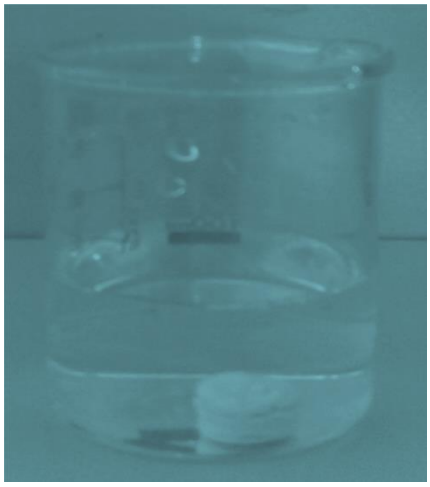

Figure 17: 30 sec

Figure 18: 40 sec

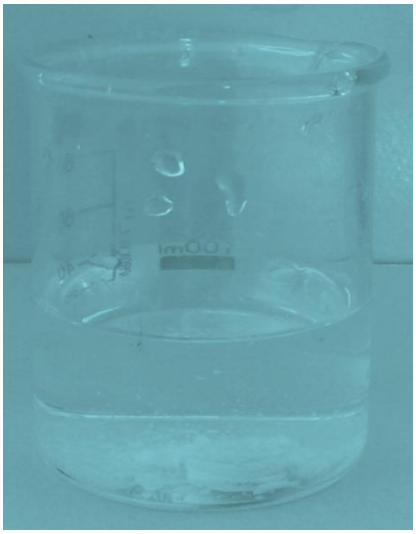

Figure 19: 50 sec

CHAPTER 13

SUMMARY & CONCLUSION

13. SUMMARY AND CONCLUSION

The present study involves formulation and evaluation of immediate release tablets of Sertraline. Endeavours with respect to Direct compression method used for formulating tablets was best suitable to achieve 100% results.

Preformulation studies involving organo-leptic bulk density, angle of repose, tapped density, compressibility index, hausner ratio, melting point range, pH and solubility were carried out as per USP specifications.

Drug excipients compatibilities were carried out physical, which showed no siginificant change in any way to the mixture.

Polymers such as Polyplasdone (Crospovidon-XL), Croscarmellose Sodium (CCS), Sodium Starch Glycolate (SSG) were utilized in the trails. All the physical evaluations carried in preformulation studies were carried out on all the three different polymers utilized. All the formulations exhibited values within the acceptable range.

Tablets were evaluated for weight variations, hardness, friability, thickness and Dissolution studies.

Release studies were carried out in 7.4 pH Saline, for 20 minutes. Evaluated samples for all the three polymer systems. Results indicated that formulation F12, gave 98.14% release within 8 minutes which is formulated with Crospovidon-XL alone. Assay was carried out for formulation F12 and was found to be 96.12%.

Remaining formulations gave fluctuating release profiles. The formulation F12 was considered to be better among the trails accomplished.

CHAPTER 14

BIBLIOGRAPAHY

14. BIBLIOGRAPHY

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