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FORMULATION AND EVALUATION OF ORO DISPERSIBLE TABLET OF CHLOROPHENIRAMINE MALEATE

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ABSTRACT
To develop Oro dispersible tablets of Chlorphenaramine Maleate to achieve rapid disintegration, dissolution to resolve the swallowing problems in Paediatric, Geriatric patients by rapid disintegration in saliva and improve the patient compliance. Oral route is the widely used route for the administration of any type of dosage form and can be made a best route by overcoming its drawbacks. Immediate release tablets by using a super disintegrant solved the problems encountered during the medication through oral route. In the present work, an attempt has been made to develop fast disintegrating tablets of Chlorphenaramine Maleate. New generation super disintegrates Polyplasdone XL, Vivasole and Explotab was selected as super disintegrates. All the formulations were prepared by Direct Compression method using 6mm punch on 10 station lab press tablet Compression Machine. The blend of all the formulations showed good flow properties such as Angle of repose, Bulk density, Tapped density. The prepared tablets were shown good post compression parameters and they passed all the quality control evaluation parameters as per I.P limits. Among all the formulations F6 formulation showed maximum % drug release i.e., 99.89% in 18±0.01 sec hence it is considered as optimized formulation.

KEYWORDS: Oro Dispersible tablets of Chlorphenaramine Maleat, Dissolution, Formulation and evaluation.

INTRODUCTION
Drug delivery systems (DDS) are a strategic tool for expanding markets/indications, extending product life cycles and generating opportunities. DDS make a significant contribution to global pharmaceutical sales through market segmentation, and are moving rapidly. Drug delivery systems are becoming increasingly sophisticated as pharmaceutical scientists acquire a better understanding of the physicochemical and biochemical parameters pertinent to their performance.

Despite of tremendous advancements in drug delivery, the oral route remains the perfect route for the administration of therapeutic agents because the low cost of therapy, ease of administration lead to high levels of patient compliance.

Fig 1.1: Fast dissolving tablets.

It is always the aim of a scientist or a dosage form designer to enhance the safety of a drug molecule while maintaining its therapeutic efficacy. Recent advances in NDDS aim for the same by formulating a dosage form, convenient to be administered so as to achieve better patient compliance. Mouth Dissolving Tablet (MDT) is one among such approaches.

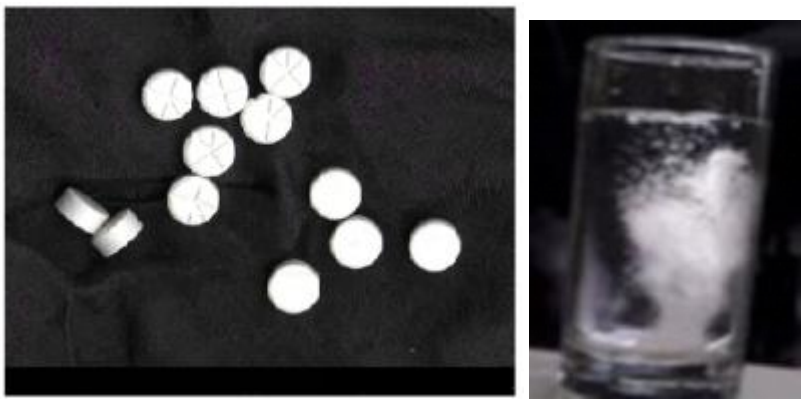


Fig 1.2: Mechanism of fast dissolving tablets.

Improved patient compliance has achieved enormous demand. Consequently demand for their technologies is also increasing many folds. To develop a chemical entity, a lot of money, hard work and time are required. So focus is rather being laid on the development of new drug delivery systems for already existing drugs, with enhanced efficacy and bioavailability, thus reducing the dose and dosing frequency to minimize the side effects.

The oral route of administration is the most preferred route due to its many advantages like ease of administration, accurate dosage, self-medication, pain avoidance, versatility and patient compliance. Tablets and capsules are the most popular dosage forms.

Fig 1.3: Commercial tablets.

But one important drawback of such dosage forms is Dysphasia or difficulty in swallowing. This is seen to afflict nearly 35% of the general population. This disorder is also associated with a number of pathological conditions including stroke, Parkinson's disease, neurological disorders, AIDS etc.

1. Parkinsonism
2. Motion sickness
3. Unconsciousness
4. Elderly patients
5. Children
6. Mentally disabled persons
7. Unavailability of water

To solve the above-mentioned problems, pharmaceutical technologists have put in their best efforts to develop a Fast dissolving drug delivery, i.e. Mouth Dissolving Tablet that disintegrates and dissolves rapidly in the saliva, within a few sec without the need of drinking water or chewing. A mouth dissolving tablet usually dissolves in the oral cavity within 10 sec to 3 min. Most of the MDTs include certain super disintegrants and taste masking agents.

1.1 Advantages of fast disintegrating tablets

Fast dissolving technology offers:

- Ease of administration for those patients who have difficulty in swallowing tablet.
- No need of water to swallow the dosage form.
- Useful for pediatric, geriatric and psychiatric patients.
- Have acceptable taste masking property.
- Achieve increased bioavailability through pregastric absorption of drugs from mouth, pharynx and oesophagus as saliva passes down.
- Have a pleasant mouth feel and leave minimal or no residue in the mouth after drug administration.
- Have rapid dissolution and absorption of the drug which will produce quick onset of action.
- It combines advantages of solid dosage form in terms of stability and liquid dosage form in term of bioavailability.

1.2 Limitations to mouth dissolving tablets

- Careful handling is required because tablets usually have insufficient mechanical strength.
- If tablets are not formulated properly they may leave unpleasant taste or grittiness in the mouth.
- Drugs difficult to formulate into FDT with relatively larger doses.
- Drugs with short half-life and frequent dosing and those whom require controlled or sustained release are unsuitable candidates of FDTs.

1.3 Salient Feature of Fast Dissolving Drug Delivery System

1. Ease of Administration to the patient who cannot swallow, such as the elderly, stroke victims, bedridden patients, patient affected by renal failure and patient who

refuse to swallow such as pediatric, geriatric & psychiatric patients.
2. No need of water to swallow the dosage form, which is highly convenient feature for patients who are traveling and do not have immediate access to water.
3. Rapid dissolution and absorption of the drug, which will produce quick onset of action.
4. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases bioavailability of drug is increased.
5. Pre-gastric absorption can result in improved bioavailability and as a result of reduced dosage; improve clinical performance through a reduction of unwanted effects.
6. Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patient.
7. The risk of chocking or suffocation during oral administration of conventional formulation due to physical obstruction is avoided, thus providing improved safety.
8. New business opportunity like product differentiation, product promotion, patent extensions and life cycle management.
9. Beneficial in cases such as motion sickness, sudden episodes of allergic attack or coughing, where an ultra rapid onset of action required.
10. An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets.
11. Stability for longer duration of time, since the drug remains in solid dosage form till it is consumed. So, it combines advantage of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability.

1.4 DESIRED CHARACTERISTICS OF FAST DISSOLVING TABLETS

Fast Disintegration

These tablets should disintegrate in the mouth without additional water or with a very small amount of water. The disintegration fluid is provided by the saliva of the patient. The disintegrated tablet should become a soft paste or liquid suspension, which can provide smooth swallowing and good mouth feel.

Drug Properties

Many drug properties could potentially affect the performance of FDTs. For example, the solubility, crystal morphology, particle size, hygroscopicity, compressibility, bioavailability, flow property and bulk density of a drug can significantly affect the final tablets characteristics, such as disintegration and tablet strength.

Taste of Active Ingredients

FDTs dissolve or disintegrate in the patient`s mouth, the drug will be partially dissolved in close proximity to the taste buds. After swallowing, there should be minimal or no residue in the mouth. An ideal taste-masking technology should provide drugs with good mouth feel and without grittiness.

Moisture Sensitivity

These tablets should have low sensitivity to humidity. This problem can be especially challenging because many highly water soluble excipients are used in formulation to enhance fast dissolving properties as well as to create good mouth feel. Those highly water soluble excipients are susceptible to moisture; some will even deliquesce at high humidity.

Tablet strength and porosity

The tablet porosity is usually maximized to ensure fast water absorption into the tablets. The key properties of the tablets are fast absorption or wetting of water into the tablets and disintegration associated particles into individual components for fast dissolution. This requires that excipients should have high wettability, and the tablet structure should also have a highly porous network. Because the strength of a tablet is related to compression pressure, and porosity is inversely related to compression pressure, it is important to find the porosity that allows fast water absorption while maintaining high mechanical strength.

1.5 DRUG SELECTION CRITERIA

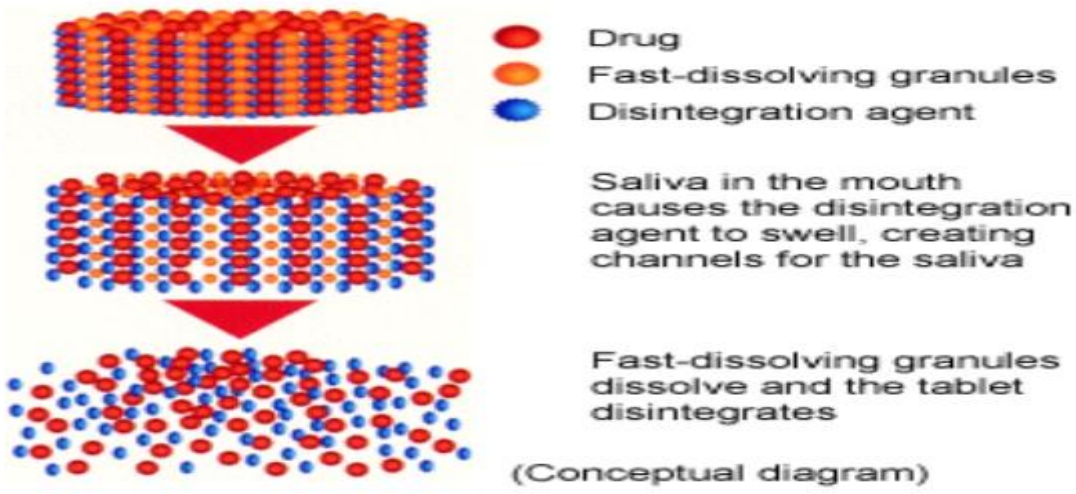
- Have better solubility. E.g. promethazine
- Low dose. E.g. terazosin hcl
- Have better availability to permeate oral mucosal tissue.
- Less or not bitter in taste.
- Good stability in both water as well as in saliva. E.g. rizatriptine benzoate

Table 1.5: Promising Drugs to be in corporated In Fast Dissolving Tablets.

S.NO.	DRUG CATEGORY	EXAMPES OF DRUG
1.	Analgesic and anti-inflammatory agents	Ibuprofen, indomethacin, naproxen, oxaprozin, phenylbutazone, piroxicam, meloxicam, ketoprofen etc.
2.	Anthelmintics	Albendazole, cambendazole, dichlorophen, mebendazole, thiabendazole, praziquantel
3.	Anti-arrhythmic agents	Quinidinesulphate, amiodrone, disopyramide, flecainide acetate
4.	Anti-coagulants	Phenindione, nicoumalone, dipyridamole, dicoumarol
5.	Anti-depressants	Trimipramine, trazodone, nortriptyline, mianserin, maprotiline, amoxapine
6.	Anti-bacterial	Trimetoprim, tetracycline, sulphapyridine, sulphafurazole, sulphadiazine, sulphacetamide, spiramycin, rifampicin, nitrofurantoin, nalidixicacid, ethionamide, erythromycin, ciprofloxacin, clarithromycin
7.	Anti-epileptics	Valproicacid, sulthiame, primidone, phensuximide, phenytoin, phenobarbitone, oxcarbazepine, methoin, ethotoin, clonazepam, carbamazepine
8.	Anti-gout agents	Sulphinpyrazone, allopurinol, probenecid
9.	Anti-fungal agents	Clotrimazole, econazole nitrate, fluconazole, flucytosine, griseofulvin, itraconazole, ketoconazole, miconazole
10.	Anti-hypertensive agents	Amlodipine, carvedilol, prazosin, benidipine, darodipine, diltiazam, diazoxide, felodipine, minoxidil, nifedipine, nimodipine, terazosin
11.	Anti-malarial agents	Proguanil, mefloquine, halofant-trine,chlorproguanil,chloroquine
12.	Anti-neoplastic agents	Busulphan, chlorambucil, cyclosporin, dacarbazine,
13.	Anti-migraine agents	Dihydroergotamine mesylate, sumatriptan, ergotamine maleate
14.	Anti-protozoal agents	Furzolidone, metronidazole, nimorazole, nitrofurazone, omidazole, tinidazole
15.	Anti-thyroid agents	Carbimazole, propylthiouracil
16.	Anxiolytic, sedative, hypnotics and neuroleptics	Alprazolam, amyiobarbitone, barbitone, chlormethiazole, chlorpromazine, clobazam, clozapine, diazepam, droperidol, lorazepam, haloperidol, oxazepam
17.	Corticosteroids	Beclomethasone, betamethasone, budesonide, cortisone acetate, prednisolone, hydrocortisone
18.	Anti-parkinsonian agents	Lysuride maleate, bromocriptine mesylate
19.	Diuretics	Acetazolamide, amiloride, bumetanide, chlorothiazide, chlorthalidone, frusemide
20.	Gastro-intestinal agents	Cimetidine, cisapride, ranitidine, domperidone, famotidine
21.	Anti-histaminic agents	Cinnarzine, cyclizine, flunarizine, loratidine, meclozine, triprolidine
22.	Local anaesthatics	Lidocaine
23.	Neuro-muscular agents	Pyridostigmine
24.	Nitrates and other anti-angina agents	Amyl nitrate, glyceryl trinitrate, isosorbide dinitrate, isosorbide mononitrate, pentaerythritol tetranitrate
25.	Nutritional agents	Betacarotene, vitamin A,B2,D,E and K
26.	Opoid analgesics	Codeine, diamorphine, dihydrocodiene, meptazinol, methadone, morphine, pentazocine
27.	Oral vaccines	Vaccines prevent against:- influenza, tuberculosis, meningitis, hepatitis,whooping cough, polio, tetanus, diphtheria, malaria, cholera, typhoid, HIV, measles, caries, mump
28.	Proteins and peptides	Insulin, glucagons, growth hormones
29.	Sex hormones	Clomiphene citrate, danazol, mestranol, methyltestosterone, norgestrel, oestradiol, conjugated oestrogens, progesterone, testosterone, tibolone
30	Stimulants	Amphetamine, pemoline, dexamphetamine, mhazindol, dexfenfluramine, fenfluramine

1.6 SUPER-DISINTEGRANTS

Superdisintegrants are the agents added to tablet formulations to promote the breakup of the tablets into smaller fragments in an aqueous environment there by increasing the available surface area and promoting a more rapid release of the drug substance.

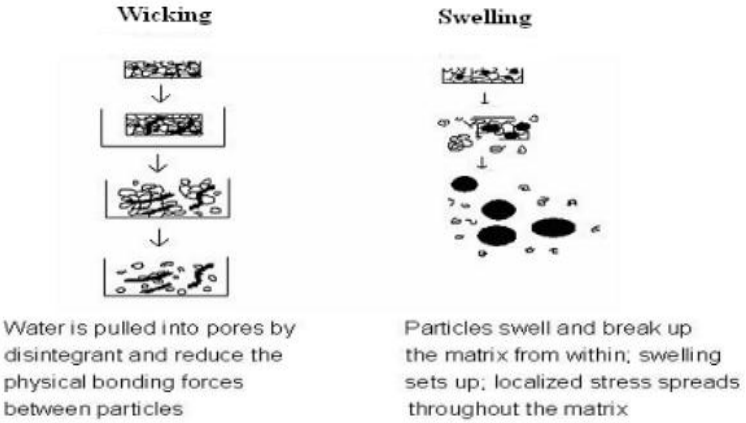


1.6.1 MECHANISM OF SUPERDISINTEGRANTS

There are four major mechanisms for tablet disintegration as follows:

- **Swelling**

General mechanism of action for tablet disintegration which is most widely accepted is swelling. Tablets with high porosity due to lack of adequate swelling force show poor disintegration. Sufficient swelling force with low porosity is exerted in the tablet. If the packing fraction is very high, fluid is unable to penetrate in the tablet & disintegration is again slows down.



- **Porosity and Capillary Action(Wicking)**

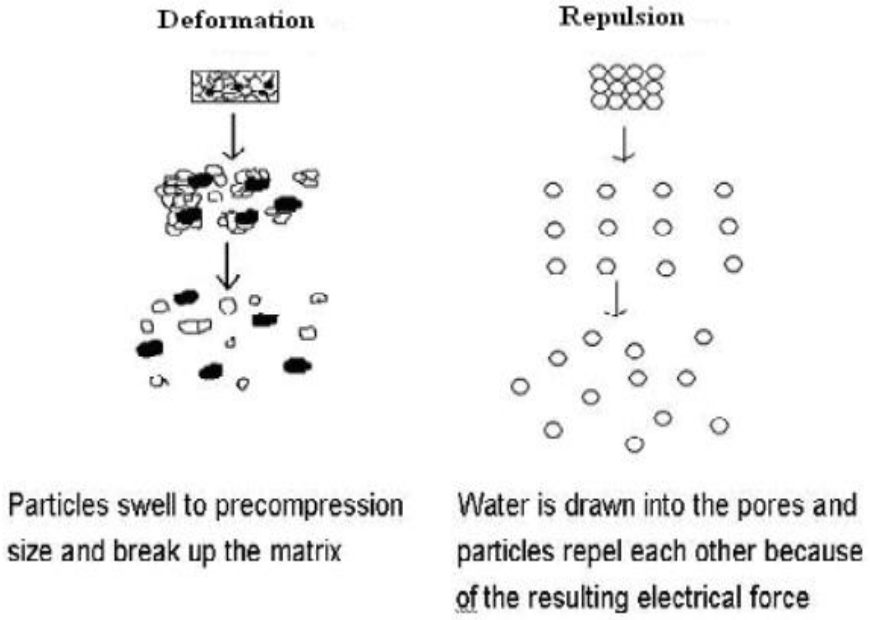
Effective disintegrates that do not swell are believed to impart their disintegrating action through porosity and capillary action. Tablet porosity provides pathways for the preparation of fluid into tablets. The disintegrate particles themselves act to enhance porosity and provide pathways into the tablet. Liquid is drawn up or "wicked" into pathways through capillary action and rupture the interparticulate bonds causing the tablet to break apart.

Due to disintegrating particle/particle repulsive forces

Another mechanism of disintegrating attempts to explain the swelling of tablet made with 'nonswellable' disintegrates. Goyt-Hermann has proposed a particle repulsion theory based on the observation that no swelling particle also causes disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it.

Due to deformation

Disintegrated particles get deformed; during tablets compression and when these deformed particles come in contact with aqueous media or water them get into their normal structure. Swelling capacity of starch was improved during compression. Due to this increase in size of the deformed particles produces a breakup of the tablet.



1.6.2 LIST OF SUPERDISINTEGRANTS

Table 1.6.2: List of Superdisintegrants.

Superdisintegrants	Example	Mechanism of action
Crosspovidone Crosspovidone M® Kollidon® Polyplasdone®	Cross linked PVP	-Swells very little and returns to original size after compression but act by capillary action
Crosscarmellose® Ac-Di-Sol® Nymce ZSX® Primellose®Solutab® Vivasol®L-HPC	Cross linked cellulose	-Swells 4-8 folds in < 10 seconds. -Swelling and Wicking both.
Sodium starch glycolate Explotab® Primogel®	Cross linked starch	-Swells 7-12 folds in < 30 seconds
Calcium silicate		-Wicking action
Alginic acid NF Satialgine®	Cross linked alginic acid	-Rapid swelling in aqueous medium or wicking action
Soy polysaccharides Emcosoy®	Natural super disintegrate	

1.7 CONVENTIONAL TECHNIQUES USED FOR PREPARATION OF FDTS

Disintegration Addition

Disintegration addition technique is one popular technique for formulating FDTs because of its easy implementation and cost- effectiveness. The basic principle involved in formulating FDTs by disintegrate addition technique is addition of superdisintegrants in optimum concentration so as to achieve rapid disintegration along with the good mouth feel.

1) Freeze drying

A process in which water is sublimated from the product after freezing. Lyophilization is a pharmaceutical technology which allows drying of heat sensitive drugs and biological at low temperature under condition that allow removal of water by sublimation. Lyophilization results in preparations which are highly porous, with a very high specific surface area, which dissolve rapidly show improved absorption and bioavailability.

1) Moulding

In this method, molded tablets are prepared by using water soluble ingredients so that the tablets dissolve completely and rapidly. The powder blend is moistened with a hydro-alcoholic solvent and is molded into tablets under pressure lower than that used in conventional tablet compression.

Sublimation

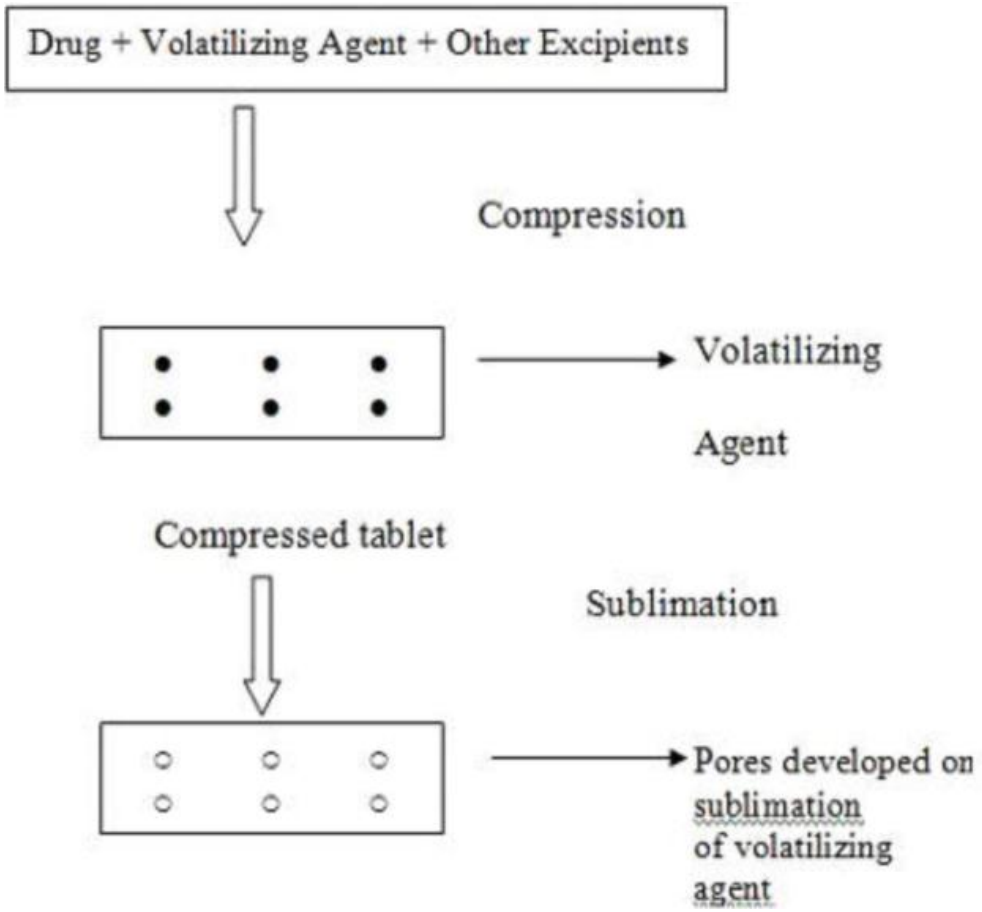


Figure 1: Steps Involved in Sublimation.

5) Spray- Drying

Spray drying can produce highly porous and fine powders that dissolve rapidly. The formulations are incorporated by hydrolyzed and non hydrolyzed gelatins as supporting agents, mannitol as bulking agent, sodium starch glycolate or crosscarmellose sodium as disintegrating and an acidic material(e.g. citric acid) and/or alkali material(e.g. sodium bicarbonate) to enhance disintegration and dissolution.

6) Mass- Extrusion

This technology involves softening the active blend using the solvent mixture of water soluble polyethylene glycol, using methanol and expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blades to form tablets.

7) Direct Compression

It is the easiest way to manufacture tablets. Conventional equipment, commonly available excipients and a limited number of processing steps are involved in direct compression. Also high doses can be accommodated and final weight of tablet can easily exceed that of other production methods. Directly compressed tablets disintegration and solubilization depends on single or combined action of disintegrants, water soluble excipients and effervescent agent.

8) Melt granulation

It is a process by which pharmaceutical powders are efficiently agglomerated by a melt able binder. The advantage of this technique compared to a conventional granulation is that no water and organic solvent is needed. Because there is no drying step, the process is less time consuming and uses less energy than wet granulation. It is a useful technique to enhance the dissolution rate of poorly water-soluble drugs.

9) Phase transition process

It is concluded that a combination of low and high melting point sugar alcohols, as well as a phase transition in the manufacturing process, are important for making FDT without any special apparatus**.**

Table 1.7: Concentration ranges of different disintegrants.

Disintegrants	Concentration
Starch USP	5-20
MCC	10-20
Alginic acid	1-5%
Sodium starch glycolate	2-8%
Crosspovidone	0.5-5%
Crosscarmellose sodium	1-3%

1.7.1 Diluents: These are commonly added to tablet formulations if the required dose is inadequate to

produce the bulk. Tablet formulation may contain diluents for secondary reasons, to provide better properties such as improved cohesion, to permit use of direct compression manufacturing or to promote flow.[16]

1.7.2 A Classification of diluents based on their solubility

Insoluble diluents: Starch, Powdered cellulose, microcrystalline cellulose, Calcium phosphate.

Soluble diluents: Lactose, Sucrose, Mannitol, Sorbitol.

1.7.3 Binding agents: Binding agents are used to hold the powders together to form granules or cohesive compacts for directly compressible materials and to ensure that the tablet remains intact after compression.

Natural polymers: Starch, gums including acacia, tragacanth and gelatin, alginic acids, pregelatinised starch.

Synthetic polymers: PVP, PEG, PVA, methyl cellulose, ethyl cellulose hydroxyl propyl cellulose, sodium carboxy methyl cellulose.

1.7.4 Anti adherents

Some material have strong adhesive properties towards the metal of punches and dies or the tablet formulation containing excessive moisture which has tendency to result in picking and sticking problem.[14,16]

Table 1.7.4: Concentration ranges of different anti-adherents.

Anti adherent	Range
Talc	1-5%
Corn starch	3-10 %
Colloidal silica	0.1-0.5%
Stearates	< 1%
Sodium lauryl sulphate	< 1%

1.7.5 Lubricants

Lubricants are used in tablet formulation to ease the ejection of the tablet from the die to prevent sticking of tablets to the punches and to prevent excessive wear on punches and dies. They function by interposing a film of lower shear strength at the interface between the tablets and die wall and punch face.[16]

1.7.5(a) Classification of lubricants based on their water solubility

1) Insoluble lubricants

Stearates (magnesium, calcium stearate), Talc, sterotex, waxes, stero wet.

2) Water soluble lubricants Boric acid, Sodium benzoate, sodium oleate, sodium acetate, sodium lauryl sulphate, magenesium lauryl sulphate.

1.8 Patended Technologies for Fast Dissolving Tablets

1) Zydis technology.
2) Durasolv technology.
3) Orasolv technology.
4) Wowtab technology.
5) Flashtab technology.
6) Ziplets/Advatab technology.
7) Pharmaburst
8) Nanocrystal technology.
9) Lyoc

Technologies for MDT

Several technologies are available for preparing Mouth dissolving tablets. But some commercially useful technologies are:

1.8.1 Zydis technology

'Zydis' is the first mouth dissolving dosage form in the market. It is a unique freeze-dried tablet in which the active drug is incorporated in a water-soluble matrix, which is then transformed into blister pockets and freeze dried to remove water by direct compression. Zydis matrix is made up of a number of ingredients in order to obtain different objectives. SUPER DISINTEGRANTS such as gelatin, dextrin or alginates are added to impart strength during handling. These form a glossy and amorphous structure. Mannitol or sorbitol is added to impart crystallinity, elegance and hardness. Various gums may be added to prevent sedimentation of dispersed drug particles. Water is used as a medium to ensure the formation of a porous dosage form. Collapse protectants like glycine may be used to prevent shrinkage of dosage form during freeze drying and long-term storage. If necessary, suspending agents and pH adjusting agents may be used. Preservatives may also be added to prevent microbial growth. Zydis products are packed in blister packs to protect the formulation from environmental moisture. A secondary moisture proof foil punch is often required as this dosage form is very moisture sensitive. When put into the mouth, Zydis unit quickly disintegrates and dissolves in saliva.

Drawbacks

1. A water insoluble drug can be incorporated only up to 400 mg per tablet or less. On the other hand water-soluble drug can be incorporated only up to 60mg.
2. Relatively expensive and time-consuming process.
3. Fragility and poor stability of dosage form during storage under stressful conditions.

1.8.2 Orasolv technology

It is CIMA lab's first mouth dissolving formulation. This technology involves taste masking of active drug. Effervescent disintegrating agent is also used. Conventional blenders and tablet equipment are used for preparation of tablets. Less force of compaction is used for manufacturing so as to obtain soft and quickly disintegrating tablets. There is a limitation of this technology that soft and fragile tablets are formed, therefore needed to be packed in specially designed pick and place package system.

1.8.3 Durasolv Technology

This too has been developed by CIMA labs. This is one of the suitable technologies to prepare products requiring low amounts of active drug. This technology uses drug, fillers and a lubricant to prepare the tablet. Conventional tabletting equipment is used to prepare the tablet. Due to higher force of compaction used, tablets prepared are rigid. Dosage form can be packaged into conventional packaging system like blisters.

1.8.4 Wowtab Technology

Yamanauchi pharmaceutical company patented this technology. 'Wow' means "without water". The active ingredients may constitute up to 50% w/w of the tablet. In this technique, saccharides of both low and high mouldability are used to prepare the granules. Mould ability is the capacity of a compound to be compressed.

Highly mouldable substance has high compressibility and thus shows slow dissolution. The combination of high and low mouldability is used to produce tablets of adequate hardness. Active ingredients are mixed with low mouldability saccharides and then granulated with high mouldabiity saccharides and then compressed into tablet. The Wowtab product dissolves quickly in 15 seconds or less. Wowtab product can be packed in both into conventional bottle and blister packs.

1.8.5 Flash dose Technology

This technology is patented by Fuisz. This system uses the combination of both Shearform and Ceform technologies in order to mask the bitter taste of the drug. A sugar based matrix, called 'Floss' is used, which is made up of a combination of excipients (crystalline sugars) alone or in combination with drugs. Nurofen meltlet, a new form of Ibuprofen, as a mouth-dissolving tablet is the first commercial product prepared by this technology and launched by Biovail Corporation.

Drawbacks

1. The dosage form can accommodate only up to 600 mg of drug.
2. Tablets produced are highly friable, soft and moisture sensitive. Therefore specialized packing is required.

1.8.6 Flashtab Technology

Prographarm labs have a patent over this technology. In this technology, micro granules of the taste-masked active drug are used. These may be prepared by using conventional techniques like coacervation, microencapsulation, and extrusion- spheronisation. All these processes utilize conventional tabletting technology. These taste-masked micro crystals of active drug, disintegrating agent, a swelling agent and other excipients like soluble diluents etc are compressed to form a multi-particulate tablet that disintegrates rapidly.

1.8.7 Shearform Technology

In this technology, a shear form matrix, 'Floss' is prepared. Feedstock prepared with a sugar carrier is subjected to flash heat processing. In this process, sugar is simultaneously subjected to centrifugal force and to a temperature gradient, which causes the temperature of the mass to rise and hence an internal flow condition is created, permitting part of it to move with respect of the mass. The flowing mass comes out through the spinning head that flings the floss. The produced floss is amorphous in nature. So by various techniques, it is further chopped and recrystallised to provide a uniform flow, thus facilitate blending. Then the recrystallised matrix, active drug and other excipients are blended together and finally compressed into tablets. Active drug and other excipients may be blended with the floss before recrystallising it.

Table 1.8. Patended Technologies for Fast Dissolving Tablets.

TECHNOLOGY	COMPANY`S NAME	TECHNOLOGY BASED
Zydis	R.P Scherer Inc.	Freeze drying
Durasolv	CIMA Labs Inc.	Compressed tablet
Orasolv	CIMA Labs Inc.	Compressed tablet
Wowtab	Yamanouchi pharma	Molding
Pharmaburst	SPI Pharma	Compressed tabled
Ziplets/ advatab	Furand	Molding
Nanocrystal	Flan Crop.	Lyophilization
Lyoc	Pharmalyoc Inc.	Freeze drying

1.9 SELECTION OF DRUG CANDIDATES FOR MOUTH DISSOLVING TABLETS

Several factors must be considered when selecting drug candidates for delivery as MDT dosage forms. In general, MDT is formulated as a bioequivalent line extension of an existing oral dosage form. Under this circumstance, it is assumed that the absorption of a drug molecule from the MDT occurs in the post-gastric GIT segments, similar to the conventional oral dosage form. But this scenario may not always be the case. MDT may have varying degrees of pre-gastric absorption and thus, the pharmacokinetic profile (including the maximum plasma concentration, time to achieve maximal plasma concentration, and area under the plasma concentration time curve of an equal dose of an MDT and a conventional oral dosage form) will vary. Therefore, the MDT will not be bioequivalent to the conventional oral dosage form. Examples are cited in the literature in which the pharmacokinetic profiles and bioavailabilities of the same dose of drug in an MDT are not

bioequivalent to the conventional oral dosage form. For example, MDT formulations of selegiline, apomorphine, and buspirone have significantly different pharmacokinetic profiles compared with the same dose administered in a conventional dosage form. It is possible that these differences may, in part, be attributed to the drug molecule, formulation, or a combination of both. If significantly higher plasma levels and systemic exposure have been observed, pre-gastric absorption leading to the avoidance of first-pass metabolism may play an important role. This situation may have implications for drug safety and efficacy, which may need to be addressed and assessed in a marketing application for a MDT. For example, safety profiles may be improved for drugs that produce significant amounts of toxic metabolites mediated by first-pass liver metabolism and gastric metabolism and for drugs that have a substantial fraction of absorption in the oral cavity and segments of the pre-gastric GIT.

1.9.1 EXAMPLES OF OTHER EXCIPIENTS USED IN FDTs

FORMULATION

- **Flavours:** Peppermint flavour, cooling flavour, flavour oils, flavouring aromatic oil, clove oil, bay oil, anise oil, eucalyptus oil, thyme oil, oil of bitter almonds. Flavouring agents include vanilla, citus oils, and fruit essences.
- **Sweeteners:** Aspartame, sugars derivatives.
- **Fillers:** Directly compressible spray dried Mannitol, sorbitol, xylitol, calcium carbonate, magnesium carbonate, calcium phosphate, calcium sulphate, pregelatinized starch, magnesium trisilicate, aluminum hydroxide.
- **Surface active agents:** sodiumdoecylsulfate, sodiumlaurylsulfate, polyoxyethylene sorbitan fatty acid esters (Tweens), sorbitan fatty acid esters (Spans), polyoxyethylene stearates.
- **Binders:** Polyvinylpyrrolidone(PVP), polyvinylalcohol(PVA)
- **Colour:** Sunset yellow, amaranth etc.
- **Lubricants:** Stearic acid, magnesium stearate, zincs state, calcium state, talc, polyethylene glycol, liquid paraffin, magnesium lauryl sulfate, colloidal silicon dioxide

5. MATERIALS AND METHODS

Table 5.1: List of Materials.

Materials	Source
Chlorphenaramine Maleate	SURALabs, Hyderabad
Vivasole(croscaramellose sodium)	SURALabs Hyderabad
Explotab(Sodium starch glycolate)	SURALabs Hyderabad
Polyplasdone X(cros povidone)	SURALabs Hyderabad
Magnesium Stearate	SURALabs Hyderabad
Talc	SURALabs Hyderabad
MCC pH 102	SURALabs Hyderabad
Mannitol	SURALabs Hyderabad
Aspartame	SURALabs Hyderabad

5.2 Equipments

Table 5.2: List of equipments.

Equipments	Model/Company
Electronic balance	Sartourious
Tablet compression machine	Lab press, India.
Tablet hardness tester	Monsanto hardness tester
Dissolution test apparatus	Lab India Dissolution Apparatus Ds 8000(USP)
Disintegration test apparatus	Lab India Disintegration Apparatus(USP)
Friability test apparatus	Lab India Friability Apparatus FT 1020 (USP)
UV-Visible Spectrophotometer	Labindia UV-2000
Hot air oven	VJ Instruments
pH meter	Lab India pH apparatus
FTIR Spectrophotometer	Lab India pH apparatus

6.1 Analytical method

6.1.1a Preparation of 6.8 pH Phosphate Buffer Solution

27.22g of monobasic potassium phosphate was weighed and transferred to a 1000 ml volumetric flask and diluted up to the mark with distilled water to get stock solution of monobasic potassium phosphate of 0.2M concentration. 8g Sodium hydroxide was weighed and transferred to a 1000 ml volumetric flask and diluted up to the mark with 250ml monobasic potassium phosphate

solution was taken from the stock solution in a 200 ml volumetric flask and 112 ml of sodium hydroxide solution from stock solution of 0.2M sodium hydroxide solution was added and then distilled water was used to make up the volume.

6.1.1b Determination of absorption maxima by UV/Visible Spectroscopy

100mg of Chlorphenaramine Maleate working standard was accurately weighed and transferred into a 100ml volumetric flask, 6.8 pH Phosphate Buffer was added and shake for 10 minutes to dissolve and diluted up to mark with 6.8 pH Phosphate buffer and mixed well. Further 10ml of above solution was added to 10ml with phosphate buffer pH 6.8 and mix well, and the resulting solution was scanned from 261 nm in UV spectrophotometer. The best possible wavelength (λ_{max}) will be chosen.

6.1.1c Preparation of standard graph for Chlorphenaramine Maleate on 6.8 pH phosphate buffer

Accurately weighed 100mg of Chlorphenaramine Maleate was dissolved in 100mL of pH 6.8 phosphate buffer to give a solution of 1mg/ml (1000µg/ml) concentration and this served as the first standard stock solution. From this stock solution 1mL was taken and diluted to 100ml using pH 6.8 phosphate buffers to get a solution of 10 µg/ml concentration and this solution served as second standard solution. In to a series of 10ml volumetric flasks, aliquots of second standard solution 1ml, 2ml, 3ml, 4ml, 5ml, was added and the volume made up to 10 ml using pH 6.8 phosphate buffer. The absorbances of these solutions were measured against the blank at 261nm using lab India UV spectrophotometer. Standard curve was plotted by taking concentration on x axis and absorbance on y axis.

6.2 Pre-formulation characteristics

Pre-formulation testing is the first step in rational development of dosage forms of a drug substance. Pre-formulation study is the process of optimizing the delivery of drug through determination of physicochemical properties of the new compound that could affect drug performance and development of an efficacious, stable and safe dosage form. It gives the information needed to define the nature of the drug substance and provide a framework for the drug combination with pharmaceutical excepient in the dosage form.

Hence, Pre-formulation studies were performed for the obtained sample of drug for identification and compatibility studies.[41,42]

6.3 Formulation of Chlorphenaramine Maleate Oro Dispersible Tablet by Direct- Compression Method

Composition of preliminary trials for chlorphenaramine maleate Dispersible Tablet by Direct Compression is shown in table 6.3. All the ingredients were weighed. Required quantity of drug and excipient mixed thoroughly in a polybag. The blend is compressed using lab press tablet Compression machine-10 station. Each tablet contains 4mg Chlorphenaramine Maleate and other Excepient.

INGREDIENT	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
Chlorphenaramine Maleate	4	4	4	4	4	4	4	4	4
Sodium starch glycolate	3.2	4.8	6.4	-	-	-	-	-	-
Cros povidone	-	-	-	3.2	4.8	6.4	-	-	-
Cros caramellose cellulose	-	-	-	-	-	-	3.2	4.8	6.4
Talc	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6
Mg. Stearate	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8
Aspartame	10	10	10	10	10	10	10	10	10
Mannitol	5	5	5	5	5	5	5	5	5
MCC pH102	55.4	53.8	52.2	55.4	53.8	52.2	55.4	53.8	52.2
TOTAL(mg)	80	80	80	80	80	80	80	80	80

6.3. Formulation of Chlorphenaramine Maleate Oro Dispersible tablets. (All ingredients are expressed in mg only).

6.4 Evaluation parameters

Pre compression parameters

1. Bulk Density (D_b)

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder (passed through standard sieve # 20) into a measuring cylinder and initial weight was noted. This initial volume is called the bulk volume. From this the bulk density is calculated according to the formula mentioned below. It is expressed in g/ml and is given by,

$$D_b = M / V_b$$

Where, M is the mass of powder

V_b is the bulk volume of the powder.

2. Tapped Density (D_t)

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 750 times and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is continued for 1250 times and tapped volume was noted. Tapping was

continued until the difference between successive volumes is less than 2% (in a bulk density apparatus). It is expressed in g/ml and is given by,

$$D_t = M / V_t$$

Where,
M is the mass of powder
V_t is the tapped volume of the powder.

RESULTS AND DISCUSSIONS

7.1 PRE-FORMULATION CHARACTERISTICS

Pre-formulation testing is the first step in rational development of dosage forms of a drug substance. Pre-formulation study is the process of optimizing the delivery of drug through determination of physicochemical properties of the new compound that could affect drug performance and development of an efficacious, stable and safe dosage form. It gives the information needed to define the nature of the drug substance and provide a framework for the drug combination with pharmaceutical excepients in the dosage form.

Hence, Pre-formulation studies were performed for the obtained sample of drug for identification and compatibility studies.[41,42]

7.1.1 Physical characteristics of API

The physical characteristics of the drug describe the appearance of the drug, taste and odour of the drug.

a) Color: A small quantity of powder was taken in butter paper and Chlorphenaramine Maleate was viewed in well-illuminated place.[41,42]

b) Taste and odour: Very less quantity of Chlorphenaramine Maleate was used to get taste with the help of tongue as well as smelled to get the odour.[41,42]

7.1.2 Determination of solubility

The approximate solubilities of substances were indicated by the descriptive terms in the accompanying table. Solvents such as methanol, water, dimethyl sulfomide, pH 6.8 Phosphate buffer used for the solubility studies.

The solubility of the Chlorphenaramine Maleate was determined adding excess amount of drug in 10ml of different solutions. These solutions were shaken well for few minutes. Then the solubility was observed.

Descriptive Term	Parts of Solvent Required for 1 part of Solute
Very soluble	Less than 1
Freely soluble	From 1 to 10
Soluble	From 10 to 30
Sparingly soluble	From 30 to 100
Slightly soluble	From 100 to 1,000
Very slightly soluble	From 1,000 to 10,000
Practically insoluble (or) Insoluble	Greater than or equal to 10,000

7.1.3 Determination of Melting Point

Melting point of Chlorphenaramine Maleate was determined by open capillary method.

7.2 DRUG-EXCEPIENT COMPATIBILITY STUDIES

7.2.1 Fourier Transform Infrared Spectroscopy

Infrared studies were conducted to rule out the interaction between the drug and polymers in the formulation.

Principle behind FT-IR studies

FT-IR stands for Fourier Transform Infra Red, the preferred method of infrared spectroscopy. In infrared spectroscopy, IR radiation is passed through a sample. Some of the infrared radiation is absorbed by the sample and some of it is passed through (transmitted). The resulting spectrum represents the molecular absorption and transmission, creating a molecular fingerprint of the sample. Like a fingerprint no two unique molecular structures produce the same infrared spectrum. This makes infrared spectroscopy useful for several types of analysis.

FTIR was performed for pure drug, pure superdisintegrants, pure sublimating agents and optimized formulation. Samples are prepared by KBr pellet method and subjected to infrared radiations. The scanning range for FTIR studies were 40.

7.3 STANDARD CALIBRATION CURVE OF CHLORPHENARAMINE MALEATE

Table 7.3: Concentration and absorbance obtained for calibration curve of Chlorphenaramine Maleate in 6.8 pH phosphate buffer.

S. No.	Concentration (µg/ml)	Absorbance* (at 261 nm)
1	0	0
2	1	0.133
3	2	0.248
4	3	0.360
5	4	0.477
6	5	0.583
Correlation Coefficient = 0.999		

It was found that the estimation of Chlorphenaramine Maleate by UV spectrophotometric method at λ_{max} 261

nm in 6.8 pH Phosphate buffer had good reproducibility and this method was used in the study. The correlation coefficient for the standard curve was found to be closer to 1, at the concentration range, 0-5µg/ml.

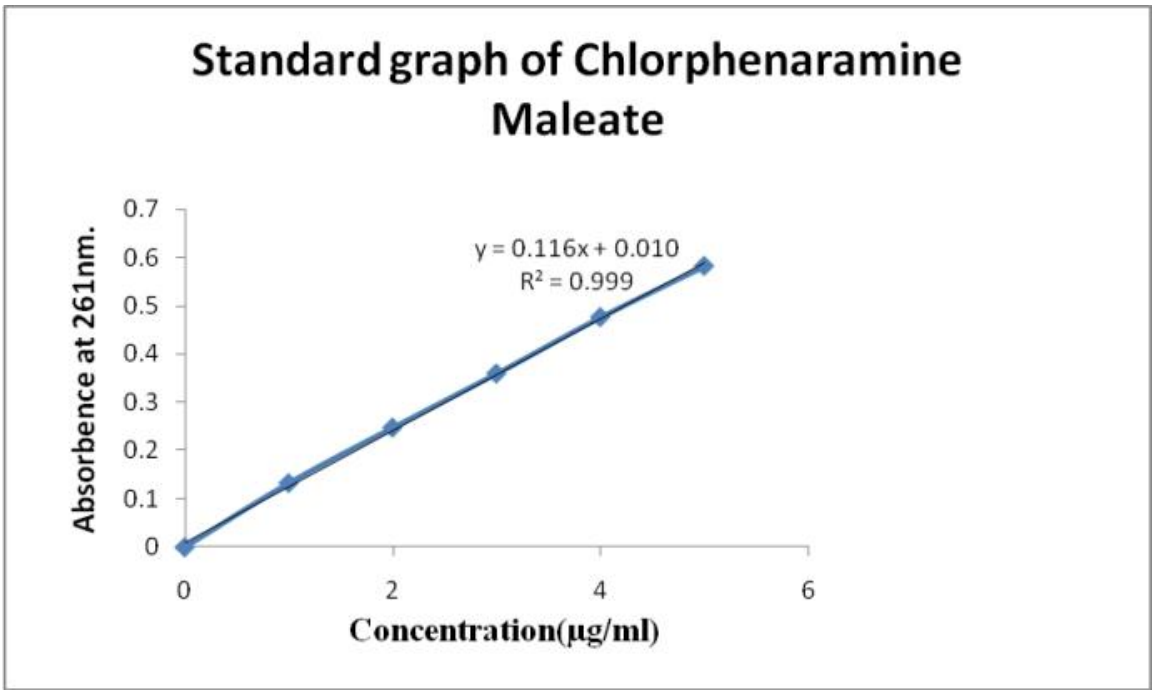


Fig 7.3: Standard Graph of Chlorphenaramine Maleate in 6.8 pH Phosphate buffer.

7.4 PRE-FORMULATION STUDIES

7.4.1 Physical characterisation of API

Physical characteristics of Chlorphenaramine Maleate which is used as the active ingredient in this project work. The physical characteristics of the drug describe the appearance of the drug and odour of the drug.

Table 7.4.1: Physical characteristics of Chlorphenaramine Maleate.

S.NO:	Description	Result
1.	Appearance	Off-White to white powder
2.	Odour	Slightly bitter

7.4.2 Solubility studies

SOLVENT	CHLORPHENARAMINE MALEATE
Water	Freely soluble
Methanol	Soluble
Ethanol	Soluble
Chloroform	Soluble
Ether, Benzene	Slightly Soluble
6.8pH buffer	Soluble

7.5 EVALUATION FOR POWDER BLEND OF DIRECT COMPRESSION PROCESS

Blend ready for compression containing drug and other excepient are subjected to pre-compression parameters (micrometric properties) to study its flow properties so as to achieve uniformity of tablet weight. The results of Pre-Compression parameters like bulk density, tapped density, compressibility index and Hausner's ratios are shown in table 7.5.

Table 7.5: Pre-compression Parameters.

Batch Code	Bulk density (gm/ml)±S.D (n=3)	Tapped density ±S.D(gm/ml) (n=3)	Carr's index (%)±S.D	Hausner's Ratio±S.D	Angle of Repose (Ɵ) ±S.D
F1	0.40±0.016	0.52±0.24	21.5±0.16	1.31±0.16	29.52±0.63
F2	0.41±0.035	0.55±0.28	24.36±0.18	1.33±0.05	28.12±1.23
F3	0.40±0.018	0.54±0.13	21.92±0.13	1.35±0.02	25.95±0.75
F4	0.38±0.024	0.45±0.19	15.55±0.19	1.19±0.02	28.92±1.58
F5	0.47±0.027	0.47±0.24	17.64±0.24	1.20±0.07	30.84±0.69
F6	0.39±0.039	0.58±0.32	19.22±0.32	1.20±0.05	29.52±0.63
F7	0.46±0.047	0.51±0.32	18.58±0.27	1.24±0.07	28.70±0.91
F8	0.41±0.034	0.52±0.24	23.77±0.19	1.23±0.10	26.98±0.80
F9	0.42±0.025	0.50±0.19	20.86±0.15	1.26±0.12	25.99±0.75

7.5.1 Bulk density

The powder blend of different formulations of direct compression was evaluated for bulk Density. The bulk density for all the formulations varied from 0.40±0.016 to 0.47±0.027. The values obtained lies within the acceptable range.

7.5.2 Tapped density

The powder blend of different formulations of direct compression was evaluated for tapped density. The tapped density for all the formulations varied from 0.45±0.19 to 0.58±0.32. The values obtained lies within the acceptable range.

The values of bulk density and tapped density lies within the acceptable range, from this the % compressibility of the powder can be calculated.

7.5.3 Compressibility index

The percentage compressibility of powder was determined using Carr's compressibility index. Compressibility index lies within the range of 15.55±0.19 to 24.36±0.18. All the formulations showed good compressibility. The results are shown in 7.5.

7.5.4 Hausner's Ratio

The flow ability of powder blend was determined using Hausner's Ratio. Hausner's Ratio lies within the range of 1.19±0.02 to 1.35±0.02. All the formulations show good flow ability. The results are shown in Table 7.5.

7.5.5 Angle of repose

The values were found to be in the range of 25.95±0.75 to 30.84±0.69. All the formulation showed angle of repose below 30^{o} which indicates a good flow property of the powder. The results obtained for all the formulations shown in Table 7.5.

7.6 POST COMPRESSION PARAMETERS

Table 7.6: Post compression Parameters.

Batch Code	Thickness(mm) ±SD (n=3)	Hardness (kg/cm^2) ±SD (n=3)	Friability (%) ±SD (n=20)	Average weight of the tablet (mg) (n=10)
F1	4.06±0.09	2.24±0.19	0.65±0.12	81.05±1.66
F2	4.18±0.08	2.20±0.23	0.62±1.03	80.40±1.31
F3	4.10±0.09	2.38±0.25	0.62±1.36	80.45±1.53
F4	4.02±0.07	2.30±0.25	0.83±1.16	76.35±1.60
F5	4.10±0.15	2.20±0.15	0.83±1.03	80.85±1.56
F6	4.08±0.12	2.15±0.11	0.65±1.04	80.55±1.43
F7	4.06±0.05	2.26±0.19	0.43±1.75	80.90±1.80
F8	4.08±0.12	2.63±0.26	0.65±1.04	80.43±1.31
F9	4.04±0.05	2.60±0.25	0.67±0.16	80.50±1.41

Weight variation test

Tablets of each batch were subjected to weight variation test, difference in weight and percent deviation was calculated for each tablet and was shown in the Table 7.6. The average weight of the tablet is approximately in range of 76.35±1.60 to 81.05±1.66. The results of the test showed that, the tablet weights were within the pharmacopoeia limit.

Hardness test

Hardness of the three tablets of each batch was checked by using Pfizer hardness tester and the data's were shown in Table 7.6. The results showed that the hardness of the tablets is in range of 2.15±0.11 to 2.63±0.26 kg/cm^2, which was within IP limits.

Thickness

Thickness of three tablets of each batch was checked by using Vernier Caliper and data shown in Table-7.6. The result showed that thickness of the tablet is raging from 4.02 ±0.072 to 4.18±0.035.

Friability

Tablets of each batch were evaluated for percentage friability and the data's were shown in the Table 7.6. The average friability of all the formulations lies in the range of 0.43±1.75 to 0.83±1.16% which was less than 1% as per official requirement of IP indicating a good mechanical resistance of tablets.

7.6.1. In -vitro Disintegration time

Different formulations have different disintegration times based upon the concentration and nature of superdisintegrant and thus compared. Prelimnary studies have been performed by direct compression technique to determine the effective superdisintegrant. Based upon the disintegration time results crospovidone found to be the best super disintegrants.

- Hence it can be concluded that superdisintegrants can be formulated along with sublimating agents for the preparation of oral disintegrating tablets.
- F6 formulation has disintegrated quickly than the other formulations because of its porous nature and wicking mechanism and of the superdisintegrant (i.e cp 8%).

Table 7.6.1: Disintegration time profiles of Chlorphenaramine Maleate in various Formulations.

Each values represents the mean ± SD (n=6)

F1 (sec)	F2 (sec)	F3 (sec)	F4 (sec)	F5 (sec)	F6 (sec)	F7 (sec)	F8 (sec)	F9 (sec)
60±1.0	42±2.5	45±1.0	35±1.6	26±1.5	18±0.01	50±2.8	55±1.63	72±2.5

7.6.2. Wetting time

Table 7.6.2: Wetting time profiles of Direct compressed tablets.

F1 (sec)	F2 (sec)	F3 (sec)	F4 (sec)	F5 (sec)	F6 (sec)	F7 (sec)	F8 (sec)	F9 (sec)
51±0.25	63±0.41	59±0.32	61±0.27	52±0.21	41±0.08	76±0.67	62±0.12	57±0.44

Each values represents the mean ± SD n=3

Table 7.6.2 summarizes the wetting time profile of all the formulated tablets. Different formulations have different wetting times these are obtained by using various types and concentration of superdisintegrants and sublimating agents for various formulations Among the directly compressed tablets with croscaramellose sodium showed less Wetting time than the tablets containing crospovidone and sodium starch glycolate.

- Hence we can conclude that oral disintegration tablets can be prepared by compession method approach of superdisintegrant.
- The results of wetting time are place in the table 7.6.2
- Figure 7.6.2 **represents** the wetting time profiles of all formulation of Chlorphenaramine Maleate.

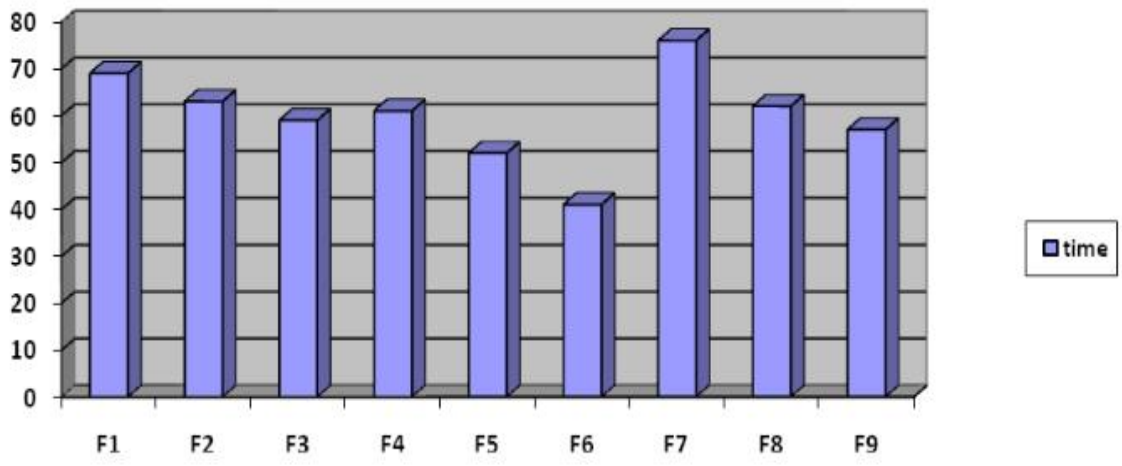


Figure 7.6.2: Wetting times of various formulations.

7.6.3. Drug Content Uniformity of various formulations of Chlorphenaramine Maleate Prepared by Direct Compression Technique.

Batch code	Drug content (%)
F1	92.34
F2	98.23
F3	96.32
F4	97.65
F5	95.84
F6	99.76
F7	97.51
F8	92.84
F9	91.65

The drug content was found to be in the range of 91.65±0.945% to 99.76±0.284% for the tablets prepared by direct compression method. The results of content uniformity are placed in the table 7.6.3.

Each values represents the mean ± SD n=6.

7.7. In-vitro drug release studies

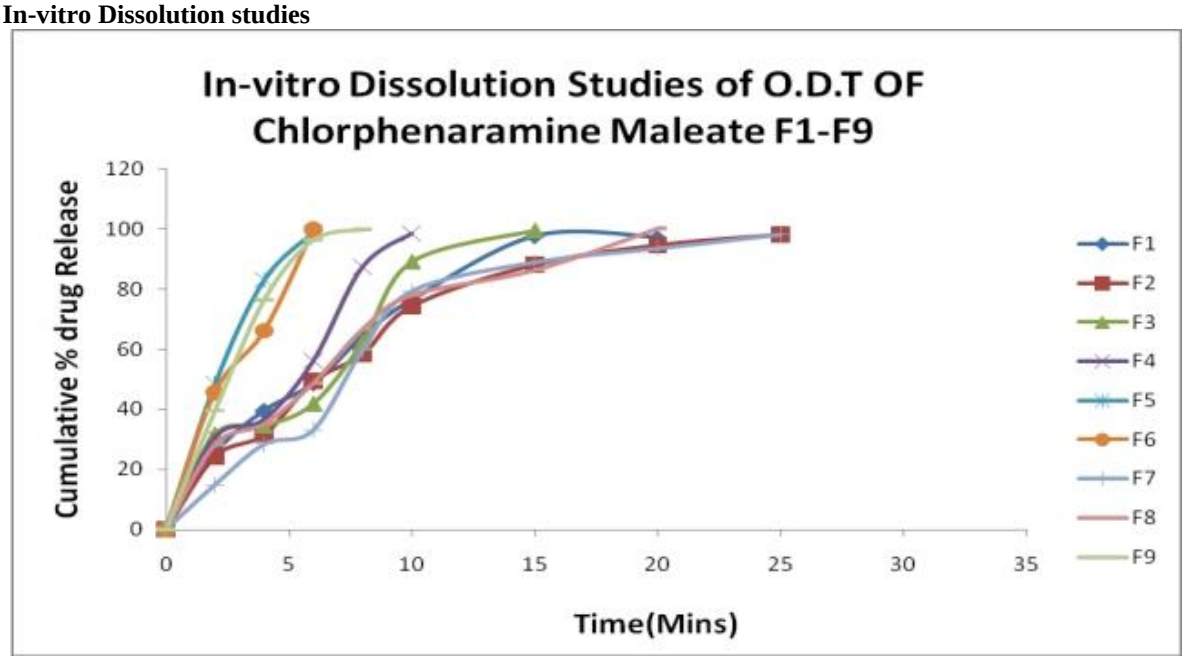
Merely disintegration studies are not judicious since all super disintegrants appear to be highly efficient. The *in-vitro* dissolution studies are done to obtain the cumulative drug release profile of the drug and to procure the optimized formulation among all.

7.8. In-vitro Dissolution studies

In-vitro dissolution studies were carried out by using 500ml of 6.8 pH phosphate buffer in USP dissolution apparatus by using paddle method. The dissolution studies were carried out for about 30 minute dissolution data for all the formulations were given in the Table 7.8.

Time(Min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
2	25.4	24.3	31.7	30.8	48.3	45.72	14.9	28.4	39.5
4	39.6	31.6	34.5	36.72	82.9	66.16	28.4	35.2	76.3
6	48.6	49.3	41.9	56.16	98.7	99.89	33.1	48.9	96.2
8	64.3	58.3	62.4	87.4			59.7	66.8	99.7
10	76.4	74.3	89.1	98.5			79.3	78.1	
15	97.6	88.1	99.5				88.9	86.4	
20	97.1	94.6					93.5	100.3	
25		98.1					98.1		
30									

7.8. In-vitro Dissolution studies



7.8 (a) In-Vitro Dissolution Studies of Chlorphenaramine Maleate.

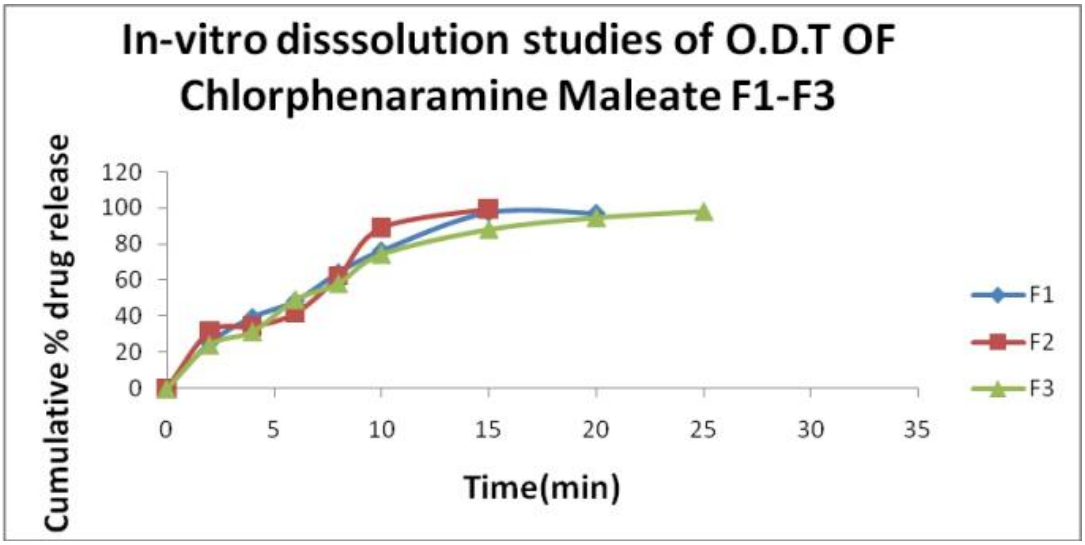


Fig: 7.8a. Dissolution profile Of F1, F2, F3 formulations prepared with Sodium Starch glycolate super disintegrants.

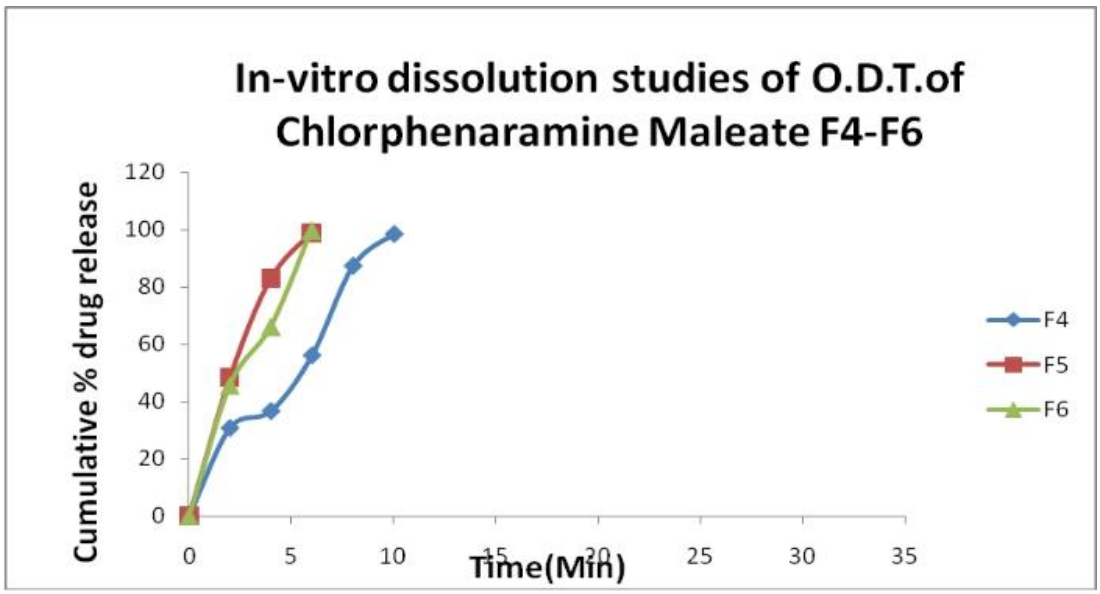


Fig 7.8b: Dissolution profile of F4, F5, F6 formulations prepared with Crospovidone as Super Disintegrants.

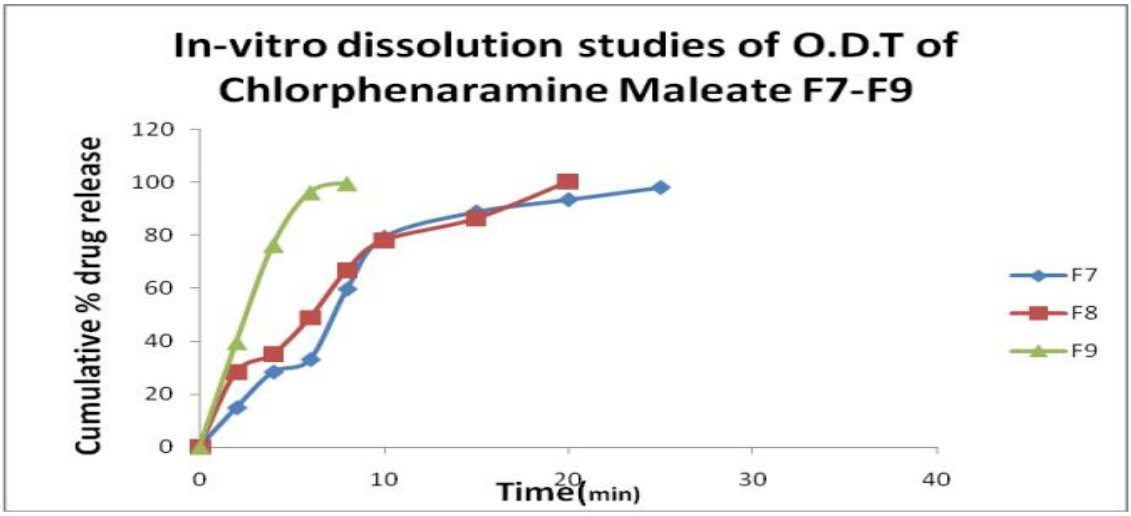


Fig 7.8c: Dissolution profile of F7, F8, F9 formulations prepared with Croscaramellose sodium as Super Disintegrants.

From the tabular column 7.4 it was evident that the formulations prepared with super disintegrate polyplasdone XL showed maximum % drug release in 6 Mins i.e. 99.89% (F6 formulation and the concentration of super disintegrate is 6.4 mg). The formulations prepared with vivasole showed maximum percentage drug release in 8 Mins i.e., 99.70% (F9 formulation and the concentration of super disintegrate is 6.4 mg).The formulation's prepared with explotab showed maximum percentage drug release in 15Mins i.e., 99.50%.

Irrespective of super disintegrate type the disintegration time decreases and Dissolution time also decreases as the concentration of super disintegrate increases. The dissolution profile was represented in above graphs.

7.9. Fourier Transform-Infrared Spectroscopy

All the prominent and primary peaks were observed in FTIR spectrum of Chlorphenaramine Maleate. Was shown in Figure 7.9 and Table 21.

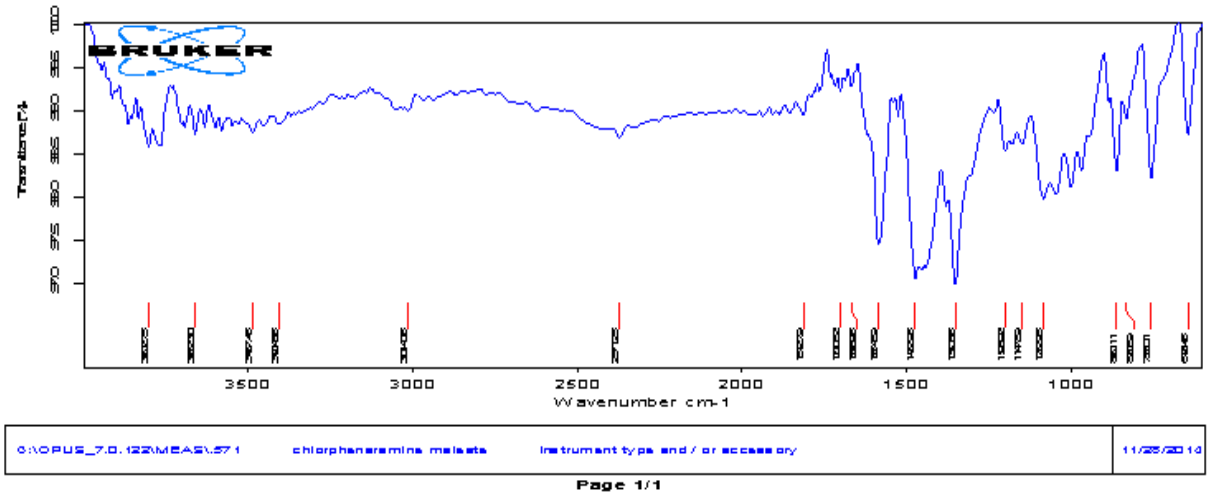
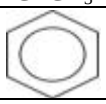


Figure 7.9: FT-TR Spectrum of Chlorphenaramine Maleate pure Drug.

Table 21: FTIR peaks and their functional groups of pure Chlorphenaraminemaleate.

Functional Group	IR range (cm^{-1})	Peak observed (cm^{-1})
N-H	2950-2800	3014.06
C=O	1430	1350.88
C- CH_3	3030-2855	756.01
	2980-2900	3404.56

All the prominent and primary peaks were observed in FTIR spectrum of Chlorphenaramine Maleate+Sodium Starch Glycolate was shown in Figure 7.9.1 and Table 22.

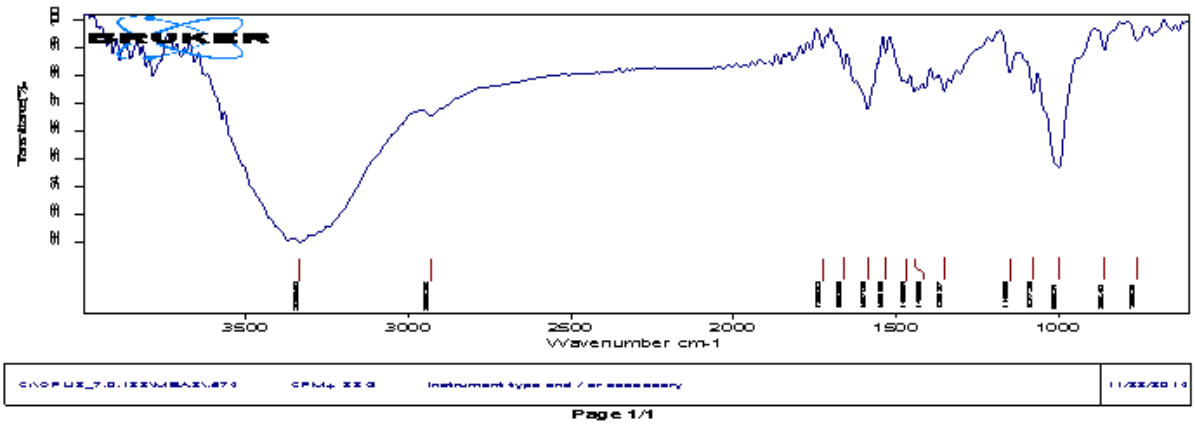
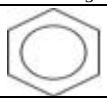


Figure 7.9.1: FT-TR Spectrum of Chlorphenaramine Maleate+Sodium Starch Glycolate.

Table 22: FTIR peaks and their functional groups of pure Chlorphenaramine Maleate+Sodium Starch Glycolate.

Functional Group	IR range (cm^{-1})	Peak observed (cm^{-1})
N-H	2950-2800	3014.06
C=O	1430	1350.88
C- CH_3	3030-2855	756.01
	2980-2900	3404.56

The infrared peak intensity of Chlorphenaramine Maleate appeared 3014.06cm-1 assigned to the N–H stretch of Secondary amines. The infrared peak intensity at 1350.88 cm-1 assigned to the corresponding to C=O stretch of ester functional group. A broad peak from 3404.56 cm-1 assigned to the C-C stretching in aromatic ring also appeared clearly. The peak corresponding to C-CH3 stretch is appeared at 756.01 cm-1. The main functional groups of Chlorphenaramine Maleate drug is COOCH3, NH, C=O and it was found in above FT-IR spectrum of Chlorphenaramine Maleate, Hence it was concluded that it confirms that given sample is Chlorphenaramine Maleate.

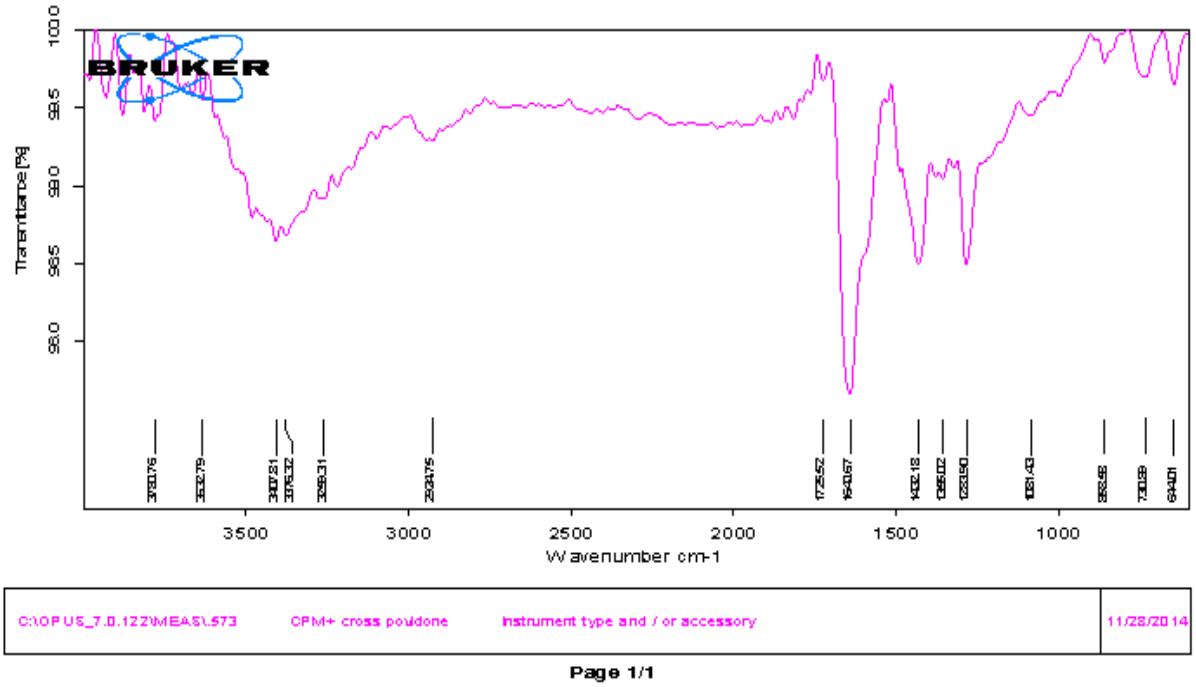


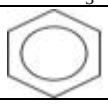
Figure 7.9.2: FT-TR Spectrum of Chlorphenaramine Maleate+Crospovidone.

Table 22: FTIR peaks and their functional groups of pure Chlorphenaramine Maleate+Sodium Starch Glycolate.

Functional Group	IR range (cm^{-1})	Peak observed (cm^{-1})
C-H	2950-2800	2902.28
C–O–H	1430	1361.87
C- CH_3	3030-2855	2902.28
	2980-2900	3003.50

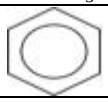
The infrared peak intensity of Chlorphenaramine Maleate+Sodium Starch Glycolate appeared 2902.28cm-1 assigned to the C–H stretch of Functional Groups. The infrared peak intensity at 1361.87 cm-1 assigned to the corresponding to C-O-H stretch of functional group. A broad peak from 3003.50 cm-1 assigned to the C-C stretching in aromatic ring also appeared clearly. The peak corresponding to C-CH3 stretch is appeared at 2902.28 cm-1. The main functional groups of Chlorphenaramine Maleate+Sodium Starch Glycolate drug is C-CH3,CH, C-O-H and it was found in above FT-IR spectrum of Chlorphenaramine Maleate+Sodium Starch Glycolate.

Table 23: FTIR peaks and their functional groups of pure Chlorphenaramine Maleate+Crospovidone.

Functional Group	IR range (cm^{-1})	Peak observed (cm^{-1})
C-H	2950-2800	2924.75
C=O	1430	1432.18
C- CH_3	3030-2855	3259.31
	2980-2900	2924.75

The infrared peak intensity of Chlorphenaramine Maleate +Crospovidone appeared 2924.75cm-1 assigned to the C–H stretch of Functional Groups. The infrared peak intensity at 1432.18 cm-1 assigned to the corresponding to C=O stretch of ester functional group. A broad peak from 2924.75 cm-1 assigned to the C-C stretching in aromatic ring also appeared clearly. The peak corresponding to C-CH3 stretch is appeared at 3259.31 cm-1. The main functional groups of Chlorphenaramine Maleate +Crospovidone drug is COOCH3, CH, C=O and it was found in above FT-IR spectrum of, Hence it was Chlorphenaramine Maleate +Crospovidone Concluded that it confirms that given sample is Chlorphenaramine Maleate +Crospovidone.

Table 24: FTIR peaks and their functional groups of pure Sodium Starch Glycolate.

Functional Group	IR range (cm^{-1})	Peak observed (cm^{-1})
N-H	2950-2800	3026.00
C=O	1430	1616.70
C- CH_3	1000-1500	1417.10
	2980-2900	3026.00

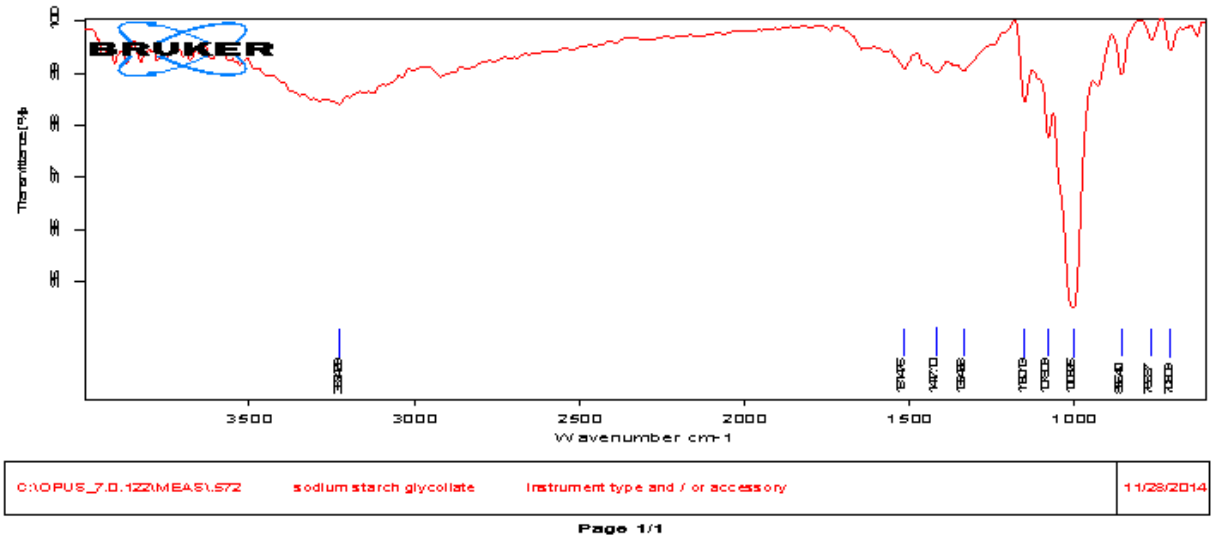


Figure 7.9.3: FT-TR Spectrum of Sodium Starch Glycolate.

The infrared peak intensity of Sodium Starch Glycolate appeared 3026.00cm-1 assigned to the N–H stretch of secondary amine. The infrared peak intensity at 1616.70cm-1 assigned to the corresponding to C=O stretch of ester functional group. A broad peak from 3026.00 cm-1 assigned to the C-C stretching in aromatic ring also appeared clearly. The peak corresponding to C-CH3 stretch is appeared at 1417.10 cm-1. The main functional groups of Sodium Starch Glycolate d rug is COOCH3, NH, C=O and it was found in above FT-IR spectrum of Sodium Starch Glycolate, Hence it was concluded that it confirms that given sample is Sodium Starch Glycolate.

CONCLUSION

Oral route is the widely used route for the administration of any type of dosage form and can be made a best route by overcoming its drawbacks.

Immediate release tablets by using a super disintegrant solved the problems encountered during the medication through oral route.

In the present work, an attempt has been made to develop fast disintegrating tablets of Chlorphenaramine Maleate.

New generation super disintegrates Polyplasdone XL, Vivasole and Explotab was selected as super

disintegrates. All the formulations were prepared by Direct Compression method using 6mm punch on 10 station lab press tablet Compression Machine.

The blend of all the formulations showed good flow properties such as Angle of repose, Bulk density, Tapped density.

The prepared tablets were shown good post compression parameters and they passed all the quality control evaluation parameters as per I.P limits.

Among all the formulations F6 formulation showed maximum % drug release i.e., 99.89% in 18±0.01 sec hence it is considered as optimized formulation.

REFERENCES

1. Ansel., 2006. 'Pharmaceutical dosage forms & drug delivery systems.' 8th Edition, 227-260.
2. Indian Pharmacopoeia, 2010; 2: 1464-1465.
3. Lachman L, liberman HA, Kanig JL., 1990. The theory and practice of industrial pharmacy. 3rd ed., 293-335.
4. Bentleys text book of pharmaceutics, 8th ed, 278-279.
5. Patel HP, Preeti karwa, Rama Bukka, Patel NJ., 2011. 'Formulation and evaluation of immediate release tablets of Zolpidem tarrate by direct compression.' Int. J pharm sci., 7(2): 80-85.
6. Remington. The science and practice of pharmacy. 20th ed., 858.
7. Alok Kumar Gupta, Anuj Mittal, Prof. K. K. Jha., 2011. 'Fast dissolving tablets-A Review' The pharma innovation, 2012; 1(1): 1-8.
8. Bradoo, R., Shahani, S., Poojary, S., Deewan, B., Sudarshan, S. (2001) Fast Dissolving Drug Delivery Systems. JAMA India, 4(10): 27-31.
9. R Chang; X Guo; B Burnside; R Couch, Pharma Tech, (North America), June, 2000; 52-58.
10. Y Bi; H Sunanda; Y Yonezawa; K Dayo; A Otsuka; K Iida, Chem Pharma Bull (Tokyo), 1996; 44: 2121-2127.
11. Yonezawa B, Y; Sunanda H, Rapidly disintegrating tablets prepared by wet compression method, Mechanism and Optimization, J. Pharm. Sci 1999; 88(1): 1004-10.
12. Shukla D, Chakraborty S, Singh S, Mishra B. Mouth Dissolving Tablets I: An Overview of Formulation Technology, Sci Pharm, 2009; 77: 309–26.
13. Bradoo R. Fast Dissolving Drug Delivery Systems. JAMA India, 2001; 4(10): 27-31.
14. Kibbe AH, ed. Hand book of Pharmaceutical Excipients., 3rd edition. Bentleys text book of pharmaceutics, 8th ed, 278-279.
15. Rowe RC, Sheskey PJ, Paul Weller., 2009. Handbook of pharmaceutical excipients 4th ed., 181-182.
16. Bhupendra G Prajapati and Nayan Ratnakar. "A Review on Recent patents on Rapid Dissolving Drug Delivery System" International Journal of Pharma. Tech Research, 2009; 1(3).
17. Debjit Bhowmik, Chiranjib.B, Krishnakanth, Pankaj, R.Margret Chandira. "Rapid Dissolving Tablet: An Overview" Journal of Chemical an Pharmaceutical Research, 2009; 1(1): 163-177.
18. Suresh Bandari, Rajendar Kumar Mittapalli, Ramesh Gannu, Yamsani Madhusudan Rao. "Orodispersible tablets: An overview." Asian journal of pharmaceutics, 2008; 2(1): 2-11.
19. Srinivas P and Mahalaxmi R., 2011. 'Preparation and invitro evaluation of nizatidine immediate release tablets.' Int. J. Pharmtech Res., 3(3): 1688-1692.
20. Syed azeem hyder, Syed ali ul hasan, Shaweta Sharma., 2011. 'Formulation and optimization of immediate release tablet of rupatadine fumarate.' Int. J. Pharma prof Res., 2(3): 345-350.
21. Tiwari AK, Shah A, Rajpoot A, Manmohan Singhal., 2011. 'Formulation and In-vitro Evaluation of Immediate release tablets of Drotaverine HCl.' J. Chem. Pharm. Res., 3(4): 333-341.
22. Naveen Pathak, Anuj Kumar, Vishal Methkar, Pankaj Pant and Rama Therdana Rao., 2011. 'Formulation and optimization of immediate release tablet of an antialcoholic drug by dry granulation method.' Int. J. com Pharm., 3(8): 1-4.
23. Sai Madhav Reddy K, Laxmidhar Sahoo, Kamalakar Reddy G, Vamsi Krishna L., 2011. 'Formulation and evaluation of immediate release tablets of Linezolid.' Int. J. Pharm & Bio Arch., 2(4): 1230-1235.
24. Seemanchala Rath, Bijan Kumar gupta, Nripendra Nath Bala, Harish Chandra Dhal., 2011. 'Formulation and optimization of immediate release telmisartan tablets using full factorial design.' Int. J. App Pharm., 3(3): 20-24.
25. Eiring AM, Khorashad JS, Kimberly Morley, Deininger MW., 2011. 'Advances in the treatment of chronic myeloid Leukemia.' BMC mededin., 9(99): 1741-7015.
26. Monica RP Rao, Visha KG, Girish SS., 2010. 'Preparation and Evaluation of immediate release tablet of metoclopramide Hcl using simplex centroid Mixture design.' Int. J. Pharmtech Res., 2(2): 1105-1111.
27. Yeole CN, Darekar SS, Amit Gupta, Ganga Shrinivasan., 2010. 'Formulation and Evaluation of Immediate Release Tablet of Paroxetine Hydrochloride.' J Phar Res., 3(8): 1736-1738.
28. Rai VK, Pathak N, Bhaskar R, Nandi BC, Dey S, Tyagi LK., 2009. 'Optimization of immediate release tablet of Raloxifene hydrochloric de by wet granulation method.' Int. J. Pharm Sci and drug Res., 1(1): 51-54.
29. Rabia Bushra, Shoaib MH, Nousheen Aslam, Durriya Hashmat and Rehman MU., 2008. 'Formulation development and optimization of ibuprofen tablets by direct compression method.' Pak. J. Sci., 21(2): 113-120.

30. Furtado.S, Deveswaran.R, Bharath.S, Basavaraj.B.V, Abraham.V, Madhavan. Development and characterization orodispersible tablets of famotidine containing a subliming agent : Journal of Pharmaceutical Research, 2008; 7: 1185-1189.
31. Patil A.B., Sumit.C, Sibaji.S. Formulation and Evaluation of Mouth Dissolving Tablet of Ketorolac Tromethaminefor Pain Management by Using Superdisintegrants: International Journal of Chem Tech Research, 2009; 14: 1008-1013.
32. Battu.S.K, Michael A. R, Soumyajit.M, Rao Y. M: Formulation and Evaluation of Rapidly Disintegrating Fenoverine Tablets: Effect of Superdisintegrants Drug Development and Industrial Pharmacy, 2007; 33: 1225–1232.
33. Dr. Raghavendra Rao N. G, Upendra Kulkarni, Formulation and Design of Fast Dissolving Tablets of Felodipine using Novel Co-Processed Superdisintegrants. International Journal of Pharma Research and Development, 2010; 2(9): 113-121.
34. S.B Shirsand, M.S para, R.G Ramani, P.V. Swamy, D. Nagendra Kumar AND \M.V Rampure, Novel Co-Processed Superdisintegrants in the Design of Fast Dissolving Tablets, International Journal Pharm Tech Research, 2010; 2(1): 222-227.
35. D.Nagendrakumar, Raju S.A.S.B.Shirsand and M.S.Para, Design of Fast Dissolving Granisetron HCl Tablet using Novel Co –Processed Superdisintegrants. Journal of Bioscience Technology, 2009; 1(1): 8-14.
36. Mukesh C.Gohel, Rajesh K.Parikh, bansari k. Brahmbhatt, and Aarohi R. Shah, Improving the tablet characteristics and dissolution profile of ibuprofen by using novel co-processed superdisintegrant: a technical note. American Association of Pharmaceutical Sciences, 2007; 8(1): 131-6.
37. www.diailymed.
38. Kuchekar B.S; Badhan A.C; Mahajan H.S, Mouth Dissolving tablets, A novel drug delivery systems, Pharma, Times, 2003; 35: 7-9.
39. Afifa Bathool, D. V. Gowda, Mohammed S. Khan, Ayaz Ahmed, S. L. Vasudha, and K. Rohitash, Development and evaluation of microporous osmotic tablets of diltiazem hydrochloride, J Adv Pharm Technol Res., 2012 Apr-Jun; 3(2): 124-26.