Determination of Flow Property of Different Groups of Excipients with Different Amounts of Disintegrants

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A thesis report, submitted to the Department of Pharmacy, East West University, in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation, entitled “Determination of Flow Property of Different Groups of Excipients with Different Amounts of Disintegrants” is an authentic and genuine thesis project carried out by me under the guidance of Md. Anisur Rahman, Senior Lecturer, Department of Pharmacy, East West University, Dhaka.

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ENDORSEMENT BY THE CHAIRPERSON

This is to certify that the dissertation entitled “Determination of Flow Property of Different Groups of Excipients with Different Amounts of Disintegrants” is a genuine research work carried out by Mynul Islam Mufti, under the supervision of Md. Anisur Rahman (Senior Lecturer, Department of Pharmacy, East West University, Dhaka). I further certify that no part of the thesis has been submitted for any other degree and all the resources of the information in this connection are duly acknowledged.

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Prof. Dr. Chowdhury Faiz Hossain

Chairperson and Ex Dean

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CERTIFICATE BY THE SUPERVISOR

This is to certify that the dissertation entitled "Determination of Flow Property of Different Groups of Excipients with Different Amounts of Disintegrants", submitted to the Department of Pharmacy, East West University, Dhaka, in partial fulfillment of the requirements for the Degree of Bachelor of Pharmacy, was carried out by Mynul Islam Mufti, ID: 2010-1-70-021 under my supervision and no part of this dissertation has been or is being submitted elsewhere for the award of any Degree/Diploma.

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Mynul Islam Mufti

This Research Paper is Dedicated

To

My Beloved Parents

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ABSTRACT

Powder flow characteristic is an important parameter during drug manufacturing process. The aim of this research work is determine the power flow characteristics of different excipients. Powder flow characteristic was determined using different parameter, for example, angle of repose, Carr's index and Hausner ratio. At first, some excipients were selected to form a mixture and then three disintegrants, eg., starch, polyvinyl pyrrolidone, carboxymethyl cellulose and microcrystalline cellulose were added in different ratios. Finally values of angle of repose, Carr's index and Hausner ratio of different ratios were determined. Variation in the values of angle of repose, Carr's index and Hausner ratio were observed after addition of different amounts of disintegrants. It was observed that flow property was improved after addition of some excipients. This research work for the thesis project has shown the improvement in flow characteristic while using different amounts of disintegrants in a drug formulation. In addition the numerical data, the regression values and equations may further be used to predict the flow characteristics of these widely used excipients, and this will be beneficial for manufacturing new products or transforming the existing one in pharmaceutical industry.

Keywords: Powder flow property, Excipients, Carr's index, Hausner's ratio, Angle of repose, Disintegrants

Chapter One

INTRODUCTION

1.1 INTRODUCTION

The objective of this research project was to determine the flow characteristics of different excipients used in pharmaceutical formulations. In this research flow characteristics of mixture of excipients were determined using individual excipients of different classes of excipients. At first the most important classes of excipients are chosen and then widely used excipients from these classes are listed. Then individual flow characteristics of selected excipients were measured using different parameters, for example, angle of repose, Carr's index or compressibility index and Hausner's ratio.

It has been anticipated that powders account for 80% of materials used in industry. Handling and processing powders, particulates and granules is essential to the pharmaceutical industry, but has traditionally been fraught with problems due to their unpredictable and irregular behavior, specifically with respect to flowability. With so many raw materials, semi-finished and finished products in powder form, pharmaceutical companies stand to increase significant manufacturing and commercial profits from improvements in the evaluation of powder flow.

Powder flow analysis is really valuable in the pharmaceutical industry, as well as in several others. Objective and repeatable testing combined with ranking of dry powder samples can provide significant opportunities and benefits. These contain optimizing batch and source selection in terms of cost and quality; the progress of best mix formulations; optimizing scaling up and process conditions; and maintaining product quality control. Innovative technology provides such data either by measuring and comparing products capable of flow, or by assessing sample behavior under test conditions reproducing in-process or product handling conditions. (Young, 2013)

Angle of repose, a powder flow determining parameter is examined by using a funnel attached with a stand. The individual powder excipient or mixture of powder excipients are freely passed over the funnel and after that using an equation, we determined the values of angle of repose of respective individual powder excipient or mixtures of

powder excipients. The values of angle of repose indicate the respective flow characteristic of individual powder excipient or mixture of powder excipients.

Carr's index or compressibility index and Hausner's ratio are another significant powder flow determining parameter calculated by using bulk volume and tapped volume of a certain amount of powder excipient in a measuring cylinder. By using the equation of Carr's index and Hausner's ratio, we determined the values of these parameters which explain the flow characteristics of respective powder excipient or mixture of powder excipients.

In this research individual flow characteristics of an excipient and flow characteristics of that excipient along with other excipients is determined. In manufacturing a solid dosage form like tablets, capsules, a single excipient is not used alone. In total manufacturing process a mixture of excipients of different classes is used. So it is necessary to determine the flow characteristics of different excipients in a mixture. By determining these, we can easily select the best suited mixture of excipient in terms of flow characteristics.

1.2 PHARMACEUTICAL EXCIPIENTS

1.2.1 Definition

Information available from their website of U.S. Pharmacopeia (Anon.,2010) Excipients are defined as any substances, other than the active drug or product, that have been appropriately evaluated for safety and are included in a drug delivery system to either aid the processing of the drug delivery system during its manufacture, protect, support or enhance stability, bioavailability, or patient acceptability, assist in product identification, or enhance any other attribute of the overall safety and effectiveness of the drug delivery system during storage or use.

Drug products contain both drug substance, commonly referred to as active pharmaceutical ingredient (API) and excipients. Reasons for this include the followings:

- ✓ Ease of administration to the target patient population by the proposed route
- ✓ Improved dosing compliance
- ✓ Consistency and control of drug bioavailability
- ✓ To enable bioavailability
- ✓ Improved API stability including protection from degradation
- ✓ To ensure a robust and reproducible physical product. (Mills, 2010)

1.2.2 Types

There are different types of excipients used in pharmaceutical manufacturing. These include the followings:

1. Antiadherents	7. Colours
2. Binders	8. Lubricants
3. Coatings	9. Glidants
4. Disintegrants	10. Sorbents
5. Fillers	11. Preservatives
6. Flavours	12. Sweeteners

1.2.2.1 Antiadherent

Antiadherents or anti-sticking agents prevent adhesion of the tablet surface to the die walls and the punches and as a consequence counter the picking or sticking of tablet.
Most commonly used antiadherent is magnesium stearate, which is also a water soluble lubricant. Talc and starch can also be used as antiadherent. (Apu, 2010)

1.2.2.2 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. Binders are usually:

- ➢ Saccharides and their derivatives:
  - ✓ Disaccharides: sucrose, lactose;

- ✓ Polysaccharides and their derivatives: starches, cellulose or modified cellulose such as microcrystalline cellulose and cellulose ethers such as hydroxypropyl cellulose (HPC);
- ✓ Sugar alcohols such as xylitol, sorbitol or maltitol;

➢ Protein: Gelatin

➢ Synthetic polymers: polyvinylpyrrolidone (PVP), polyethylene glycol (PEG)...

❖ Binders are classified according to their application:

- Solution binders are dissolved in a solvent (for example water or alcohol can be used in wet granulation processes). Examples include gelatin, cellulose, cellulose derivatives, polyvinylpyrrolidone, starch, sucrose and polyethylene glycol.
- Dry binders are added to the powder blend, either after a wet granulation step, or as part of a direct powder compression formula. Examples include cellulose, methyl cellulose, polyvinyl pyrrolidone and polyethylene glycol. (Excipients, 2013)

1.2.2.3 Coatings

Tablet coatings protect tablet ingredients from deterioration by moisture in the air and make large or unpleasant-tasting tablets easier to swallow. For most coated tablets, a cellulose ether hydroxypropyl methylcellulose (HPMC) film coating is used which is free of sugar and potential allergens. Occasionally, other coating materials are used, for example synthetic polymers, shellac, corn protein zein or other polysaccharides. (Excipients, 2013)

1.2.2.4 Disintegrants

The purpose of a disintegrant is to facilitate the breakup of a tablet when they contact water in gastrointestinal tract.A disintegrant is added to most tablet formulations to facilitate a breakup or disintegration of the tablet when placed in an aqueous environment. (Apu, 2010)

Disintegrants expand and dissolve when wet causing the tablet to break apart in the digestive tract, releasing the active ingredients for absorption.

They ensure that when the tablet is in contact with water, it rapidly breaks down into smaller fragments, facilitating dissolution.

Examples of disintegrants include:

- Crosslinked polymers: crosslinked polyvinyl pyrrolidone (crospovidone), crosslinked sodium carboxymethyl cellulose (croscarmellose sodium).
- The modified starch sodium starch glycolate. (Excipients, 2013)

1.2.2.5 Diluents

Dilents are also known as bulking agents or fillers. Diluents added to the active ingredient in sufficient quantity to make a reasonably sized tablet. A tablet should at least 50mg and therefore very low dose drugs (diazepam, clonidine hydrochloride) will invariably require a diluent to bring the overall tablet weight to at least 50mg.

This agent may not be necessary if dose of drug per tablet is high (e.g. aspirin and certain antibiotics). Usually the range of diluents may vary from 5-80%. (Apu, 2010)

Fillers or diluents typically also fill out the size of a tablet or capsule, making it practical to produce and convenient for the consumer to use.A good filler should typically be inert, compatible with the other components of the formulation, non-hygroscopic, relatively cheap, compactible, and preferably tasteless or pleasant tasting. Plant cellulose (pure plant filler) is popular filler in tablets or hard gelatin capsules. Dibasic calcium phosphate is popular tablet filler. A range of vegetable fats and oils can be used in soft gelatin capsules. Other examples of fillers include: lactose, sucrose, glucose, mannitol, sorbitol, calcium carbonate, and magnesium stearate. Sometimes other noted kinds of excipients are in effect doubling in function as fillers. (Excipients, 2013)

1.2.2.5.1 Reasons for using Diluents

- Inert substance designed to make up the required bulk of tablet when the drug dosage itself is inadequate to produce its bulk.
- To provide better tablet properties such as:
  - ✓ Improved cohesion (maintain proper shape of tablet)
  - ✓ To permit use of direct compression manufacturing

- ✓ To promotes flow
- ✓ To adjust weight of tablet as per die capacity. (Apu, 2010)

1.2.2.5.2 Influence of diluents on bioavailability

- Although diluents are normally thought of as inert ingredients, they can significantly affect the biopharmaceutical, chemical and physical properties of tablet. The calcium salts interfering with the absorption of tetracycline from the gastrointestinal tract. They make half the bioavailability of standard product.
- Antiepileptic drug sodium phenytoin will form poorly absorbable calcium-phenytoin complex, when calcium sulphate dihydrate used as diluent in the formulation. But using of lactose as diluent improves bioavailability of the antiepileptic drug significantly. (Apu, 2010)

1.2.2.5.3 Influence of diluents on incompatibility

- Sometimes diluents cause discoloration of tablet. In case of amine drugs, lactose used as dilent along with metal stearate (Magnesium stearate) used as lubricant, cause's discoloration of tablets with time. (Apu, 2010)

1.2.2.6 Lubricants

Lubricants are supposed to help in the reduction of friction:

- ✓ Between particles during compression and
- ✓ Between the walls of tablet and the walls of the cavity in which tablet was formed

The lubricants are believed to form a coat around each granule and this effect also gets extended to the tablet surface. The lubricants may show some inherent drawbacks:

- ✓ Lessen tensile strength (may interfere with the particle – particle bonding)
- ✓ Extension of disintegration and dissolution time (waterproofing properties)

Since primarily lubricants are required to act at the tooling or material interface, lubricants should be incorporated in the final mixing step, after granulation is complete. Concentration should not exceed to 1% for producing maximum flow rate. (Apu, 2010)

Lubricants prevent ingredients from clumping together and from sticking to the tablet punches or capsule filling machine. Lubricants also ensure that tablet formation and ejection can occur with low friction between the solid and die wall.

Common minerals like talc or silica, and fats, e.g. vegetable stearin, magnesium stearate or stearic acid are the most frequently used lubricants in tablets or hard gelatin capsules. Lubricants are agents added in small quantities to tablet and capsule formulations to improve certain processing characteristics.

❖ There are three roles identified with lubricants as follows:

1. True lubricant role:
   - ✓ To decrease friction at the interface between a tablet's surface and the die wall during ejection and reduce wear on punches & dies.

2. Anti-adherent role:
   - ✓ Prevent sticking to punch faces or in the case of encapsulation, lubricants
   - ✓ Prevent sticking to machine dosators, tamping pins, etc.

3. Glidant role:
   - ✓ Enhance product flow by reducing interparticulate friction.

1.2.2.6.1 Types

There are two major types of lubricants:

1. Hydrophilic

- ✓ Generally poor lubricants, no glidant or anti-adherent properties.

2. Hydrophobic

- ✓ Hydrophobic lubricants are generally good lubricants and are usually effective at relatively low concentrations. Hydrophobic lubricants are used much more frequently than hydrophilic compounds. E.g., magnesium stearate. (Excipients, 2013)

1.2.2.7 Glidants

Glidants are used to promote powder flow by reducing inter particle friction and cohesion. These are used in combination with lubricants as they have no ability to reduce die wall friction. (Excipients, 2013)

The commonly used glidants are talcum, starch, colloidal silica, silicates, stearates, calcium phosphate etc.

Concentration of starch is common up to 10%, but should be limited otherwise it will worsen the flow of material. Talc is a glidant which is superior to starch; its concentration should be limited because it has retardant effect on dissolution-disintegration profile.

The most important and traditional glidant used is talcum (talc). Recently, silica type glidants are becoming popular due to their small particle size.

Magnesium oxide and other magnesium salts are generally added as auxiliaries to silica type glidants where granules have hygroscopic inclinations. The magnesium compounds mop up the excess moisture keeping the granules dry and free flowing. (Apu, 2010)

1.2.2.8 Preservatives

Some typical preservatives used in pharmaceutical formulations are

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

1.3 INDIVIDUAL BRIEF DESCRIPTION ON DIFFERENT PHARMACEUTICAL EXCIPIENTS

1.3.1 Lactose

In the solid state, lactose appears as various isomeric forms, depending on the crystallization and drying conditions, i.e. α-lactose monohydrate, β-lactose anhydrous, and α –lactose anhydrous. The stable crystalline forms of lactose are α –lactose monohydrate, β-lactose anhydrous, and stable α –lactose anhydrous.

Lactose occurs as white to off-white crystalline particles or powder. Lactose is odorless and slightly sweet-tasting; α –lactose is approximately 20% as sweet as sucrose, while β-lactose is 40% as sweet.

- Empirical Formula: $C_{12}H_{22}O_{11}$. H_2O

- Molecular Weight: 360.31

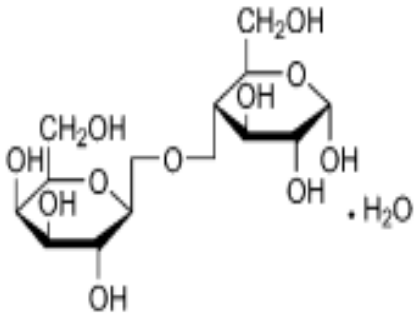

Figure 1.1: α-lactose monohydrate (Rowe, Sheskey, Owen, 2005)

1.3.1.1 Functional Category

Binding agent, Diluents for dry-powder inhalers, Tablet binder, Tablet and capsule diluent.

1.3.1.2 Applications in Pharmaceutical Formulation or Technology

Lactose is widely used as filler or diluents in tablets and capsules, and to a more limited extent in lyophilized products and infant formulas. Lactose is also used as diluents in dry-powder inhalation.

Various lactose grades are commercially available that have different physical properties such as particle size distribution and flow characteristics. This permits the selection of the most suitable material for a particular application; for example, the particle size range selected for capsules is often dependent on the type of encapsulating machine used. Usually, fine grades of lactose are used in the preparation of tablets by the wet-granulation method or when milling during processing is carried out, since the fine size permits better mixing with other formulation ingredients and utilizes the binder more efficiently.

Other applications of lactose include use in lyophilized products, where lactose is added to freeze-dried solutions to increase plug size and aid cohesion. Lactose is also used in combination with sucrose (approximately1:3) to prepare sugar-coating solutions.

Direct-compression grades of lactose monohydrate are available as granulated/agglomerated α-lactose monohydrate, containing small amounts of anhydrous lactose.

Direct-compression grades are often used to carry lower quantities of drug and this permits tablets to be made without granulation. (Rowe, Sheskey, Owen, 2005)

1.3.2 Talc

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

- Empirical Formula: Talc is a purified, hydrated, magnesium silicate, approximating to the formula $Mg_6(Si_2O_5)_4(OH)_4$. It may contain small, variable amounts of aluminum silicate and iron.

1.3.2.1 Functional Category

Anticaking agent; glidant; tablet and capsule diluent; tablet and capsule lubricant.

Table 1.1: Uses of Talc

Use	Concentration (%)
• **Dusting powder**	90.0-99.0
• **Glidant and tablet lubricant**	1.0-10.0
• **Tablet and capsule diluent**	5.0-30.0

1.3.2.2 Applications in Pharmaceutical Formulation or Technology

Talc was once widely used in oral solid dosage formulations as a lubricant and diluent, see Table I,(1–3) although today it is less commonly used. However, it is widely used as a dissolution retardant in the development of controlled-release products. Talc is also used as a lubricant in tablet formulations; in a novel powder coating for extended-release, pellets; and as an adsorbent.

In topical preparations, talc is used as a dusting powder, although it should not be used to dust surgical gloves. Talc is a natural material; it may therefore frequently contain microorganisms and should be sterilized when used as a dusting powder;

Talc is additionally used to clarify liquids and is also used in cosmetics and food products, mainly for its lubricant properties. (Rowe, Sheskey, Owen, 2005)

1.3.3 Starch

Starch occurs as an odorless and tasteless, fine, white-colored powder comprising very small spherical or ovoid granules whose size and shape are characteristic for each botanical variety.

- Empirical Formula: $(C_6H_{10}O_5)_n$; Where, n =300–1000.

Starch consists of amylase and amylopectin, two polysaccharides based on α-glucose.

- Molecular weight: 50000–160000

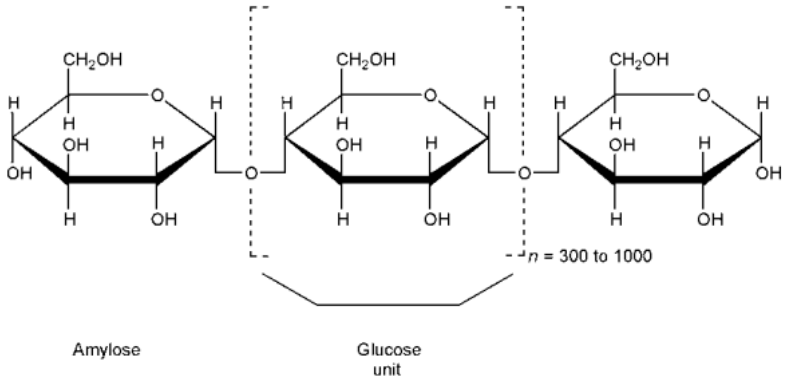

Figure 1.2: Starch

1.3.3.1 Functional Category

Glidant; tablet and capsule diluent; tablet and capsule disintegrant; tablet binder.

1.3.3.2 Applications in Pharmaceutical Formulation or Technology

Starch is used as an excipient primarily in oral solid-dosage formulations where it is utilized as a binder, diluent, and disintegrant.

As a diluent, starch is used for the preparation of standardized triturates of colorants or potent drugs to facilitate subsequent mixing or blending processes in manufacturing operations. Starch is also used in dry-filled capsule formulations for volume adjustment of the fill matrix.

In tablet formulations, freshly prepared starch paste is used at a concentration of 5–25% w/w in tablet granulations as a binder. Selection of the quantity required in a given system is determined by optimization studies, using parameters such as granule friability, tablet friability, hardness, disintegration rate, and drug dissolution rate.

Starch is one of the most commonly used tablet disintegrants at concentrations of 3–15% w/w. However, unmodified starch does not compress well and tends to increase tablet friability and capping if used in high concentrations. In granulated formulations, about half the total starch content is included in the granulation mixture and the balance as part of the final blend with the dried granulation.

Starch is also used in topical preparations; for example, it is widely used in dusting powders for its absorbency, and is used as a protective covering in ointment formulations applied to the skin. Starch mucilage has also been applied to the skin as an emollient, has formed the base of some enemas, and has been used in the treatment of iodine poisoning. (Rowe, Sheskey, Owen, 2005)

1.3.4 Sodium Lauryl Sulfate

Sodium lauryl sulfate consists of white or cream to pale yellow colored crystals, flakes, or powder having a smooth feel, a soapy, bitter taste, and a faint odor of fatty substances.

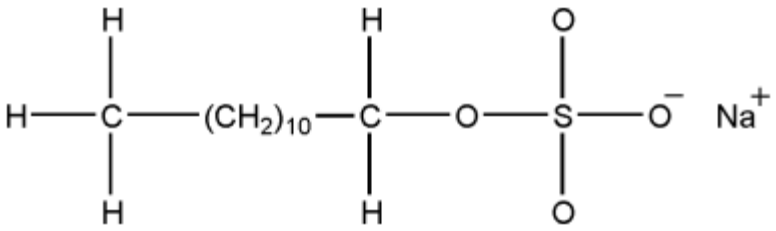

Figure 1.3: Sodium lauryl sulfate (Rowe, Sheskey, Owen, 2005)

- Empirical Formula: $C_{12}H_{25}NaO_4S$
- Molecular Weight: 288.38

1.3.4.1 Functional Category

Anionic surfactant; detergent; emulsifying agent; skin penetrant; tablet and capsule lubricant; wetting agent.

1.3.4.2 Applications in Pharmaceutical Formulation or Technology

Sodium lauryl sulfate is an anionic surfactant employed in a wide range of non parenteral pharmaceutical formulations and cosmetics. It is a detergent and wetting agent effective in both alkaline and acidic conditions. In recent years it has found application in analytical electrophoretic techniques, SDS (sodium dodecyl sulfate) polyacrylamide gel electrophoresisis one of the more widely used techniques for the analysis of proteins; and sodium lauryl sulfate has been used to enhance the selectivity of micellar electrokinetic chromatography (MEKC).

Table 1.2: Uses of sodium lauryl sulfate

Use	Concentration (%)
• Anionic emulsifier, forms self-emulsifying bases with fatty alcohols	0.5-2.5
• Detergent in medicated shampoos	≈ 10
	1

• Skin cleanser in topical applications	› 0.0025
• Solubilizer in concentrations greater than critical micelle concentration	1.0–2.0
• Tablet lubricant	1.0–2.0
• Wetting agent in dentrifices	

1.3.5 Magnesium Stearate

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.

- Empirical Formula: $C_{36}H_{70}MgO_4$
- Molecular Weight: 591.34

1.3.5.1 Functional Category

Tablet and capsule lubricant.

1.3.5.2 Applicationsin 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. (Rowe, Sheskey, Owen, 2005)

1.3.6 Carboxy Methyl Cellulose Calcium

Carboxy methyl cellulose calcium occurs as a white to yellowish-white, hygroscopic, fine powder.

- Empirical Formula: The USP NF 23 describes carboxymethylcellulose calcium as the calcium salt of polycarboxy methyl ether of cellulose.

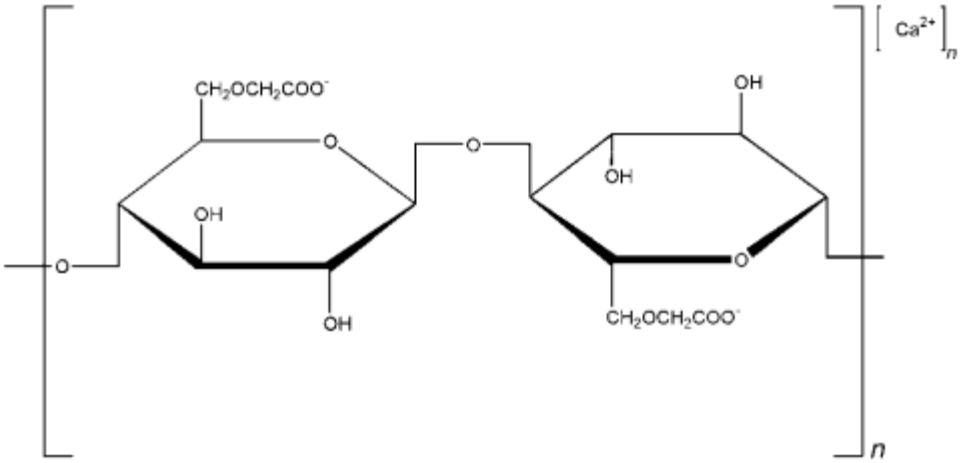

Figure 1.4: Carboxymethyl cellulose (Rowe, Sheskey, Owen, 2005)

1.3.6.1 Functional Category

Stabilizing agent; suspending agent; tablet and capsule disintegrant; viscosity-increasing agent; water-absorbing agent.

Table 1.3: Uses of Carboxymethyl cellulose calcium

Use	Concentration (%)
Tablet binder	5-15
Tablet disintegrant	1-15

1.3.6.2 Applications in Pharmaceutical Formulation or Technology

The main use of carboxymethylcellulose calcium is in tablet formulations, where it is used as a binder, diluent, and disintegrant. Although carboxymethylcellulose calcium is insoluble in water, it is an effective tablet disintegrant as it swells to several times its original bulk on contact with water. Concentrations up to 15% w/w may be used in tablet formulations; above this concentration, tablet hardness is reduced.

Carboxymethyl cellulose calcium is also used in other applications similarly to Carboxymethyl cellulose sodium; for example, as a suspending or viscosity increasing agent in oral and topical pharmaceutical formulations. Carboxymethyl cellulose calcium

is also used in modern wound dressings for its water absorption, retention and hemostatic properties. (Rowe, Sheskey, Owen, 2005)

1.3.7 Polyvinyl Pyrrolidone (PVP)

Polyvinyl Pyrrolidone is also known as Povidone (USP), 1-vinyl-2-pyrrolidinone polymer. Povidone or PVP occurs as a fine, white to creamy-white colored, odorless or almost odorless, hygroscopic powder.

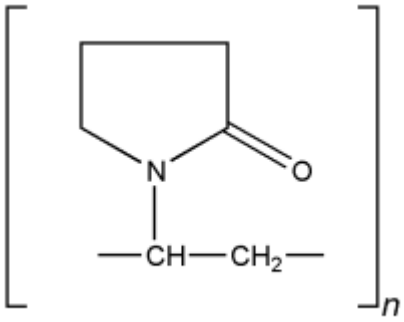

Figure 1.7: Polyvinyl Pyrrolidone or Povidone

- Empirical Formula: $(C_6H_9NO)_n$
- Molecular Weight: 2500–3000000

1.3.7.1 Functional Category

Disintegrant; dissolution aid; suspending agent; tablet binder.

Table 1.4: Uses of povidone or PVP

Use	Concentration (%)
✓ **Carrier for drugs**	10–25
✓ **Dispersing agent**	Up to 5
✓ **Eye drops**	2-10
✓ **Suspending agent**	Up to 5

✓ **Tablet binder, tablet diluent, or coating agent**	0.5-5.0

1.3.7.2 Applications in Pharmaceutical Formulation or Technology

Although povidone is used in a variety of pharmaceutical formulations, it is primarily used in solid dosage forms. In tableting, povidone solutions are used as binders in wet granulation processes.

Povidone is also added to powder blends in the dry form and granulated *in situ* by the addition of water, alcohol, or hydroalcoholic solutions. Povidone is used as a solubilizer in oral and parenteral formulations and has been shown to enhance dissolution of poorly soluble drugs from solid dosage forms.

Povidone solutions may also be used as coating agents. Povidone is additionally used as a suspending, stabilizing, or viscosity increasing agent in a number of topical and oral suspensions and solutions. The solubility of a number of poorly soluble active drugs may be increased by mixing with povidone. (Rowe, Sheskey, Owen, 2005)

1.3.8 Calcium Phosphate, Dibasic Anhydrous

Anhydrous dibasic calcium phosphate is a white, odorless, tasteless powder or crystalline solid. It occurs as triclinic crystals.

- Empirical Formula: $CaHPO_4$
- Molecular Weight: 136.06

1.3.8.1 Functional Category

Tablet and capsule diluent.

1.3.8.2 Applications in Pharmaceutical Formulation or Technology

Anhydrous dibasic calcium phosphate is used both as an excipient and as a source of calcium in nutritional supplements. It is used particularly in the nutritional/health food

sectors. It is also used in pharmaceutical products because of its compaction properties, and the good flow properties of the coarse grade material.

The predominant deformation mechanism of anhydrous dibasic calcium phosphate coarse grade is brittle fracture and this reduces the strain-rate sensitivity of the material, thus allowing easier transition from the laboratory to production scale. However, unlike the dihydrate, anhydrous dibasic calcium phosphate when compacted at higher pressures can exhibit lamination and capping. This phenomenon can be observed when the material represents a substantial proportion of the formulation and is exacerbated by the use of deep concave tooling. This phenomenon also appears to be independent of rate of compaction. Anhydrous dibasic calcium phosphate is abrasive and a lubricant is required for tableting, for example 1% w/w magnesium stearate or 1% w/w sodium stearyl fumarate.

Two particle size grades of anhydrous dibasic calcium phosphate are used in the pharmaceutical industry. Milled material is typically used in wet granulated or roller compacted formulations. The ‘unmilled’ or coarse grade material is typically used in direct compression formulations. Anhydrous dibasic calcium phosphate is non hygroscopic and stable at room temperature. It does not hydrate to form the dihydrate.

Anhydrous dibasic calcium phosphate is used in toothpaste and dentifrice formulations for its abrasive properties. (Rowe, Sheskey, Owen, 2005)

1.4 POWDER FLOWABILITY

1.4.1 Definition

A simple definition of powder flowability is the ability of a powder to flow. By this definition, flowability is sometimes thought of as a one-dimensional characteristic of a powder, whereby powders can be ranked on a sliding scale from “free-flowing” to “non-flowing”. Unfortunately, this simplistic view lacks science and understanding sufficient to address common problems encountered by formulators, equipment designers and production personnel.

Flowability is the result of a combination of material physical properties that affect flow, and the equipment used for handling, storing, or processing the material. Equal

consideration must be given to both the material characteristics and the equipment. The same powder may flow well in one hopper but poorly in another; likewise, a given hopper may handle one powder well but cause another powder to hang-up. Therefore, a more accurate definition of powder flowability is the ability of a powder to flow in a desired manner in a specific piece of equipment. (Rx times, 2013)

1.4.2 Flow Properties

The specific properties of a powder that affect its flow are known as flow properties. Examples of flow properties include bulk density, permeability, coheive strength, and wall friction. These flow properties arise from the collective forces acting on individual particles, such as van der Waals, electrostatic, surface tension, interlocking, friction, etc. Although beyond the scope of this article, substantial amount of literature [1-3] is available on measurement of flow properties. (Rx times, 2013)

1.4.3 Benefits of Accurate Flow Measurement

Even the most rudimentary methods of assessing powder flow can be time consuming. However, the benefits of accurately characterizing powder flow measurement can far outweigh this investment of time.

1. New product development

Product development teams can evaluate new excipients, active ingredients and formulations, predicting their behavior prior to commencing large-scale production. They can also check how new powders interact with existing constituents. This speeds up development time and minimizes "trial and error" tactics; especially important when active ingredients are extremely valuable and may have only been produced in small quantities.

2. Improving quality

Predictable powder flow enables constituent selection, manufacturing procedures and equipment to be optimized. This in turn maximizes speed of production, reduces the risk of stoppages and improves blend quality, filling procedures and end product quality.

3. Delivering cost-savings

As costs are required to be driven down, the substitution of expensive constituents with lower cost powders is an attractive prospect. Although these substitutes may be produced to the same specification as the original substance, they may not necessarily store, convey and process as easily. Discovering this after production has started would incur downtime and additional cost. Final product quality may also be compromised. (Young, 2013)

1.5 METHODS OF DETERMINING POWDER FLOW CHARACTERISTICS

The widespread use of powders in the pharmaceutical industry has generated a variety of methods for characterizing powder flow. In addition, while it is clear that no single and simple test method can adequately characterize the flow properties of pharmaceutical powders, this part proposes the standardization of test methods that may be valuable during pharmaceutical development.

Three commonly reported methods for testing powder flow are:

1) Angle of repose
2) Compressibility index or Carr's index
3) Hausner's ratio,
4) Flow rate through an orifice,
5) Shear cell. (US Pharmacopeia, 2010)

In this research work, we worked through first three methods and rest two method were our out of concern.

1.5.1 Compressibility Index or Carr's Index and Hausner's Ratio

In recent years the compressibility index and the closely related Hausner's ratio have become the simple, fast, and popular methods of predicting powder flow characteristics. The compressibility index has been proposed as an indirect measure of bulk density, size and shape, surface area, moisture content, and cohesiveness of materials because all of these can influence the observed compressibility index. The compressibility index and the Hausner's ratio are determined by measuring both the bulk volume and the tapped volume of a powder.

Although there are some variations in the method of determining the compressibility index and Hausner's ratio, the basic procedure is to measure (1) the unsettled apparent volume, V_O, and (2) the final tapped volume, V_f, of the powder after tapping the material until no further volume changes occur. The compressibility index and the Hausner's ratio are calculated as follows: (US Pharmacopeia, 2010)

$$Compressibility\ Index = 100 \times \left(\frac{V_o - V_f}{V_o} \right)$$

$$Hausner\ Ratio = \frac{V_o}{V_f}$$

For the compressibility index and the Hausner's ratio, the generally accepted scale of flowability is given in the following table:

Table 1.5: Scale of Flowability

Compressibility Index (%)	Flow Character	Hausner's Ratio
≤10	Excellent	1.00–1.11
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

1.5.1.1 Experimental Considerations

Compressibility index and Hausner's ratio are not intrinsic properties of the powder; i.e., they depend on the methodology used. In the existing literature, there are discussions of

the following important considerations affecting the determination of (1) the unsettled apparent volume, Vo, (2) the final tapped volume, Vf, (3) the bulk density, ρbulk, and (4) the tapped density, ρtapped. The following factors are considered during experiment:

- ✓ The diameter of the cylinder used
- ✓ The number of times the powder is tapped to achieve the tapped density
- ✓ The mass of material used in the test
- ✓ Rotation of the sample during tapping. (US Pharmacopeia, 2010)

1.5.2 Angle of Repose

The angle of repose has been used in several branches of science to characterize the flow properties of solids. Angle of repose is a characteristic related to interparticulate friction or resistance to movement between particles. Angle of repose test results are reported to be very dependent upon the method used. Experimental difficulties arise as a result of segregation of material and consolidation or aeration of the powder as the cone is formed. Despite its difficulties, the method continues to be used in the pharmaceutical industry, and a number of examples demonstrating its value in predicting manufacturing problems appear in the literature.

The angle of repose is the constant, three-dimensional angle assumed by a cone-like pile of material formed by any of several different methods

A variety of angle of repose test methods are described in the literature. The most common methods for determining the static angle of repose can be classified on the basis of the following two important experimental variables:

The height of the “funnel” through which the powder passes may be fixed relative to the base, or the height may be varied as the pile forms.

The base upon which the pile forms may be of fixed diameter or the diameter of the powder cone may be allowed to vary as the pile forms. (US Pharmacopeia, 2010)

1.5.2.1 Angle of Repose General Scale of Flowability

There are examples in the literature of formulations with an angle of repose in the range of 40° to 50° that were manufactured satisfactorily. When the angle of repose exceeds 50°, the flow is rarely acceptable for manufacturing purposes.

Table 1.6: Flow Properties and Corresponding values Angles of Repose

Flow Property	Angle of Repose (degrees)
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

1.5.2.2 Experimental Considerations for Angle of Repose

Angle of repose is not an intrinsic property of the powder; i.e., it is very much dependent upon the method used to form the cone of powder. The following important considerations are raised in the existing literature:

The peak of the cone of powder can be distorted by the impact of powder from above. By carefully building the powder cone, the distortion caused by impact can be minimized.

The nature of the base upon which the powder cone is formed influences the angle of repose. It is recommended that the powder cone be formed on a "common base," which can be achieved by forming the cone of powder on a layer of powder. This can be done by using a base of fixed diameter with a protruding outer edge to retain a layer of powder upon which the cone is formed. (US Pharmacopeia, 2010)

1.5.2.3 Recommended Procedure for Angle of Repose

Form the angle of repose on a fixed base with a retaining lip to retain a layer of powder on the base. The base should be free of vibration. Vary the height of the funnel to carefully build up a symmetrical cone of powder. Care should be taken to prevent vibration as the funnel is moved. The funnel height should be maintained approximately 2–4 cm from the top of the powder pile as it is being formed in order to minimize the impact of falling powder on the tip of the cone. If a symmetrical cone of powder cannot be successfully or reproducibly prepared, this method is not appropriate. Determine the angle of repose by measuring the height of the cone of powder and calculating the angle of repose, α, from the following equation: (US Pharmacopeia, 2010)

$$\tan(\alpha) = \text{height} / 0.5 \text{ base}$$

$$\text{So that, } \alpha = \tan^{-1}(\text{height} / 0.5 \text{ base})$$

Chapter Two

LITERATURE REVIEW

Flow property of individual Active Pharmaceutical Ingredients (API) and excipients both has an important role in drug manufacturing. If flow property of an excipient or an API is not good then it may affects many parameters of both tablets and capsules. Realizing the significance of flow property of excipients and APIs in mind, many scientists and researchers tried to study and finally determined the flow characteristics of different excipients and APIs. In last few decades lots of research works took place regarding different parameters of flow characteristics of different powder excipients and APIs.

In the year 1979, Bolhuis and his team (Bolhuis, Lerk, Moes, 1979) studied on the flow and lubrication properties of a high dosage range drug, acetylsalicylic acid with different particle size distributions, which was formulated with directly compressible excipients and compressed into tablets. They investigated the weight variation, drug content, crushing strength, friability, disintegration time, dissolution rate of the drug and stability after storage for eight weeks at 20‡C and 50% or 85% relative humidity of 500 mg acetylsalicylic acid. Their result showed that knowledge of the properties and interactions of drug, directly compressible excipients and other tablet vehicles makes possible the formulation and compression of different particle size acetylsalicylic acid powders into good quality tablets.

After four year back in 1983, Chowhan and Yang (1983) in their research paper determined the tensile strength of consolidated powder beds of spray-dried lactose and binary mixtures of lactose including different concentrations of glidants and/or lubricants. They measured the orifice flow rate of these powders by choosing an appropriate orifice diameter. They found that powder mixtures containing up to 1% glidant resulted in general in a decrease in the tensile strength and a raise in the flow rate as well as flow rate of powder mixtures containing simple glidants such as corn starch and microcrystalline cellulose at different concentrations was linearly related to the tensile strength.

Then subsequent to seven year later, Tan and Newton (1990) worked on 5 pharmaceutical excipients in the middle of 1990 and found that the flowability of size fractions of 5 pharmaceutical excipients was related to their capsule filling performance. They used angular, packing and shear tests, the samples were ranked in different relative orders of flowability. Flowability was reliant on the particle size, morphology and bulk density of the powder. They found that there was a major correlation between the values of coefficient of variation and the flow parameters of Carr's compressibility, Hausner's's ratio, angle of repose, Kawakita's equation constant and Jenike's flow factor. They also found that coefficient of variation was also related to the coefficient of variation of the powder bed bulk density and the variation in the compression stress.

Later in 1994, Schmidt and Rubensdorfer (1994) in their research paper evaluated and compared powder characteristics and tableting properties of Ludipress, a lactose-based, free flowing granule containing povidone and crospovidon. They evaluated flowability, bulk density, tapped density, Hausner's ratio, angle of repose and particle size distribution of Ludipress. They examined the particle morphology by using scanning electron microscopy (SEM). They found that Ludipress samples revealed a good batch-to-batch uniformity and flow characteristics compared to the physical blend and other excipients investigated.

The next year, in middle of 1995, Amidon and Houghton (1995) worked on the effects of moisture on the mechanical and powder flow properties of microcrystalline cellulose and finally they found powder flow was shown to decrease with increasing moisture content.

In afterward 2000, Podczeck and Newton (2000) in their research paper studied Granulated powdered cellulose in terms of powder bulk properties and capsule filling performance on a tamp-filling machine with and without the addition of a range of concentrations of magnesium stearate. They found that Carr's compressibility reached its minimum value at 0.4% magnesium stearate signifying an improvement of powder flow

compared to the unlubricated material. They also found that shear cell measurements and the use of a powder rheometer specified that the addition of 0.2% magnesium stearate and more impairs powder flow.

In the same year, Taylor his research fellows (Taylor et al. 2000) worked on the flow properties of typical tablet and capsule formulation excipients, active compounds as well as representative formulation blends were tested with current and novel flow measurement techniques to identify a reliable bench test to measure powder flow as a screening method in early tablet and capsule formulation development. Test methods used by them were vibrating spatula, critical orifice, and angle of repose, compressibility index, and avalanching analysis. They established empirical composite index and ranked powder flow in accordance with formulator experience. The data that they found were not reproducible from vibrating spatula and avalanching methods.

In the subsequently year 2001, Hancock and his team determined the powder flow and compact mechanical properties of two recently developed matrix-forming polymers. The polymers were cross-linked high-amylose starch and poly acrylic acid. They compared the properties of polymers with those of two established matrix-forming polymers, hydroxypropyl methylcellulose and hydroxypropyl cellulose. They found that the particle morphology, size distribution and true density of the four materials were quite different as well as they exhibited quantifiable performance differences with respect to powder flow, compact ductility, compact elasticity and compact tensile strength. (Hancock et al., 2001)

Again two year later, in early 2003, Mullarney and his research fellow worked on the physical, flow, and mechanical properties of four common pharmaceutical sweeteners, such as Sucrose, acesulfame potassium (Sunett®), saccharin sodium, and aspartame to assess their relative manufacturability in solid dosage formulations. They measured powder flow and cohesivity as well as compact mechanical properties such as ductility,

elasticity, and tensile strength. They found sucrose and acesulfame potassium demonstrated excellent flowability. Saccharin sodium and aspartame demonstrated poor flowability and superior compact strength relative to sucrose and acesulfame, despite their noticeably higher brittleness. (Mullarney et al., 2003)

In the same year, Zhang and his research fellows (Zhang, Law, Chakrabarti, 2003) investigated the basic physico-chemical property and binding functionality of commonly used commercial direct compression binders in 2003. They analyzed the compressibility of microcrystalline cellulose (MCC), starch, lactose, dicalcium phosphate (DCP), and sugar using compression parameters derived from the Heckel, Kawakita, and Cooper-Eaton equations. They demonstrated that MCC had moderate flowability, excellent compressibility, and extremely good compact hardness; with some exceptions, starch, lactose, and sugar generally demonstrated moderate flowability, compressibility, and hardness on the other hand dicalcium phosphate had outstanding flowability, but poor compressibility and hardness.

In the next year 2004, Bhattachar and his research fellows (Bhattachar et al., 2004) studied on the flow properties of pharmaceutical powders and blends used in solid oral dosage forms which are important consideration during dosage form development. They adapted vibratory feeder method which is a flow measurement technique that quantifies avalanche flow that used for measurement of the flow properties of common pharmaceutical powders used in solid oral dosage forms. They measured 17 different powders with the instrument and results are described as a powder flow index (PFI). They found the PFI tendency of the powders show a relationship with flow properties. They also measured the flow property with a commercially available avalanche instrument, the Aero-Flow™, and the results were detailed as the mean time to avalanche (MTA). in view of the fact that the two instruments analyze the avalanche by different algorithms, the results were compared with nonparametric statistical evaluation of ranked

data. Finally they recommended a procedure for measurement of powder flow with the vibratory feeder.

In the similar year, Thalberg and his research fellows (Thalberg, Lindholm, Axelsson, 2004) in their research paper characterized a series of placebo powders for inhalation concerning bulk density and powder flowability using different techniques. They found a modified Hausner's Ratio was obtained by measurement of the poured and the compressed bulk densities as well as they investigated angle of repose, the avalanching behaviour using the AeroFlow, and the yield strength using the Uniaxial tester. They found a good correlation between the modified Hausner's Ratio and the angle of repose and AeroFlow was suitable for powders with a low percentage of fine particles, but could not discriminate between the more cohesive powders. They determined that the addition of micronized particles has a strong manipulate on the flowability of ordered mixtures, while in-between sized particles have little impact on the powder flow.

Again in the same year 2004, Jonat along with his research group (Jonat et al., 2004) studied the glidant properties of compacted hydrophilic and hydrophobic colloidal silicon dioxides and compared with respect to mixing time and mixer type using microcrystalline cellulose, pregelatinized starch and α-lactose-monohydrate as model excipients. They also performed flowability studies, including angle of repose measurements and a novel dynamic conveyor belt method and found differences in the flow enhancement between the colloidal silicon dioxide types. They found that an influence of mixing conditions on flowability was hydrophilic colloidal silicon dioxide. They identified the influence of size and distribution of the colloidal silicon dioxide particles on the surface of the excipient, mixing time, mixer type. In addition, they found after moisture studies that colloidal silicon dioxide protects the excipients against a flowability decrease caused by humidity.

In the next year 2005, Kim and his research fellows studied on the surface composition of four industrial spray-dried dairy powders, skim milk powder, whole milk powder, cream

powder and whey protein concentrate by electron spectroscopy for chemical analysis (ESCA). They also studied its influence on powder flowability. They found that skim milk powder flows well compared to the other powders because the surface is made of lactose and protein with a small amount of fat, whereas the high surface fat composition inhibits the flow of whole milk, cream and whey protein powders. They identified poor flowability of the powders with high surface fat coverage was drastically improved by removal of fat present on the surface through a brief wash with petroleum ether. Finally they concluded that even though there are several parameters including particle size, which influence the flowability of powders, the flowability of powders is powerfully influenced by the surface composition of powders, chiefly for fat-containing powders. (Kim, Chen, Pearce, 2005)

In the same year 2005, Kachrimanis along with his research fellows studied effects of cylindrical orifice length and diameter on the flow rate of three commonly used pharmaceutical direct compression diluents lactose, dibasic calcium phosphate dihydrate and pregelatinised starch. They also evaluated the powder particle characteristics e.g., particle size, aspect ratio, roundness and convexity) and the packing properties e.g.,true, bulk and tapped density. They determined the flow rate was for three different sieve fractions through a series of tiny tableting dies of different orifice diameter and thickness. They found that flow rate decreased with the increase of the orifice length for the small diameter but for the large diameter was increased with the orifice length. Finally they stated that orifice length is the third most influential variable after the orifice diameter and particle size, followed by the bulk density, the difference between bulk and tapped densities and the particle convexity. (Kachrimanis, Petrides, Malamataris, 2005)

Then two year later, in the year 2007, Jacob and his research fellows conducted a study on flow property of co-processed particles of microcrystalline cellulose (MCC) and mannitol. They fabricated both the excipients by spray drying process to be used as a direct compression excipient in fast dissolving tablet formulation. They examined

composite particles for their powder and compression properties. They observed that that an increase in the MCC proportion imparted greater compressibility to the composite particles, but the flowability of these mixtures was decreased. MCC and mannitol have been widely used in the formulation of fast dissolving tablets. They found the non-wetting property of the hard compact central core may delay the disintegration time. They optimized the ratio of mannitol and MCC and found have optimized powder and compressibility characteristics with fast disintegrating property. They concluded that higher rate of powder flow can indirectly influence the rate of disintegration. (Jacob et al., 2007)

In earlier of the same year, Faqih and his research fellows (Faqih et al., 2007) studied on flow in a rotating drum and flow in bench scale hoppers. They studied flow characteristics of 13 cohesive granular materials in the gravitational displacement Rheometer (GDR). They compared it to flow in hoppers of varying angle and discharge diameter at fixed temperature and moisture conditions. They found that GDR was an effective and convenient tool for examining flow properties of pharmaceutical materials, both pure and mixtures. A flow Index acquired from GDR measurements is directly correlated to the flow through hoppers, providing a predictive method for hopper design and a convenient experimental test for screening materials and determining their suitability for specific hopper systems.

Then next year, Shah and his team (Shah, Tawakkul, Khan, 2008) evaluated the flow of pharmaceutical powders and granules using compendial and non-compendial methods. They evaluated Angle of repose, bulk density, tapped density, Carr's compressibility index, and Hausner's ratios. They also determined cohesivity index, caking strength, and flow stability of samples which includes different grades of magnesium stearate powder including bovine, vegetable, and food grade, physical mixture powder blend consisting of a model formulation, granules prepared by various methods including slugging, high shear granulator, and fluid bed dryer. They observed that the compendial methods were

often non-discriminating for minor variations in powder flow. They stated that cohesivity, and caking strength was helpful in understanding the flow characteristics of pharmaceutical systems.

In the same year 2008, Feeley and his research fellows (Feeley et al., 2008) employed Inverse gas chromatography (IGC) to characterise the surface thermodynamic properties of two nominally equivalent batches of salbutamol sulphate. They highlighted on surface energetic changes induced on micronisation. They used powder flow avalanching analyser which explore the relationship between powder flow and the surface energetic properties. They found a result which demonstrated the potential of these techniques to detect and quantify differences in powder samples, before and after micronisation. They also indicated that the surface energy differences detected by Inverse gas chromatography (IGC) can be linked to important secondary processing properties such as powder flow.

Again in the same year 2008, Hou and Sun (2008) investigated the effects of particle size, morphology, particle density, and surface silicification, on powder flow properties using a ring shear tester. They took 11 powders from three series of microcrystalline cellulose (MCC) (a) Avicel, regular MCC, elongated particles, (b)Prosolv, silicified MCC, elongated particles, and (c) Celphere, spherical MCC, and studied them. They found that smaller particles always led to poorer powder flow properties. They identify that mechanism of the detrimental effect of particle size reduction on flow properties and that was the larger powder specific surface area. They found that flow properties of Celphere were considerably better than Avicel of comparable particles size and finally suggested that spherical morphology promoted better powder flow properties. They identified that flow properties of powders different in densities but similar in particle size, shape, as well as they found similar surface properties.

In early of the next year 2009, Emery and his co research workers worked on the effect of moisture content on four pharmaceutical powders, an active pharmaceutical ingredient

(API), Aspartame, Hydroxypropyl Methylcellulose (HPMC), and Respitose. They found the API and Respitose powders were nonhygroscopic. They measured the flow property using the Jenike shear index, the Hausner's Ratio, the Carr Index, and the static and dynamic angles of repose. Finally they found that flowability of Aspartame improved with an increase in moisture content, which is credited to the formation of large, round agglomerates as well as the flowability of HPMC decreased with a raise in moisture content, recognized to the increasing strength of liquid bridges. (Emery et al., 2009)

Then one year later, in early 2010, Seppala and his research team developed a new method to get a reliable powder flow characteristics using only 1 to 2 g of powder. In pharmaceutical industry, it is frequently significant to directly measure real powder flow rate from a small amount of powder. It is necessary to determine powder flow properties of new active pharmaceutical ingredient (API) in an early stage of the development when the amount of API is limited. They introduced a new direct method to measure powder flow when the material is poorly flowing and the amount of material is small. Their system was very simple and consisted of a flow chamber and electronic balance and an automated optical detection system. They stated that for each measurement only 1 to 2 g of sample was required. They selected sugar excipients, three grades of microcrystalline cellulose, and APIs e.g., caffeine, carbamazepine, and paracetamol. They also classified freely flowing, intermediate flowing, and poorly flowing powders, respectively. This classification was based on their results. Their method provided a new tool for a rapid determination of flowing characteristics of powders (e.g., inhalation powders) and granules at a small scale. (Seppala et al., 2010)

Then in the same year 2010, Yu and his research fellows (Yu et al., 2010) established a modeling approach that can be used to predict bulk powder flowability of pharmaceutical materials from their particle size and shape distributions. They characterized the particle size and shape distributions of 23 commonly used pharmaceutical excipients and 38 binary blends. They analyzed the flow properties using Schulze Ring Shear Tester at a

fixed humidity condition and used partial least squares (PLS) approach to construct the mathematical model. Finally they found that particle size and shape play an important role in determining the powder flow behavior.

Over again in the year 2010, Sarraguca and his co-research fellows (Sarraguca et al., 2010) studied the flow properties of pharmaceutical excipientss using near infrared spectroscopy. They demonstrated that physical properties of pharmaceutical powders are of topmost significance in the pharmaceutical industry. They observed the critical major properties of flowability using processes like blending, tablet compression, capsule filling and transportation using angle of repose, Carr's index and Hausner's ratio. They used near infrared spectroscopy because it is fast and low-cost analytical technique to determine the parameters of flow properties of pharmaceutical powders based on active ingredient paracetamol. They recorded the spectra on a Fourier-transform near infrared spectrometer in which the parameters were the angle of repose, true and tapped density. They made a comparison between near infrared based properties and reference methods results. They found that the physical properties affect the flowability of pharmaceutical powders.

Chapter Three

MATERIALS & METHODS

3.1 MATERIALS

3.1.1 Excipients Collection

For the research purpose different classes of excipients were collected from the different labs of Pharmacy Dept. of East West University.

3.1.2 Excipients

The list of excipients those were used during this research is given below with their individual source (supplier name):

Table 3.1: List of excipients through this research work

SL no.	Name of Excipients	Source (Supplier Name)
1.	Carboxymethyl Cellulose	MERK, Germany
2.	Calcium Phosphate	MERK, Germany
3.	Lactose	MERK, Germany
4.	Magnesium Stearate	MERK, Germany
5.	Polyvinyl pyrrolidine	MERK, Germany
6.	Sodium Lauryl Sulphate	MERK, Germany
7.	Starch	MERK, Germany
8.	Talc	MERK, Germany

3.1.3 Equipments and Instruments

Table 3.2: List of instruments through this research work

Serial No.	Equipments	Source (Supplier Name)	Origin
1.	Weight Balance	SHIMADZU	Japan
2.	Mixture Machine	Locally Produced	Bangladesh

3.1.4 Images of Instruments

Some images of important instruments those were used in different times during this research work.

Figure 3.1: Mixture Machine

Figure 3.2: Electronic Balance

3.1.5 Apparatus

Some apparatus are listed in the following table those were used through the research work.

Table 3.3: List of apparatus used throughout this research work

Serial No.	Apparatus
1.	Beaker
2.	Test tubes
3.	Aluminum Foil Paper
4.	Cling Wrap (Transparent Plastic Paper)
5.	Mortar & Pastels
6.	Spatula
7..	Funnel
8.	Measuring Cylinder
9.	Conical Flask
10.	White Paper
11.	Desiccant
12.	Black Marker
13.	Ruler

3.2 METHODS

In this research work, we determined the flow characteristics of powder excipients by approved methods descried in US Pharmacopeia. The methods that we followed in this research work are briefly described in Introduction portion. The process that started from the beginning to the end for determining the flow characteristics of powder excipients is given below:

3.2.1 Formation of Different Mixtures

Different mixtures were formed choosing different excipients from different classes of excipients. During my research work, I was able to form eight mixtures which contain four to five excipients from different classes. The mixture composition was given below:

Table 3.4: Percentage of excipients in different mixtures

Name of Mixture	Excipients in Mixture	Justification	Amount in respective Mixture
Mixture 1 (M1)	Starch	Diluent	50%
	Lactose	Binder	35%
	Talc	Lubricant	10%
	Magnesium Stearate	Lubricant	5%
	Calcium Phosphate	Diluent	78%
Mixture 2 (M2)	Polyvinyl Pyrrolidone	Binder	10%
	Talc	Lubricant	10%
	Sodium Lauryl Sulphate (SLS)	Lubricant	2%
	Calcium Phosphate	Diluent	50%
Mixture 3 (M3)	Lactose	Binder	35%
	Talc	Lubricant	10%
	Magnesium Stearate	Lubricant	5%
	Lactose	Diluent	50%

Mixture 4 (M4)	Starch	Binder	35%
	Talc	Lubricant	10%
	Sodium Lauryl Sulphate (SLS)	Lubricant	5%
	Calcium Phosphate	Diluent	75%
Mixture 5 (M5)	Polyvinyl Pyrrolidone	Binder	10%
	Talc	Lubricant	10%
	Magnesium Stearate	Lubricant	5%
	Starch	Binder	25%
	Calcium Phosphate	Diluent	25%
Mixture 6 (M6)	Lactose	Diluent	35%
	Talc	Lubricant	10%
	Magnesium Stearate	Lubricant	5%
	Lactose	Diluent	40%
	Calcium Phosphate	Diluent	35%
Mixture 7 (M7)	Polyvinyl Pyrrolidone (PVP)	Binder	10%
	Talc	Lubricant	10%
	Magnesium Stearate	Lubricant	5%

After that I selected some specific excipients to which the previously described mixtures were mixed again in specified as well as justified ratio. The mentioned specific excipients belong to the disintegrant type of excipients, for example Polyvinyl pyrrolidone (PVP), Starch, Caroxymethyl Cellulose (CMC) and Microcrystalline Celulose. Then different ratios are formed using these excipients with previously formed different mixtures. The mixing process was performed using Mixture Machine available in Pharmacy Laboratory, East West University. Before using this machine, each time the machine was washed thoroughly and dried the machine clearly to reduce the cross contamination between the powder excipients.

3.2.1.1 Amount of Excipients Needed for 20gm Mixture 1 (M1)

Table 3.4: Amount Needed to Prepare 20gm of M1

Name of Excipients in M1	Amount in M1	Amount for 20gm in M1
• Starch	50%	10 gm
• Lactose	35%	7 gm
• Talc	10%	2 gm
• Magnesium Stearate	5%	1 gm
	Total = 100%	Total = 20 gm

3.2.1.2 Amount of Excipients Needed for 20gm Mixture 2 (M2)

Table 3.6: Amount Needed to Prepare 20gm of M2

Name of Excipients in M2	Amount in M2	Amount for 25gm in M2
• Calcium Phosphate	78%	19.5 gm
• Polyvinyl Pyrrolidone	10%	2.5 gm
• Talc	10%	2.5 gm
• Sodium Lauryl Sulphate (SLS)	2%	0.5 gm
	Total = 100%	Total = 25 gm

3.2.1.3 Amount of Excipients Needed for 20gm Mixture 3 (M3)

Table 3.7: Amount Needed to Prepare 20gm of M3

Name of Excipients in M3	Amount in M1	Amount for 20gm in M1
• Calcium Phosphate	50%	10 gm
• Lactose	35%	7 gm

• Talc	10%	2 gm
• Magnesium Stearate	5%	1 gm
	Total = 100%	Total = 20 gm

3.2.1.4 Amount of Excipients Needed for 20gm Mixture 4 (M4)

Table 3.8: Amount Needed to Prepare 20gm of M4

Name of Excipients in M4	Amount in M4	Amount for 20gm in M4
• Lactose	50%	10 gm
• Starch	35%	7 gm
• Talc	10%	2 gm
• Sodium Lauryl Sulphate (SLS)	5%	1 gm
	Total = 100%	Total = 20 gm

3.2.1.5 Amount of Excipients Needed for 20gm Mixture 5 (M5)

Table 3.9: Amount Needed to Prepare 20gm of M5

Name of Excipients in M6	Amount in M6	Amount for 25gm in M6
• Calcium Phosphate	75%	18.75 gm
• Polyvinyl Pyrrolidone	10%	2.5 gm
• Talc	10%	2.5 gm
• Magnesium Stearate	5%	1.25 gm
	Total = 100%	Total = 25 gm

3.2.1.6 Amount of Excipients Needed for 20gm Mixture 6 (M6)

Table 3.10: Amount Needed to Prepare 20gm of M6

Name of Excipients in M6	Amount in M6	Amount for 20gm in M6
• Starch	25%	5 gm
• Calcium Phosphate	25%	5 gm
• Lactose	35%	7 gm
• Talc	10%	2 gm
• Magnesium Stearate	5%	1 gm
	Total = 100%	Total = 20 gm

3.2.1.7 Amount of Excipients Needed for 20gm Mixture 7 (M7)

Table 3.11: Amount Needed to Prepare 20gm of M7

Name of Excipients in M7	Amount in M7	Amount for 25gm in M7
• Lactose	40%	10.0 gm
• Calcium Phosphate	35%	8.75 gm
• Polyvinyl Pyrrolidone (PVP)	10%	2.5 gm
• Talc	10%	2.5 gm
• Magnesium Stearate	5%	1.25 gm
	Total = 100%	Total = 25 gm

3.2.2 Formation of Different Ratio

Different ratios were formed between the mixtures those are described before with polyvinyl pyrrolidone, starch, carboxymethyl cellulose and microcrystalline cellulose. The ratios of mixtures with these excipients are given below:

3.2.2.1 Mixture 1 (M1) with Polyvinyl Pyrrolidone (PVP)

Table 3.12: Ratio concentration of M1 with PVP and amount needed for 5gm

Ratio	M1 (%) : PVP (%)	Amount for 5gm
▪ *Ratio 1*	98 : 2	4.9 gm M1 + 0.1 gm PVP
▪ *Ratio 2*	96 : 4	4.8 gm M1 + 0.2 gm PVP
▪ *Ratio 3*	94 : 6	4.7 gm M1 + 0.3 gm PVP
▪ *Ratio 4*	92 : 8	4.6 gm M1 + 0.4 gm PVP

3.2.2.2. Mixture 1 (M1) with Carboxymethyl Cellulose (CMC)

Table 3.13: Ratio concentration of M1 with CMC and amount needed for 5gm

Ratio	M1 (%) : CMC (%)	Amount for 5gm
▪ *Ratio 1*	94 : 6	4.70 gm M1 + 0.30 gm CMC
▪ *Ratio 2*	91 : 9	4.55 gm M1 + 0.45 gm CMC
▪ *Ratio 3*	88 : 12	4.40 gm M1 + 0.60 gm CMC
▪ *Ratio 4*	85 : 15	4.25 gm M1 + 0.75 gm CMC

3.2.2.3. Mixture 1 (M1) with Microcrystalline Cellulose (MCC)

Table 3.14: Ratio concentration of M1 with MCC and amount needed for 5gm

Ratio	M1(%) : MCC (%)	Amount for 5gm
▪ *Ratio 1*	95 : 5	4.75 gm M1 + 0.25 gm MCC
▪ *Ratio 2*	92 : 8	4.60 gm M1 + 0.40 gm MCC
▪ *Ratio 3*	89 : 11	4.45 gm M1 + 0.55 gm MCC
▪ *Ratio 4*	86 : 14	4.30 gm M1 + 0.70 gm MCC

3.2.2.4. Mixture 2 (M2) with Starch

Table 3.15: Ratio concentration of M2 with Starch and amount needed for 5gm

Ratio	M2 (%) : Starch (%)	Amount for 5gm
▪ *Ratio 1*	97 : 3	4.85 gm M2 + 0.15 gm Starch
▪ *Ratio 2*	94 : 6	4.70 gm M2 + 0.30 gm Starch
▪ *Ratio 3*	91 : 9	4.55 gm M2 + 0.45 gm Starch
▪ *Ratio 4*	88 : 12	4.40 gm M2 + 0.60 gm Starch
▪ *Ratio 5*	85 : 15	4.25 gm M2 + 0.75 gm Starch

3.2.2.5. Mixture 3 (M3) with Polyvinyl Pyrrolidone (PVP)

Table 3.16: Ratio concentration of M3 with PVP and amount needed for 5gm

Ratio	M3 (%) : PV (%)	Amount for 5gm
▪ *Ratio 1*	98 : 2	4.9 gm M3 + 0.1 gm PVP
▪ *Ratio 2*	96 : 4	4.8 gm M3 + 0.2 gm PVP
▪ *Ratio 3*	94 : 6	4.7 gm M3 + 0.3 gm PVP
▪ *Ratio 4*	92 : 8	4.6 gm M3 + 0.4 gm PVP

3.2.2.6. Mixture 3 (M3) with Starch

Table 3.17: Ratio concentration of M3 with Starch and amount needed for 5gm

Ratio	M3 (%) : Starch (%)	Amount for 5gm
▪ *Ratio 1*	97 : 3	4.85 gm M3 + 0.15 gm Starch
▪ *Ratio 2*	94 : 6	4.70 gm M3 + 0.30 gm Starch

▪ *Ratio 3*	91 : 9	4.55 gm M3 + 0.45 gm Starch
▪ *Ratio 4*	88 : 12	4.40 gm M3 + 0.60 gm Starch

3.2.2.7. Mixture 4 (M4) with Polyvinyl Pyrrolidone (PVP)

Table 3.18: Ratio concentration of M4 with Starch and amount needed for 5gm

Ratio	M4 (%) : PVP (%)	Amount for 5gm
▪ *Ratio 1*	98 : 2	4.9 gm M4 + 0.1 gm PVP
▪ *Ratio 2*	96 : 4	4.8 gm M4 + 0.2 gm PVP
▪ *Ratio 3*	94 : 6	4.7 gm M4 + 0.3 gm PVP
▪ *Ratio 4*	92 : 8	4.6 gm M4 + 0.4 gm PVP

3.2.2.8. Mixture 5 (M5) with Starch

Table 3.19: Ratio concentration of M5 with Starch and amount needed for 5gm

Ratio	M5 (%) : Starch (%)	Amount for 5gm
▪ *Ratio 1*	97 : 3	4.85 gm M5 + 0.15 gm Starch
▪ *Ratio 2*	94 : 6	4.70 gm M5 + 0.30 gm Starch
▪ *Ratio 3*	91 : 9	4.55 gm M5 + 0.45 gm Starch
▪ *Ratio 4*	88 : 12	4.40 gm M5 + 0.60 gm Starch
▪ *Ratio 5*	85 : 15	4.25 gm M5 + 0.75 gm Starch

3.2.2.9. Mixture 6 (M6) with Polyvinyl Pyrrolidone (PVP)

Table 3.20: Ratio concentration of M6 with PVP and amount needed for 5gm

Ratio	M6 (%) : PVP (%)	Amount for 5gm
▪ *Ratio 1*	98 : 2	4.9 gm M6 + 0.1 gm PVP

▪ *Ratio 2*	96 : 4	4.8 gm M6 + 0.2 gm PVP
▪ *Ratio 3*	94 : 6	4.7 gm M6 + 0.3 gm PVP
▪ *Ratio 4*	92 : 8	4.6 gm M6 + 0.4 gm PVP

3.2.2.10 Mixture 7 (M7) with Starch

Table 3.21: Ratio concentration of M7 with Starch and amount needed for 5gm

Ratio	M7 (%) : Starch (%)	Amount for 5gm
▪ *Ratio 1*	97 : 3	4.85 gm M7 + 0.15 gm Starch
▪ *Ratio 2*	94 : 6	4.70 gm M7 + 0.30 gm Starch
▪ *Ratio 3*	91 : 9	4.55 gm M7 + 0.45 gm Starch
▪ *Ratio 4*	88 : 12	4.40 gm M7 + 0.60 gm Starch
▪ *Ratio 5*	85 : 15	4.25 gm M7 + 0.75 gm Starch

3.2.3 Determination of Hausner's Ratio and Carr's Index:

Amounts of powder excipients of different ratio were weighed correctly and put into a conical flask. Then mixing is done by hand shaking of the conical flask. Then the mixture was transferred into a measuring cylinder. The measurement of volume that we obtained from the measuring cylinder without shaking is known as bulk volume. The obtained bulk volume was recorded into the laboratory note book. Then 40-50 times hand tapping per 30 second was done. After that, we obtained the tapped volume of the mixture and recorded into the laboratory note book again. This process was done three times repetitively. The maximum bulk volume from the three obtained values was selected as most acceptable value as well as used for further calculation of Hausner's Ratio and Carr's Index. Again the minimum tapped volume from the three obtained values was selected as most acceptable values as well as used for further calculation.

Hausner's ratio and Carr's index was calculated by using the following equation:

- **Carr's Index or Compressibility Index**

  $$= [(\text{Bulk volume} - \text{Tapped volume}) / \text{Bulk volume}] \times 100$$

- **Hausner's Ratio** = [Bulk volume ÷ Tapped volume]

3.2.4 Determination of Angle of Repose:

Angle of repose is another parameter that characterizes the powder flow behavior. For determination of angle of repose, we first set up a stand over the table. A cleaned funnel was hung on the stand and a white paper was attached in the base of the stand.

Then appropriate amounts of excipients were weighed using electronic balance. Then the weighed materials were mixed by hand shaking using a conical flask. Then the mixed excipients was poured through the funnel carefully thus a pile was formed upon the white paper. A round mark was made using a pencil upon the base of the pile. This was done with carefully thus the pile would vibrate and break.

Then the height of the pile was measured by using a ruler in cm. This data was recorded into the laboratory log book. The base of pile was measured removing the powder from the paper and recorded into laboratory log book. The angle of repose was determined by using the following formula:

$$\tan\alpha = [\text{height} / (0.5 \text{ diameter})]$$

- **Angle of Repose**, $\alpha = \tan^{-1}(\text{height} / 0.5 \text{ base})$

This process of determining angle of repose was done three times repeatedly and finally the average value of angle of repose was recorded for further calculation.

Chapter Four

RESULTS

4.1 RESULT

4.1.1 Data of Hausner's Ratio and Carr's Index of Individual Excipient

Compressibility Index and Hausner's Ratio of different excipients were measured in previously described method and the obtained data are given below:

Table 4.1: Values of Hausner's Ratio and Carr's Index of Individual Excipient

Name of Excipients	Bulk Volume, V_o ml	Most Acceptable Value of V_o ml	Tapped Volume (V_f)	Most Acceptable Value of V_f	Hausner's ratio = (V_o/V_f)	Carr's Index = 100 ×{(V_o - V_f)/ $V_{o)}$ }
Sodium Lauryl Sulphate	17.0	17.0	14.0	14.0	**1.21**	**17.6**
	16.5		14.0			
	17.0		14.5			
Magnesium Stearate	52.0	52.5	40.0	40.5	**1.28**	**22.8**
	52.5		40.0			
	52.5		40.5			
Lactose	10.0	10.0	6.5	6.5	**1.54**	**35.0**
	9.5		7.0			
	9.5		7.0			
Talc	5.0	5.0	3.0	3.0	**1.67**	**40**
	4.5		3.0			
	5.0		3.0			
Starch	8.5	8.5	3.5	3.5	**2.43**	**58.82**
	8.5		4.0			
	8.0		3.5			
Carboxy methyl Celllose	7.0	7.5	4.0	4.0	**1.87**	**47.0**
	7.5		4.0			
	7.5		4.5			

Name of Excipients	**Bulk Volume, V_o ml**	**Most Acceptable Value of V_o ml**	**Tapped Volume (V_f)**	**Most Acceptable Value of V_f**	**Hausner's ratio = (V_o/V_f)**	**Carr's Index = 100 ×{(V_o - V_f)/ V_o) }**
Polyvinyl pyrrolidine	13.5	13.5	10.0	10.0	**1.35**	**25.92**
	13.0		10.0			
	13.5		10.5			
Calcium Phosphate	10.0	10.5	7.0	7.0	**1.50**	**33.33**
	10.0		7.0			
	10.5		7.5			

4.1.2 Data of Angle of Repose of Individual Excipient

Angle of Repose of Different Excipient was measured and the obtained values of angle of repose are given below:

Table 4.2 Values of Angle of Repose of Individual Excipient

Name of Excipients	**Height (cm)**	**Base (cm)**	**Angle of Repose = [$\tan^{-1}$(Height/ 0.5 base)]**	**Average Value of Angle of repose**
Sodium Lauryl Sulphate	2.8	6.0	43.03	**44.18**
	3.0	5.9	45.48	
	2.9	6.0	44.03	
Magnesium Stearate	2.0	5.2	37.57	**38.13**
	2.1	5.4	38.87	
	2.0	5.1	37.95	

Name of Excipients	**Height (cm)**	**Base (cm)**	**Angle of Repose = [$\tan^{-1}$(Height/ 0.5 base)]**	**Average Value of Angle of repose**
Talc	2.1	3.8	47.86	**47.65**
	2.1	3.7	48.62	
	2.0	3.8	46.47	
Starch	2.6	5.0	46.12	**46.33**
	2.6	4.9	46.70	
	2.5	4.8	46.17	
Carboxymethyl Celllose	1.7	4.0	40.36	**41.63**
	1.8	3.8	41.82	
	1.8	3.9	42.71	
Polyvinyl pyrrolidine	2.1	5.8	35.91	**36.51**
	2.2	5.6	38.16	
	2.1	5.9	35.45	
Calcium Phosphate	2.5	4.8	46.17	**46.75**
	2.6	4.6	48.50	
	2.5	4.9	45.58	
Lactose	2.0	4.6	41.01	**40.67**
	1.9	4.4	40.82	
	1.9	4.5	40.18	

4.1.3 Data of Mixture 1 (M1) with Polyvinyl Pyrrolidone (PVP)

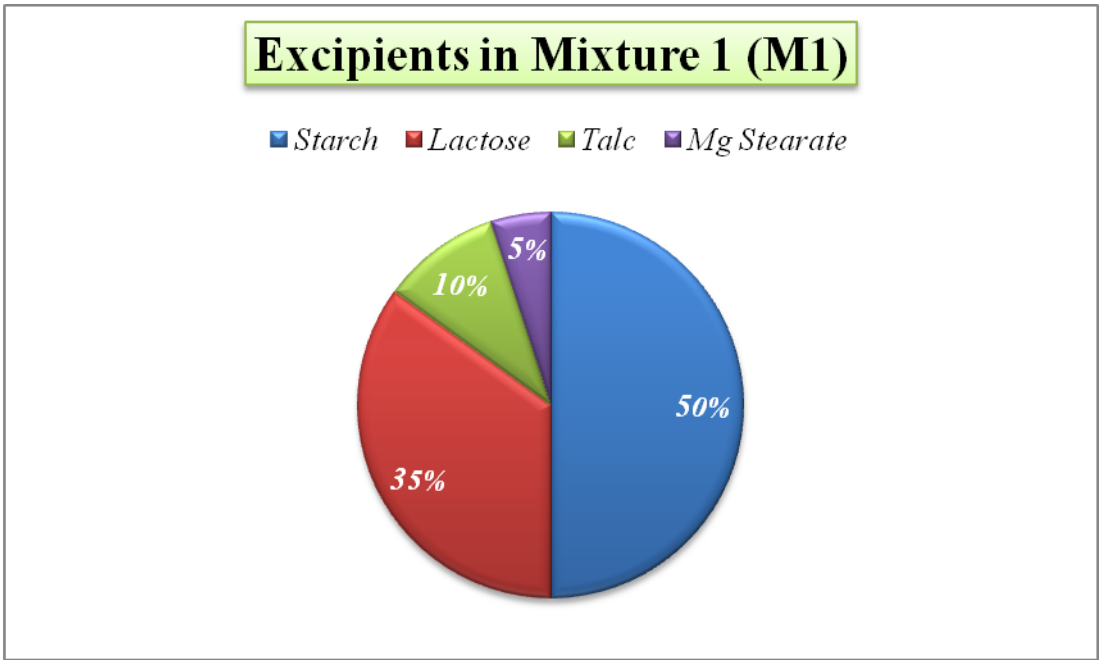

Figure 4.1: A *1* pie chart showing the composition of M1

4.1.3.1 Values of Carr's Index and Hausner's Ratio of Mixture 1 (M1) with Polyvinyl Pyrrolidone (PVP)

Table 4.3: Values of Compressibility Index and Hausner's Ratio of Mixture 1 (M1) with Polyvinyl Pyrrolidone (PVP)

Ratio	Bulk Volume, V_o ml	Most Acceptable Value of V_o ml	Tapped Volume (V_f)	Most Acceptable Value of V_f	Hausner's ratio = (V_o/ V_f)	Carr's Index = 100 ×{(V_o - V_f)/ $V_{o)}$ }
Ratio 1	10.5	10.5	7.5	7.5	1.40	**28.57**
	10.5		7.5			
	10.0		8.0			
Ratio 2	10.5	11.0	8.0	7.5	1.47	**31.82**
	10.5		7.5			
	11.0		7.5			

Ratio 3	10.5	10.5	7.0	7.0	1.50	**33.33**
	10.5		7.0			
	11.0		7.5			
Ratio 4	11.0	11.2	7.5	7.0	1.60	**37.50**
	11.0		7.5			
	10.5		7.0			

The following graph was obtained putting the amount of PVP into X-axis and Carr's index into Y-axis.

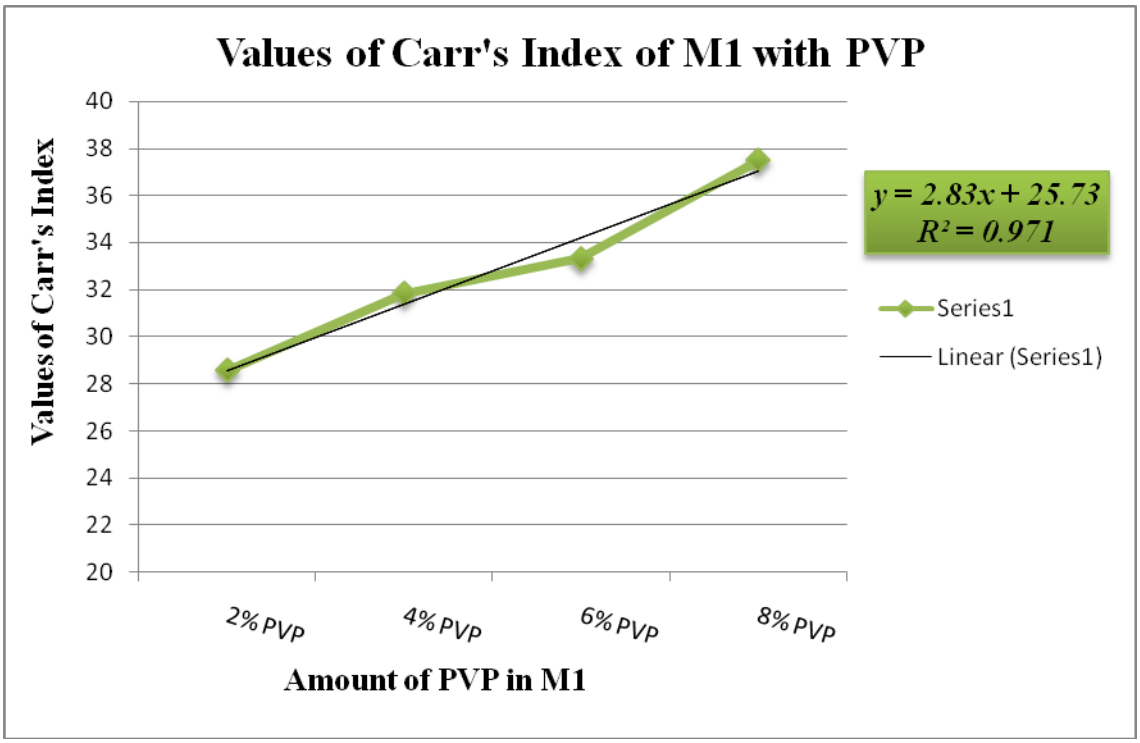

Figure 4.2: Scattered Plot showing the values of Carr's index of different mixture ratio (M1 with PVP)

The following graph was obtained putting the amount of PVP ratio into X-axis and Hausner's ratio into Y-axis.

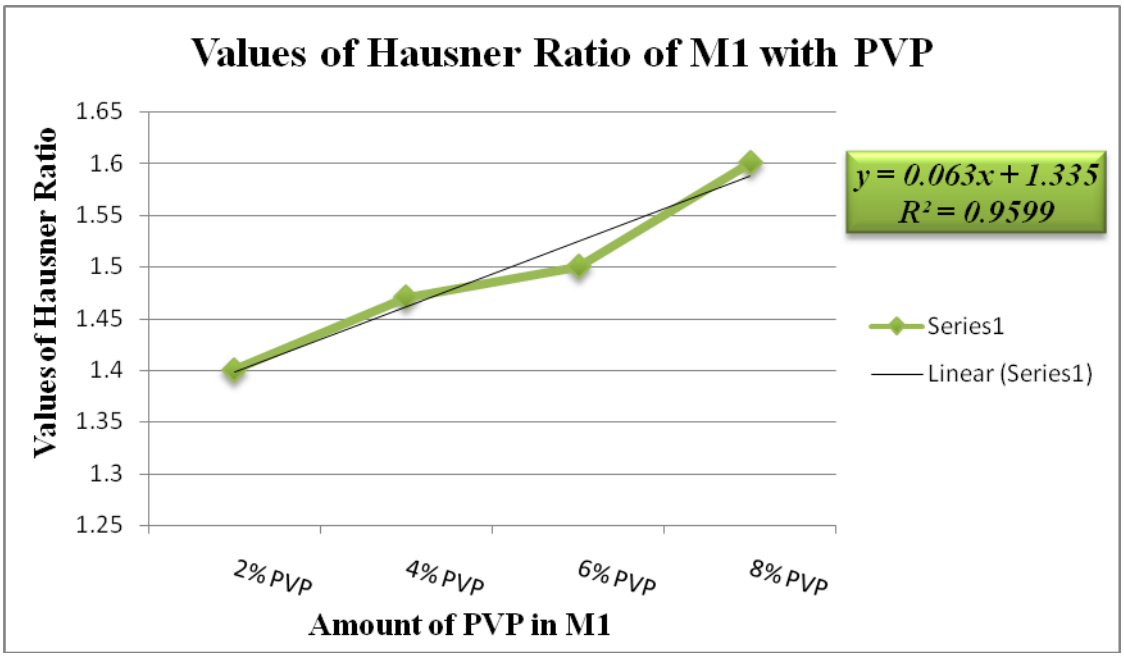

Figure 4.3: Scattered Plot showing the values Hausner's ratio of different mixture ratio (M1 with PVP)

4.1.3.2 Values of Angle of Repose of Mixture 1 (M1) with Polyvinyl Pyrrolidone (PVP)

Table 4.4: Values of Angle of Repose of Mixture 1 (M1) with Polyvinyl Pyrrolidone (PVP)

Ratio	Height (cm)	Base (cm)	Angle of Repose = $\tan^{-1}$(Height/ 0.5 base)	Average Value of Angle of repose
Ratio 1	2.2	5.6	38.16	**38.75**
	2.3	5.4	40.43	
	2.2	5.7	37.67	
Ratio 2	1.9	5.4	35.13	**35.60**
	2.0	5.3	37.04	
	1.9	5.5	34.64	

Ratio 3	2.0	5.2	37.57	**37.62**
	2.2	5.8	37.18	
	2.0	5.1	38.11	
Ratio 4	1.7	5.3	32.68	**31.69**
	1.6	5.5	30.19	
	1.7	5.4	32.20	

The following graph was obtained putting the amount of PVP into X-axis and angle of repose into Y-axis.

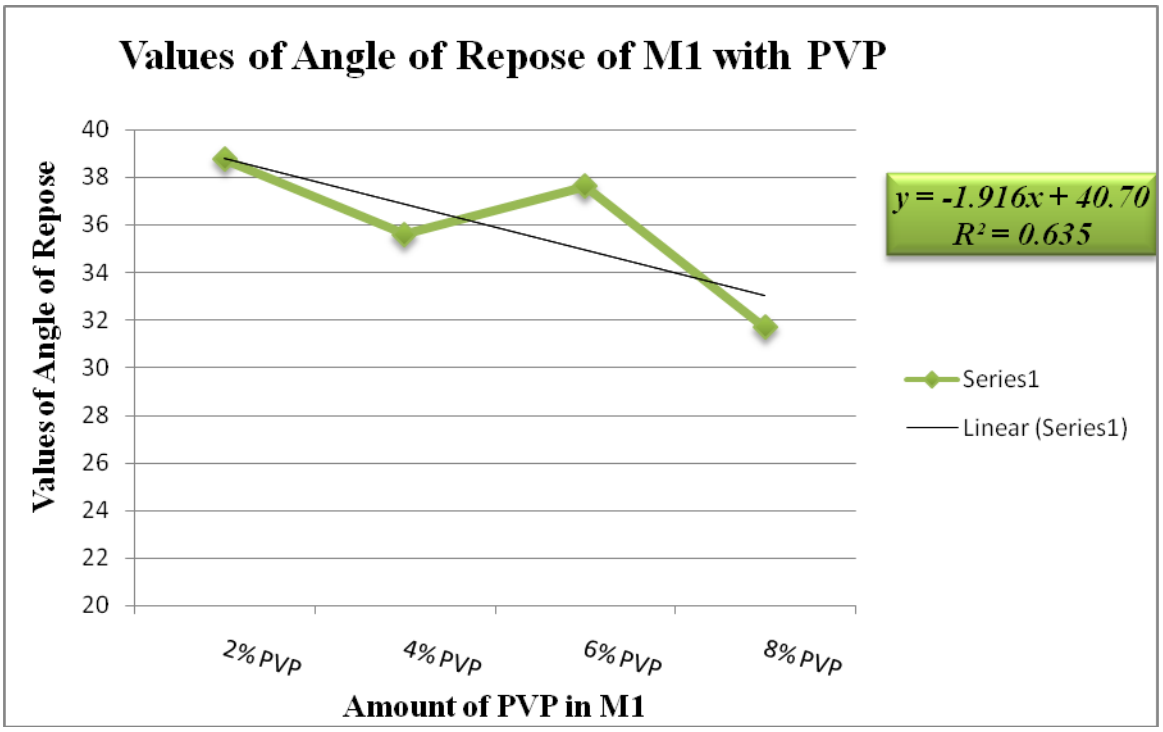

Figure 4.4: Scattered Plot showing the values of angle of repose of different mixture ratio (M1 with PVP)

4.1.4 Data of Mixture 1 (M1) with Carboxymethyl Cellulose (CMC)

4.1.4.1 Values of Compressibility Index and Hausner's Ratio of Mixture 1 (M1) with Carboxymethyl Cellulose (CMC)

Table 4.5: Values of Compressibility Index and Hausner's Ratio of Mixture 1 (M1) with Carboxymethyl Cellulose (CMC)

Ratio	Bulk Volume, V_o ml	Most Acceptable Value of V_o ml	Tapped Volume (V_f)	Most Acceptable Value of V_f	Hausner's ratio = (V_o/ V_f)	Compressibility Index = 100 ×{(V_o - V_f)/ V_o) }
Ratio 1	10.5	10.5	7.5	7.0	**1.50**	**33.33**
	10.0		7.0			
	10.5		7.0			
Ratio 2	10.5	11.0	8.0	7.5	**1.47**	**31.81**
	11.0		7.5			
	11.0		7.5			
Ratio 3	10.5	11.0	7.0	7.0	**1.57**	**36.36**
	11.0		7.0			
	11.0		7.5			
Ratio 4	11.2	11.5	7.5	7.0	**1.64**	**39.13**
	11.5		7.0			
	11.5		7.0			

The following graph was obtained putting the amount of CMC into X-axis and values of Carr's index into Y-axis.

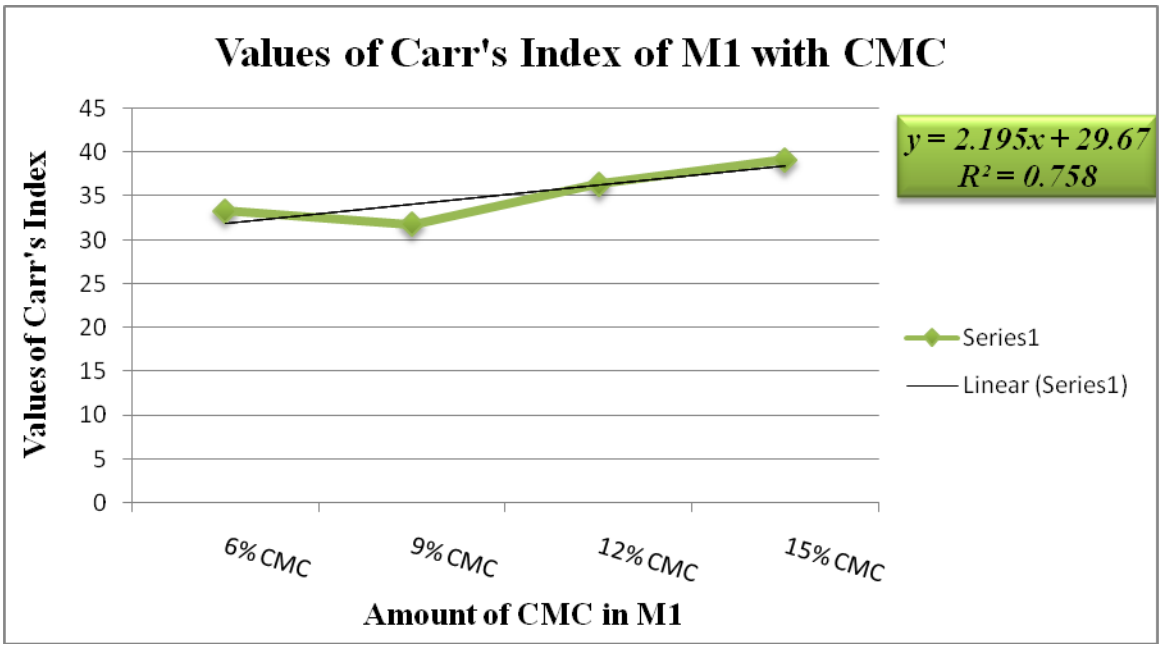

Figure 4.5: Scattered Plot showing the values of Carr's index of different mixture ratio (M1 with CMC)

The following graph was obtained putting the amount of CMC into X-axis and values of Hausner's ratio into Y-axis:

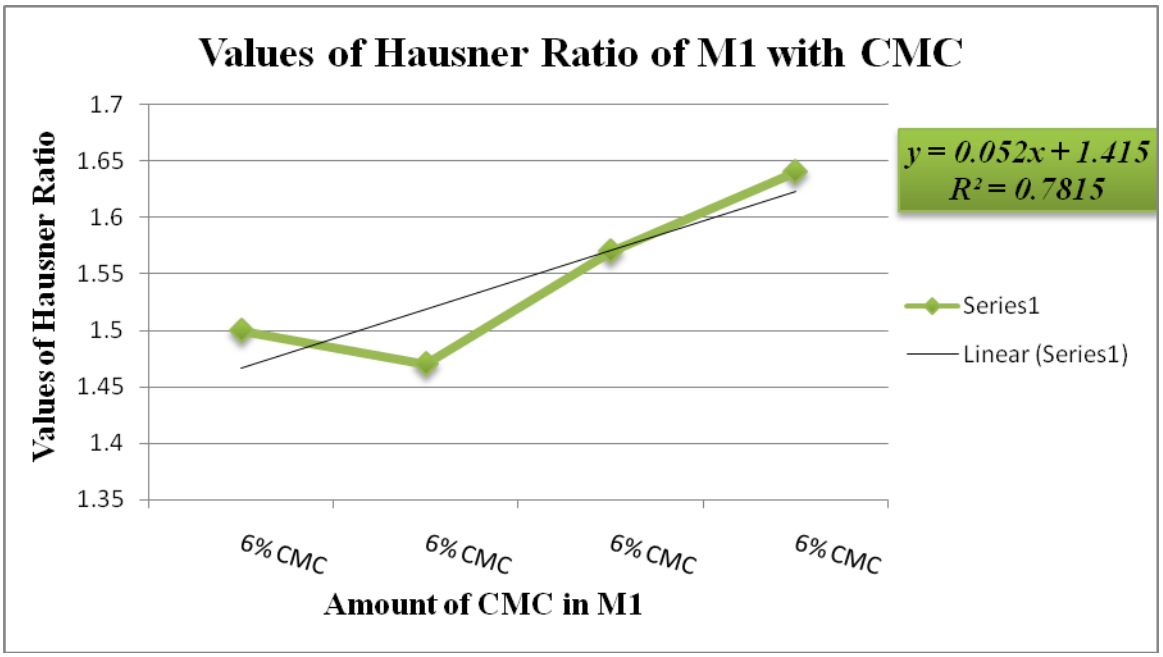

Figure 4.6: Scattered Plot showing the values of Hausner's ratio of different mixture ratio (M1 with CMC)

4.1.4.2 Values of Angle of Repose of Mixture 1 (M1) with Carboxymethyl Cellulose (CMC)

Table 4.6: Values of Angle of Repose of Mixture 1 (M1) with Carboxymethyl Cellulose (CMC)

Ratio	Height (cm)	Base (cm)	Angle of Repose = $\tan^{-1}$(Height/ 0.5 base)	Average Value of Angle of repose
Ratio 1	1.9	5.0	37.23	**37.16**
	2.0	5.2	37.55	
	1.9	5.1	36.69	
Ratio 2	1.8	5.5	33.21	**33.37**
	1.7	5.6	31.26	
	1.9	5.3	35.64	
Ratio 3	2.5	5.1	44.43	**43.66**
	2.4	5.0	43.83	
	2.4	5.2	42.71	
Ratio 4	2.3	4.6	45.00	**45.60**
	2.4	4.6	46.22	
	2.4	4.7	45.60	

The following graph was obtained putting the amount of CMC into X-axis and values of angle of repose into Y-axis:

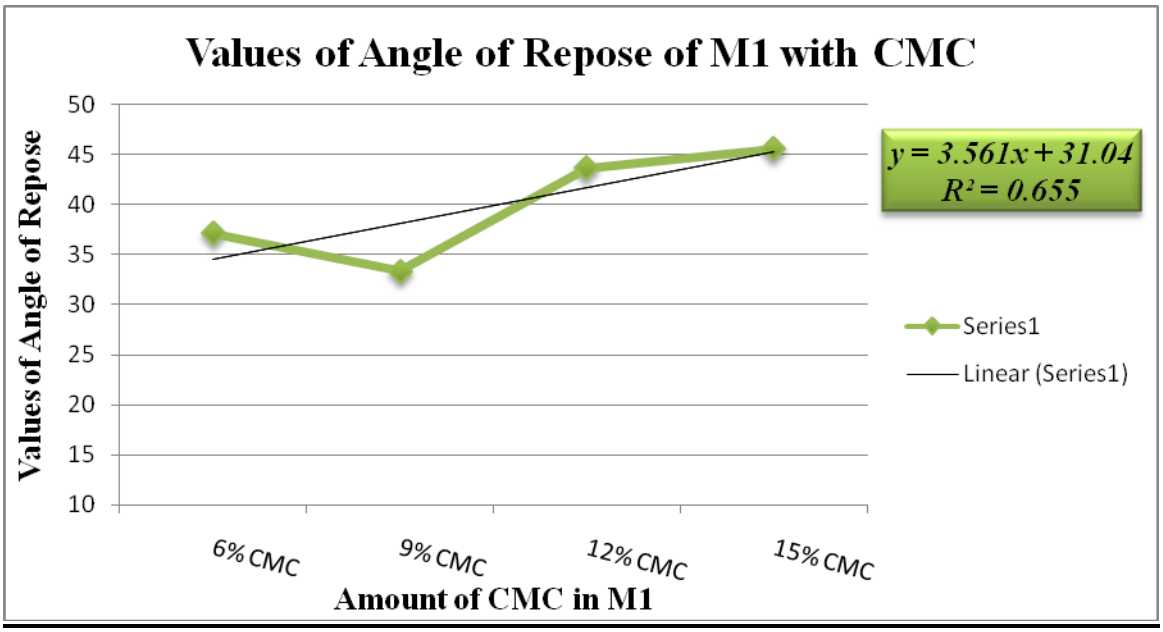

Figure 4.7: Scattered Plot showing the values of angle of repose of different mixture ratio (M1 with CMC)

4.1.5 Data of Mixture 1 (M1) with Microcrystalline Cellulose (MCC)

4.1.5.1 Values of Carr'sIndex Index and Hausner's Ratio of Mixture 1 (M1) with Microcrystalline Cellulose (MCC)

Table 4.7: Values of Compressibility Index and Hausner's Ratio of Mixture 1 (M1) with Microcrystalline Cellulose (MCC)

Ratio	Bulk Volume, V_o ml	Most Acceptable Value of V_o ml	Tapped Volume (V_f)	Most Acceptable Value of V_f	Hausner's ratio = (V_o/ V_f)	Carr's Index = 100 ×{(V_o - V_f)/ V_o) }
Ratio 1	10.5	11.0	7.5	7.5	1.47	**31.81**
	11.0		7.5			
	11.0		8.0			
Ratio 2	10.5	11.0	8.0	7.5	1.47	**31.81**
	11.0		7.5			
	11.0		7.5			

Ratio 3	12.0	12.0	7.0	7.5	1.60	**37.50**
	11.5		7.0			
	12.0		7.5			
Ratio 4	11.2	11.5	7.5	7.0	1.64	**39.13**
	11.5		7.0			
	11.5		7.0			

The following graph was obtained putting the amount of MCC into X-axis and values of Carr's index into Y-axis:

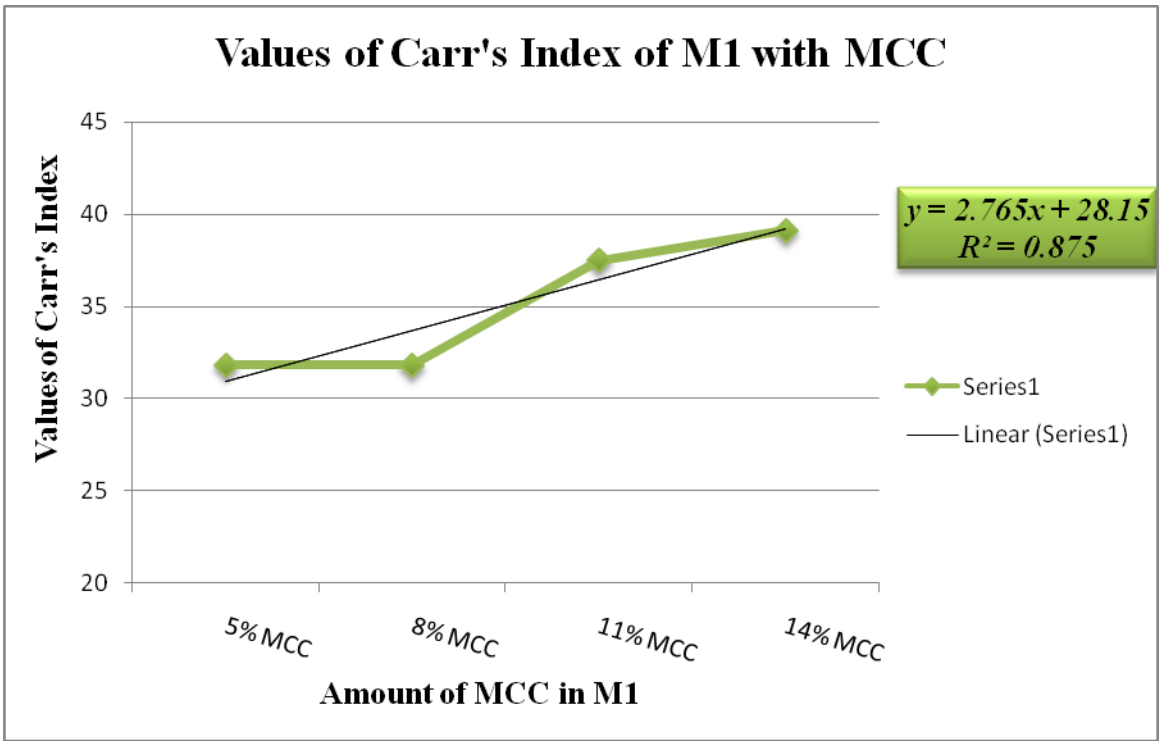

Figure 4.8: Scattered Plot showing the values of Carr's index of different mixture ratio (M1 with MCC)

The following graph was obtained putting the amount of MCC into X-axis and values of Hausner's ratio into Y-axis:

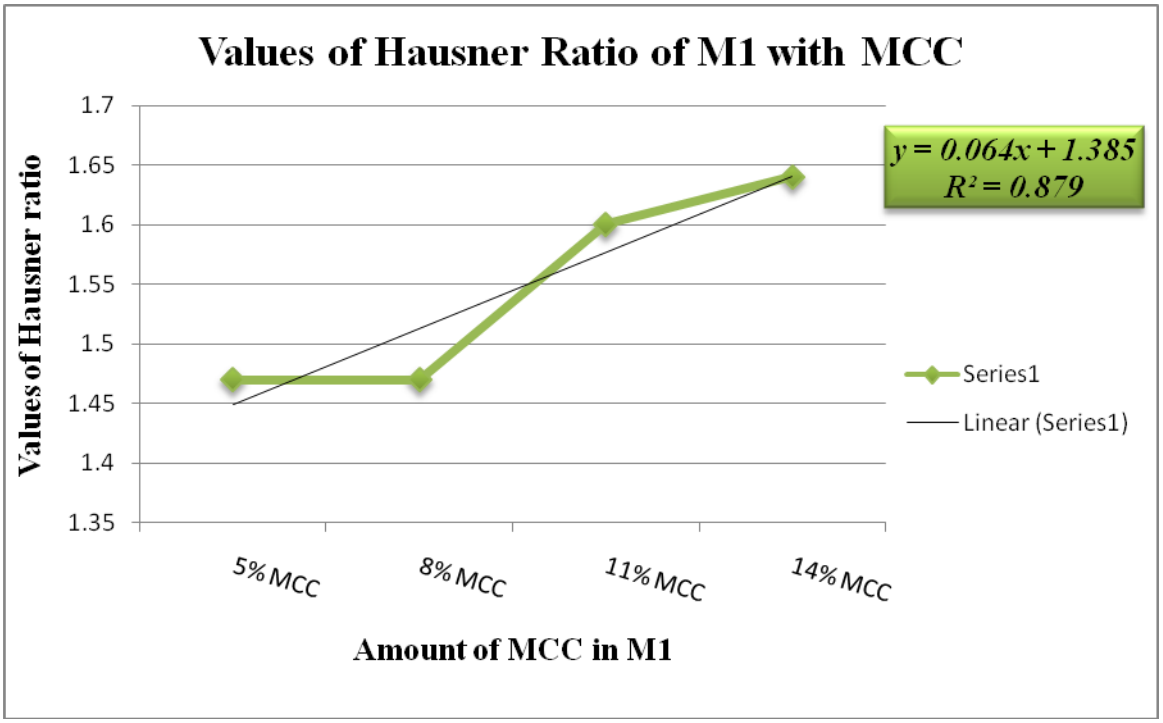

Figure 4.9: Scattered Plot showing the values of Hausner's ratio of different mixture ratio (M1 with MCC)

4.1.5.2 Values of Carr's Index and Hausner's Ratio of Mixture 1 (M1) with Microcrystalline Cellulose (MCC)

Table 4.8: Values of Angle of Repose of Mixture 1 (M1) with Microcrystalline Cellulose (MCC)

Ratio	Height (cm)	Base (cm)	Angle of Repose = $\tan^{-1}$(Height/ 0.5 base)	Average Value of Angle of repose
Ratio 1	2.3	4.8	43.78	**44.19**
	2.3	4.9	43.19	
	2.4	4.7	45.60	

Ratio 2	2.4	4.9	44.41	**43.81**
	2.4	5.0	43.83	
	2.3	4.9	43.19	
Ratio 3	2.2	5.1	40.79	**39.73**
	2.1	5.2	38.93	
	2.1	5.1	39.47	
Ratio 4	2.2	4.9	41.92	**40.85**
	2.1	4.9	40.60	
	2.1	5.0	40.03	

The following graph was obtained putting amount of MCC into X-axis and values of angle of repose into Y-axis:

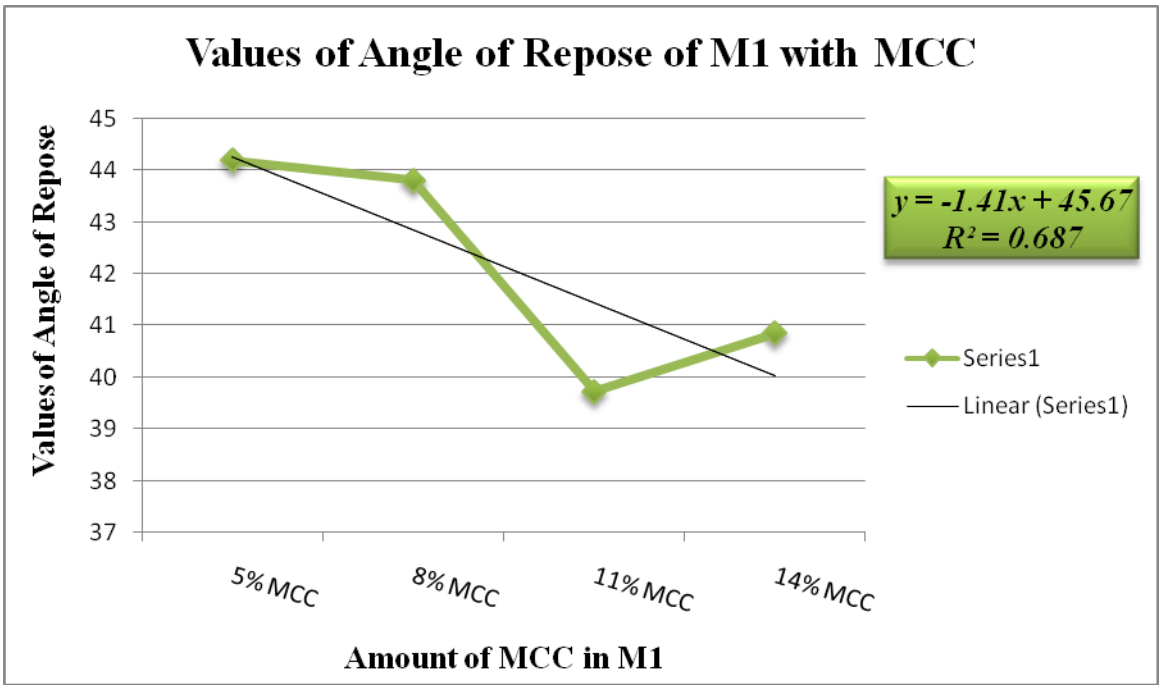

Figure 4.10: Scattered Plot showing the values of angle of repose of different mixture ratio (M1 with MCC)

4.1.6 Data of Mixture 2 (M2) with Starch

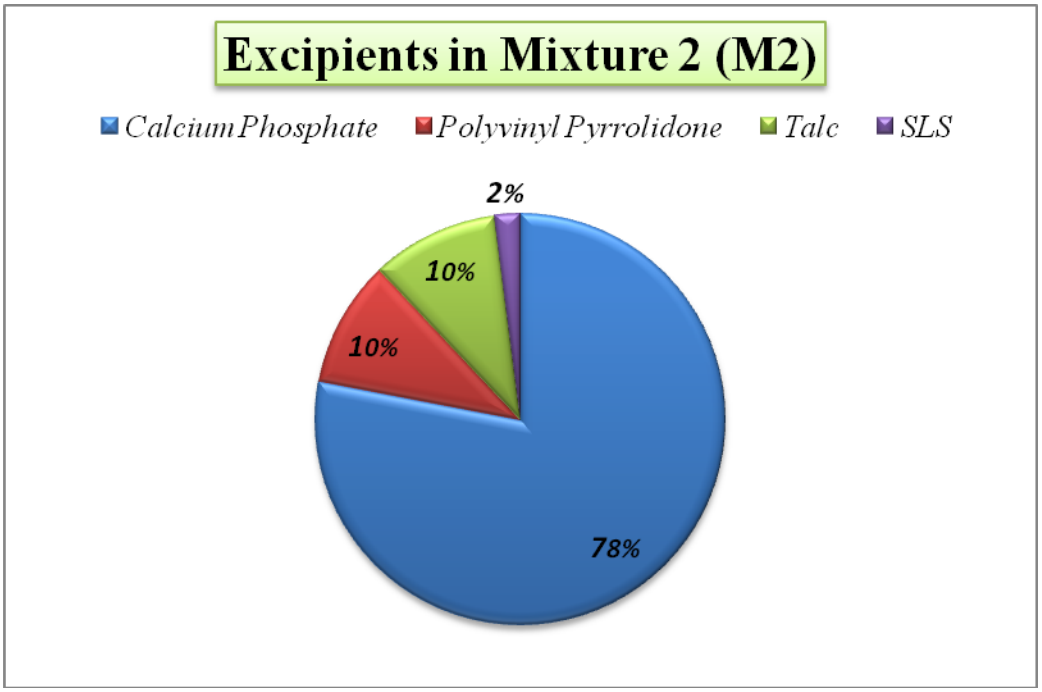

Figure 4.11: A pie chart showing the composition of M2

4.1.6.1 Values of Compressibility Index and Hausner's Ratio of Mixture 2 (M2) with Starch

Table 4.9: Values of Compressibility Index and Hausner's Ratio of Mixture 2 (M2) with Starch

Ratio	Bulk Volume, V_o ml	Most Acceptable Value of V_o ml	Tapped Volume (V_f)	Most Acceptable Value of V_f	Hausner's ratio = (V_o/ V_f)	Carr's Index = 100 ×{(V_o - V_f)/ V_o) }
Ratio 1	10.0	10.0	7.0	7.0	1.42	30.00
	10.0		7.5			
	10.0		7.0			
Ratio 2	11.1	11.1	7.0	7.1	1.56	36.04
	11.0		7.0			
	11.1		7.1			

Ratio 3	11.1	11.1	7.8	7.8	1.42	29.73
	11.1		7.8			
	11.0		8.0			
Ratio 4	10.5	10.5	7.5	7.5	1.40	28.57
	10.5		7.5			
	10.0		8.0			
Ratio 5	9.5	9.5	7.0	7.0	1.36	26.32
	9.5		7.5			
	9.2		7.0			

The following graph was obtained putting the amount of Starch into X-axis and values of Carr's index into Y-axis.

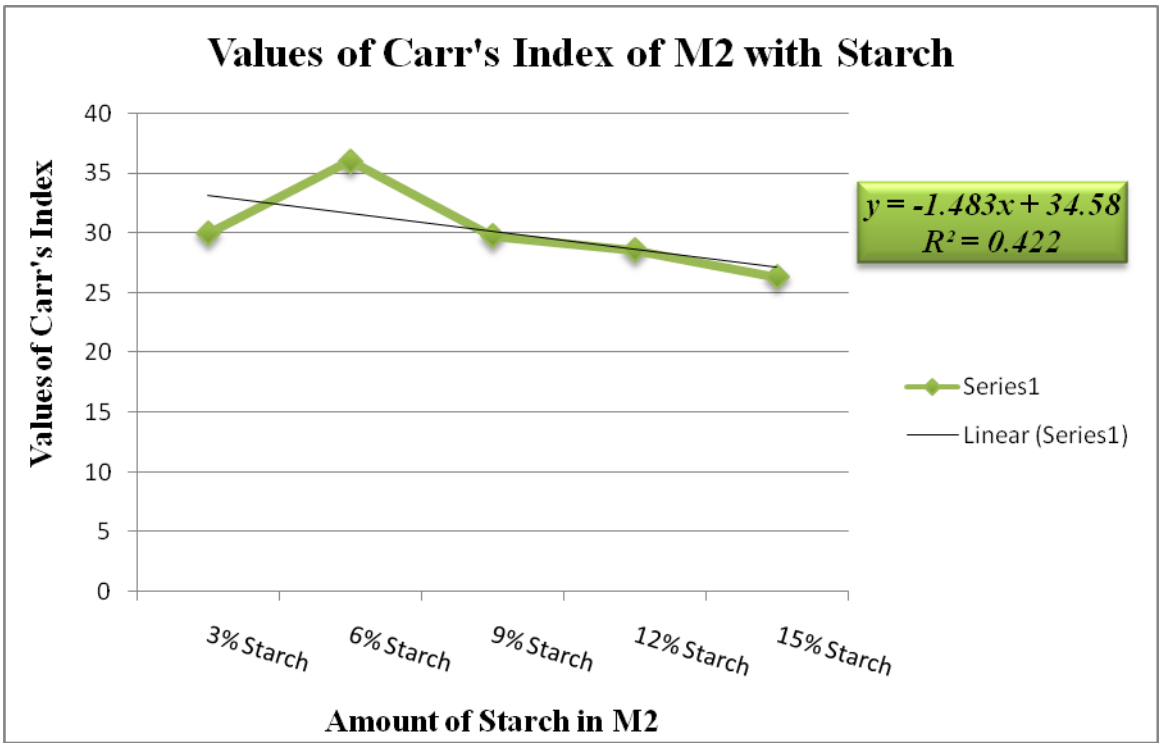

Figure 4.12: Scattered Plot showing the values of Carr's index of different mixture ratio (M2 with Starch)

The following graph was obtained putting the amount of Starch into X-axis and values of Hausner's ratio into Y-axis:

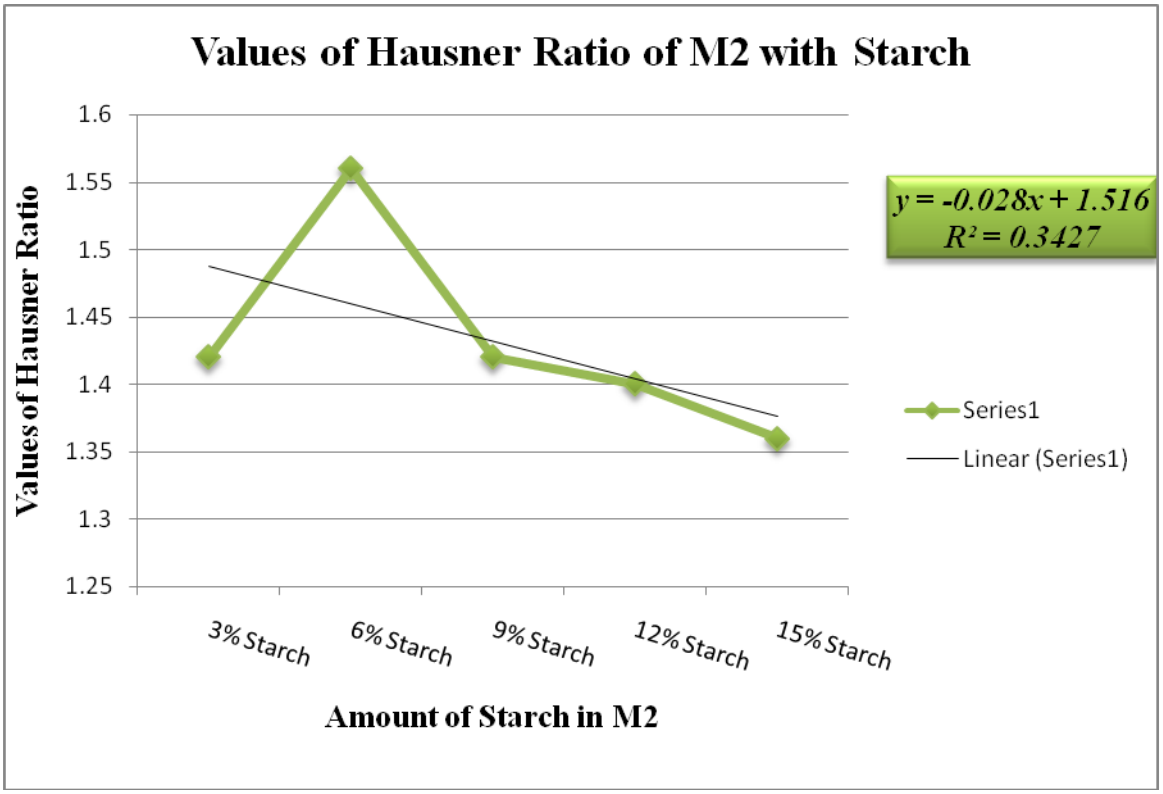

Figure 4.13: Scattered Plot showing the values of Hausner's ratio of different mixture ratio (M2 with Starch)

4.1.6.2 Values of Angle of Repose of Mixture 2 (M2) with Starch

Table 4.10: Values of Angle of Repose of Mixture 2 (M2) with Starch

Ratio	Height (cm)	Base (cm)	Angle of Repose = $\tan^{-1}$(Height/ 0.5 base)	Average Value of Angle of repose
Ratio 1	2.0	4.5	41.63	**41.68**
	2.1	4.6	42.40	
	2.0	4.6	41.01	

Ratio 2	2.2	5.0	41.35	**41.29**
	2.1	4.9	40.60	
	2.2	4.9	41.92	
Ratio 3	2.2	5.0	41.35	**41.10**
	2.2	4.9	41.92	
	2.1	5.0	40.03	
Ratio 4	1.8	4.3	39.94	**39.19**
	1.7	4.4	37.69	
	1.8	4.3	39.94	
Ratio 5	2.0	4.8	39.81	**38.94**
	1.9	4.9	37.79	
	2.0	4.9	39.23	

The following graph was obtained putting the amount of Starch into X-axis and values of angle of repose into Y-axis:

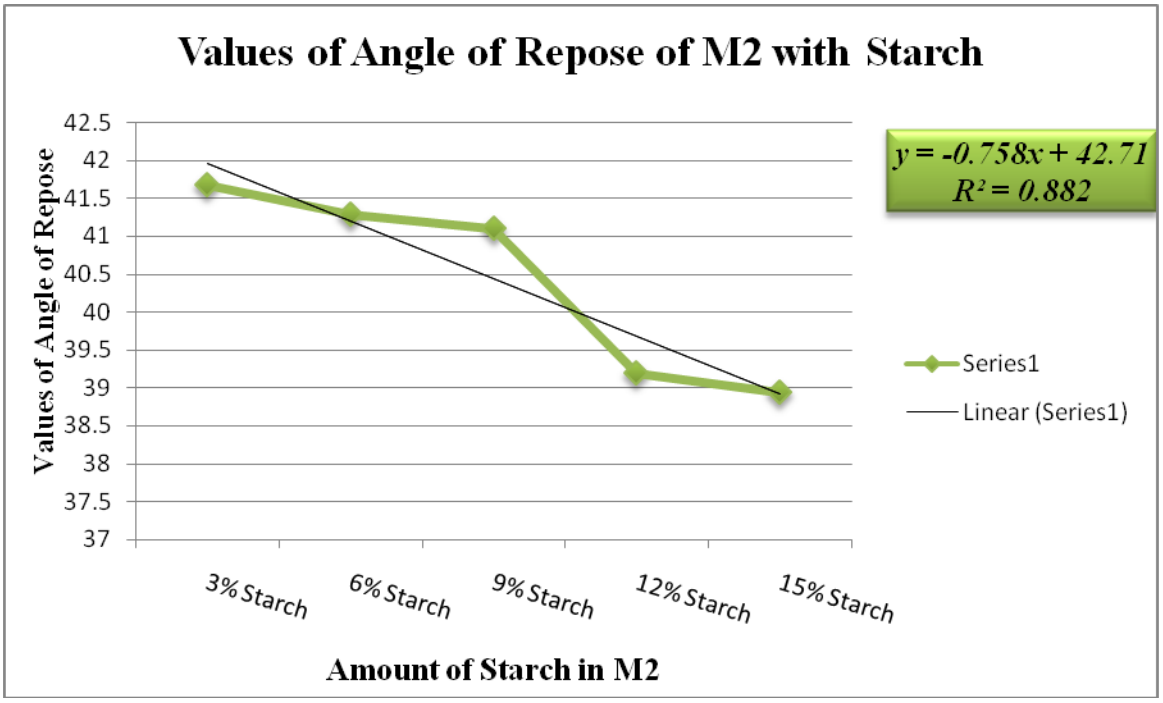

Figure 4.14: Scattered Plot showing the values of angle of repose of different mixture ratio (M2 with Starch)

4.1.7 Data of Mixture 3 with polyvinyl pyrrolidone (PVP)

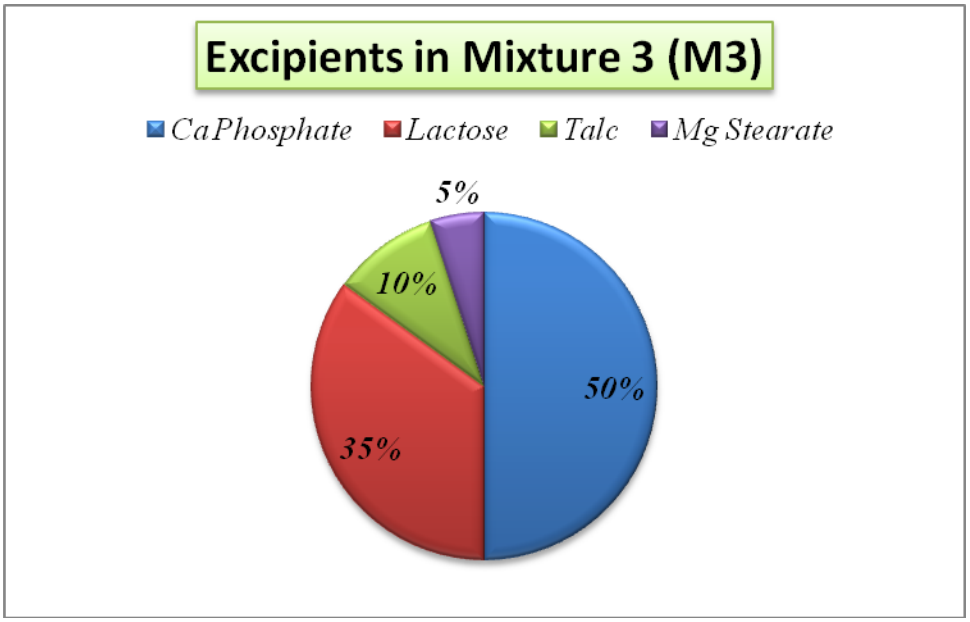

Figure 4.15: A pie chart showing the composition of M3

4.1.7.1 Values of Compressibility Index and Hausner's Ratio of Mixture 3 (M3) with Polyvinyl Pyrrolidone (PVP)

Table 4.11: Values of Compressibility Index and Hausner's Ratio of Mixture 3 (M3) with Polyvinyl Pyrrolidone (PVP)

Ratio	Bulk Volume, V_o ml	Most Acceptable Value of V_o ml	Tapped Volume (V_f)	Most Acceptable Value of V_f	Hausner's ratio = (V_o/ V_f)	Carr's Index = 100 ×{(V_o - V_f)/ V_o) }
Ratio 1	10.5	10.5	7.0	7.0	1.50	**33.33**
	10.0		7.0			
	10.5		7.5			
Ratio 2	10.2	10.2	7.0	6.5	1.57	**36.27**
	10.2		7.0			
	10.0		6.5			

Ratio 3	11.5	11.5	7.0	7.0	1.64	**39.13**
	11.5		7.5			
	11.0		7.5			
Ratio 4	10.5	10.5	6.5	6.5	1.62	**38.10**
	10.0		6.5			
	10.5		7.0			

The following graph was obtained putting the amount of PVP into X-axis and values of Carr's index into Y-axis:

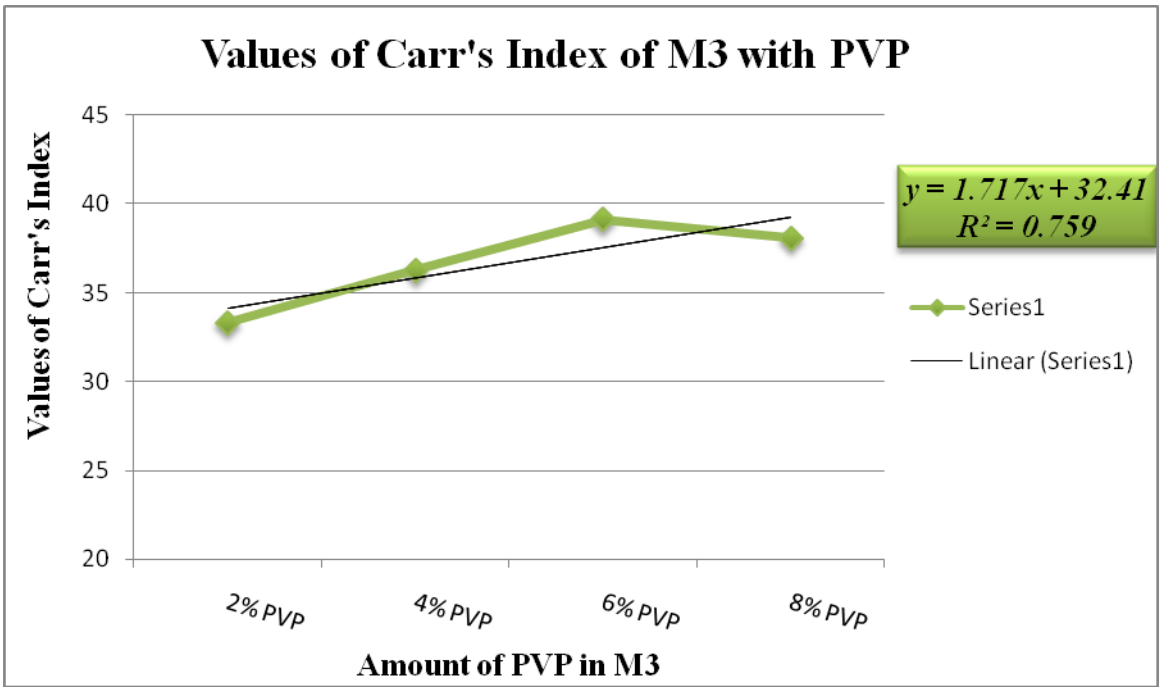

Figure 4.16: Scattered Plot showing the values of Carr's index of different mixture ratio (M3 with PVP)

The following graph was obtained putting the amount of PVP into X-axis and values of Hausner's ratio into Y-axis:

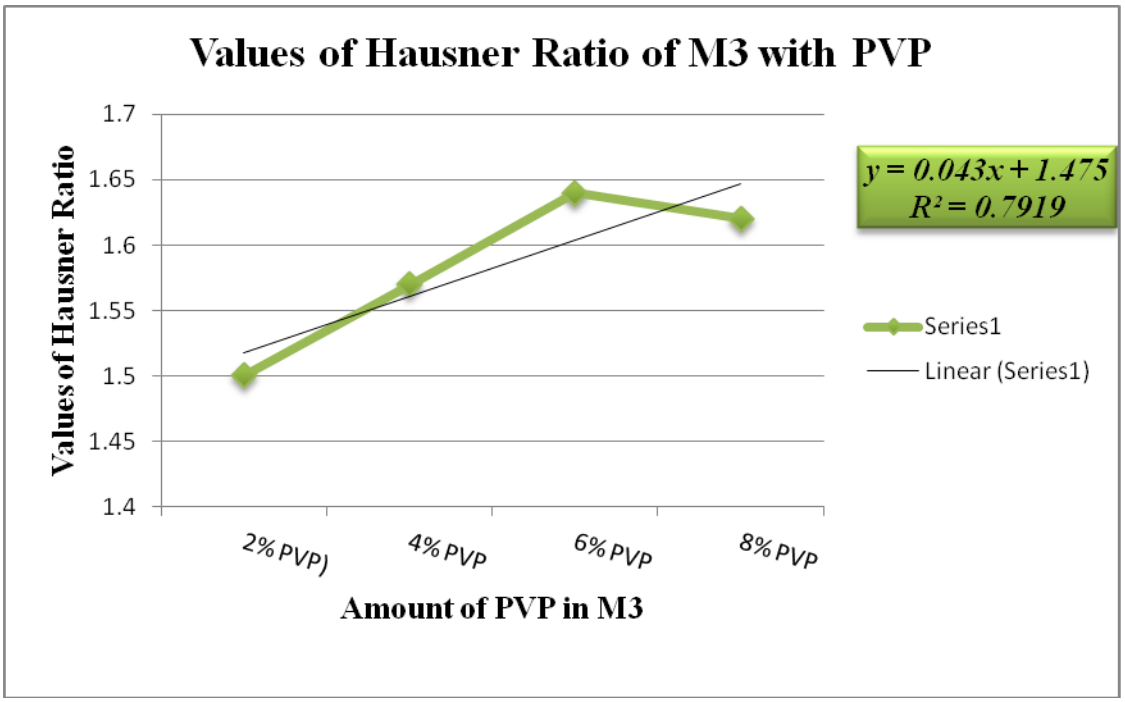

Figure 4.17: Scattered Plot showing the values of Hausner's ratio of different mixture ratio (M3 with PVP)

4.1.7.2 Values of Angle of Repose of Mixture 3 (M3) with Polyvinyl Pyrrolidone (PVP)

Table 4.12: Values of Angle of Repose of Mixture 3 (M3) with Polyvinyl Pyrrolidone (PVP)

Ratio	Height (cm)	Base (cm)	Angle of Repose = $\tan^{-1}$(Height/ 0.5 base)	Average Value of Angle of repose
Ratio 1	1.8	5.2	34.70	**35.36**
	1.9	5.2	36.16	
	1.8	5.1	35.22	
Ratio 2	1.6	4.9	33.15	**32.59**
	1.6	5.0	32.62	
	1.5	4.8	32.01	

Ratio 3	2.0	4.6	41.01	**40.79**
	2.1	4.6	42.40	
	1.9	4.7	38.96	
Ratio 4	2.3	4.5	45.63	**44.58**
	2.3	4.6	45.00	
	2.2	4.7	43.11	

The following graph was obtained putting the amount of PVP into X-axis and values of angle of repose into Y-axis:

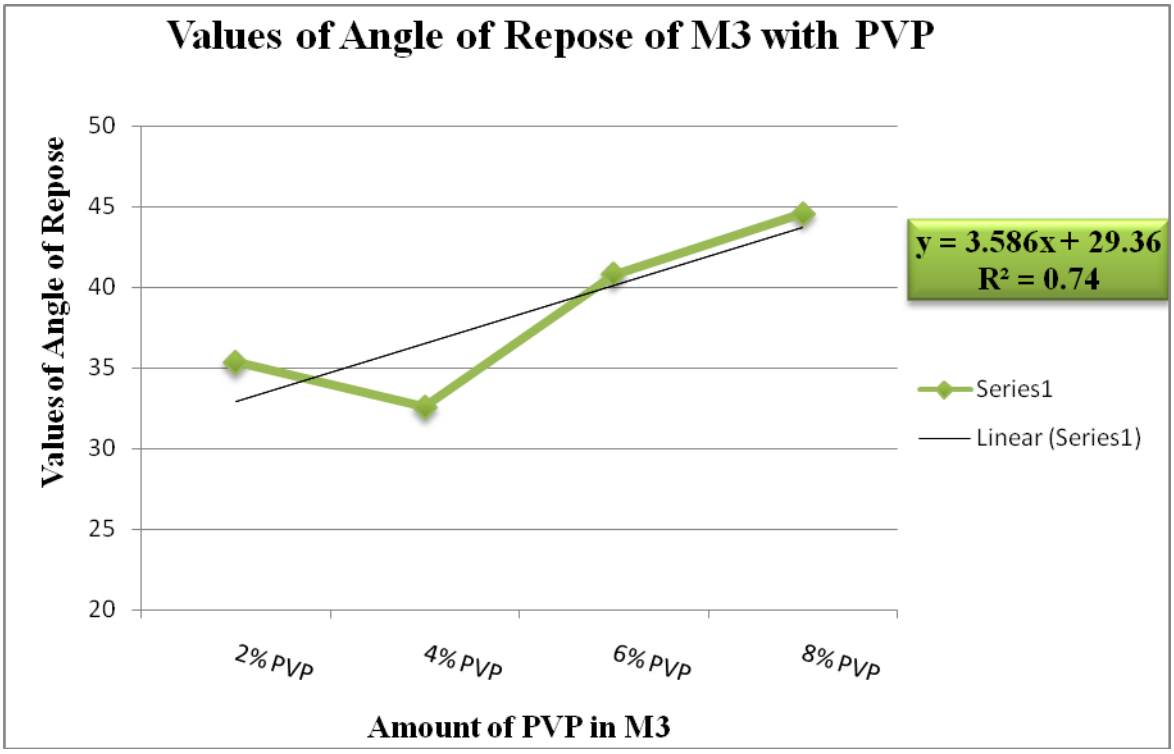

Figure 4.18: Scattered Plot showing the values of angle of repose of different mixture ratio (M3 with PVP)

4.1.8 Data of Mixture 3 (M3) with Starch

4.1.8.1 Values of Compressibility Index and Hausner's Ratio of Mixture 3 (M3) with Starch

Table 4.13: Values of Compressibility Index and Hausner's Ratio of Mixture 3 (M3) with Starch

Ratio	Bulk Volume, V_o ml	Most Acceptable Value of V_o ml	Tapped Volume (V_f)	Most Acceptable Value of V_f	**Hausner's ratio = (V_o/ V_f)**	**Carr's Index = 100 ×{(V_o - V_f)/ V_o) }**
Ratio 1	10.0	10.0	7.0	6.5	**1.54**	**35.0**
	10.0		6.5			
	10.0		6.5			
Ratio 2	10.5	10.5	7.0	7.0	**1.50**	**35.0**
	10.5		7.0			
	10.0		7.5			
Ratio 3	10.0	10.5	7.5	7.0	**1.50**	**35.0**
	10.5		7.0			
	10.0		7.0			
Ratio 4	10.5	11.0	7.5	7.5	**1.47**	**31.82**
	11.0		7.5			
	11.0		8.0			

The following graph was obtained putting the amount of Starch into X-axis and values of Carr's index into Y-axis:

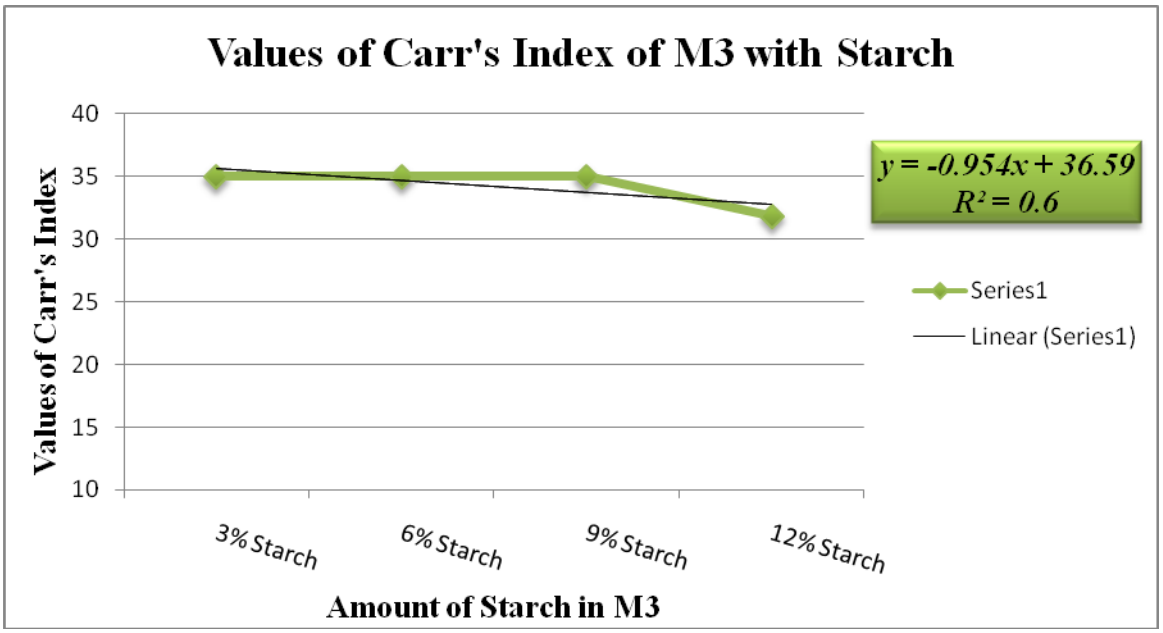

Figure 4.19: Scattered Plot showing the values of Carr's index of different mixture ratio (M3 with Starch)

The following graph was obtained putting the values of mixture ratio into X-axis and values of Hausner's ratio into Y-axis:

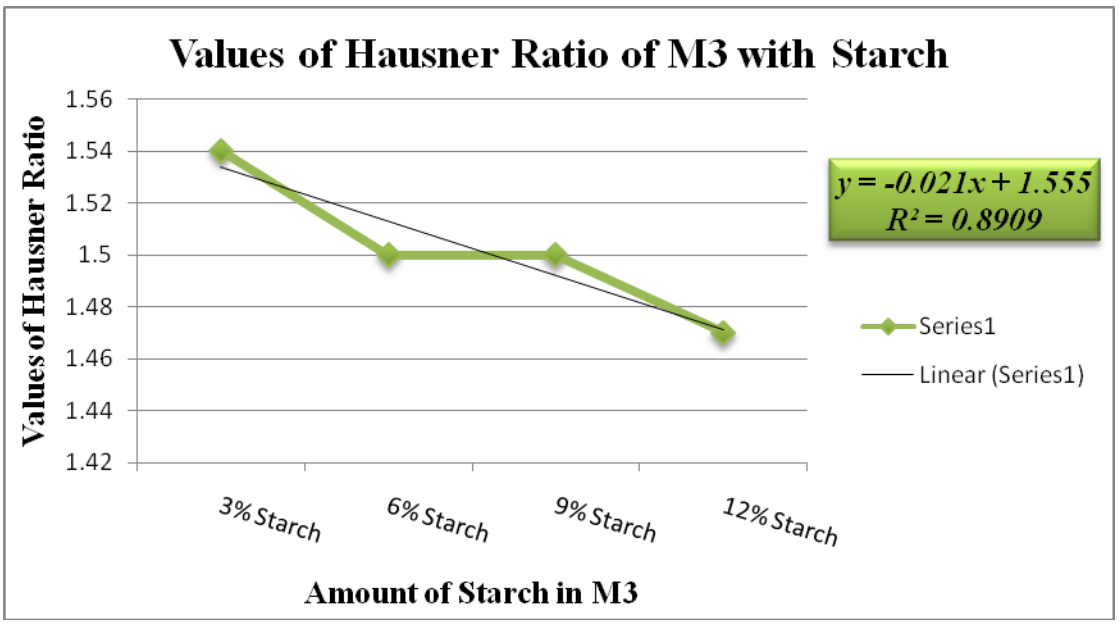

Figure 4.20: Scattered Plot showing the values of Hausner's ratio of different mixture ratio (M3 with Starch)

4.1.8.2 Values of Angle of Repose of Mixture 3 (M3) with Starch

Table 4.14: Values of Angle of Repose of Mixture 3 (M3) with Starch

Ratio	Height (cm)	Base (cm)	Angle of Repose = $\tan^{-1}$(Height/ 0.5 base)	Average Value of Angle of repose
Ratio 1	2.2	4.8	42.51	**42.55**
	2.3	4.8	43.78	
	2.1	5.0	41.35	
Ratio 2	2.1	5.3	38.40	**39.01**
	2.2	5.3	39.70	
	2.1	5.2	38.93	
Ratio 3	1.4	4.8	30.26	**31.81**
	1.5	4.7	32.55	
	1.6	5.0	32.62	
Ratio 4	1.7	5.5	31.72	**32.70**
	1.8	5.4	33.69	
	1.7	5.3	32.68	

The following graph was obtained putting the amount of Starch into X-axis and values of Hausner's ratio into Y-axis.

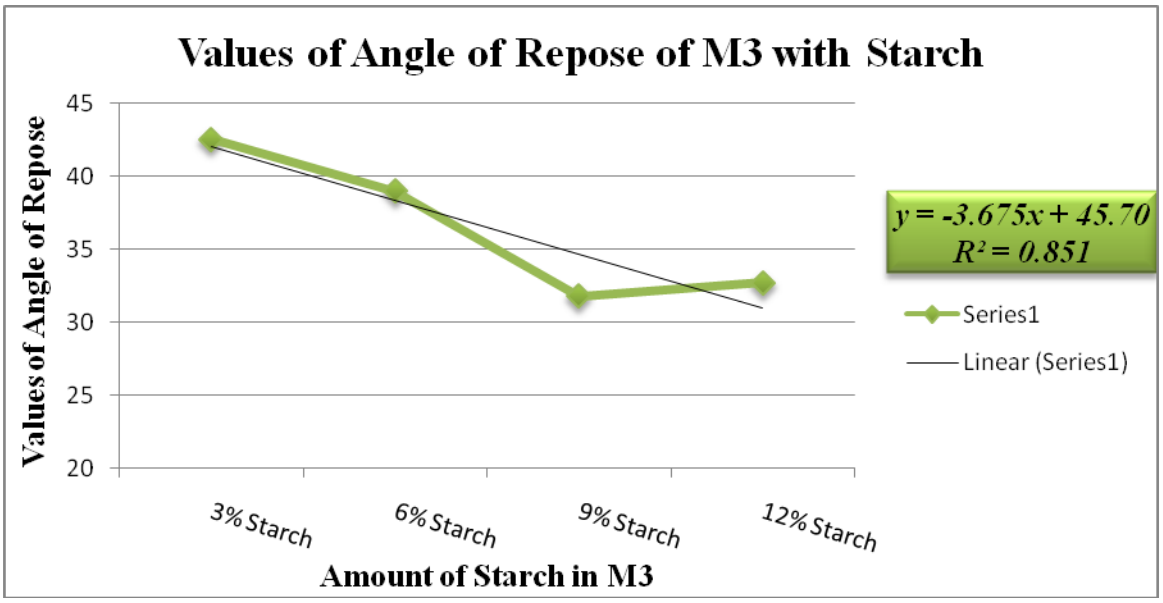

Figure 4.21: Scattered Plot showing the values of angle of repose of different mixture ratio (M3 with Starch)

4.1.9 Data of Mixture 4 (M4) with Polyvinyl Pyrrolidone (PVP)

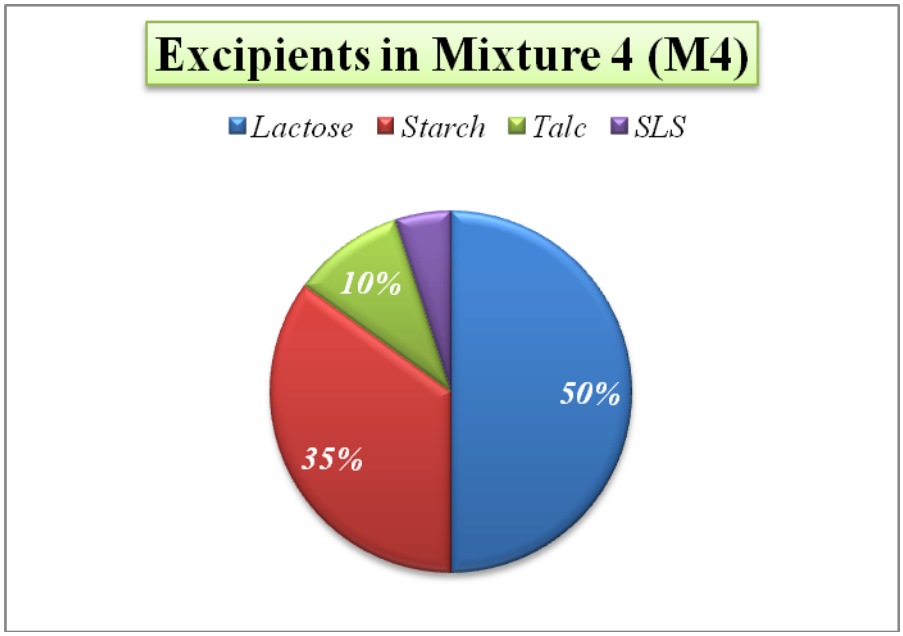

Figure 4.22: A pie chart showing the composition of Mixture 4

4.1.9.1 Values of Compressibility Index and Hausner's Ratio of Mixture 4 (M4) with Polyvinyl pyrrolidone (PVP)

Table 4.15: Values of Compressibility Index and Hausner's Ratio of Mixture 4 (M4) with Polyvinyl pyrrolidone (PVP)

Ratio	Bulk Volume, V_o ml	Most Acceptable Value of V_o ml	Tapped Volume (V_f)	Most Acceptable Value of V_f	**Hausner's ratio = (V_o/ V_f)**	**Carr's Index = 100 ×{(V_o - V_f)/ V_o) }**
Ratio 1	10.5	10.5	7.0	7.0	**1.50**	**33.33**
	10.5		7.0			
	10.0		7.5			
Ratio 2	10.2	10.2	6.5	6.5	**1.57**	**36.27**
	10.0		6.5			
	10.2		6.5			
Ratio 3	10.0	10.5	7.0	6.5	**1.62**	**38.10**
	10.5		6.5			
	10.5		6.5			
Ratio 4	11.5	11.5	7.0	7.0	**1.64**	**39.13**
	11.0		7.0			
	11.0		7.5			

The following graph was obtained putting the amount of PVP into X-axis and values of Carr's index into Y-axis:

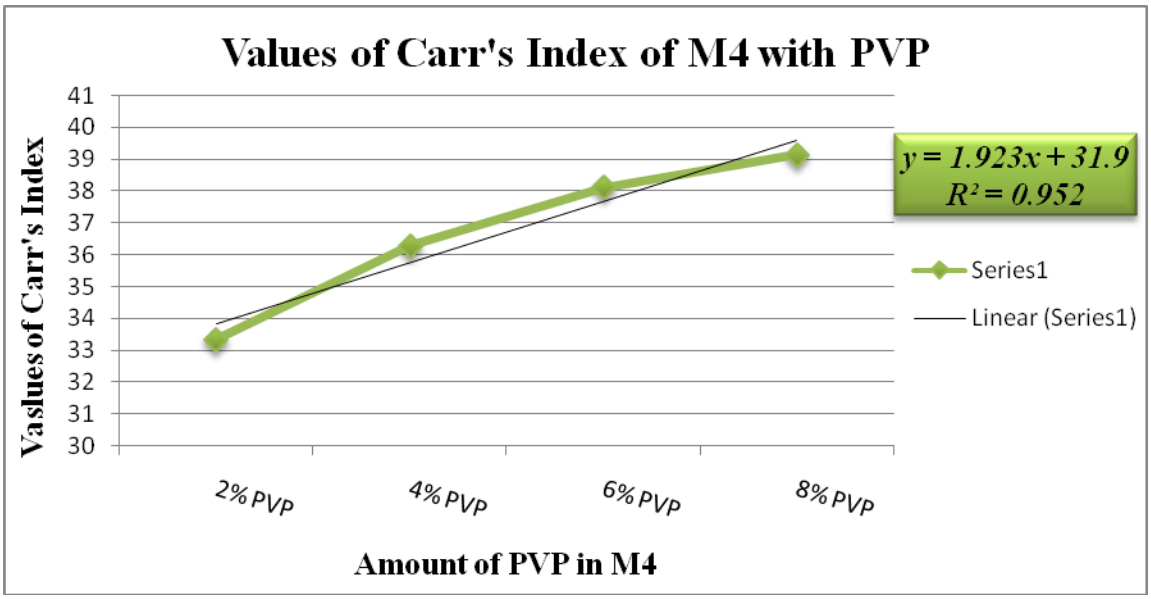

Figure 4.23: Scattered Plot showing the values of Carr's index of different mixture ratio (M4 with PVP)

The following graph was obtained putting the amount of PVP into X-axis and values of Hausner's ratio into Y-axis:

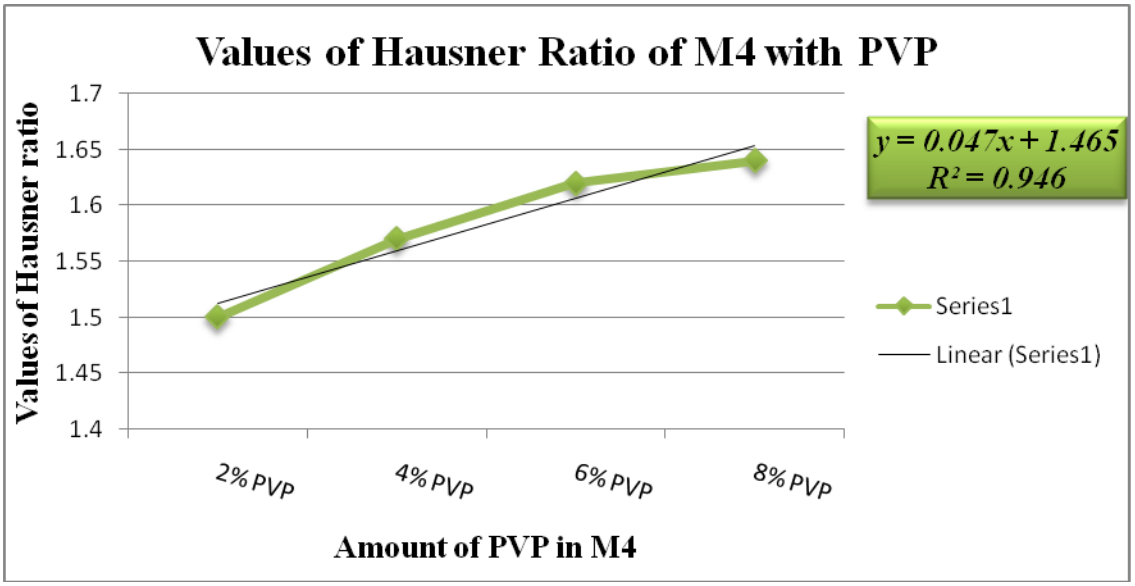

Figure 4.24: Scattered Plot showing the values of Hausner's ratio of different mixture ratio (M4 with PVP)

4.1.9.2 Values of Angle of Repose of Mixture 4 (M4) with Polyvinyl Pyrrolidone (PVP)

Table 4.16: Values of Angle of Repose of Mixture 4 (M4) with Polyvinyl Pyrrolidone (PVP)

Ratio	Height (cm)	Base (cm)	Angle of Repose = $\tan^{-1}$(Height/ 0.5 base)	Average Value of Angle of repose
Ratio 1	1.9	5.2	36.16	**35.85**
	1.9	5.3	35.64	
	2.0	5.0	35.75	
Ratio 2	1.9	5.1	36.69	**36.46**
	1.9	5.2	36.16	
	2.0	5.4	36.53	
Ratio 3	2.2	4.8	42.51	**41.49**
	2.2	4.9	41.92	
	2.1	5.0	40.03	
Ratio 4	2.2	4.9	41.92	**42.94**
	2.3	4.8	43.78	
	2.2	4.7	43.11	

The following graph was obtained putting the amount of PVP into X-axis and values of angle of repose into Y-axis:

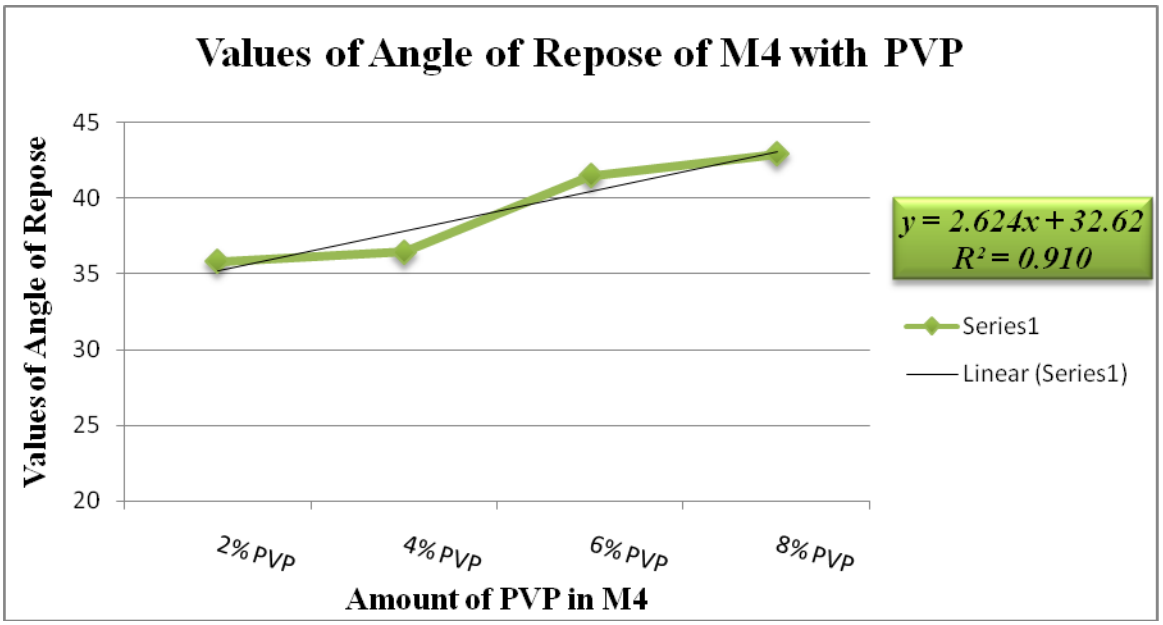

Figure 4.25: Scattered Plot showing the values of angle of repose of different mixture ratio (M4 with PVP)

4.1.10 Data of Mixture 5 (M5) with Starch

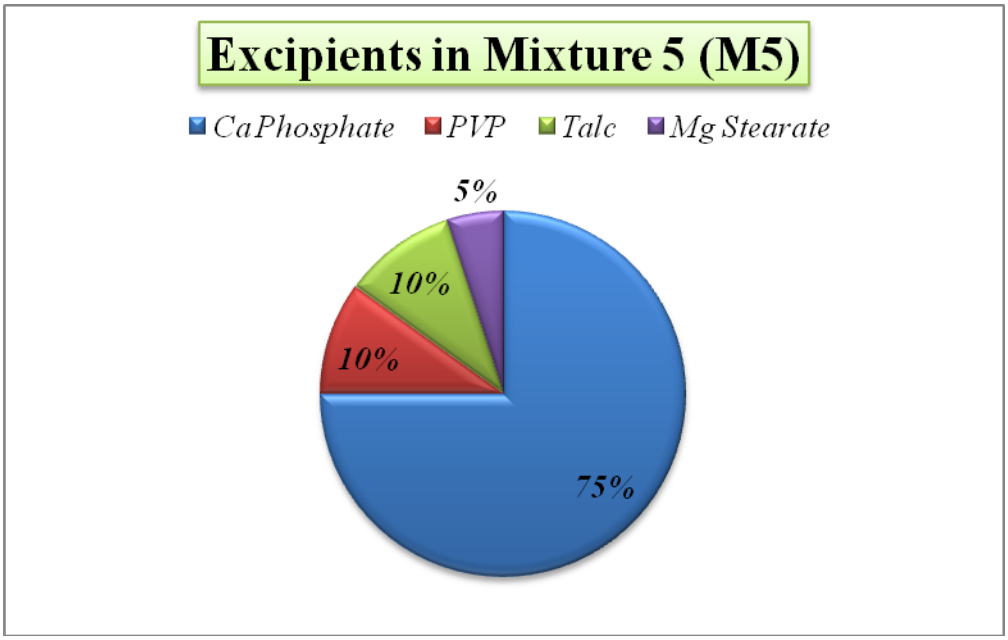

Figure 4.26: A pie chart showing the composition of Mixture 5

4.1.10.1 Values of Compressibility Index and Hausner's Ratio of Mixture 5 (M5) with Starch

Table 4.17: Values of Compressibility Index and Hausner's Ratio of Mixture 5 (M5) with Starch

Ratio	Bulk Volume, V_o ml	Most Acceptable Value of V_o ml	Tapped Volume (V_f)	Most Acceptable Value of V_f	Hausner's ratio = (V_o/ V_f)	Carr's Index = 100 ×{(V_o - V_f)/ V_o) }
Ratio 1	11.2	11.5	8.0	8.0	**1.44**	**30.43**
	11.5		7.5			
	11.5		7.5			
Ratio 2	11.5	11.5	7.5	7.5	**1.53**	**34.78**
	11.0		8.0			
	11.5		7.5			
Ratio 3	11.0	11.0	7.0	7.0	**1.57**	**36.36**
	11.0		7.5			
	11.0		7.0			
Ratio 4	11.0	11.0	7.0	7.0	**1.57**	**36.36**
	11.0		7.0			
	10.5		7.2			
Ratio 5	11.5	11.5	7.0	7.0	**1.64**	**39.13**
	11.5		7.0			
	11.0		7.5			

The following graph was obtained putting the amount of Starch into X-axis and values of Carr's index into Y-axis:

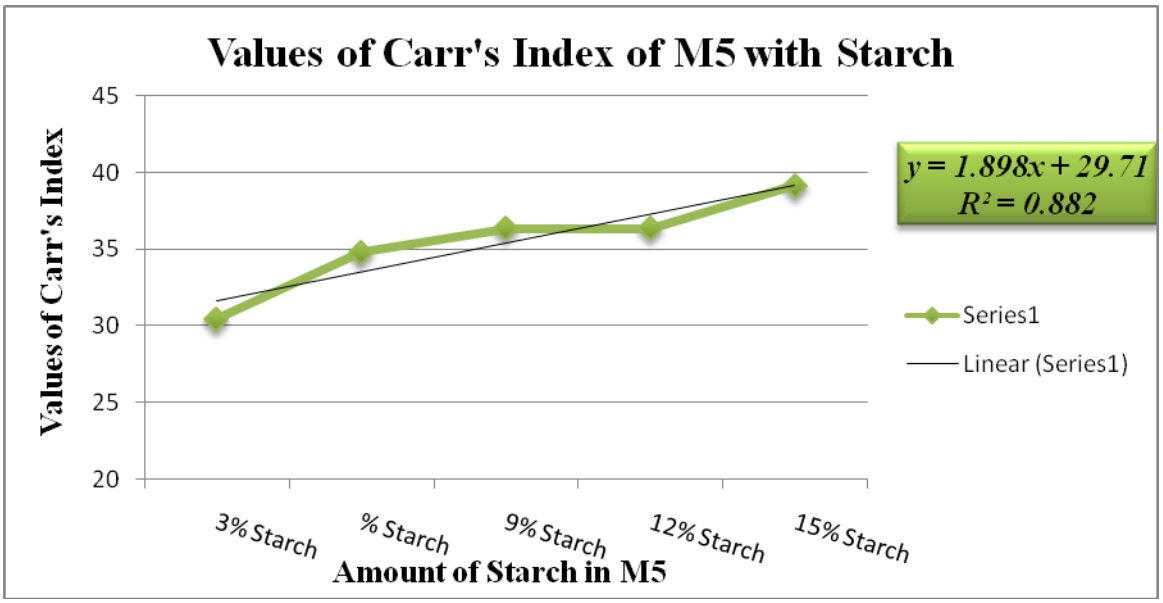

Figure 4.27: Scattered Plot showing the values of Carr's index of different mixture ratio (M5 with Starch)

The following graph was obtained putting the amount of Starch into X-axis and values of Hausner's ratio into Y-axis:

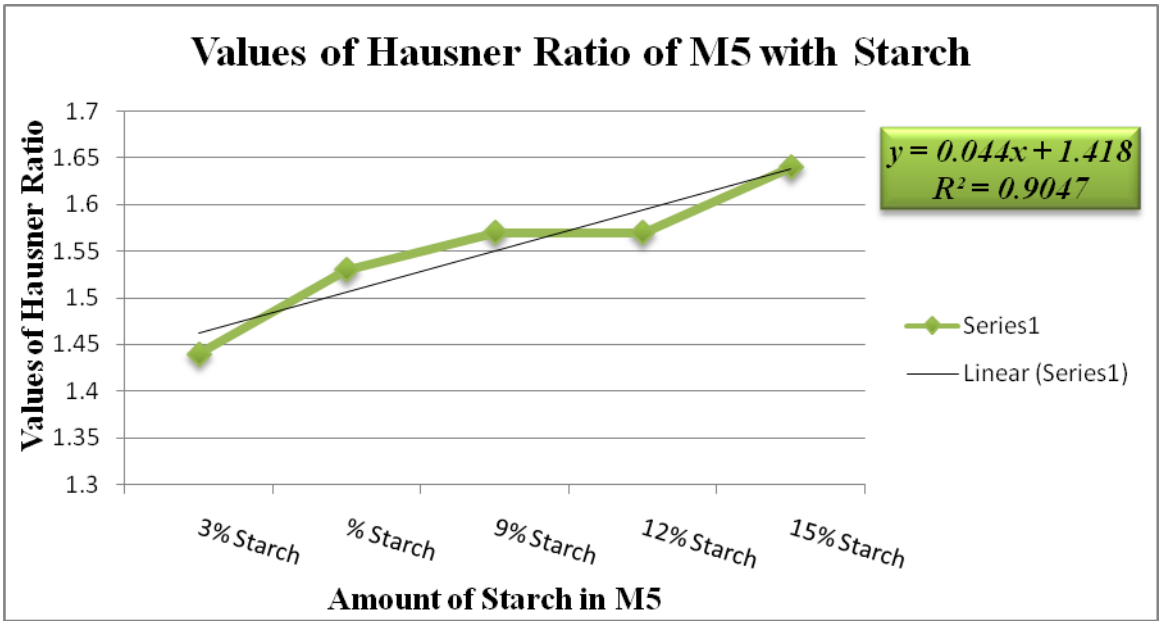

Figure 4.28: Scattered Plot showing the values of Hausner's ratio of different mixture ratio (M5 with Starch)

4.1.10.2 Values of Angle of Repose of Mixture 5 (M5) with Starch

Table 18: Values of Angle of Repose of Mixture 5 (M5) with Starch

Ratio	Height (cm)	Base (cm)	Angle of Repose = $\tan^{-1}$(Height/ 0.5 base)	Average Value of Angle of repose
Ratio 1	2.4	4.0	50.19	**49.56**
	2.4	4.1	49.50	
	2.3	4.0	48.99	
Ratio 2	2.0	5.2	37.57	**38.03**
	2.1	5.3	38.40	
	2.0	5.1	38.11	
Ratio 3	2.0	4.9	39.23	**38.84**
	2.1	4.9	40.60	
	1.9	5.1	36.69	
Ratio 4	1.9	5.0	37.23	**37.40**
	1.8	5.0	35.75	
	2.0	4.9	39.23	
Ratio 5	1.7	5.1	33.69	**34.55**
	1.8	5.0	35.75	
	1.7	5.0	34.22	

The following graph was obtained putting the amount of Starch into X-axis and values of angle of repose into Y-axis.

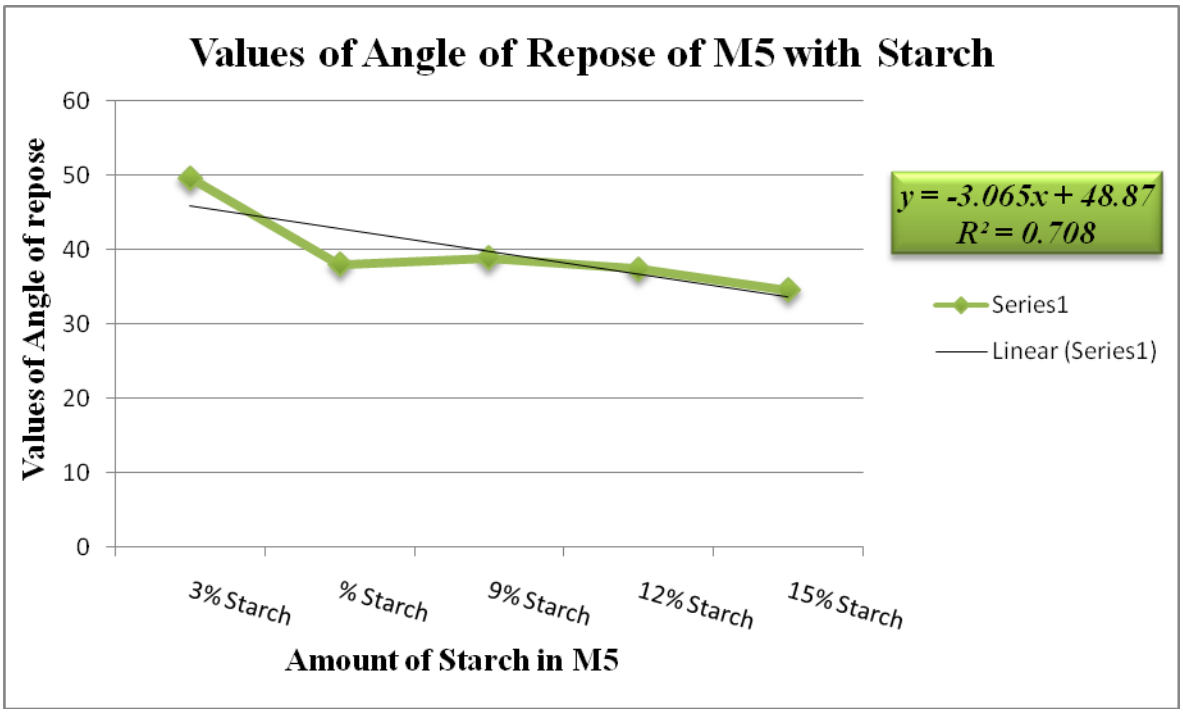

Figure 4.29: Scattered Plot showing the values of angle of repose of different mixture ratio (M5 with Starch)

4.1.11 Data of Mixture 6 (M6) with Polyvinyl Pyrrolidone (PVP)

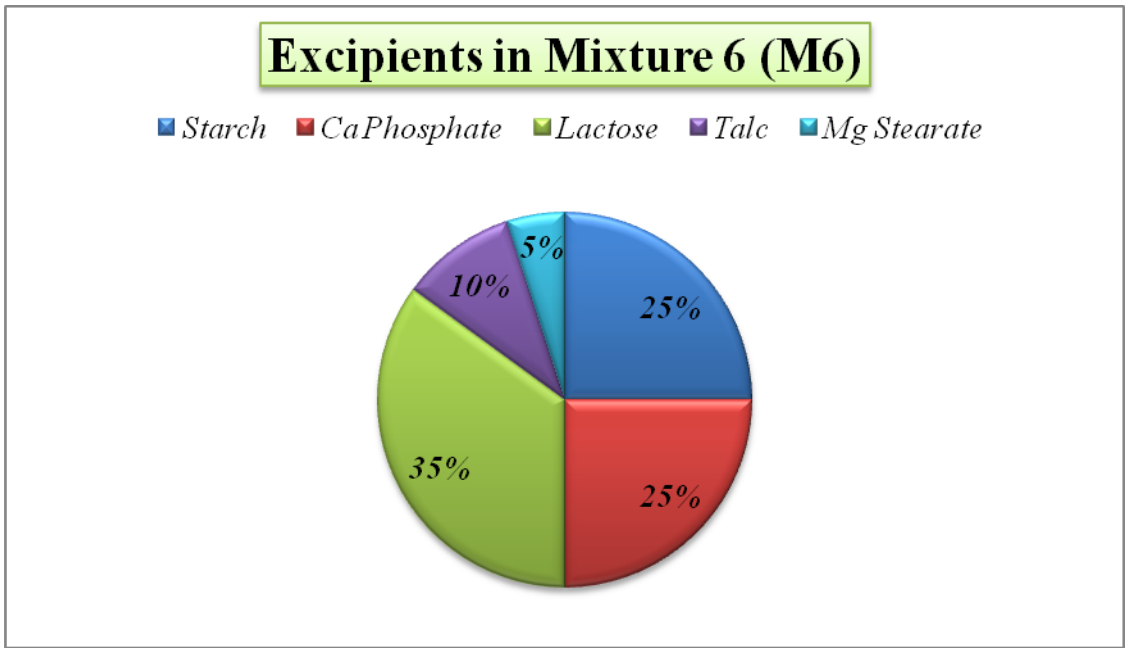

Figure 4.30: A pie chart showing the composition of Mixture 6

4.1.11.1 Values of Compressibility Index and Hausner's Ratio of Mixture 6 (M6) with Polyvinyl Pyrrolidone (PVP)

Table 4.19: Values of Compressibility Index and Hausner's Ratio of Mixture 6 (M6) with Polyvinyl Pyrrolidone (PVP)

Ratio	Bulk Volume, V_o ml	Most Acceptable Value of V_o ml	Tapped Volume (V_f)	Most Acceptable Value of V_f	Hausner's ratio = (V_o/ V_f)	Compressibility Index = 100 ×{(V_o - V_f)/ $V_{o)}$ }
Ratio 1	10.5	11.2	7.5	7.0	**1.60**	**37.50**
	11.2		7.0			
	11.0		7.0			
Ratio 2	10.5	11.0	7.0	7.0	**1.57**	**36.36**
	11.0		7.0			
	11.0		7.5			
Ratio 3	10.5	10.5	7.0	7.0	**1.50**	**33.33**
	10.5		7.0			
	10.0		7.5			
Ratio 4	10.0	10.5	7.0	7.0	**1.46**	**31.37**
	10.5		7.0			
	10.5		7.2			

The following graph was obtained putting the amount of PVP into X-axis and values of Carr's index into Y-axis:

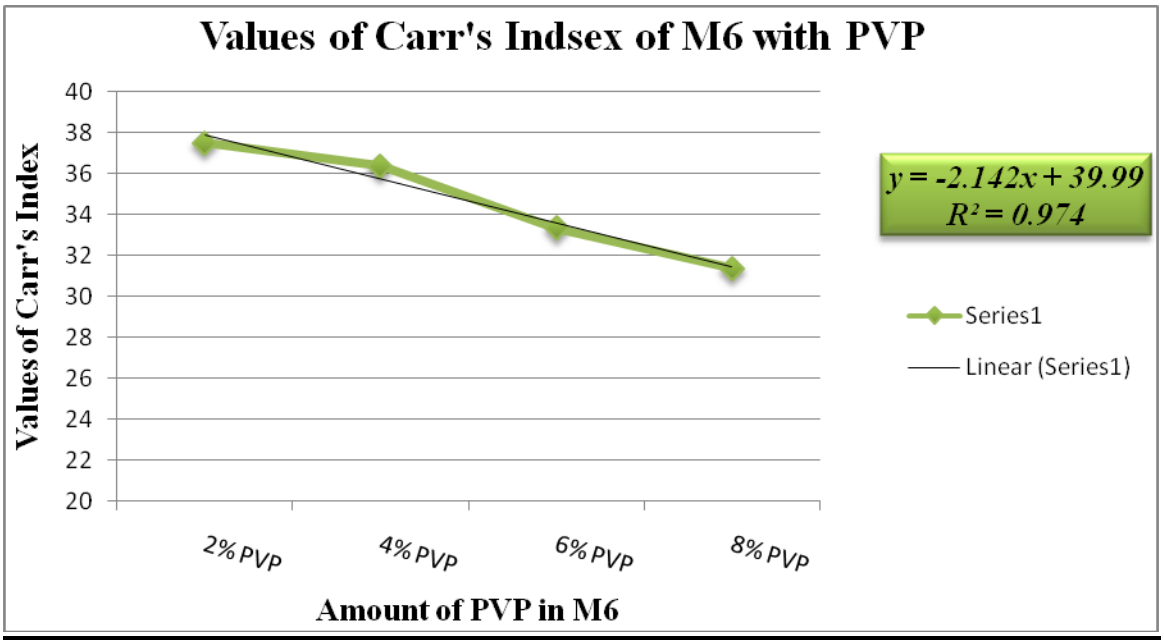

Figure 4.31: Scattered Plot showing the values of Carr's index of different mixture ratio (M6 with PVP)

The following graph was obtained putting the values of mixture ratio into X-axis and values of Hausner's ratio into Y-axis:

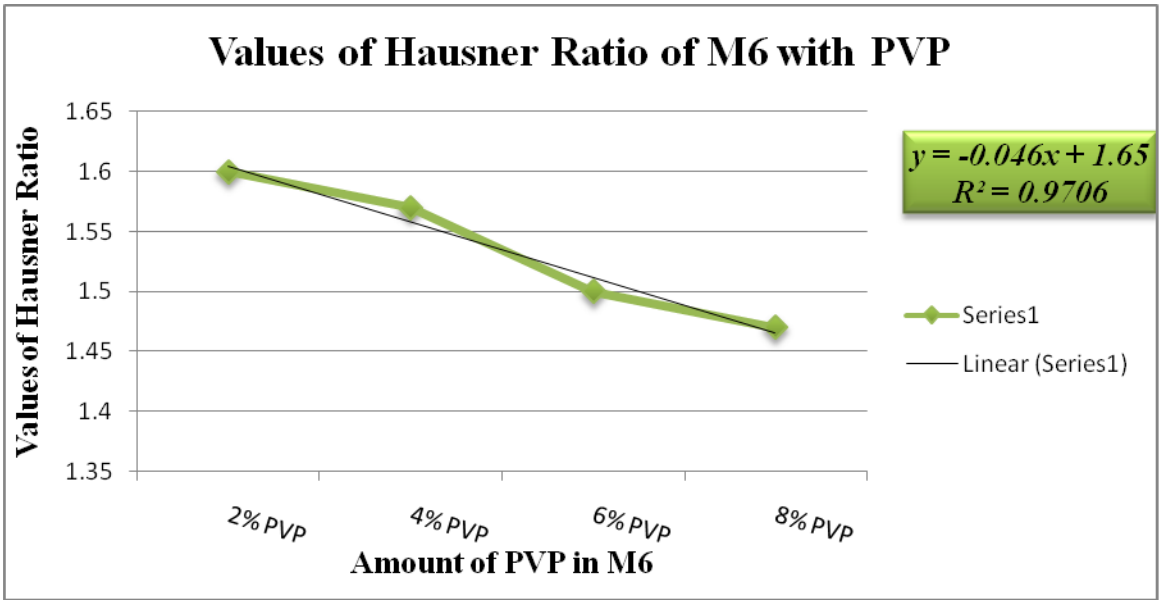

Figure 4.32: Scattered Plot showing the values of Hausner's ratio of different mixture ratio (M6 with PVP)

4.1.11.2 Values of Angle of Repose of MIXTURE 6 (M6) with Polyvinyl Pyrrolidone (PVP)

Table 4.20: Values of Angle of repose of Mixture 6 (M6) with Polyvinyl Pyrrolidone (PVP)

Ratio	Height (cm)	Base (cm)	Angle of Repose = $\tan^{-1}$(Height/ 0.5 base)	Average Value of Angle of repose
Ratio 1	2.0	4.9	39.23	**39.69**
	2.1	4.8	41.19	
	2.0	5.0	38.66	
Ratio 2	1.9	4.8	38.37	**38.66**
	2.0	4.8	39.81	
	1.9	4.9	37.79	
Ratio 3	2.0	5.2	37.57	**38.38**
	2.1	5.1	39.47	
	2.0	5.1	38.11	
Ratio 4	1.8	5.0	35.75	**34.21**
	1.7	5.1	33.69	
	1.7	5.2	33.18	

The following graph was obtained putting the amount of PVP into X-axis and values of angle of repose into Y-axis:

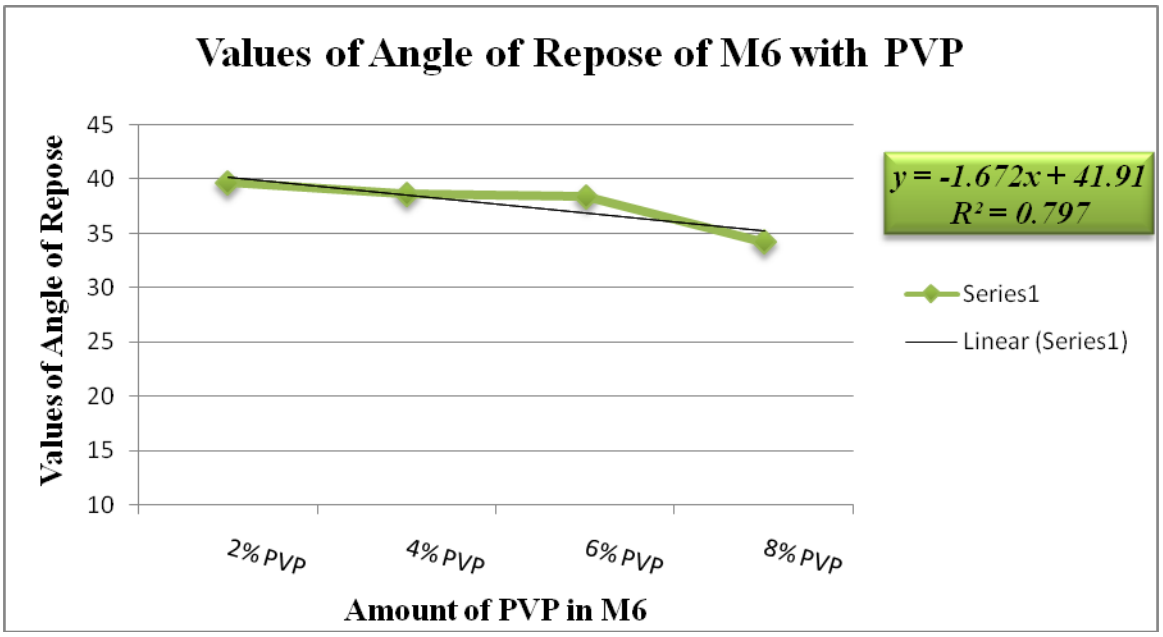

Figure 4.33: Scattered Plot showing the values of angle of repose of different mixture ratio (M6 with PVP)

4.1.12 Data of Mixture 7 (M7) with Starch

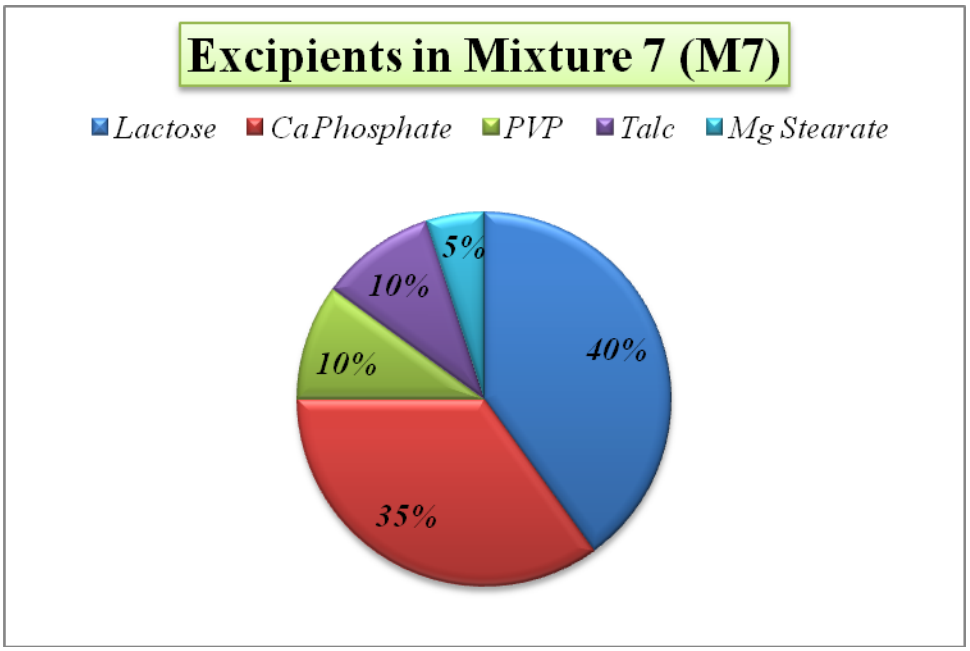

Figure 4.34: A pie chart showing the composition of Mixture 7

4.1.12.1 Values of Compressibility Index and Hausner's Ratio of Mixture 7 (M7) with Starch

Table 4.21: Values of Compressibility Index and Hausner's Ratio of Mixture 7 (M7) with Starch

Ratio	Bulk Volume, V_o ml	Most Acceptable Value of V_o ml	Tapped Volume (V_f)	Most Acceptable Value of V_f	Hausner's ratio = (V_o/ V_f)	Compressibility Index = 100 ×{(V_o - V_f)/ V_o) }
Ratio 1	10.5	10.5	7.0	7.0	**1.50**	**33.33**
	10.0		7.0			
	10.0		7.5			
Ratio 2	13.0	13.0	8.5	8.5	**1.53**	**34.62**
	12.5		8.5			
	12.5		9.0			
Ratio 3	11.0	11.0	7.0	7.0	**1.57**	**36.36**
	10.5		7.5			
	10.2		7.0			
Ratio 4	11.0	11.0	7.0	7.0	**1.57**	**36.36**
	11.0		7.0			
	10.5		6.5			
Ratio 5	11.5	11.5	7.0	7.0	**1.64**	**39.13**
	11.0		7.5			
	11.0		7.0			

The following graph was obtained putting the amount of Starch into X-axis and values of Carr's index into Y-axis.

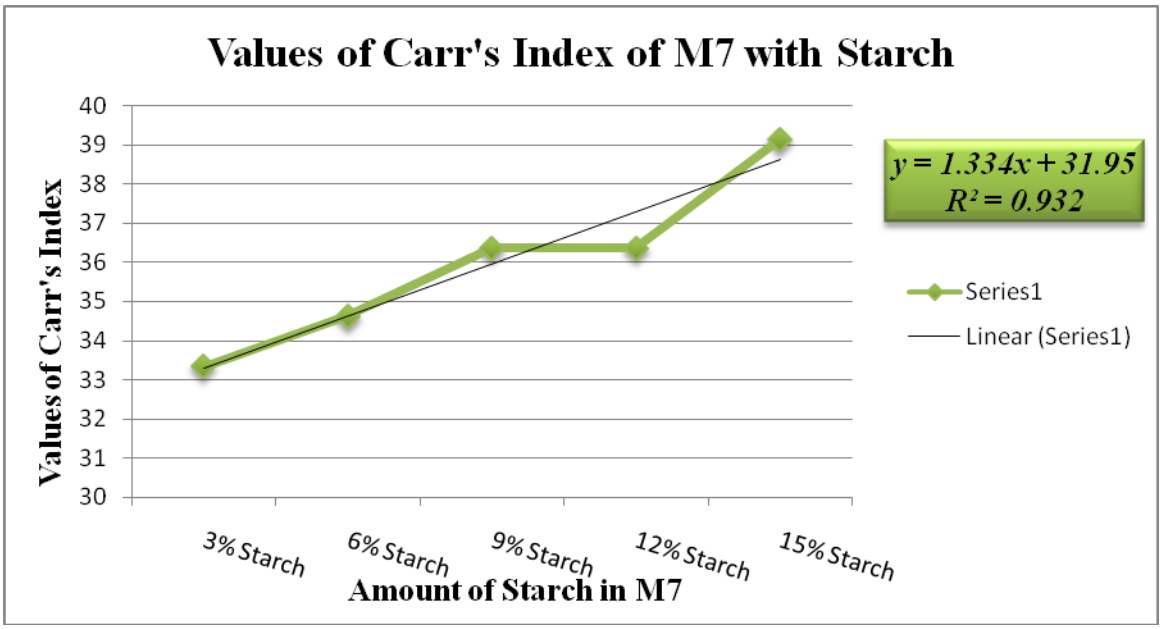

Figure 4.35: Scattered Plot showing the values of Carr's index of different mixture ratio (M7 with Starch)

The following graph was obtained putting the values of mixture ratio into X-axis and values of Hausner's ratio into Y-axis:

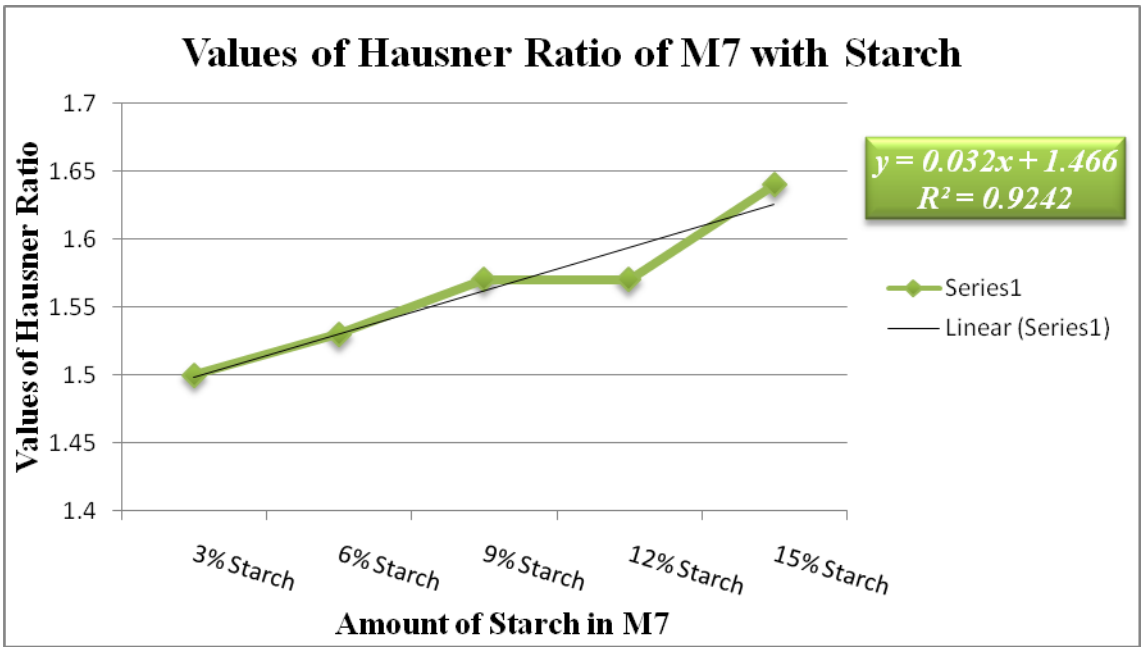

Figure 4.36: Scattered Plot showing the values of Hausner's ratio of different mixture ratio (M7 with Starch)

4.1.12.2 Values of Angle of Repose of Mixture 7 (M7) with Starch

Table 4.22: Values of Angle of Repose of Mixture 7 (M7) with Starch

Ratio	Height (cm)	Base (cm)	Angle of Repose = $\tan^{-1}$(Height/ 0.5 base)	Average Value of Angle of repose
Ratio 1	2.0	5.4	36.53	**37.60**
	2.1	5.4	37.87	
	2.0	5.3	38.40	
Ratio 2	1.8	4.8	36.87	**37.87**
	1.9	4.7	38.96	
	1.8	4.9	37.79	
Ratio 3	1.9	4.9	37.79	**38.28**
	2.0	4.8	39.81	
	1.9	5.0	37.23	
Ratio 4	2.1	4.9	40.60	**39.58**
	2.0	5.1	38.11	
	2.1	5.0	40.03	
Ratio 5	2.0	4.7	40.40	**40.87**
	2.1	4.6	42.40	
	2.0	4.8	39.81	

The following graph was obtained putting the amount of Starch into X-axis and values of angle of repose into Y-axis.

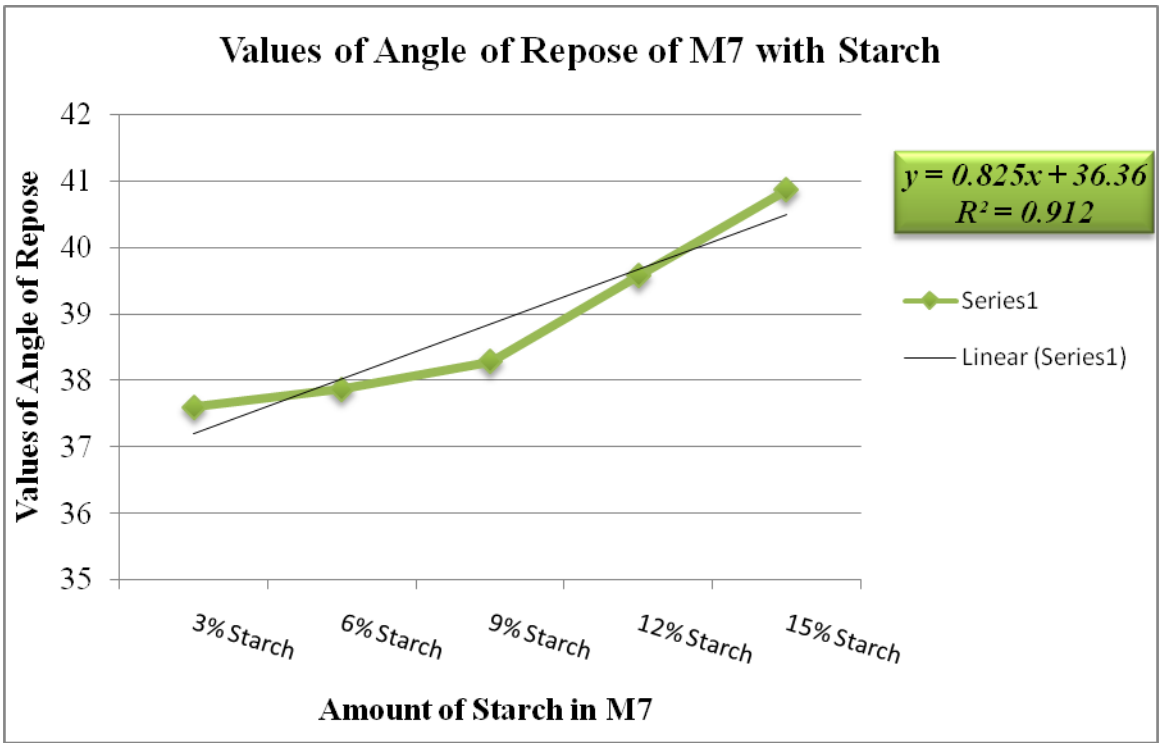

*Figure 4.*37: Scattered Plot showing the values of angle of repose of different mixture ratio (M7 with Starch)

Chapter Five

DISCUSSION

5.1 DISCUSSION

In this experiment it was found that variations occurred in the values of Carr's index, Hausner's ratio and angle of repose with the variation of Excipients and their amounts.

5.1.1 Mixture 1 (M1) with Polyvinyl Pyrrolidone (PVP)

In the experiment, it was found that values of Carr's index increases gradually with the increases amount of PVP. Figure 4.2 showed that, values Carr's index is highest in ratio 4 (92% M1 + 8% PVP). It means that flow property gradually decreased with the increased amount of PVP.

The values of Hausner's ratio were also increased with increased amount of PVP. So that, flow property gradually decreased. But in case of angle of repose value, the scenario is slightly different. Ratio 4 (92% M1 + 8% PVP) showed lowest value of angle of repose, that means good flow property obtained at Ratio 4.

5.1.2 Mixture 1 (M1) with Carboxymethyl Cellulose (CMC)

From this experiment, it can be said that flow property of Mixture 2 decreased with the increased amount of CMC. Figure 4.5, Figure 4.6 and Figure 4.7 showed that good flow property obtained when the amount of CMC is the lowest in total mixture.

According to obtained angle of repose values, Ratio 2 (91% M1 + 9% CMC) can be classified as 'good' powder flowing mixture.

5.1.3 Mixture 1 (M1) with Microcrystalline Cellulose (MCC)

The values of Carr's index and Hausner's ratio gradually increased with the increased amount of MCC. It showed that, flow property gradually decreased of M1 with the increased amount of MCC.

In case of angle of repose, the values were decreased with the increased amount of MCC. It means that ratio 4 showed good flow property compared to other ratios.

5.1.4 Mixture 2 (M2) with Starch

From this experiment, it can be said that the flow property of M2 increased with the increased amount of starch in the total ratio. The value of Carr's index, Hausner's ratio and angle of repose decreased with the increased amount of starch in ratios. It showed that ratio 4 had the maximum flow property compared to other ratios. Ratio 5 (85% PVP + 15% starch) can be classified as 'fair' flowing powder in terms of angle of repose values.

5.1.5 Mixture 3 with polyvinyl pyrrolidone (PVP)

The values of angle of repose, Hausner's ratio and Carr's index gradually increased with increased amount of PVP. It showed that maximum flow property was obtained in case ratio 2 (96% M3 + 4% PVP) compared to the other mixture ratios in terms of angle of repose values.

5.1.6 Mixture 3 (M3) with Starch

The flow property of M3 with starch increased with the increased amount of starch. The values of Carr's index, Hausner's ratio and angle of repose decreased with the increased amount of starch in the ratio. So it can be said that ratio 4 had the maximum flow property compared to the other ratios.

5.1.7 Mixture 4 (M4) with Polyvinyl Pyrrolidone (PVP)

In this research work, it was obtained that flow property M4 with PVP decreased with the increased amount of PVP. Ratio 1 had the maximum flow property compared to the other ratio. Ratio 1 (98% M4 + 2% PVP) can be classified as 'good' flowing powder according to the angle of repose values.

5.1.8 Mixture 5 (M5) with Starch

The values of Carr's index and Hausner's ratio increased with the increased amount of starch in ratios. It means that, ratio 4 had relatively low flow property compared to the other ratios.

But in case of angle of repose, the values decreased with the increased amount of starch in the ratios. It signified that, ratio 4 had good flow property compared to other rartios.

5.1.9 Mixture 6 (M6) with Polyvinyl Pyrrolidone (PVP)

From this experiment it can be said that flow property was improved with the increased amount of PVP in the mixture. Ratio 4 (92% M6 + 8% PVP) showed the maximum flow property compared to other mixture ratios and can be classified as ‘poor’ flowing powder in terms Carr’s index values.

5.1.10 Mixture 7 (M7) with Starch

The values of Carr’s index, Hausner’s ratio and angle of repose were increased with the increased amount of starch in M7. It means that flow property gradually decreased with the increased amount of starch. Ratio 1 (97% M7 + 3% starch) showed the maximum flow property compared with the other ratios.

Chapter Six

CONCLUSION

6.1 CONCLUSION

These research findings revealed that starch, PVP, CMC, MCC had great impact on flow property of a group of excipients. In this research work we tried our best to determine the flow characteristics of mixture of excipients with different amounts of some selected excipients. It can be stated that variation in amounts of excipients in the mixture showed a variation in the powder flow characteristics. It is also true that due to some lacking during the research work, we could not achieve our main objective. Overall this research work will be beneficial in formulation development of new drug product as well as this research work will be advantageous for Research & Development department of pharmaceutical company.

Chapter Seven

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7.1 REFERENCES

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