Variation of Flow Property of different set of Formulas of excipients against various ratios of different Binders

Submitted by

Md. Shafiul Azam

ID: 2010-1-70-014

East West University, Dhaka, Bangladesh

In partial fulfillment of the requirements for the award of the degree

Bachelor of Pharmacy

Under the Guidance of-

Md. Anisur Rahman,

Senior Lecturer

Department of Pharmacy

East West University.

January 17, 2014

Endorsement by Head of the Department

This is to certify that the thesis "Variation of Flow Property of different set of Formulas of excipients against various ratios of different Binder” submitted to the department of pharmacy, East West University in partial fulfillment of the requirements of the degree of Bachelor of Pharmacy was carried out by Md. Shafiul Azam (ID: 2010-1-70-014) under our guidance and supervision and that no part of the thesis has been submitted for any other degree. We further certify that all the sources of information and laboratory facilities availed of in this connection is duly acknowledged.

Dr. Chowdhury Faiz Hossain

Chairperson

Department of Pharmacy

East West Unviersity,

Aftabnagar, Dhaka, Bangladesh

Certificate by the Supervisor

This is to certify that the dissertation "Variation of Flow Property of different set of Formulas of excipients against various ratios of different Binder" submitted to the department of pharmacy, East West University was carried out by Md. Shafiul Azam (ID: 2010-1-70-014) in partial fulfillment of the requirements of the degree of Bachelor of Pharmacy.

Md. Anisur Rahman

Senior Lecturer

Department Of Pharmacy

East West University,

Aftabnagar, Dhaka, Bangladesh

Declaration by the Research Candidate

I, Md. Shafiul Azam, hereby declare that the dissertation entitled "Variation of Flow Property of different set of Formulas of excipients against various ratios of different Binder” submitted by me to the Department of Pharmacy, East West University, in the partial fulfillment of the requirement for the award of the degree of Bachelor of Pharmacy (Honors) is a bonafide record of original research work carried out by me during 2013 (January —December) under the supervision and guidance of Md. Anisur Rahman, Senior Lecturer Dept. of Pharmacy, East West University and it has not formed the basis for the award of any other Degree/Diploma/Fellowship or other similar title to any candidate of any University

----

Signature of the candidate

Md. Shafiul Azam

2010-1-70-014

Dhaka

ACKNOWLEDGEMENTS

At the beginning, I would like to remember the mercy and kindness of Almighty Allah for completing my research work appropriately.

It is my pleasure and proud privilege to express my heartiest regards and gratitude to my respected teacher and supervisor Md. Anisur Rahman, Senior Lecturer, Department of Pharmacy, East West University, for his mastermind direction,constant supervision and support, optimistic counseling and continuous backup to carry out the research work as well asto prepare this dissertation.

I feel my deepest admiration to the chairperson, Dr. Chowdhury Faiz Hossain, Department of Pharmacy, and the administration, East West University for giving me the honor to perform the research in partial fulfillment of the requirements for the award of the degree Bachelor of Pharmacy.

I also give my thanks to the Laboratory Officers of the Department of Pharmacy, East West University for guiding and helping me with their utmost abilities throughout my project.

I am thankful to my coworkersMahjabinHaque,MynulIslam Muftiand Sumaiya AhmedBhasha.

I am sincerely thankful to my caring parents for guiding me all through my life including that my research project. I am very grateful to my sisters and friends who encouraged me enormously. It is because of the inspiration of the people around me that I have come all the way. I remember here the inspiring words of my family members and to all my well-wishers. I say many thanks to them for their wholehearted inspiration during my thesis work.

Table of Content

List of Tables	
Topic	Page No.

Abstract

Flow property means the physical properties of moving ability of pharmaceutical powders. It is very much important in the pharmaceutical industry for the operations such as blending, tablet compression, capsule filling, transportation, and in scale-up operation. Our purpose is to isolate that ratio of pharmaceutical excipients in a mixture that will provide maximum flow property. Our proposed equations will be helpful for determining the flow property of new drug formulations. We had measured several parameters, such as, bulk density, tapped density, Carr's index, Hausner ratio and angle of repose for different mixture of same pharmaceutical excipients but in different ratio, and were able to resolve an equation. We had done this for different mixtures of different excipients to determine different equations. We used several software, such as Microsoft excel, SPSS etc. to determine these equations. By evaluating the laboratory experimental data, we were able to determine several specific equations (y= mx + c) for particular mixtures of specific pharmaceutical excipients. My work was based on the variation in flowability of mixtures due to the presence of different amount of bingers. Flow property of pharmaceutical excipients for a new drug formulations can be predicted and measured by these equations.

Keywords: Binder, Flowability, Bulk density, Tapped density, Carr's index, Hausner ratio and Angle of Repose

CHAPTER ONE

INTRODUCTION

1 Introduction

Our objective is to evaluate that ratio of pharmaceutical excipients in a mixture that will provide maximum flow property. We are focusing to isolate a specific equation which will explain the flowability of a formulation. Our proposed equations will be helpful for determining the flow property of new drug formulations. We had measured several parameters, such as, bulk density, tapped density, Carr's index, Hausner ratio and angle of repose for different mixture of same pharmaceutical excipients but in different ratio, and were able to resolve an equation. We had done this for different mixtures of different excipients to determine different equations. Our proposed equation will help the future researcher to evaluate the flowability variation occurred due to the variable percentages of different excipients.

1.1 Powder Flow

The extensive use of powders in the pharmaceutical industry has created a variety of methods for symbolizing powder flow (USP29-NF24, 2013). Not surprisingly, scores of references appear in the pharmaceutical literature, trying to relate the various measures of powder flow to manufacturing properties. The development of such a variety of test methods was unavoidable and the behaviors of powder flow properties are many-sided and this complicates the effort to characterize the powder flow. The reason of this part is to review the methods for characterizing powder flow. 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. Four commonly described methods for testing powder flow are-

(1) Angle of repose,

(2) Compressibility index or Hausner ratio,

(3) Flow rate through an orifice, and

(4) Shear cell.

1.2 Excipient

Excipient means any component other than the active pharmaceutical ingredient(s) intentionally added to the formulation of a dosage form. Many guidelines exist to aid in selection of nontoxic excipients such as IIG (Inactive Ingredient Guide), GRAS (Generally Regarded as Safe), Handbook of Pharmaceutical Excipients and others(USP29-NF24, 2013).

1.2.1 Functionalities of Excipients

Excipients play a crucial role in design of the delivery system, determining its quality and performance. Excipients though usually regarded as nontoxic there are examples of known excipient induced toxicities which include renal failure and death from diethylene glycol, osmotic diarrhoea caused by ingested mannitol, hypersensitivity reactions from lanolin and cardiotoxicity induced by propylene glycol (USP29-NF24, 2013).

Excipients are chosen in tablet formulation to perform a variety of functions like-

i) For providing essential manufacturing technology functions (binders, glidants, lubricants may be added),

ii) For enhancing patient acceptance (flavors, colourants may be added),

iii) For providing aid in product identification (colourants may be added),

iv) For Optimizing or modifying drug release (disintegrants, hydrophilic polymers, wetting agents, biodegradable polymers may be added),

v) For enhancing stability (antioxidant, UV absorbers may be added)

Table 1.1: **Excipient with their functions in solid dosage forms**

EXCIPIENT	**FUNCTION**
Diluents or Fillers	Diluents make the required bulk of the tablet when the drug dosage itself is inadequate to produce tablets of adequate weight and size.

Binders or Granulating agents or Adhesives	Binders are added to tablet formulations to add cohesiveness to powders, thus providing the necessary bonding to form granules, which under compaction form a cohesive mass or a compact which is referred to as a tablet.
Disintegrants	A disintegrant is added to most tablet formulations to facilitate a breakup or disintegration of the tablet when placed in an aqueous environment.
Lubricants	Lubricants are intended to reduce the friction during tablet formation in a die and also during ejection from die cavity.
Antiadherents	Antiadherents are added to reduce sticking or adhesion of any of the tablet granulation or powder to the faces of the punches or to the die wall.
Glidants	Glidants are intended to promote the flow of tablet granulation or powder mixture from hopper to the die cavity by reducing friction between the particles.

***Table1.2*: Percentage of excipients used in different powder formulation**

Ingredient	**Diluent (% w/w)**	**lubricant (% w/w)**	**Disintegrant (% w/w)**	**Binder (% w/w)**	**Antiadhearent (% w/w)**
Starch	5–75		3–15	5–25	
Boric acid		Present			
Sodium Lauryl sulfate (SLS)		1–2			Present
Calcium phosphates	Present			Present	
Lactose	Present			Present	
Sucrose	Present			2–20	
Stearates(Magnesium		0.25–5		Present	Present

Stearate)					
Powdered cellulose	Present		5–15	5–25	
Microcrystalline cellulose	20-30		5–15	20–90	5–20
Cellulose			5–15	5–25	
Carboxy methylcellulose	20-30		Present	1–6	
Crosslinked cellulose			5–15	20–90	5–20
Hydroxypropyl methylcellulose (HPMC)			Present	2–5	
Polyvinylpyrrolidone (PVP) (Povidone)			2–8	0.5–5	
Polyethylene glycol (PEG)			5	10–15	
Talc	5–30	1–10			Present

1.3 Binders

Binder is one of an important excipient to be added in tablet formulation. In simpler words, binders or adhesives are the substances that promotes cohesiveness. It is utilized for converting powder into granules through a process known as Granulation. Granulation is the unit operation by which small powdery particles are agglomerated into larger entities called granules.

1.3.1 Types of Binders

Table 1.3: **Classification of Binders**

Sugars	Natural Binders	Synthetic/Semisynthetic Polymer
Sucrose	Acacia	Methyl Cellulose

Liquid glucose	Tragacanth	Ethyl Cellulose
	Gelatin	Hydroxy Propyl Methyl Cellulose (HPMC)
	Starch Paste	Hydroxy Propyl Cellulose
	Pregelatinized Starch	Sodium Carboxy Methyl Cellulose
	Alginic Acid	Polyvinyl Pyrrolidone (PVP)
	Cellulose	Polyethylene Glycol (PEG)
		Polyvinyl Alcohols
		Polymethacrylates

CHAPTER TWO

LITERATURE REVIEW

2 Literature Review

In 1999, two scientists E.C. Abdullah and D. Geldart measured the bulk density of powders with two equipments to evaluate the flow property of porous and nonporous powders. The Hosokawa Powder Tester and the Copley Tap Density Volumeter were the two equipments.The Hosokawa Powder Tester gave accurate measurement of the aerated and tapped bulk densities due to the use of a fixed volume of powder and an accurately measured mass of powder. The Copley Tap Density Volumeter gave inaccurate measurements using a fixed mass of powder because it is difficult to measure the volume from the graduated cylinder. However, flow property of the powder increases with the increase of particle size though there is a critical particle size range above which flow property does not improve (Abdullah and Geldart, 1999).

In 2002, a Chinese scientist, Anthony Chi-Ying Wong did an experiment on theangle of repose (AOR), tapped bulk densities (ρT), and aerated bulk densities (ρA) of 18 fractions of spherical glass beads which mean particle size was 12–190µm. It had been found that the ratio of angle of repose to aerated bulk densities was correlated with the ratio of aerated bulk densities to tapped bulk densities for free-flowing powder. Results of this experiment suggested that the ρA in the angle of repose can be replaced by ρT which will reduce the errors followed by the sensitivity of ρA measurements (Wong, 2002).

While determining the angle of repose (AOR), cohesive and semi-cohesive powders have the tendency to block the funnel which makes it difficult to measure the AOR for these powders. In 1996, Ilse M. F. Wouters and Derek Geldart did an experiment on 73 powders consisting of four materials including covering agents. The results showed that AOR of different combination increases with the decrease of mean particle size. AOR of these combinations were measured with the aerated bulk density which made this method a quick, sensitive and effective one for characterizing a wide range of powders (Wouters andGeldart, 1996).

In 2013, Traina and other five researcher from Belgium carried out measurements of compressibility on five granular materials; those are two different lactose powders, hydrated lime $Ca(OH)_2$, yttrium stabilized zirconia balls and polystyrene balls. Here, additional air volume was added to the optimal granular packing. The found that if the powder is cohesive, it traps more air compared with the non-cohesive or free flowing powder which traps very small amount of air in static state and this free flowing powder improves the speed of packaging (Trainaa, et al., 2013).

In 1995, Eino Nelson studied the problems of granulation flow in tablet manufacturing. He studied the angle of repose of sulfathiazole where he found that the AOR increased with decrease of particle size. Addition of talc to the granules in small portion decreased the repose angle. He also found that Magnesium stearate caused little or no effect on the repose angle of the granulation. However, addition of fines to coarse granules had a striking increase in AOR (Nelson, 1995).

In1996, Gerald Gold, Ronald N. Duvall, Blaze T. Palermo and James G. Slater studied the effect of glidants on flow rate and angle of repose in drug formulation. They used fumed silicon dioxide, magnesium stearate, starch, and talc in combination with a set of selective materials. They had found that most glidants actually decreased the flow rate and glidants with lower AOR did not significantly increase the flow rate. However, they also suggested that for evaluating the flow rate of these materials, the AOR was not a reliable method (Gold, et al., 1996).

1n 2000, Taylor and Ginsburg measured flow property of powders by vibrating spatula, critical orifice, angle of repose, compressibility index and angle of repose. They found 72.4% variability in results and the results are not reproducible (Taylor and Ginsburg, 2000).

In 2013, Silva and Splendor evaluated Bulk Density and Tapped Density of commonly used excipients according to European Pharmacopeia monograph (seventh edition) in order to study the influence of the procedure conditions. The results suggested that the leveling of the powder inside the cylinder ought to be avoided (Silva and Splendor, 2013).

In 2008, Rakhi Shah evaluated Angle of repose, bulk density, tapped density, Carr's compressibility index, and Hausner ratios of different grades of magnesium stearate powder. It was observed that the compendial methods were often non-discriminating for minor variations in powder flow. The additional characterization such as cohesivity, and caking strength were helpful in understanding the flow characteristics of pharmaceutical systems (Shah, et al., 2008).

In 2009, Erica Emerya and Jasmine Oliver evaluated the Hausner Ratio, the Carr Index, and the Angles of repose of Hydroxypropyl methylcellulose (HPMC). The flowability of HPMC decreased with an increase in moisture content (Emerya, et al., 2009).

In 2013, Garett and Lauren investigated the effect of magnesium stearate, magnesium silicate, stearic acid, and calcium stearate on powder flowability. The Carr Index, and the Angles of repose were evaluated for those excipients. Of the tested lubricants, magnesium stearate provided the best increase in flowability even in the low amounts commonly added in formulations (Garett and Lauren, 2013).

In 2008, Tawakkul and Mansoor Khan did a systematic evaluation of flow of pharmaceutical powders and granules using compendial and non-compendial methods. Angle of repose, bulk density, tapped density, Carr's compressibility index, and Hausner ratios were evaluated. Additionally, flow was characterized using a powder rheometer in which a sensitive force transducer monitors the forces generated as a result of the sample displacement. The critical attributes such as cohesivity index, caking strength, and flow stability were determined for samples. It was observed that the compendial methods were often non-discriminating for minor variations in powder flow. The additional characterization such as cohesivity, and caking strength were helpful in understanding the flow characteristics of pharmaceutical systems (Tawakkul and Khan, 2008).

In 2013,Allison Crouter and Briens investigated the effect of moisture content on flowability of six pharmaceutical powders (microcrystalline cellulose (MCC), hydroxypropyl methylcellulose (HPMC), carboxymethyl cellulose (CMC), polyvinylpyrrolidone (PVP), corn starch, and potato starch) by Carr's index, and Hausner ratios. The flowability of MCC, CMC, PVP, and potato starch decreased after a critical moisture content, flowability of corn starch increased and flowability did not significantly change for HPMC (Crouter and Briens, 2013).

In 2009, Meer Saiful Hassan and Raymond Wai Man Lau compared the flowability with similar size range particles of different shapes such as sphere, needle, cube, plate, and pollen. Flowability of the particles was characterized by Carr's compressibility index and angle of slide (θ) method. Pollen-shaped particles are found to exhibit better flowability than particles of other shapes in similar size range. They showed minimum θ of 35°. They suggested that the use of pollen-shaped particles can be a potential improvement in dry particle inhalation (Hassan and Raymond, 2009).

In 1990, Tan and Newton evaluated the flowability of pharmaceutical excipients related to their capsule filling performance. 20 capsules was used as an indicator of capsule filling performance. As flowability was dependent on the particle size, morphology and bulk density of the powder there was a significant correlation between the values of X_{cv} and the flow parameters of Carr's compressibility, Hausner's ratio, angle of repose, Kawakita's equation constant (a) and Jenike's flow factor. X_{cv} was also related to the coefficient of variation of the powder bed bulk density and the variation in the compression stress. There was, however, no correlation between the values of X_{cv} and the angle of internal flow and the angle of effective friction (Tan and Newton, 1990).

In 2000, FridrunPodczeck and .Michael Newton studied powder bulk properties and capsule filling performance on a tamp-filling machine with and without the addition of various concentrations of magnesium stearate. They found that the Carr's compressibility reaches its minimum value at 0.4% magnesium stearate. They suggested an improvement of powder flow in a mixture of powder containing lubricating agent compared to that of unlubricated material (Podczeck and Newton, 2000).

In 1996, Rajesh Patel and FridrunPodczeck investigated 8 microcrystalline cellulose samples on the capsule filling performance. Different sources of fine, medium and coarse grade microcrystalline cellulose were used. They determined the Kawakita constant and Hausner's ratio as the indicators of the capsule filling performance. A fine grade microcrystalline cellulose such as Avicel® PH105 cannot be used in capsule filling because of unsatisfactory flow properties. Medium and coarse grade microcrystalline cellulose can be classified as a good capsule filling excipient, but not all sources are suitable (Patel and Podczeck, 1996).

In 2013, Crouter and Briens investigated the flowability of MCC, HPMC, CMC, PVP, corn starch, and potato starch. Flowability of MCC, CMC and PVP decreased after a critical moisture content and for corn starch, it was increased. Flowability of HPMC was not changed that much. The moisture decreased flowability by forming stronger interparticle liquid bridges and increased flowability by acting as a lubricant. The dynamic density of the celluloses and PVP decreased linearly with increasing moisture content as the particles swelled with water. The starches also swelled and decreased in dynamic density, but only after a moisture content corresponding to monolayer coverage of water around the particles had been reached (Crouter and Briens, 2013).

In 2013, Morin and Briens investigated the effect of lubricants on powder flowability as flowability into the tablet press is critical. Four lubricants (magnesium stearate, magnesium silicate, stearic acid, and calcium stearate) were mixed, in varying amounts, with spray-dried lactose. Among the tested lubricants, magnesium stearate increased the flowability most (Morin and Briens, 2013).

In 2010, Gerald Gold studied the commonly used glidants, fumed silicon dioxide, magnesium stearate, starch, and talc in combination with selected materials. Many of the more widely used glidants actually decreased the flow rate. Glidants which lowered the angle of repose did not necessarily increase the flow rate. Flow rate were not always detectable by angle of repose measurement. By doing the comparison of the angle of repose and the flow rate they suggested that the angle of repose was not a reliable method for evaluating the flow of these materials (Gold, et al., 2006).

In 2009, Erica Emery investigated the effect of moisture content on four pharmaceutical powders (an active pharmaceutical ingredient (API), Aspartame, Hydroxypropyl Methylcellulose (HPMC), and Respitose). The Aspartame was tested at moisture contents of 0%, 2%, 5%, and 8% and the HPMC was also tested at moisture contents of 0%, 2%, 5%, and 10%. Powder flowability was measured using the Jenike shear index, the Hausner Ratio, the Carr Index, and the static and dynamic angles of repose. The flowability of Aspartame increased with an increase in moisture content, which is attributed to the formation of large, round agglomerates. The flowability of HPMC decreased with an increase in moisture content due to the increasing strength of liquid bridges (Emerya, et al., 2009).

In 2004, Thalberg, Lindholm and Axelsson, investigated the comparison of different flowability tests for powders for inhalation. A series of placebo powders for inhalation was examined. A modified Hausner Ratio, the Aero Flow, Uniaxial tester and the angle of repose was measured. The modified Hausner Ratio discriminated well between the investigated powders and seemed to have the widest measuring range. It was also found that the poured and compressed bulk densities provide information about the packing of the particles in the powders. A good correlation was obtained between the modified Hausner Ratio and the angle of repose (Thalberg, et al. 2004).

In 2006, Bagster and Crooks evaluated a number of methods of estimating flowability of some direct compression vehicles. There was little or no inter-relationship between angle of repose, compressibility and flow rate values. In addition, there was no correlation between any of these three values and tablet weight variation (Bagster and Crooks, 2006).

In 2003, Yeli Zhang, Yuet Law and SibuChakrabarti investigated the flowability of commonly used direct compression binders. Five classes of excipients were evaluated, including microcrystalline cellulose (MCC), starch, lactose, dicalcium phosphate (DCP), and sugar. In general, the starch category exhibited the highest moisture. DCP displayed the highest density. MCC, starch, lactose, and sugar had shown moderate whereas DCP had shown excellent flowability (Zhang, Law and Chakrabarti, 2003).

In 2005, Jun Yang and Ales Sliva indicated that surface-treated hydrophobic silica is more effective in improving the flowability of cornstarch particles than untreated hydrophilic silica (Yang, et al., 2005).

CHAPTER THREE

MATERIALS & METHOD

3 MATERIAL & METHOD

3.1 Materials

3.1.1 Collection of Excipients

We offered the East West University, Dhaka-1200, Bangladesh; to give as some research grant. Our respected supervisor, Md. Anisur Rahman, Senior Lecturer, Department of Pharmacy, East West University send a requisition letter to the authority for some specific excipients on February, 2013 and after six month we got most of the ingredient we asked for.

3.1.2 Excipients

All the excipients we had used are given bellow,

1. Starch
2. Boric acid
3. Sodium Lauryl sulfate (SLS)
4. Calcium phosphates
5. Lactose
6. Sucrose
7. Stearates(Magnesium Stearate)
8. Powdered cellulose
9. Microcrystalline cellulose
10. Cellulose
11. Carboxy methylcellulose
12. Crosslinked cellulose
13. Hydroxypropyl methylcellulose (HPMC)
14. Polyvinylpyrrolidone (PVP) (Povidone)
15. Polyethylene glycol (PEG)
16. Talc

3.1.3 Equipments and Instruments

The equipments and instruments that were used in this experiment are described below.

***Table 3.1:*Equipments used in this research**

Serial No.	**Equipments**	**Source (Supplier Name)**	**Origin**
1	Electronic Balance	Precisa XB 120A	Switzerland
2	Double Cone Blender		

3.1.4 Image of Instruments

Some image of important instruments those were used in different tests during research work.

Figure 3.1:

Figure 3.2: **Double Cone Blender**

3.1.5 Apparatus

The apparatus that were used in this experiment are described below.

Table 3.2: Apparatus used in this research

Serial No.	**Apparatus**
1	Beaker
2	Test tube
3	Plastic container
4	Aluminum foil papper
5	Transparent tracing paper
6	Filter paper
7	Mortar & Pestles
8	Spatula
9	Measuring cylinder
10	Glass and plasticFunnel
11	Glassrod
12	Stand

3.2 Method

3.2.1 DENSITY

Granule density, True Density, Bulk Density may influence compressibility, tablet porosity, flow property, dissolution and other properties. Higher compression load was required in case of dense and hard granules which in turn increases the tablet disintegration and drug dissolution times. Density is usually determined by Pycnometer (USP29-NF24, 2013).

3.2.2 ANGLE OF REPOSE

The angle of repose is used in the several branches of science to characterize the flow properties of solids. Angle of repose is interring particulate friction or resistance to movement between particles. Angle of repose test results is 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. The method continues to be used in the pharmaceutical industry.

The angle of repose contains, three-dimensional angle (relative to the horizontal base) supposed by a cone shape (USP29-NF24, 2013).

3.2.2.1 Basic Methods for Angle of Repose

A variety of angle of repose test methods are described in these part. The most common method static angle of repose can be determined and it can be classified on the basis of the following two important experimental variables:

1. The powder passes from the height of the funnel which is fixed relative to the base, or the height may be varied as the pile forms.

2. The base diameter of the pile may be fixed or the diameter of the powder cone may be varied as the pile forms.

3.2.2.2 Variations in Angle of Repose Methods

In addition to the above methods, the following variations are used to some extent in the pharmaceutical literature:

- Drained angle of repose is determined by allowing an excess quantity of material positioned above a fixed diameter base to "drain from the container. Formation of a cone of powder on the fixed diameter base allows determination of the drained angle of repose.
- The filling of a cylinder (with a clear, flat cover on one end) and its rotation at a specified speeds is determined the dynamic angle of repose. It is the angle (relative to the horizontal) formed by the flowing powder. The internal angle of kinetic friction is defined by the plane separating those particles sliding down the top layer of the powder .Those particles that are rotating with the drum (with roughened surface) (USP29-NF24, 2013).

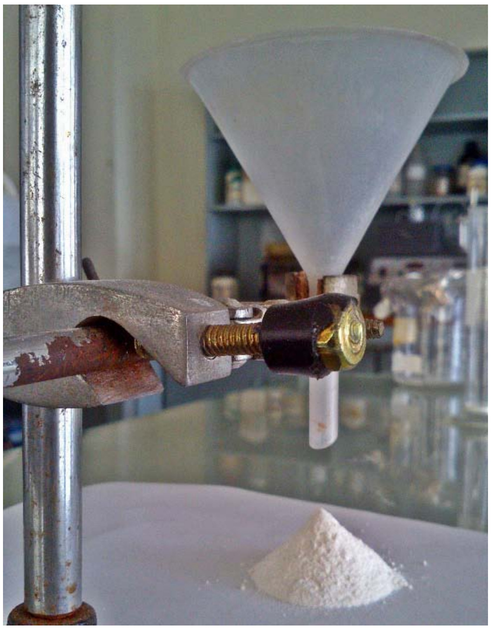

Figure 3.3: **Measuring Angle of Repose**

3.2.2.3 Angle of Repose General Scale of Flow ability

By using the angle of repose, there is some variation in the qualitative description of powder flow properties. The classification of Carr: This is shown in Table 1. There are examples in the formulations with an angle of repose in the range of 40° to 500 that were manufactured satisfactorily, when the angle of repose exceeds 500. The flow is rarely acceptable for manufacturing purposes (USP29-NF24, 2013).

3.2.2.4 Experimental Considerations for Angle of Repose

The properties of the powder is not an intrinsic in angle of repose i.e. It is dependent upon the method used to form the cone of powder. The following important considerations are:

• By carefully building the powder cone because the peak of the cone of powder can be distorted by the impact of powders from above.

• The nature of the base upon which the powder cone is formed that is influenced by 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 (USP29-NF24, 2013).

3.2.2.5 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.

1. The base should not be vibrated.

2. The height of the funnel is varied to carefully build up a symmetrical cone of powder.

3. The vibration should be prevented when the funnel is moved.

4. The funnel height should be maintained approximately 2-4 cm from the top of the powder pile.

5. If a symmetrical cone of powder cannot be successfully prepared then this method is not appropriate. 6. The determination of the angle of repose by measuring the height of the cone of powder and calculate the angle of repose, α, from the following equation:

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

Angle of Repose (α) is the maximum angle between the surface of a pile of powder and horizontal plane. It is usually determined by Fixed Funnel Method and is the measure of the flowability of powder/granules (USP29-NF24, 2013).

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

Where, h = height of heap of pile

r = radius of base of pile

Table 3.3: Angle of Repose (Φ)

ANGLE OF REPOSE	TYPE OF FLOW
< 25	Excellent
25 – 30	Good
30 – 40	Passable
> 40	Very Poor

3.2.3 COMPRESSIBILITY INDEX AND HAUSNER RATIO

In recent years the compressibility index and the closely related Hausner ratio are the simple, fast and popular methods of predicting powder flow characteristics. The compressibility index is indirect measurement of bulk density, size and shape, surface area, moisture content and cohesiveness of materials because all of these can influence the observed compressibility index. Measurement of both the bulk volume and the tapped volume of a powder can be determined by using the compressibility index and the Hausner ratio (USP29-NF24, 2013).

3.2.3.1 Basic Methods for Compressibility Index and Hausner Ratio

There are some variations in the method of determining the compressibility index and Hausner ratio. The basic procedure is to measure

(1) The unsettled apparent volume. Vo

(2) The final tapped volume. Vf, of the powder after tapping the material until no further volume changes occur.

The compressibility index and the Hausner ratio are calculated as follows:

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

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

Alternatively, the compressibility index and Hausner ratio is calculated by using measured values for bulk density (P_{bulk}) and tapped density (P_{tapped}) as follows:

$$Compressibility\ Index = 100 \times \left(\frac{\rho_{tapped} - \rho_{bulk}}{\rho_{tapped}} \right)$$

$$Hausner\ \ Ratio = \left(\frac{\rho_{tapped}}{\rho_{bulk}} \right)$$

Table 3.4: **Scale of Flowability**

Compressibility Index (%)	***Flow Character***	***Hausner 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	1.46-1.56
>38	Very, very poor	>1.60

3.2.3.2 Experimental Considerations for the Compressibility Index and Hausner Ratio

Compressibility index and Hausner ratio are not intrinsic properties of the powder; i.e., they depend on the methodology used. 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, P_{bulk},anD

(4) The tapped density, P_{tapped} :

Few things that were considered are,

- The diameter of the cylinder used
- The number of times the powder tapped to determine the tapped density
- The mass of material used in the test
- Rotation of the sample during tapping

3.2.3.3 Recommended Procedure for Compressibility Index and Hausner Ratio

Use a 250-mL volumetric cylinder with a test sample weight of 100 g. smaller weights and volumes was used, but variations in the method should be described with the results. An average of three determinations was recommended.

3.3 Preparation of the Formulations

Selecting excipients for any formulation considers the following things:

- The excipients should kept to a minimum in number minimize the quantity of each

- Excipients and multifunctional excipients may be given preference over unifunctional excipients.

Four formulations were formed following two formulations described in the Handbook of Pharmaceutical Manufacturing Formulations. The first formulation was (Rowe, Sheskey and Quinn, 2009),

***Table 3.5:* Formulation of Acetaminophen, Dextropropoxyphen hydrochloride**

Material Name	**Scale (mg/tablet)**	**%**
Acetaminophen	325	83.44
Dextropropoxyphen hydrochloride	32	8.22
Povidone	8	2.05
Starch (maize)	7.5	1.93
Cellulose microcrystalline	10	2.57
Talc	5	1.28
Magnesium stearate	2	0.51
Total	**389.5**	**100.00**

This formulation was taken as a reference and two formulation was made consisting only excipients excepting binder and API (Active Pharmaceutical Ingredient). They are,

3.3.1 F1

***Table 3.6:* Formulation of F1**

Ingredient	**Use**	**%**
PVP	Disintigrant	30
Carboxy methylcellulose	Diluent	40
Magnesium Stearate	Lubricant	10
Talc	Antiadhearent	20
Total		**100**

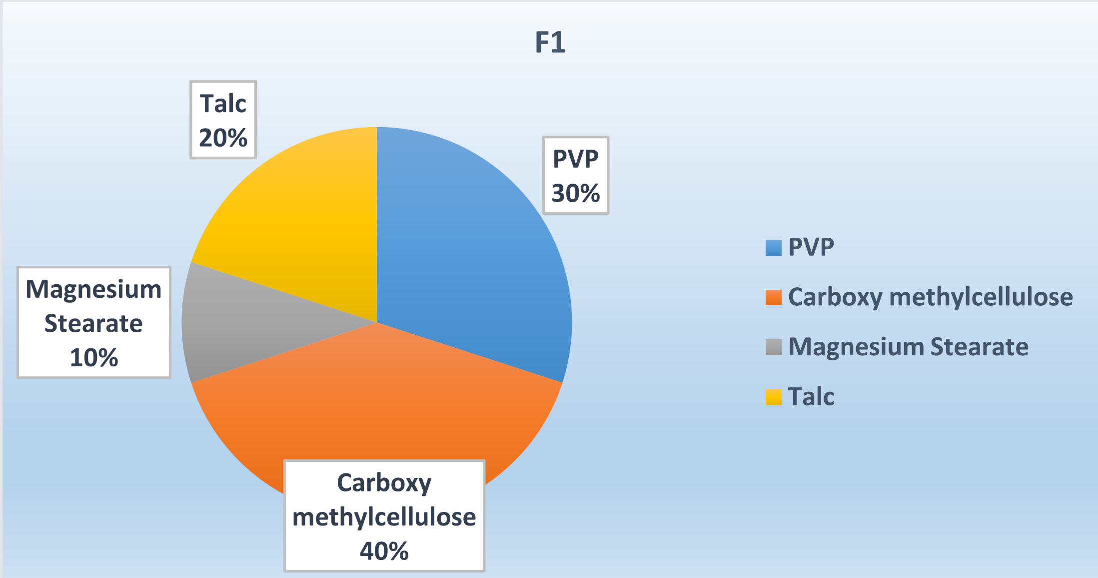

Figure 3.1: **Pie diagram of F1**

3.3.2 F2

Table 3.7: **Formulation of F2**

Ingredient	Use	%
Starch (maize)	Disintigrant	30.6
Carboxy methylcellulose	Diluent	40.8
Talc	Antiadhearent	20.4
Magnesium stearate	Lubricant	8.2
Total		**100.0**

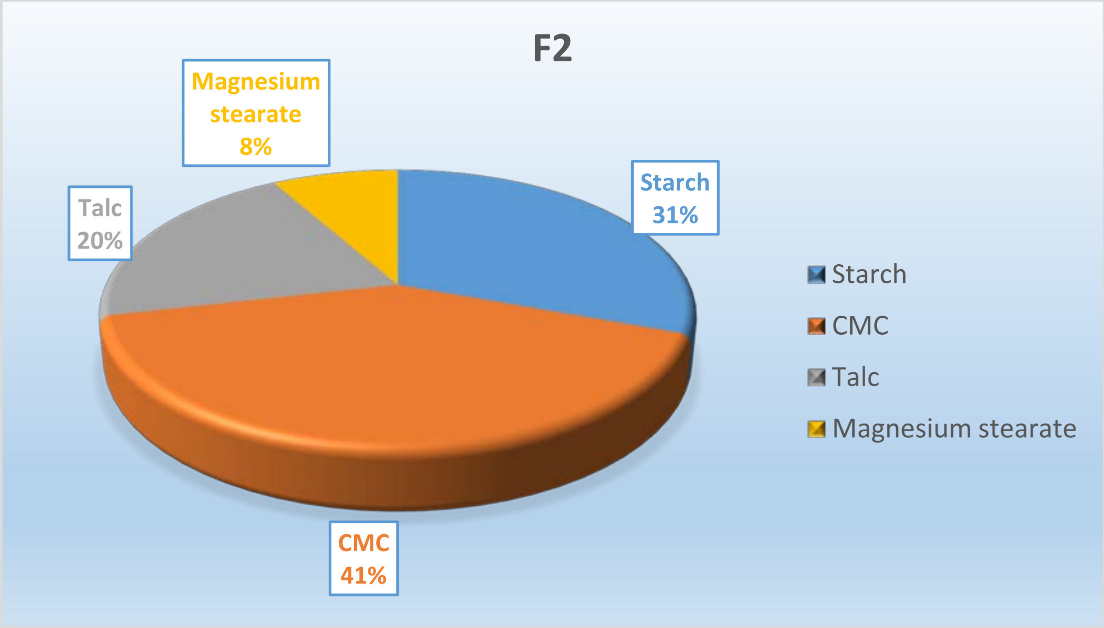

Figure 3.2: **Pie diagram of F2**

The second reference formulation (Rowe, Sheskey and Quinn, 2009) is given bellow.

Table 3.8: **Formulation of Imipramine hydrochloride**

Ingredient	**Amount**	**%**
Imipramine hydrochloride	26	18.03
Polyvinyl pyrroidone	1.4	0.97
Magnesium stearate	1.4	0.97
Talc	1.4	0.97
Lactose monohydrate	50	34.67
Dicalcium phosphate	50	34.67
Starch (maize)	14	9.71
Total	**144.2**	**100.00**

This formulation was taken as a reference and two formulation was made consisting only excipients excepting binder and API (Active Pharmaceutical Ingredient). They are

3.3.3 F3

Table 3.9: Formulation of F3

Ingredient	**Use**	**%**
Magnesium stearate	Lubricant	1.2
Talc	Antiadhearent	1.2
Lactose	Disintegrant	42.8
Dicalcium phosphate	Diluent	42.8
Starch (maize)	Diluent	12.0
Total		**100.0**

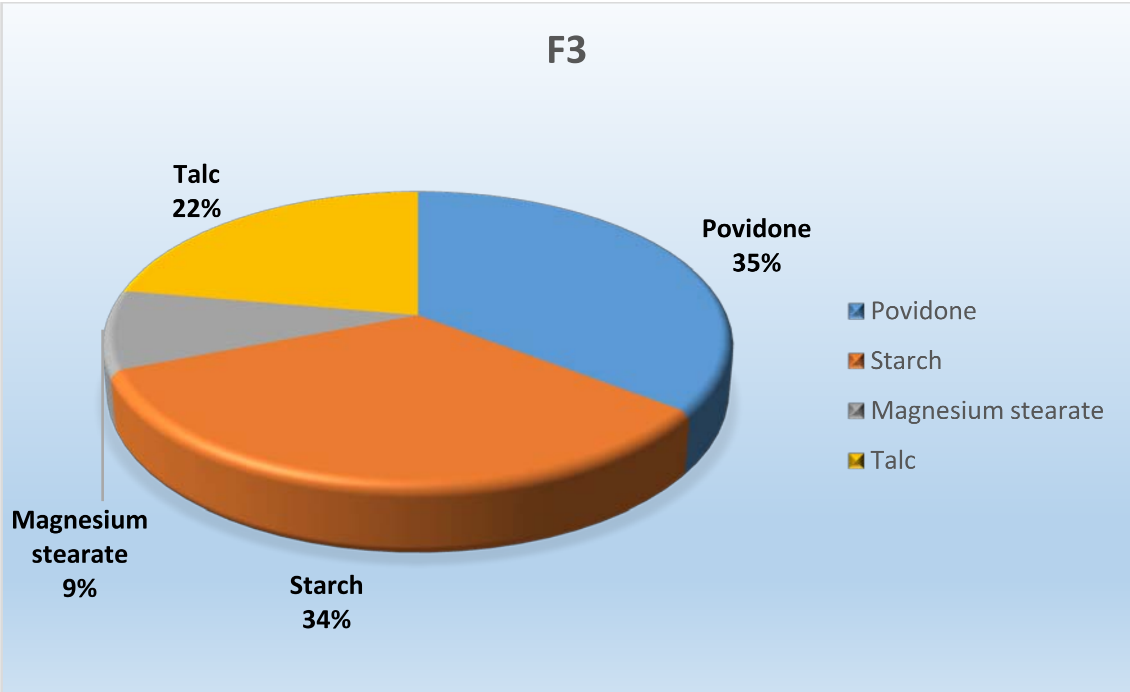

Figure 3.3: **Pie diagram of F3**

3.3.4 F4

Table 3.10: Formulation of F4

Ingredient	**Use**	**%**
Polyvinyl pyrroidone	Disintigrant	1.3
Magnesium stearate	Lubricant	1.4
Talc	Antiadhearent	1.3
Lactose	Disintegrant	48.0
Dicalcium phosphate	Diluent	48.0
Total		**100.0**

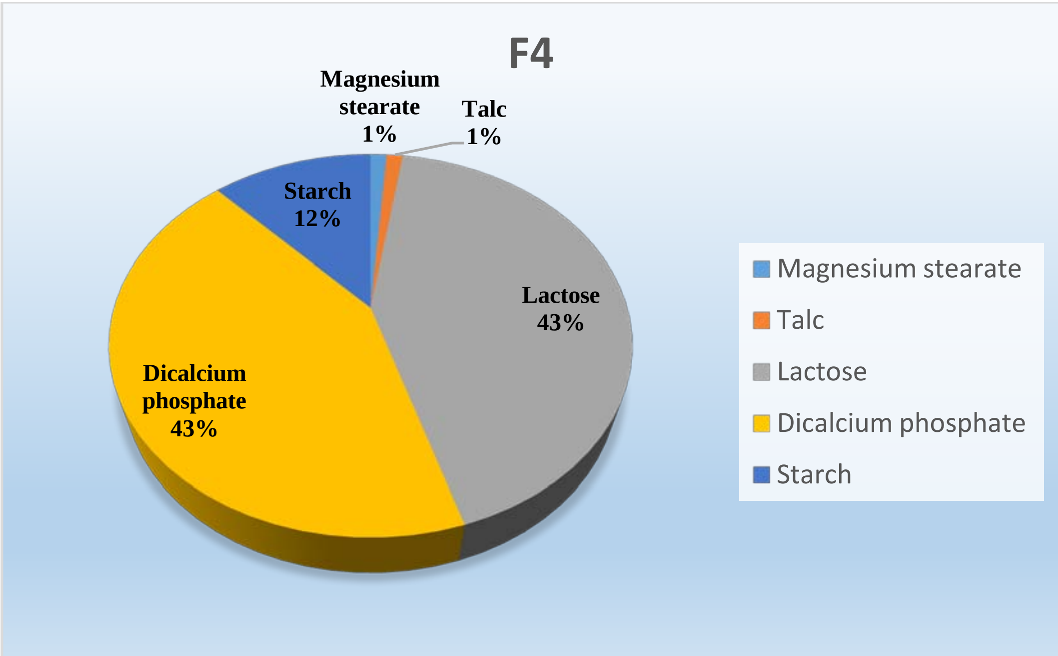

Figure 3.4: **Pie diagram of F4**

3.4 Procedure

1. Bulk density, Tapped density, Carr's index, Hausner ratio and Angle of Repose were measured for each excipients.
2. The four formulations were measured with the help of Electronic Balance
3. Different binders were mixed with different formulations in different ratio.

4. Carr’s index, Hausner ratio and Angle of Repose were measured for each mixtures.
5. This measurements were plotted in the graph by using Microsoft Excel- 2013 Workbook.

3.4.1 Process of measuring Bulk Volume

1. Mixture was taken in a 25ml measuring cylinder.
2. The upper level of the powder was taken as a measurement of bulk volume.
3. This process was performed three times
4. An average of three determinations was considered as a bulk volume

3.4.2 Process of measuring Tapped Volume

1. Mixture was taken in a 25ml measuring cylinder.
2. Then the measuring cylinder was tapped 30 times.
3. The lower level of the powder was taken as a measurement of tapped volume.
4. This process was performed three times.
5. An average of three determinations was considered as a bulk volume.

3.4.3 Process of measuring Angle of Repose

1. Plastic or glass funnel was attached to a stand
2. 5gm mixture was poured through the orifice of the funnel
3. The radius and the height of the peak was determined.
4. This process was performed three times.
5. An average of three determinations was considered as the measurement.

3.5 Flow property of ingredients

Table 3.11: **Carr’s index and Hausner Ratio of excipients**

Ingredient	***Bulk Volume***	***Average Bulk Volume (V0)***	***Tapped Volume***	***Average Tapped Volume (Vf)***	***Carr's Index***	***Hausner ratio***
Boric acid	5.5	5	3.5	3.2	36.67	1.53
	5		3			

	4.5		3			
Starch	8.5	8.3	3.5	3.3	60.80	1.95
	8		3			
	8.5		3.3			
CMC	7.5	7.3	4.5	4.3	41.82	1.02
	7		4			
	7.5		4.3			
HPMC	9.5	9.7	7	7.2	25.86	1.54
	10		7.5			
	9.5		7			
PVP	8.5	8.3	6.3	6.3	24.19	0.57
	8		6.5			
	8.3		6			
SLS	16.5	17.0	14.5	14.5	14.71	0.42
	17.5		15			
	17		14			
Mg Stearate	52.5	52.3	40	40.2	23.25	15.70
	52		40.5			
	52.5		40			
Sugar	4.5	4.3	3.5	3.3	23.08	0.86
	4		3			
	4.5		3.5			
Lactose	6	5.8	5.1	5.1	13.14	1.90
	5.5		5			
	6		5.1			
Talc	4.5	4.7	3.1	3.1	34.29	0.82
	4.5		3			
	5		3.1			
PEG	8	8.3	5.5	5.7	32.00	1.47
	8.5		6			
	8.5		5.5			

Table 3.12: **Angle of Repose of excipients**

Ingredient	***Diameter***	***Average Diameter (d)***	***Radious (r)***	***Hight***	***Average Hight (h)***	***Angle of Repose***
Boric acid	3.7	3.7	1.9	1.7	1.6	40.60
	3.9			1.6		
	3.6			1.5		
Starch	5.2	5.2	2.6	1.5	1.6	31.07
	5.1			1.7		
	5.3			1.5		
CMC	4.5	4.3	2.2	1.7	1.7	38.12
	4			1.8		
	4.5			1.6		
HPMC	4.5	4.6	2.3	2	2.2	43.29
	4.7			2.3		
	4.6			2.2		
PVP	5	5.1	2.6	1.8	1.8	35.22
	5.2			1.7		
	5.1			1.9		
SLS	6.1	6.1	3.1	2.7	2.7	41.52
	6			2.8		
	6.2			2.6		
Magnesium Stearate	1.9	2.0	1.0	5	5.1	78.84
	2			5.2		
	2.1			5		
Sugar	4	4.1	2.0	1	1.0	26.94
	4.2			1.1		
	4			1		
Lactose	5.1	5.1	2.5	2.5	2.6	45.74
	5			2.6		

	5.1			2.7		
Talc	4.1	4.0	2.0	1.8	1.8	41.75
	4			1.9		
	4			1.7		
PEG	4.7	4.8	2.4	1.1	1.1	23.96
	4.9			1		
	4.8			1.1		

CHAPTER FOUR

RESULTS

4 Results

4.1 F1: Starch

We experimented on the mixture of F1 and Starch at different intervals. Carr's index and Hausner ratio was calculated for powder mixtures at different ratio of F1 and Starch in the table below.

Table 4.1: **Carr's index and Hausner Ratio for different mixtures of F1 and Starch**

% of F1	% of Starch	Bulk Volume	Average Bulk Volume (V0)	Tapped Volume	Average Tapped Volume (Vf)	Carr's Index	Hausner Ratio
95	5	13.5	14.3	11.1	11.0	22.66	1.29
		13		11			
		13.4		11			
90	10	14	13.3	10.2	9.8	26.32	1.36
		14.5		9.2			
		14.3		10			
85	15	15.2	15.5	11	11.5	25.65	1.34
		16.2		11			
		15		12.5			
80	20	15	15.2	11.1	11.0	27.41	1.38
		15.2		11			
		15.4		11			
75	25	15	15.3	10	10.3	32.46	1.48
		15.5		11			
		15.4		10			

By plotting Carr's index against the percentages of Starch a straight line was obtained and the following equation was derived.

$$y = 0.4139x + 20.692 \text{ and } R^2 = 0.8387$$

Here, y denotes Carr's index and X denotes the percentage of starch

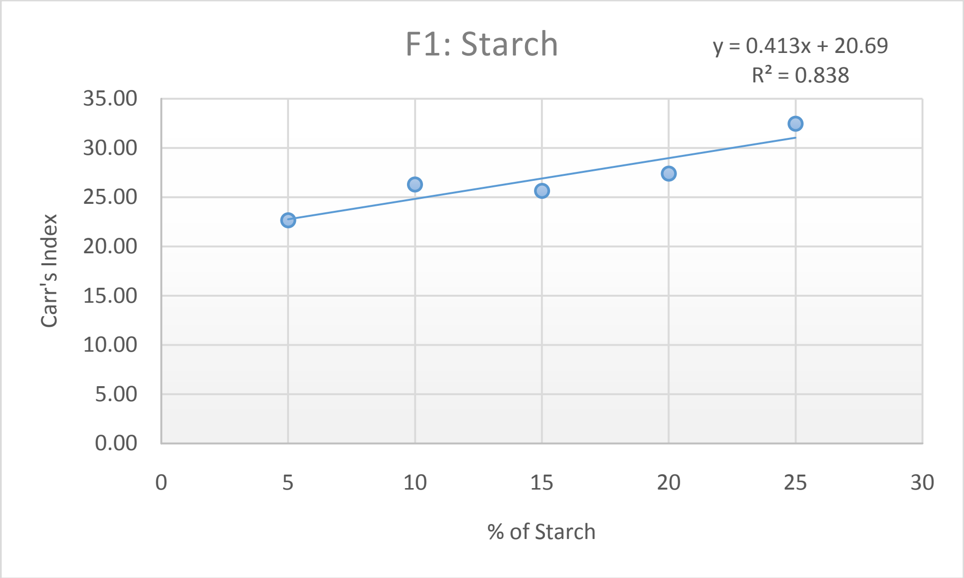

Figure 4.1: **Scatter chart of Carr's Index for different percentages of Starch**

By plotting Hausner Ratio against the percentages of Starch a straight line was obtained and the following equation was derived.

$$y = 0.0079x + 1.252 \text{ and } R^2 = 0.8235$$

Here, y denotes Hausner Ratio and X denotes the percentage of starch.

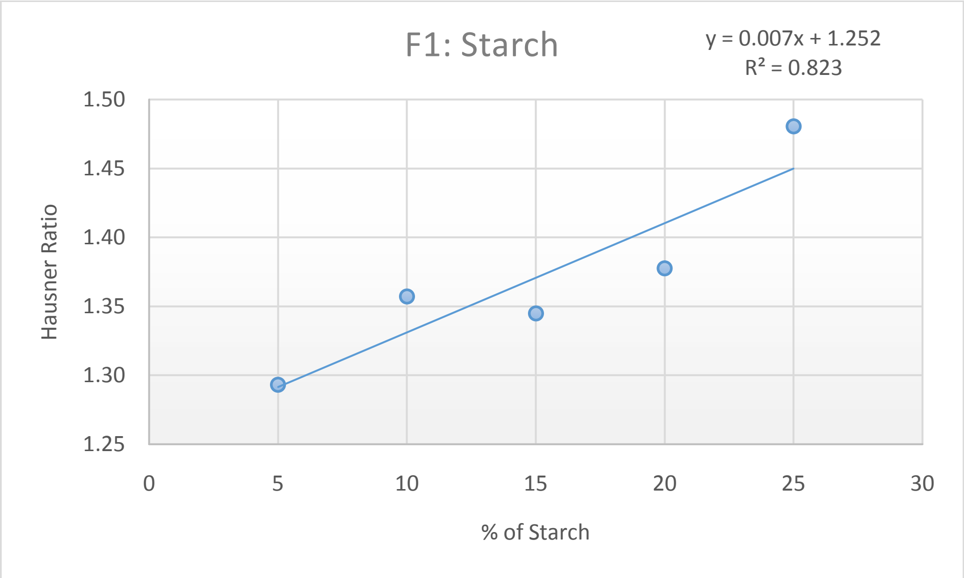

Figure 4.2: **Scatter chart of Hausner Ratio for different percentages of Starch**

Angle of Reposewas calculated for powder mixtures at different ratio of F1 and Starch in the table below.

Table 4.2:**Angle of Repose for different mixtures of F1 and Starch**

% of F1	**% of Starch**	**Diameter**	**Average Diameter (d)**	**Radius (r)**	**Height**	**Average Height (h)**	**Angle of Repose**
95	5	5	5.0	2.5	2.1	2.1	39.84
		5			2		
		5.1			2.2		
90	10	4.8	4.8	2.4	2	2.1	40.99
		4.9			2.1		
		4.8			2.2		
85	15	5.6	5.5	2.8	1.8	1.9	34.48
		5.5			2.2		
		5.5			1.7		
80	20	5.7	5.6	2.8	2	1.9	34.47
		5.6			2		
		5.6			1.8		
75	25	5.4	5.4	2.7	1.6	1.7	31.53
		5.4			2		
		5.5			1.4		

From table 4.2, we got Angle of repose for different percentages of starch used in the mixture. By plotting Angle of repose against the percentages of Starch a straight line was obtained and the following equation was derived.

$$y = -0.463x + 43.207 \text{ and } R^2 = 0.8378$$

Here, y denotes Angle of repose and X denotes the percentage of starch

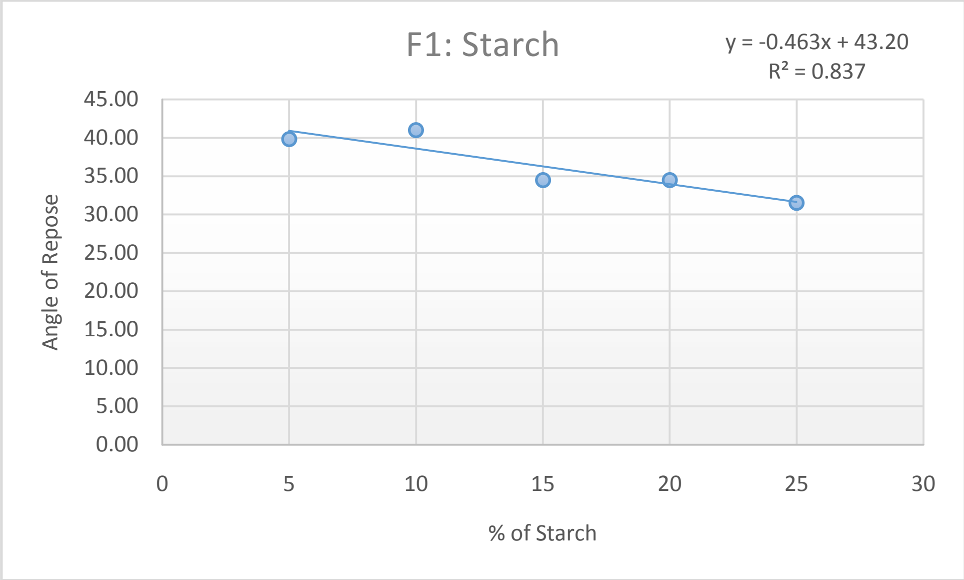

Figure 4.3: **Scatter chart of Angle of Repose for different percentages of Starch**

4.2 F1: Lactose

We experimented on the mixture of F1 and Lactose at different intervals. Lactose is usually used 5-25% w/w as a binder. Carr's index and Hausner ratio was calculated for powder mixtures at different ratio of F1 and Lactose in the table below.

Table 4.3: **Carr's index and Hausner Ratio for different mixtures of F1 and Lactose**

F1 (%)	Lactose (%)	Bulk Volume	Average Bulk Volume (V0)	Tapped Volume	Average Tapped Volume (Vf)	Carr's Index	Hausner Ratio
95	5	16	15.3	8	8.7	43.48	1.77
		15		9			
		15		9			
90	10	14.5	13.7	8.5	8.2	40.24	1.67
		13		8			
		13.5		8			
85	15	14	13.2	8.5	8.0	39.24	1.65
		13		7.5			
		12.5		8			
80	20	13	12.8	7.5	7.8	38.96	1.64
		12		8			
		13.5		8			

75	25	13	12.3	7.5	7.7	37.84	1.61
		12		8			
		12		7.5			

From table 4.3, we got Carr's index and Hausner ratio for different percentages of lactose used in the mixture. By plotting Carr's index against the percentages of lactose a straight line was obtained and the following equation was derived.

$$y = -0.2513x + 43.721 \text{ and } R^2 = 0.8543$$

Here, y denotes Carr's index and X denotes the percentage of lactose.

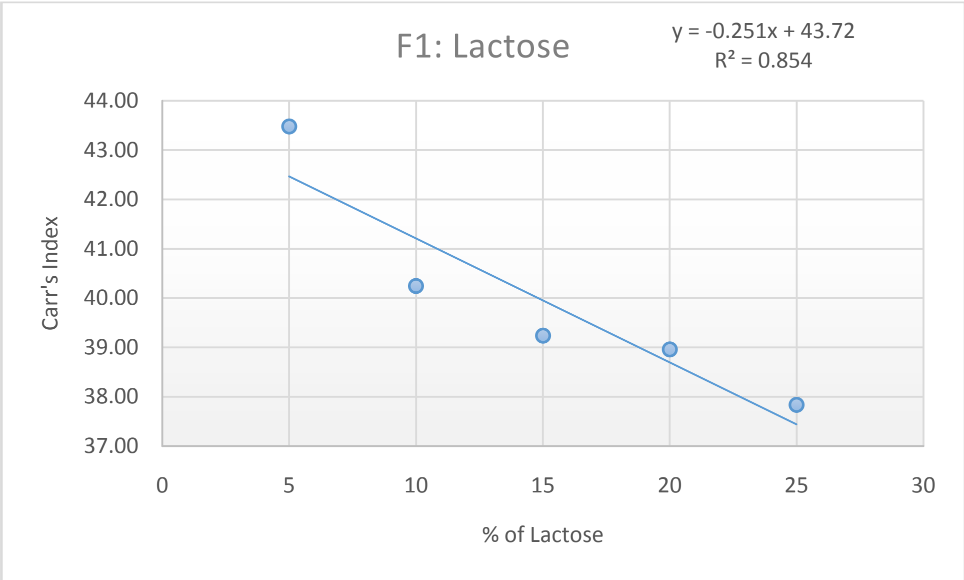

Figure 4.4: **Scatter chart of Carr's Index for different percentages of Lactose**

By plotting Hausner Ratio against the percentages of Lactose a straight line was obtained and the following equation was derived.

$$y = -0.0071x + 1.774 \text{ and } R^2 = 0.8369$$

Here, y denotes Hausner Ratio and X denotes the percentage of lactose.

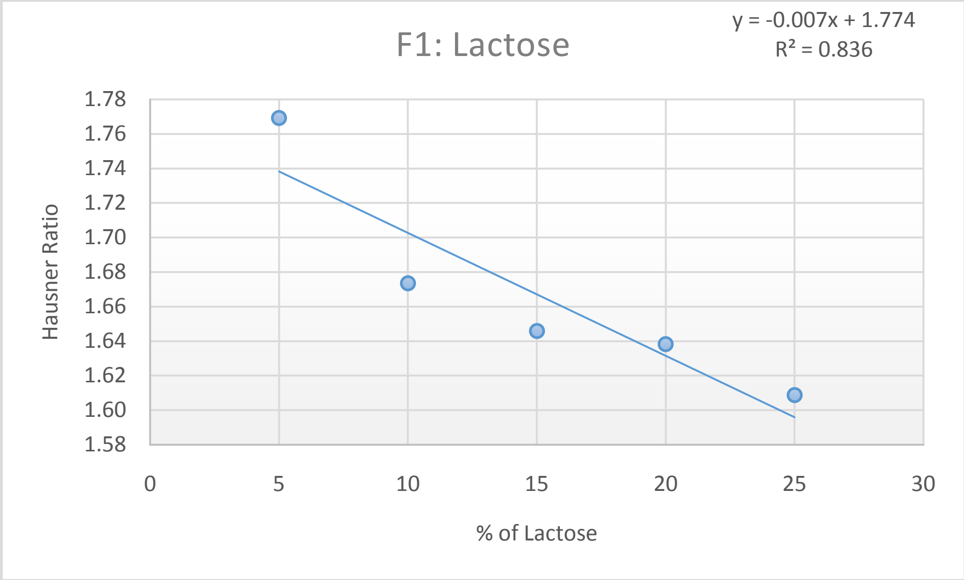

***Figure 4.5:* Scatter chart of Hausner Ratio for different percentages of Lactose**

Angle of Reposewas calculated for powder mixtures at different ratio of F1 and Lactose in the table below.

***Table 4.4:*Angle of Repose for different mixtures of F1 and Lactose**

F1 (%)	Lactose (%)	Diameter	Average Diameter (d)	Radius (r)	Height	Average Height (h)	Angle of Repose
95	5	5.1	5.1	2.5	2.7	2.6	46.11
		5			2.7		
		5.1			2.5		
90	10	5	4.8	2.4	2.6	2.6	47.09
		4.8			2.6		
		4.7			2.6		
85	15	4.8	4.9	2.4	2.5	2.5	45.39
		4.9			2.5		
		4.9			2.4		
80	20	4.8	4.8	2.4	2.3	2.3	43.17
		4.8			2.3		
		4.9			2.2		
75	25	4.8	4.7	2.4	2.1	2.1	42.03

		4.7			2.1		
		4.7			2.2		

From table 4.4, we got Angle of repose for different percentages of lactose used in the mixture. By plotting Angle of repose against the percentages of Lactose a straight line was obtained and the following equation was derived.

$$y = -0.2416x + 48.382 \text{ and } R^2 = 0.8273$$

Here, y denotes Angle of repose and X denotes the percentage of lactose.

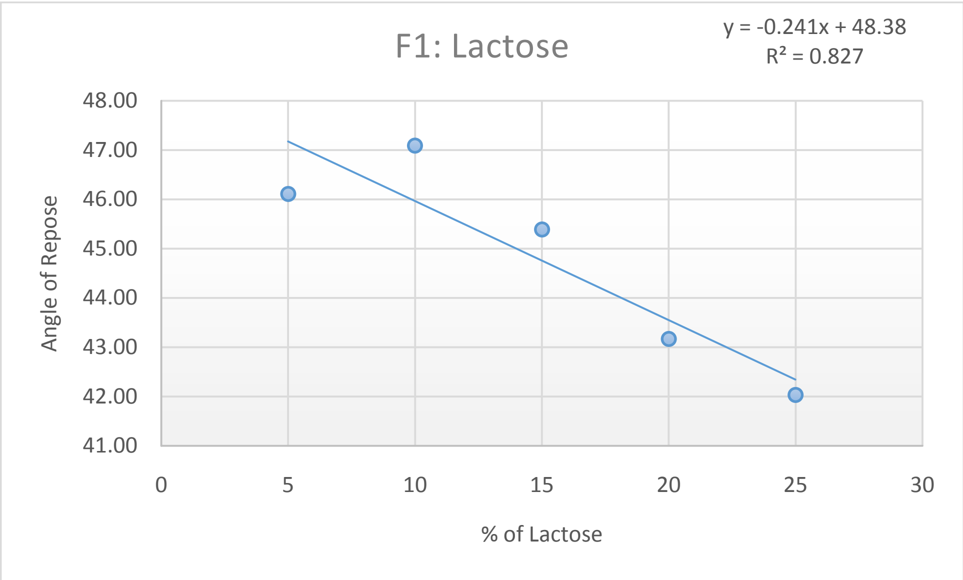

Figure 4.6: **Scatter chart of Angle of Repose for different percentages of Lactose**

4.3 F2: PVP

We experimented on the mixture of F2 and PVP at different intervals. PVP is usually used 0.5-5% w/w as a binder. Carr's index and Hausner ratio was calculated for powder mixtures at different ratio of F2 and PVP in the table below.

Table 4.5: **Carr's index and Hausner Ratio for different mixtures of F2 and PVP**

F2 (%)	**PVP (%)**	**Bulk Volume**	**Average Bulk Volume (V0)**	**Tapped Volume**	**Average Tapped Volume (Vf)**	**Carr's Index**	**Hausner Ratio**
99.5	0.5	12.5	12.3	9	8.5	31.08	1.45
		12		8			
		12.5		8.5			
98	2	11.5	11.3	7.5	7.3	35.29	1.55
		11.5		7			
		11		7.5			
97	3	11.5	11.5	7	6.8	40.58	1.68
		11.5		6.5			
		11.5		7			
96	4	11	11.2	6	6.2	44.78	1.81
		11.5		6			
		11		6.5			
95	5	10.5	10.7	5.5	5.3	50.00	2.00
		11		5.5			
		10.5		5			

From table 4.5, we got Carr's index and Hausner ratio for different percentages of PVP used in the mixture. By plotting Carr's index against the percentages of PVP a straight line was obtained and the following equation was derived.

$$y = 4.2584x + 27.997 \text{ and } R^2 = 0.9866$$

Here, y denotes Carr's index and X denotes the percentage of PVP.

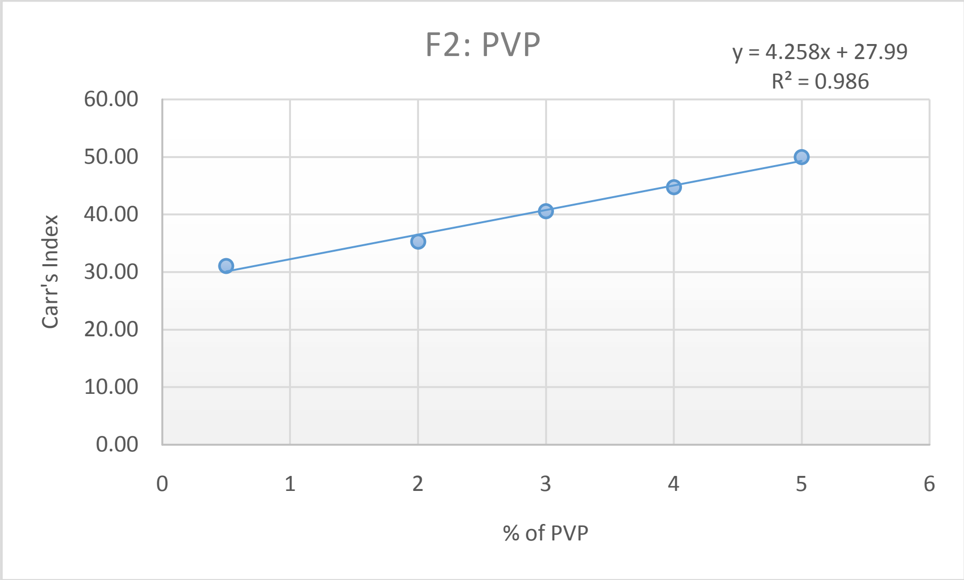

Figure 4.7: **Scatter chart of Carr's Index for different percentages of PVP**

By plotting Hausner Ratio against the percentages of PVP a straight line was obtained and the following equation was derived.

$$y = 0.1219x + 1.3446 \text{ and } R^2 = 0.9617$$

Here, y denotes Hausner Ratio and X denotes the percentage of PVP.

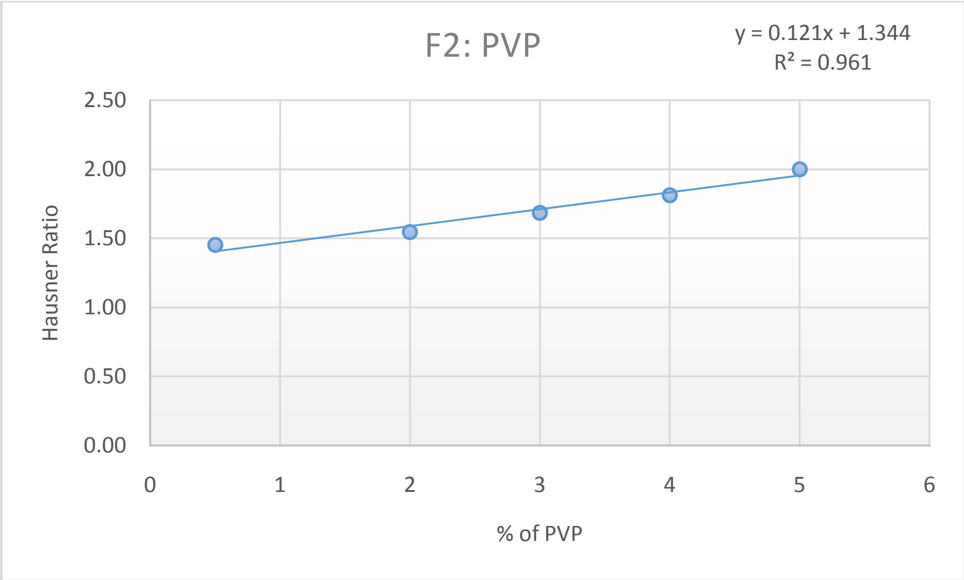

Figure 4.8: **Scatter chart of Hausner Ratio for different percentages of PVP**

Angle of Repose was calculated for powder mixtures at different ratio of F2 and PVP in the table below.

Table 4.6: **Angle of Repose for different mixtures of F2 and PVP**

F2 (%)	**PVP (%)**	**Diameter**	**Average Diameter (d)**	**Radius (r)**	**Height**	**Average Height (h)**	**Angle of Repose**
99.5	0.5	5.1	5.1	2.5	1.5	1.5	31.18
		5.1			1.5		
		5			1.6		
98	2	5	5.0	2.5	1.7	1.6	33.33
		4.9			1.6		
		5			1.6		
97	3	4.8	4.9	2.4	1.8	1.8	35.98
		4.9			1.7		
		4.9			1.8		
96	4	4.8	4.8	2.4	2	2.0	39.61
		4.8			2.1		
		4.9			1.9		
95	5	4.8	4.7	2.4	2.2	2.2	42.47
		4.7			2.1		
		4.7			2.2		

From table 4.6, we got Angle of repose for different percentages of PVP used in the mixture. By plotting Angle of repose against the percentages of PVP a straight line was obtained and the following equation was derived.

$$y = 2.5837x + 29.024 \text{ and } R^2 = 0.9706$$

Here, y denotes Angle of repose and X denotes the percentage of PVP.

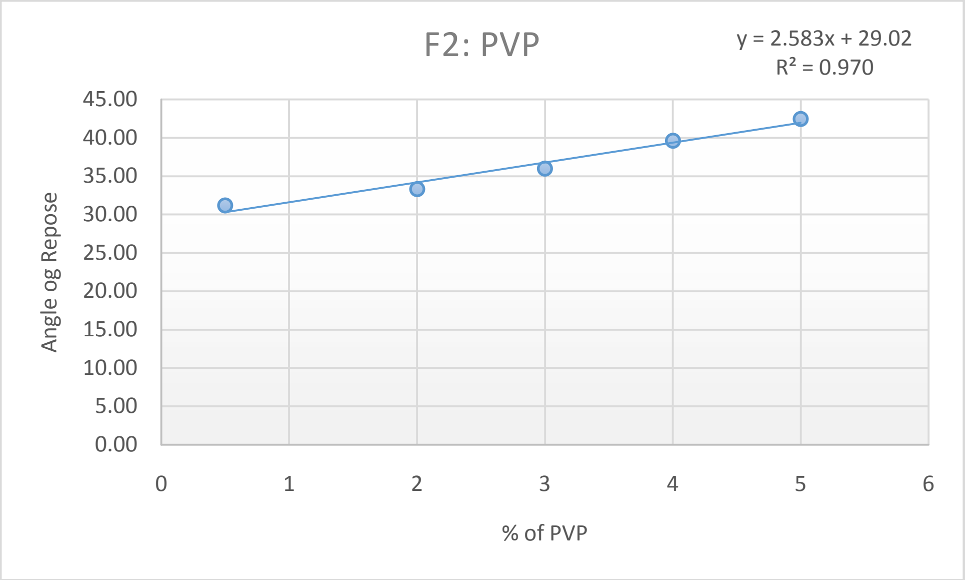

Figure 4.9: **Scatter chart of Angle of Repose for different percentages of PVP**

4.4 F2: HPMC

We experimented on the mixture of F2 and HPMC at different intervals. HPMC is usually used 2-5% w/w as a binder. Carr's index and Hausner ratio was calculated for powder mixtures at different ratio of F2 and HPMC in the table below.

Table 4.7: **Carr's index and Hausner Ratio for different mixtures of F2 and HPMC**

F2 (%)	HPMC (%)	Bulk Volume	Average Bulk Volume (V0)	Tapped Volume	Average Tapped Volume (Vf)	Carr's Index	Hausner Ratio
98	2	12.5	12.3	7.5	7.3	40.54	1.68
		12		7.5			
		12.5		7			
97	3	12	11.8	7.5	7.7	35.21	1.54
		11.5		8			
		12		7.5			
96	4	11	10.8	7	7.0	35.38	1.55
		10.5		7			

		11		7			
95	5	11	10.8	7.5	7.5	30.77	1.44
		10.5		7.5			
		11		7.5			

From table 4.7, we got Carr's index and Hausner ratio for different percentages of HPMC used in the mixture. By plotting Carr's index against the percentages of HPMC a straight line was obtained and the following equation was derived.

$$y = -2.9141x + 45.676 \text{ and } R^2 = 0.8867$$

Here, y denotes Carr's index and X denotes the percentage of HPMC.

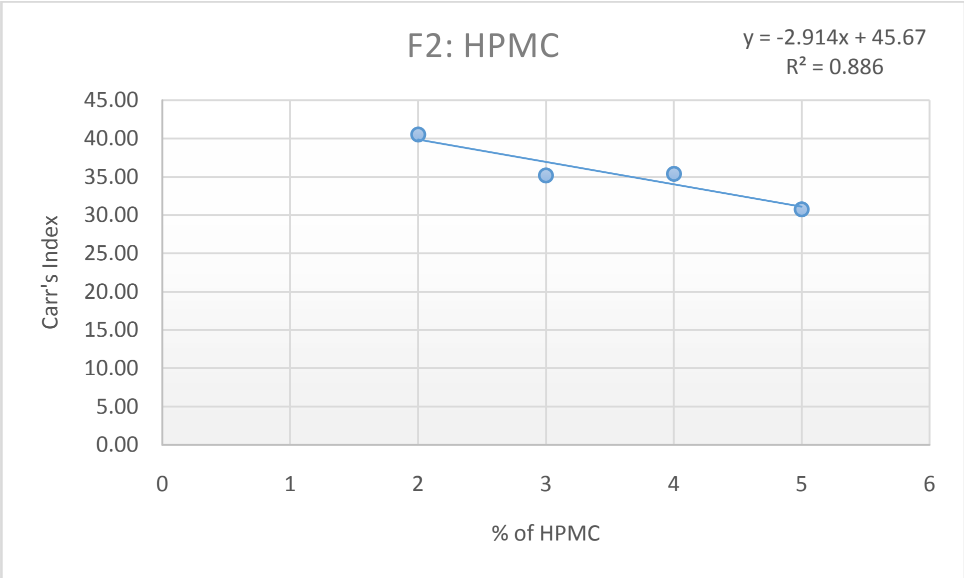

Figure 4.10: **Scatter chart of Carr's Index for different percentages of HPMC**

By plotting Hausner Ratio against the percentages of HPMC a straight line was obtained and the following equation was derived.

$$y = -0.0708x + 1.8021 \text{ and } R^2 = 0.8796$$

Here, y denotes Hausner Ratio and X denotes the percentage of HPMC.

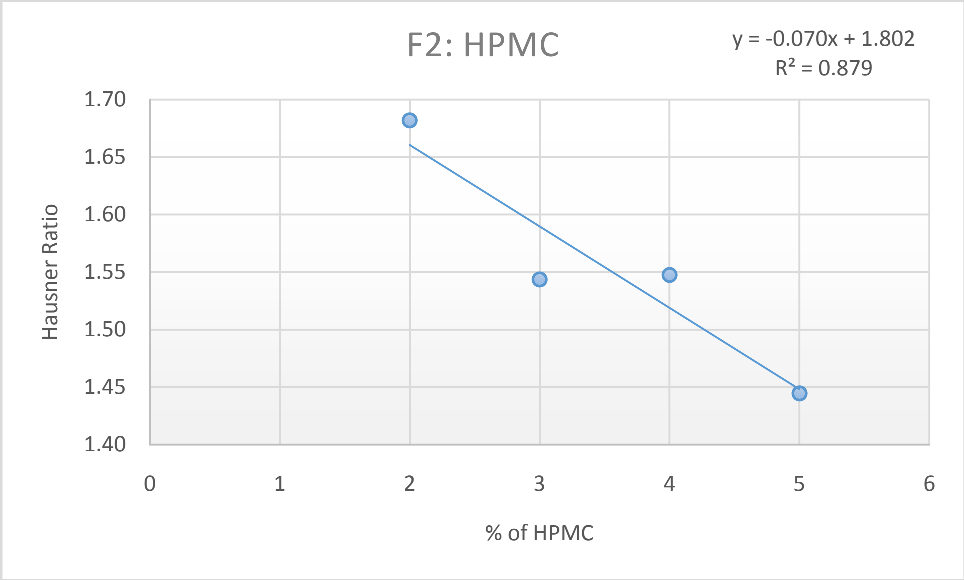

Figure 4.11: **Scatter chart of Hausner Ratio for different percentages of HPMC**

Angle of Repose was calculated for powder mixtures at different ratio of F2 and HPMC in the table below.

Table 4.8: **Angle of Repose for different mixtures of F2 and HPMC**

F2 (%)	HPMC (%)	Diameter	Average Diameter (d)	Radius (r)	Height	Average Height (h)	Angle of Repose
98	2	4.9	5.0	2.5	1.8	1.8	36.25
		5			1.8		
		5.1			1.9		
97	3	4.7	4.7	2.4	2.2	2.2	42.68
		4.7			2.1		
		4.7			2.2		
96	4	4.6	4.6	2.3	2.3	2.3	44.58
		4.7			2.3		
		4.5			2.2		
95	5	4.5	4.5	2.3	2.4	2.4	46.24
		4.6			2.3		
		4.5			2.4		

From table 4.8, we got Angle of repose for different percentages of HPMC used in the mixture. By plotting Angle of repose against the percentages of HPMC a straight line was obtained and the following equation was derived.

$$y = 3.1854x + 31.288 \text{ and } R^2 = 0.885$$

Here, y denotes Angle of repose and X denotes the percentage of HPMC.

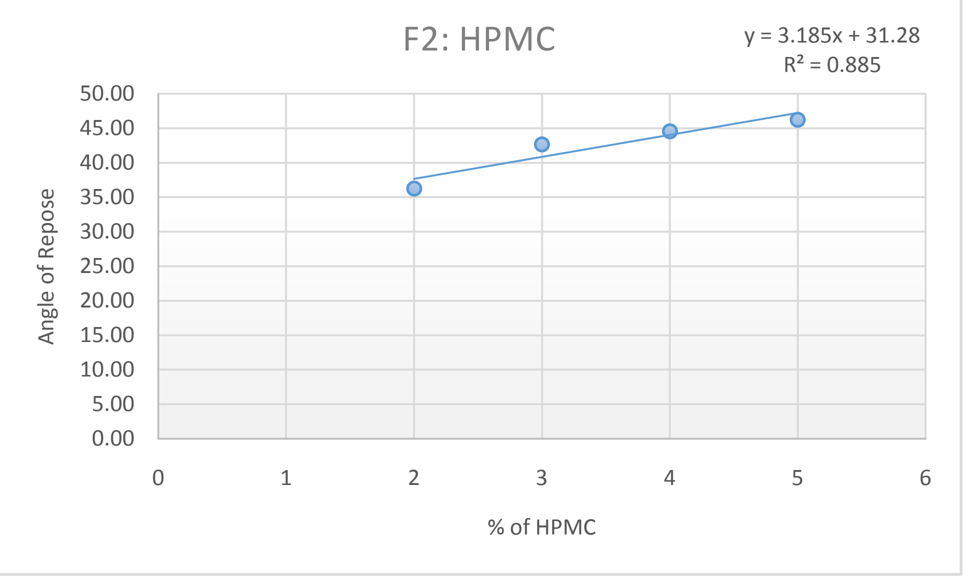

Figure 4.12: **Scatter chart of Angle of Repose for different percentages of HPMC**

4.5 F2: PEG

We experimented on the mixture of F2 and PEG at different intervals. PEG is usually used 10-15% w/w as a binder. Carr’s index and Hausner ratio was calculated for powder mixtures at different ratio of F2 and PEG in the table below.

Table 4.9: **Carr’s index and Hausner Ratio for different mixtures of F2 and PEG**

F2 (%)	**PEG (%)**	**Bulk Volume**	**Average Bulk Volume (V0)**	**Tapped Volume**	**Average Tapped Volume (Vf)**	**Carr's Index**	**Hausner Ratio**
90	10	12.5	12.3	8	8.5	31.08	1.45
		12		9			

		12.5		8.5			
89	11	12.5	12.3	8	7.5	39.19	1.64
		12.5		7			
		12		7.5			
88	12	11.5	11.2	6.5	6.7	40.30	1.68
		10.5		6			
		11.5		7.5			
87	13	11	11.0	6.5	6.3	42.42	1.74
		11		6.5			
		11		6			
85	15	10.5	10.8	6	5.5	49.23	1.97
		11		5			
		11		5.5			

From table 4.9, we got Carr's index and Hausner ratio for different percentages of PEG used in the mixture. By plotting Carr's index against the percentages of PEG a straight line was obtained and the following equation was derived.

$$y = 3.2649x + 0.613 \text{ and } R^2 = 0.9259$$

Here, y denotes Carr's index and X denotes the percentage of PEG.

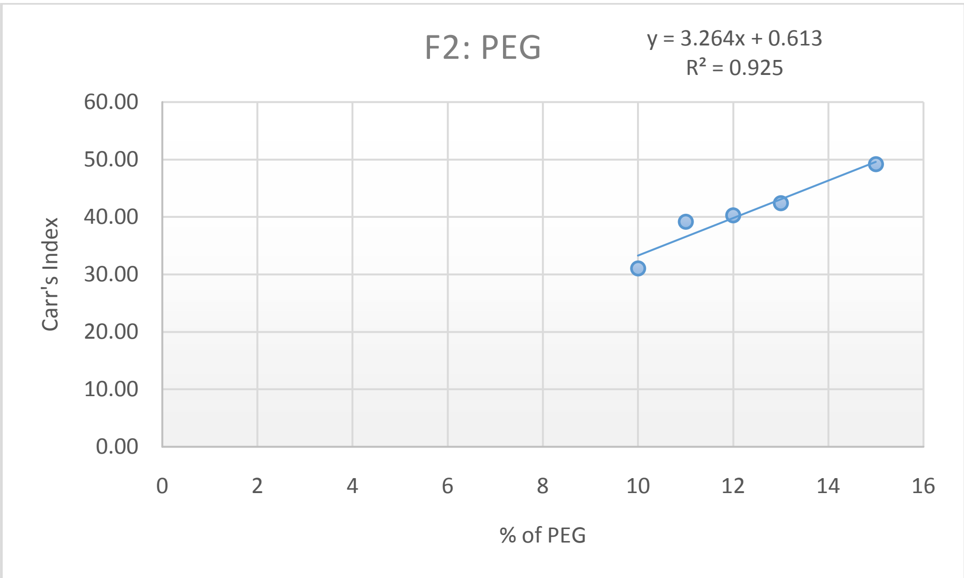

Figure 4.13: **Scatter chart of Carr's Index for different percentages of PEG**

By plotting Hausner Ratio against the percentages of PEG a straight line was obtained and the following equation was derived.

$$y = 0.0949x + 0.5379 \text{ and } R^2 = 0.9535$$

Here, y denotes Hausner Ratio and X denotes the percentage of PEG.

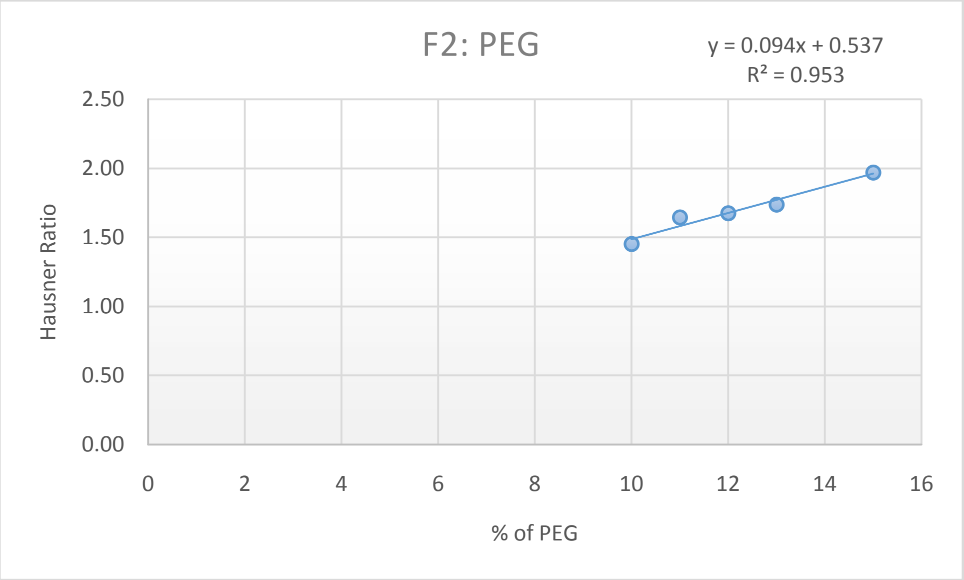

Figure 4.14: **Scatter chart of Hausner Ratio for different percentages of PEG**

Angle of Repose was calculated for powder mixtures at different ratio of F2 and PEG in the table below.

Table 4.10:**Angle of Repose for different mixtures of F2 and PEG**

F2 (%)	PEG (%)	Diameter	Average Diameter (d)	Radius (r)	Height	Average Height (h)	Angle of Repose
90	10	4.9	5.0	2.5	1.8	1.8	36.25
		5			1.8		
		5.1			1.9		
89	11	4.7	4.7	2.4	2.2	2.2	42.68
		4.7			2.1		
		4.7			2.2		
88	12	4.6	4.6	2.3	2.3	2.3	44.58
		4.7			2.3		

		4.5			2.2		
87	13	4.5	4.5	2.3	2.4	2.4	46.24
		4.6			2.3		
		4.5			2.4		
85	15	4.8	4.7	2.4	2.2	2.2	42.47
		4.7			2.1		
		4.7			2.2		

From table 4.10, we got Angle of repose for different percentages of PEG used in the mixture. By plotting Angle of repose against the percentages of PEG, a straight line was obtained and the following equation was derived.

$$y = 2.1172x + 17.65 \text{ and } R^2 = 0.8237$$

Here, y denotes Angle of repose and X denotes the percentage of PEG.

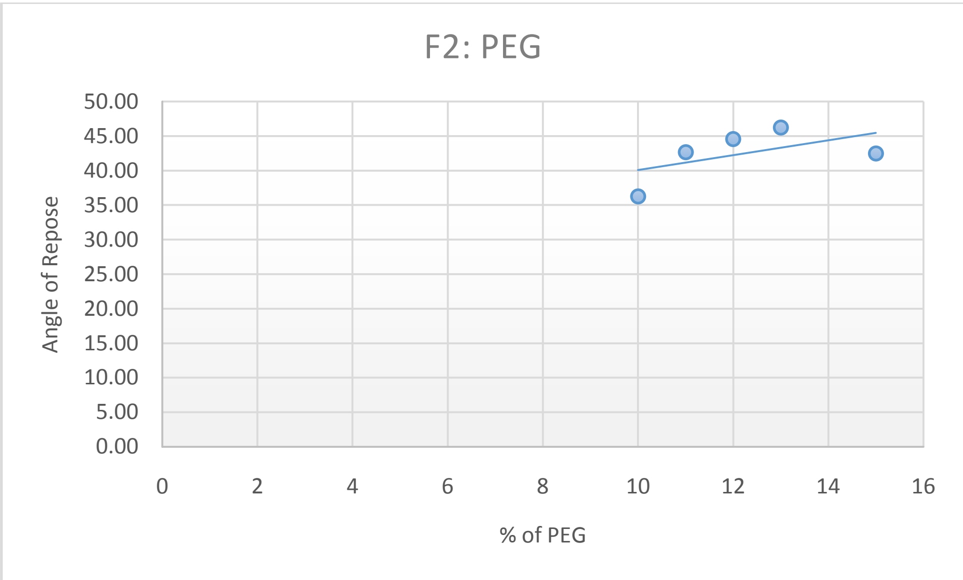

Figure 4.15: **Scatter chart of Angle of Repose for different percentages of PEG**

4.6 F3: PVP

We experimented on the mixture of F3 and PVP at different intervals. PVP is usually used 0.5-5% w/w as a binder. Carr's index and Hausner ratio was calculated for powder mixtures at different ratio of F3 and PVP in the table below.

Table 4.11: **Carr's index and Hausner Ratio for different mixtures of F3 and PVP**

F3 (%)	**PVP (%)**	**Bulk Volume**	**Average Bulk Volume (V0)**	**Tapped Volume**	**Average Tapped Volume (Vf)**	**Carr's Index**	**Hausner Ratio**
99.5	0.5	9	8.8	7.5	7.8	11.32	1.13
		9		8			
		8.5		8			
98	2	9	8.8	7.5	7.5	15.09	1.18
		8.5		7.5			
		9		7.5			
97	3	8.5	8.7	7	7.0	19.23	1.24
		9		7			
		8.5		7			
96	4	8.5	8.7	6.5	6.7	23.08	1.30
		9		7			
		8.5		6.5			
95	5	9	9.0	6	6.2	31.48	1.46
		9		6			
		9		6.5			

By plotting Carr's index against the percentages of PVP a straight line was obtained and the following equation was derived.

$$y = 4.3167x + 7.5223 \text{ and } R^2 = 0.9422$$

Here, y denotes Carr's index and x denotes the percentage of PVP.

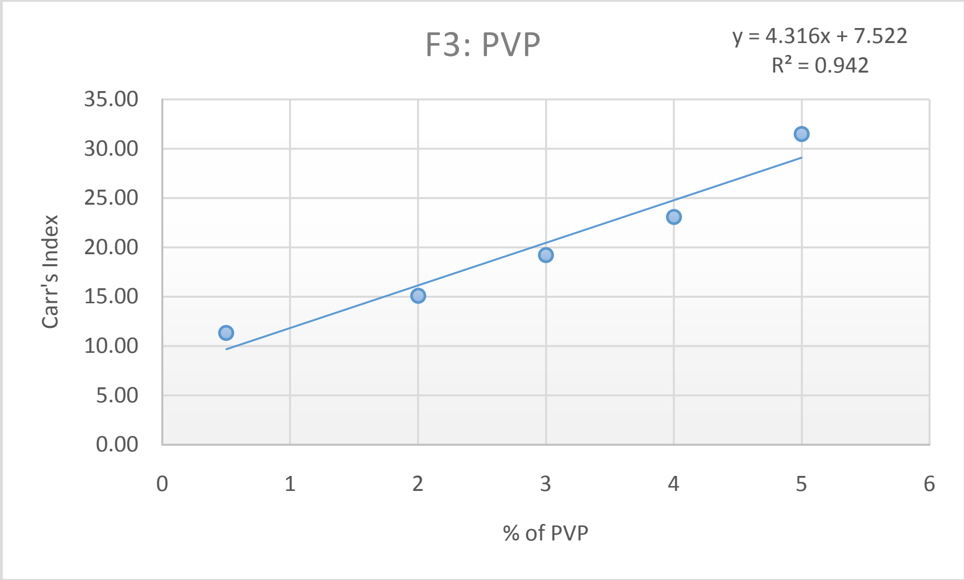

Figure 4.16: **Scatter chart of Carr's Index for different percentages of PVP**

By plotting Hausner Ratio against the percentages of PVP a straight line was obtained and the following equation was derived.

$$y = 0.0699x + 1.058 \text{ and } R^2 = 0.9003$$

Here, y denotes Hausner Ratio and x denotes the percentage of PVP.

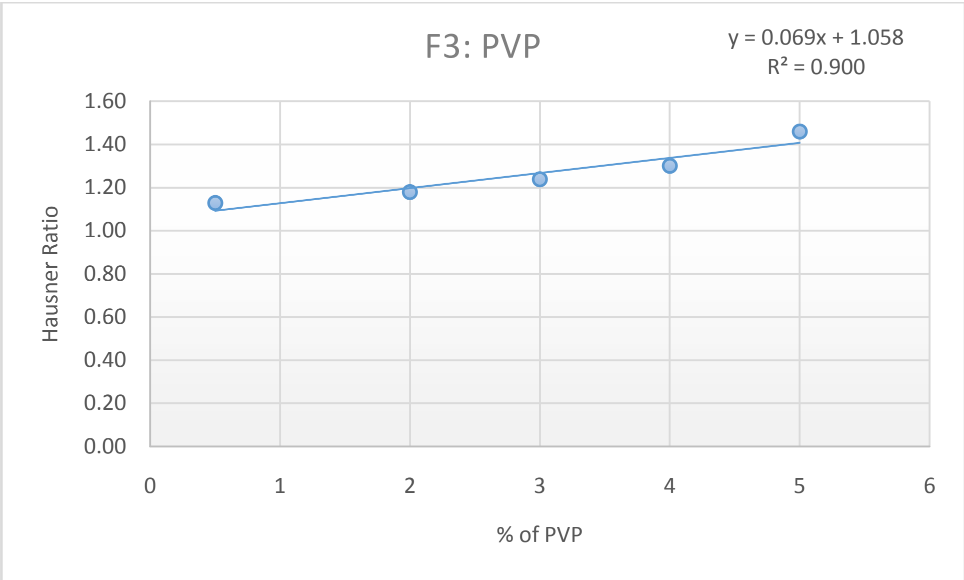

Figure 4.17: **Scatter chart of Hausner Ratio for different percentages of PVP**

Angle of Repose was calculated for powder mixtures at different ratio of F3 and PVP in the table below.

Table 4.12: **Angle of Repose for different mixtures of F3 and PVP**

F3 (%)	**PVP (%)**	**Diameter**	**Average Diameter (d)**	**Radius (r)**	**Height**	**Average Height (h)**	**Angle of Repose**
99.5	0.5	4.3	4.3	2.1	1.5	1.6	36.29
		4.2			1.6		
		4.3			1.6		
98	2	4.4	4.4	2.2	1.5	1.5	33.69
		4.4			1.4		
		4.4			1.5		
97	3	4.5	4.5	2.3	1.4	1.4	31.70
		4.6			1.4		
		4.5			1.4		
96	4	4.6	4.5	2.3	1.3	1.3	30.47
		4.5			1.4		
		4.5			1.3		
95	5	4.8	4.8	2.4	1.3	1.2	27.36
		4.8			1.2		
		4.7			1.2		

From table 4.12, we got Angle of repose for different percentages of PVP used in the mixture. By plotting Angle of repose against the percentages of PVP, a straight line was obtained and the following equation was derived.

$$y = -1.9085x + 37.437 \text{ and } R^2 = 0.9831$$

Here, y denotes Angle of repose and x denotes the percentage of PVP.

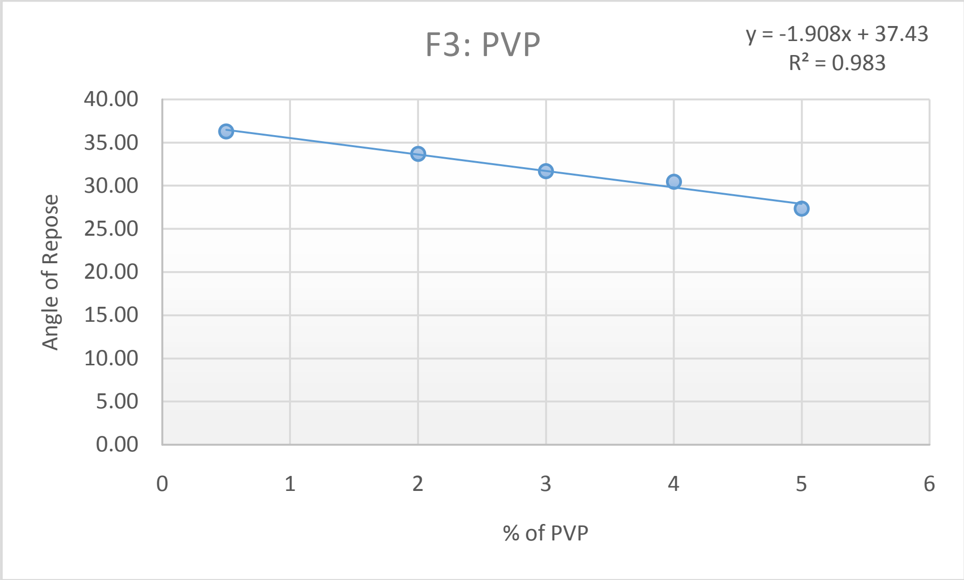

Figure 4.18: **Scatter chart of Angle of Repose for different percentages of PVP**

4.7 F3: HPMC

We experimented on the mixture of F3 and HPMC at different intervals. HPMC is usually used 2-5% w/w as a binder. Carr's index and Hausner ratio was calculated for powder mixtures at different ratio of F3 and HPMC in the table below.

Table 4.13: **Carr's index and Hausner Ratio for different mixtures of F3 and HPMC**

F3 (%)	HPMC (%)	Bulk Volume	Average Bulk Volume (V0)	Tapped Volume	Average Tapped Volume (Vf)	Carr's Index	Hausner Ratio
98	2	8.5	8.7	7.5	7.3	15.38	1.18
		9		7			
		8.5		7.5			
97	3	8.5	8.8	7.5	7.2	18.87	1.23
		9		7			
		9		7			
96	4	9.5	9.2	7	6.7	27.27	1.38
		9		6			

		9		7			
95	5	9	8.8	6.5	6.2	30.19	1.43
		8.5		6			
		9		6			

From table 4.13, we got Carr's index and Hausner ratio for different percentages of HPMC used in the mixture. By plotting Carr's index against the percentages of HPMC a straight line was obtained and the following equation was derived.

$$y = 5.2817x + 4.4425 \text{ and } R^2 = 0.9621$$

Here, y denotes Carr's index and x denotes the percentage of HPMC.

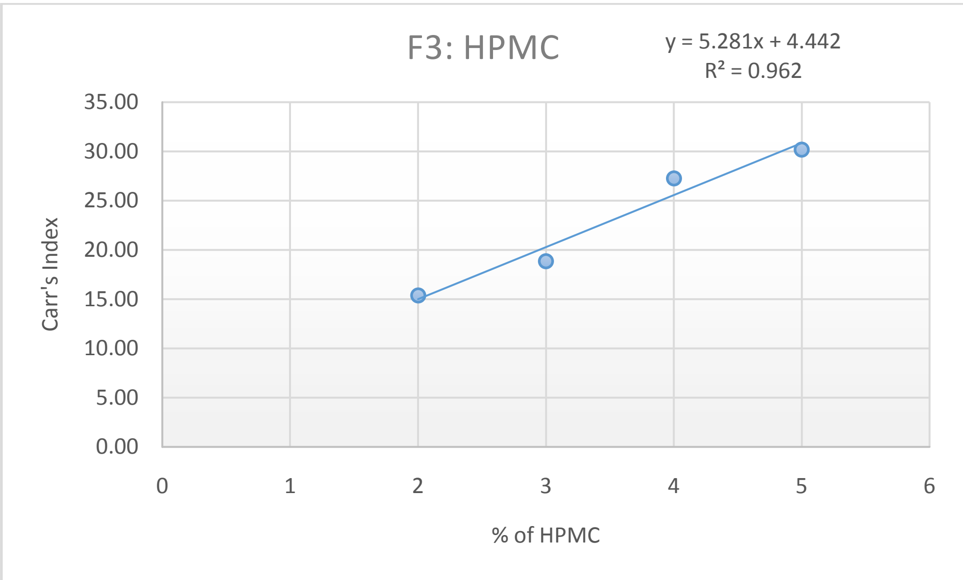

Figure 4.19: **Scatter chart of Carr's Index for different percentages of HPMC**

By plotting Hausner Ratio against the percentages of HPMC a straight line was obtained and the following equation was derived.

$$y = 0.0894x + 0.9925 \text{ and } R^2 = 0.9622$$

Here, y denotes Hausner Ratio and x denotes the percentage of HPMC.

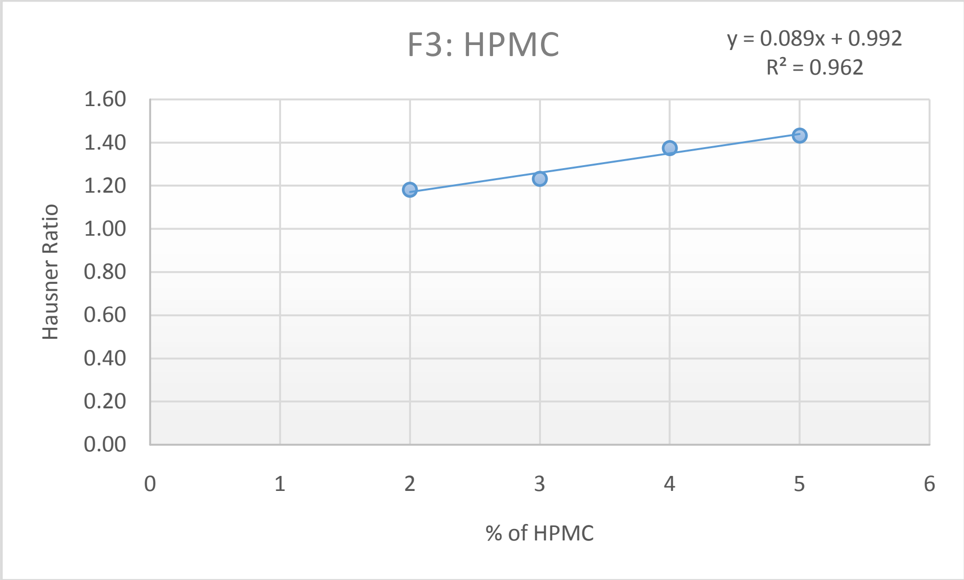

Figure 4.20: **Scatter chart of Hausner Ratio for different percentages of HPMC**

Angle of Repose was calculated for powder mixtures at different ratio of F3 and HPMC in the table below.

Table 4.14:**Angle of Repose for different mixtures of F3 and HPMC**

F3 (%)	HPMC (%)	Diameter	Average Diameter (d)	Radius (r)	Height	Average Height (h)	Angle of Repose
98	2	4.5	4.5	2.3	1.8	1.8	39.17
		4.5			1.9		
		4.5			1.8		
97	3	4.6	4.6	2.3	1.7	1.7	35.73
		4.6			1.7		
		4.7			1.6		
96	4	4.6	4.7	2.4	1.6	1.5	31.97
		4.8			1.3		
		4.7			1.5		
95	5	4.5	4.7	2.4	1.1	1.1	25.59
		4.9			1.2		
		4.8			1.1		

From table 4.14, we got Angle of repose for different percentages of HPMC used in the mixture. By plotting Angle of repose against the percentages of HPMC, a straight line was obtained and the following equation was derived.

$$y = -4.4519x + 48.697 \text{ and } R^2 = 0.9761$$

Here, y denotes Angle of repose and x denotes the percentage of HPMC.

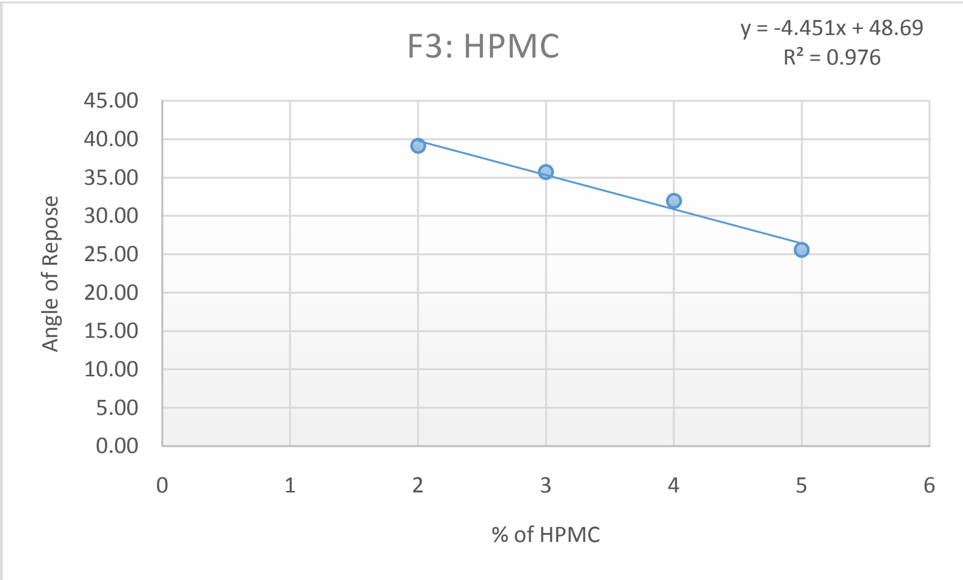

Figure 4.21: **Scatter chart of Angle of Repose for different percentages of HPMC**

4.8 F3: PEG

We experimented on the mixture of F3 and PEG at different intervals. PEG is usually used 10-15% w/w as a binder. Carr's index and Hausner ratio was calculated for powder mixtures at different ratio of F3 and PEG in the table below.

Table 4.15: **Carr's index and Hausner Ratio for different mixtures of F3 and PEG**

F3 (%)	PEG (%)	Bulk Volume	Average Bulk Volume (V0)	Tapped Volume	Average Tapped Volume (Vf)	Carr's Index	Hausner Ratio
90	10	8	8.2	7	7.3	10.20	1.11

		8		7.5			
		8.5		7.5			
89	11	8.5	8.2	7	7.2	12.24	1.14
		8		7			
		8		7.5			
88	12	8.5	8.3	6	6.0	28.00	1.39
		8.5		6			
		8		6			
87	13	8	8.2	6	5.8	28.57	1.40
		8		6			
		8.5		5.5			
85	15	8	8.3	5.5	5.3	36.00	1.56
		8.5		5			
		8.5		5.5			

From table 4.15, we got Carr's index and Hausner ratio for different percentages of PEG used in the mixture. By plotting Carr's index against the percentages of PEG a straight line was obtained and the following equation was derived.

$$y = 5.4672x - 43.696 \text{ and } R^2 = 0.8769$$

Here, y denotes Carr's index and x denotes the percentage of PEG.

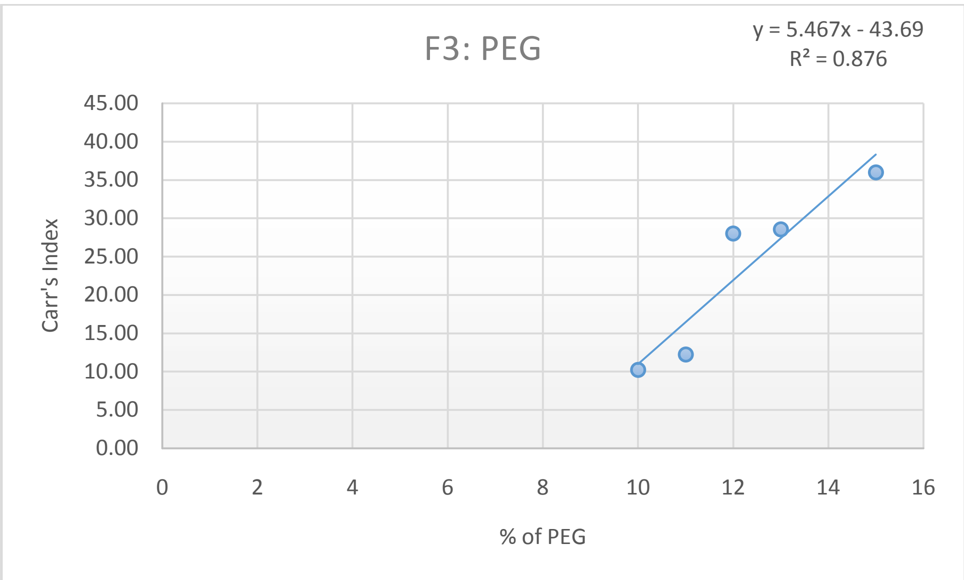

Figure 4.22: **Scatter chart of Carr's Index for different percentages of PEG**

By plotting Hausner Ratio against the percentages of PEG a straight line was obtained and the following equation was derived.

$$y = 0.0946x + 0.167 \text{ and } R^2 = 0.9124$$

Here, y denotes Hausner Ratio and x denotes the percentage of PEG.

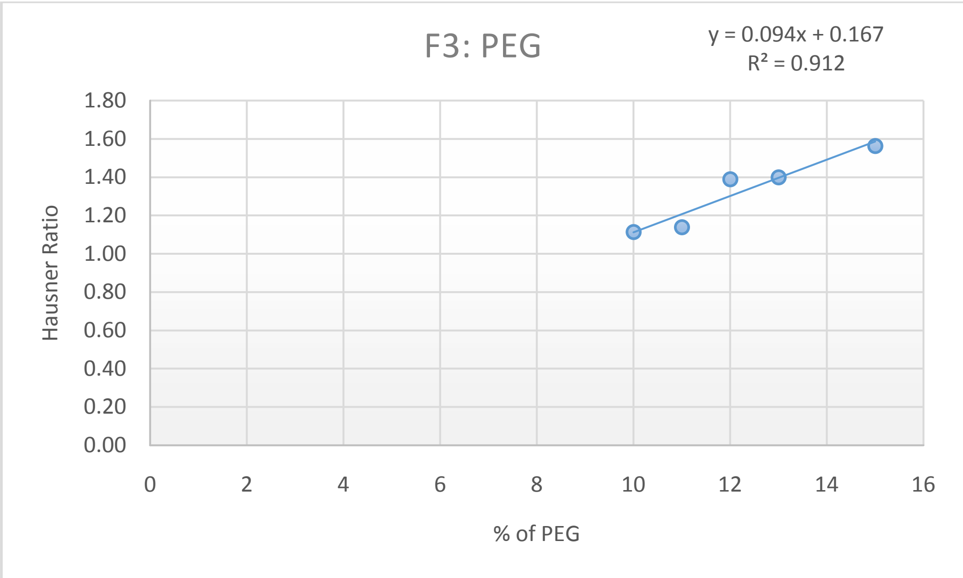

Figure 4.23: **Scatter chart of Hausner Ratio for different percentages of PEG**

Angle of Repose ratio was calculated for powder mixtures at different ratio of F3 and PEG in the table below.

Table 4.16: **Angle of Repose for different mixtures of F3 and PEG**

F3 (%)	**PEG (%)**	**Diameter**	**Average Diameter (d)**	**Radius (r)**	**Height**	**Average Height (h)**	**Angle of Repose**
90	10	3.8	3.8	1.9	1.5	1.4	36.15
		3.8			1.4		
		3.9			1.3		
89	11	4	4.0	2.0	1.5	1.5	36.25
		4			1.4		
		4			1.5		

88	12	4.2	4.2	2.1	1.6	1.6	37.52
		4.1			1.6		
		4.2			1.6		
87	13	4.2	4.3	2.1	1.6	1.6	37.44
		4.3			1.7		
		4.3			1.6		
85	15	4.4	4.5	2.2	1.7	1.7	37.82
		4.5			1.7		
		4.5			1.8		

From table 4.16, we got Angle of repose for different percentages of PEG used in the mixture. By plotting Angle of repose against the percentages of PEG, a straight line was obtained and the following equation was derived.

$$y = 0.3584x + 32.663 \text{ and } R^2 = 0.7881$$

Here, y denotes Angle of repose and x denotes the percentage of PEG.

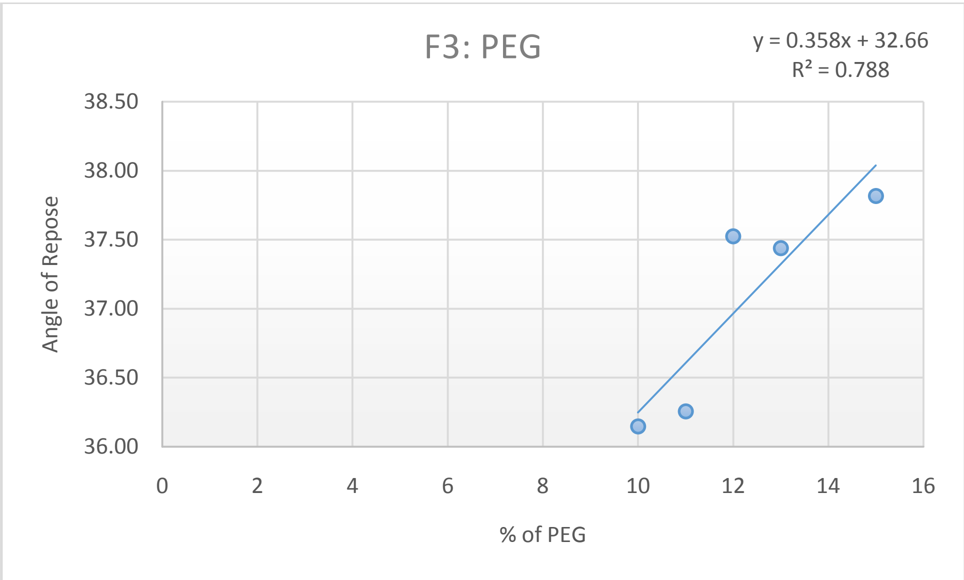

Figure 4.24: **Scatter chart of Angle of Repose for different percentages of PEG**

4.9 F4: Lactose

We experimented on the mixture of F4 and lactose at different intervals. Lactose is usually used 5-25% w/w as a binder. Carr's index and Hausner ratio was calculated for powder mixtures at different ratio of F4 and Lactose in the table below.

Table 4.17: **Carr's index and Hausner Ratio for different mixtures of F4 and Lactose**

F4 (%)	Lactose (%)	Bulk Volume	Average Bulk Volume (V0)	Tapped Volume	Average Tapped Volume (Vf)	Carr's Index	Hausner Ratio
95	5	8	8.2	6.5	6.2	24.49	1.32
		8		6			
		8.5		6			
90	10	8.5	8.7	6.5	6.3	26.92	1.37
		9		6.5			
		8.5		6			
85	15	9	9.0	6.5	6.5	27.78	1.38
		9		6.5			
		9		6.5			
80	20	9	9.3	6	6.2	33.93	1.51
		9.5		6			
		9.5		6.5			
75	25	10	9.8	6	6.2	37.29	1.59
		9.5		6			
		10		6.5			

From table 4.17, we got Carr's index and Hausner ratio for different percentages of lactose used in the mixture. By plotting Carr's index against the percentages of lactose a straight line was obtained and the following equation was derived.

$$y = 0.652x + 20.301 \text{ and } R^2 = 0.9383$$

Here, y denotes Carr's index and x denotes the percentage of lactose.

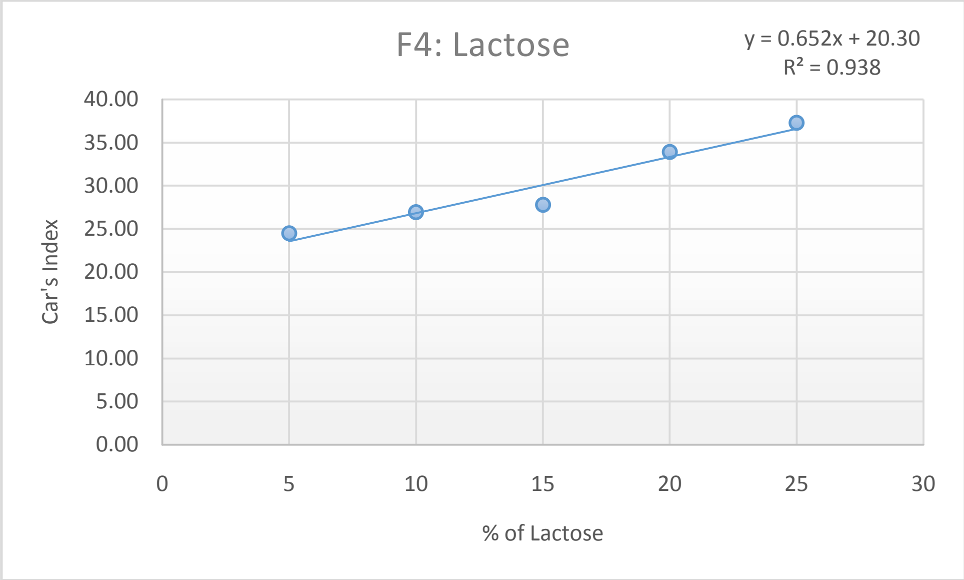

Figure 4.25: **Scatter chart of Carr's Index for different percentages of Lactose**

By plotting Hausner Ratio against the percentages of lactose a straight line was obtained and the following equation was derived.

$$y = 0.0137x + 1.2314 \text{ and } R^2 = 0.9248$$

Here, y denotes Hausner Ratio and x denotes the percentage of lactose.

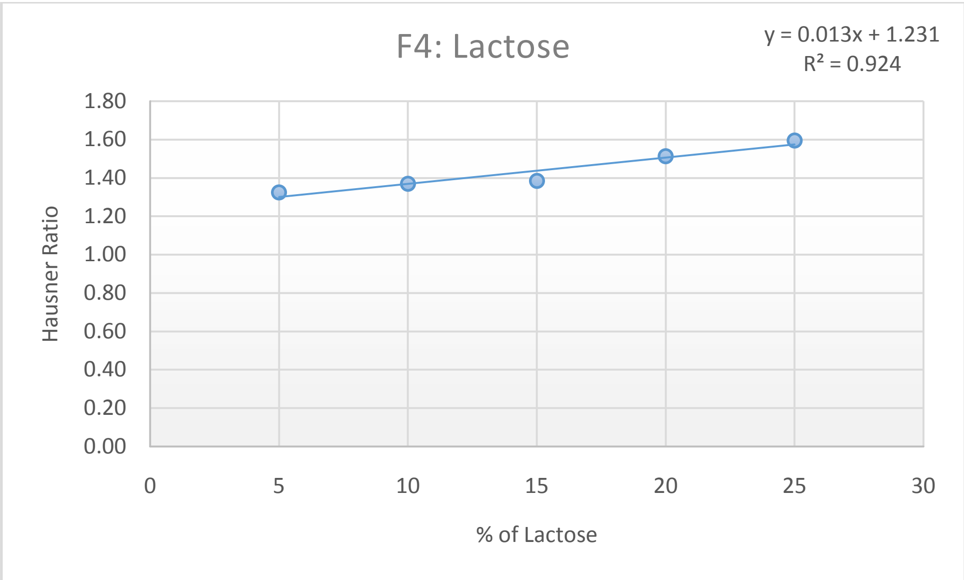

Figure 4.26: **Scatter chart of Hausner Ratio for different percentages of Lactose**

Angle of Repose was calculated for powder mixtures at different ratio of F4 and Lactose in the table below.

***Table 4.18:*Angle of Repose for different mixtures of F4 and Lactose**

F4 (%)	Lactose (%)	Diameter	Average Diameter (d)	Radius (r)	Height	Average Height (h)	Angle of Repose
95	5	4.5	4.5	2.2	1.6	1.6	35.62
		4.4			1.6		
		4.5			1.6		
90	10	4.4	4.4	2.2	1.6	1.7	37.36
		4.3			1.7		
		4.4			1.7		
85	15	4.3	4.3	2.2	1.8	1.7	38.88
		4.3			1.7		
		4.3			1.7		
80	20	4.2	4.2	2.1	1.9	1.8	40.90
		4.2			1.8		
		4.3			1.8		
75	25	4.1	4.1	2.1	1.9	1.9	42.59
		4.2			1.9		
		4.1			1.9		

From table 4.18, we got Angle of repose for different percentages of lactose used in the mixture. By plotting Angle of repose against the percentages of lactose, a straight line was obtained and the following equation was derived.

$$y = 0.3498x + 33.821 \text{ and } R^2 = 0.9984$$

Here, y denotes Angle of repose and x denotes the percentage of lactose.

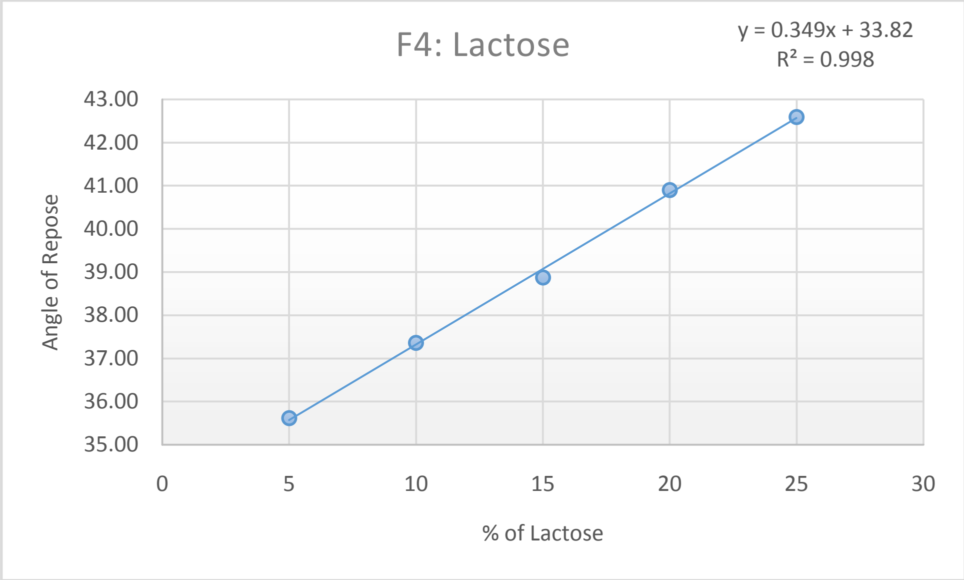

Figure 4.27: **Scatter chart of Angle of Repose for different percentages of Lactose**

4.10 F4: Starch

We experimented on the mixture of F4 and starch at different intervals. Starch is usually used 5-25% w/w as a binder. Carr's index and Hausner ratio was calculated for powder mixtures at different ratio of F4 and Starch in the table below.

Table 4.19: **Carr's index and Hausner Ratio for different mixtures of F4 and Starch**

F4 (%)	Starch (%)	Bulk Volume	Average Bulk Volume (V0)	Tapped Volume	Average Tapped Volume (Vf)	Carr's Index	Hausner Ratio
95	5	6.5	6.7	5.5	5.7	15.00	1.18
		7		6			
		6.5		5.5			
90	10	7	6.8	6	5.8	14.63	1.17
		7		5.5			
		6.5		6			
85	15	7.5	7.3	6.5	6.2	15.91	1.19
		7.5		6			

		7		6			
80	20	8	8.2	6	6.3	22.45	1.29
		8		6.5			
		8.5		6.5			
75	25	9	9.0	6.5	6.3	29.63	1.42
		9		6			
		9		6.5			

From table 4.19, we got Carr's index and Hausner ratio for different percentages of starch used in the mixture. By plotting Carr's index against the percentages of starch a straight line was obtained and the following equation was derived.

$$y = 0.7415x + 8.4021 \text{ and } R^2 = 0.8175$$

Here, y denotes Carr's index and x denotes the percentage of starch.

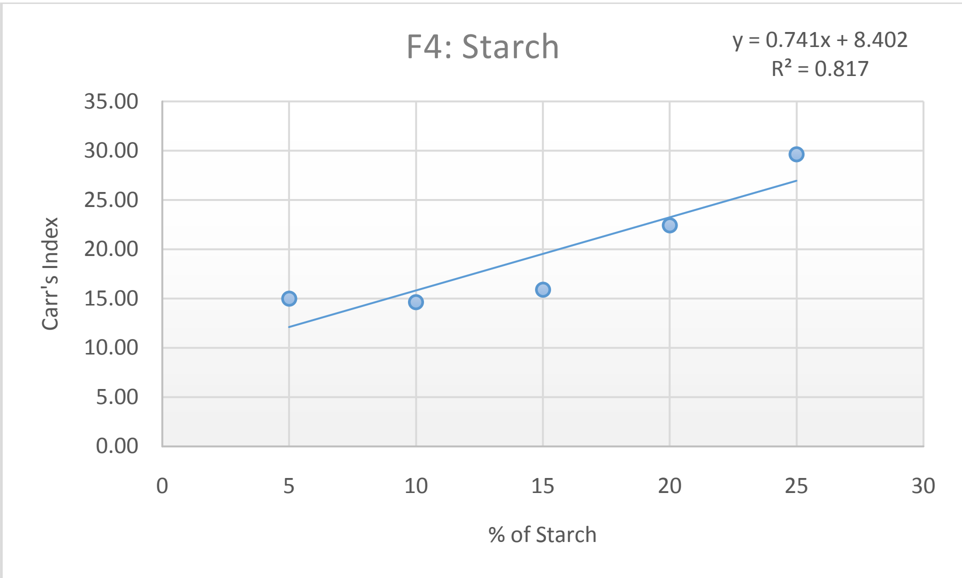

Figure 4.28: **Scatter chart of Carr's Index for different percentages of Starch**

By plotting Hausner Ratio against the percentages of starch a straight line was obtained and the following equation was derived.

$$y = 0.0121x + 1.0674 \text{ and } R^2 = 0.7999$$

Here, y denotes Hausner Ratio and x denotes the percentage of starch.

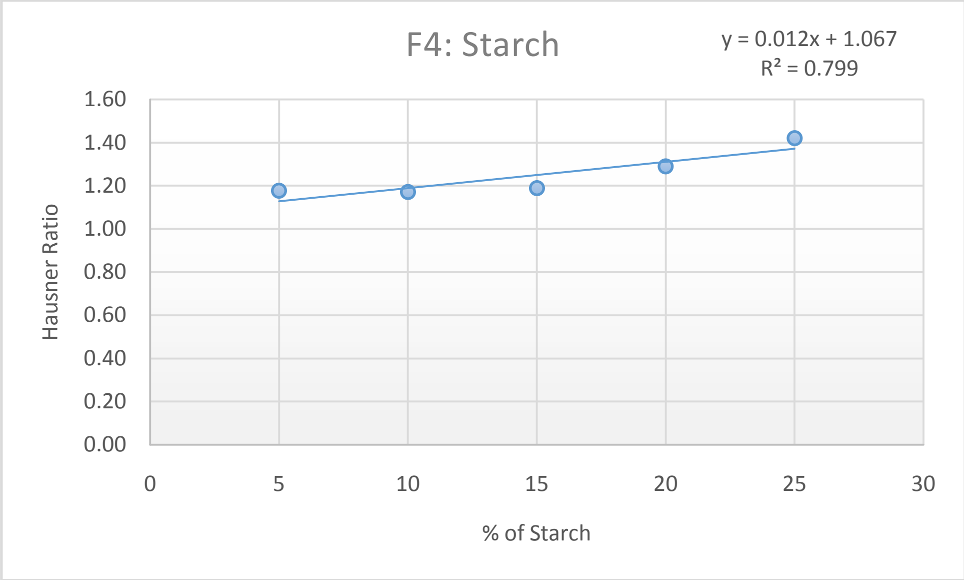

Figure 4.29: **Scatter chart of Hausner Ratio for different percentages of Starch**

Angle of Repose was calculated for powder mixtures at different ratio of F4 and Starch in the table below.

Table 4.20:**Angle of Repose for different mixtures of F4 and Starch**

F4 (%)	**Starch (%)**	**Diameter**	**Average Diameter (d)**	**Radius (r)**	**Height**	**Average Height (h)**	**Angle of Repose**
95	5	4.5	4.5	2.3	1.4	1.4	31.27
		4.4			1.3		
		4.6			1.4		
90	10	4.2	4.3	2.2	1.5	1.5	35.50
		4.3			1.5		
		4.4			1.6		
85	15	4.1	4.1	2.1	1.6	1.6	38.32
		4.2			1.7		
		4.1			1.6		
80	20	4	4.0	2.0	1.6	1.6	39.24
		4			1.7		
		4			1.6		
75	25	3.8	3.8	1.9	1.7	1.7	41.57

		3.8			1.7		
		3.9			1.7		

From table 4.20, we got Angle of repose for different percentages of starch used in the mixture. By plotting Angle of repose against the percentages of starch, a straight line was obtained and the following equation was derived.

$$y = 0.4867x + 29.879 \text{ and } R^2 = 0.9471$$

Here, y denotes Angle of repose and x denotes the percentage of starch.

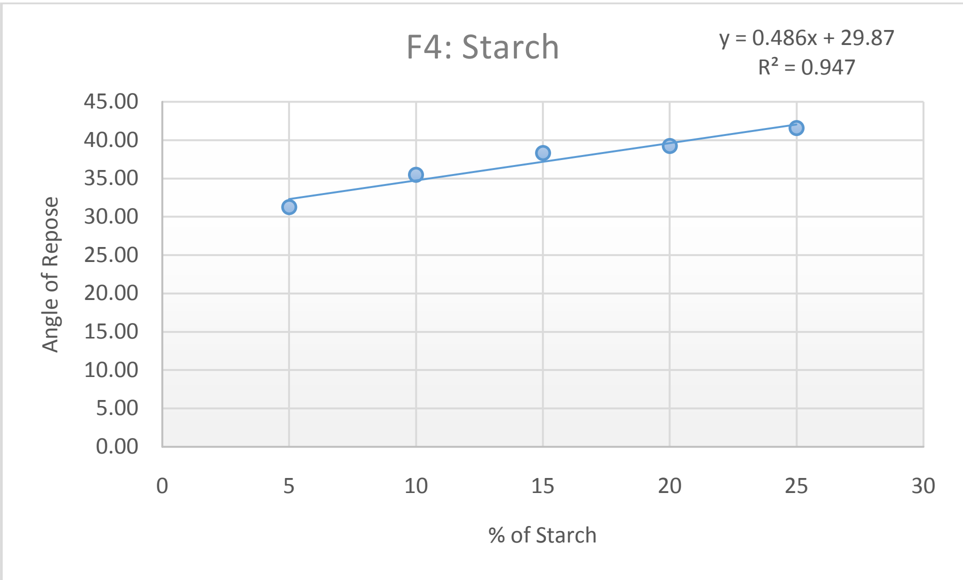

Figure 4.30: **Scatter chart of Angle of Repose for different percentages of Starch**

CHAPTER FIVE

DISCUSSION

5.1 Discussion

This experiment was done to isolate several equation of some pharmaceutical binders which helps to determine the flow property of the powder mixture. At what percentage the flow property will be maximum can be determined by those equations.

***Table 5.1*: Carr's Index Equations and best percentages with flow property**

Mixture				**Flow**
Formulation	**Binder**	**Equation and Regression value**	**Best % of Binder**	**property According to USP29**
F1	Starch	y = 0.4139x + 20.692 and R^2 = 0.8387	5	Good
F1	Lactose	y = -0.2513x + 43.721 and R^2 = 0.8543	25	Very Poor
F2	PVP	y = 4.2584x + 27.997 and R^2 = 0.9866	0.5	Very Poor
F2	HPMC	y = -2.9141x + 45.676 and R^2 = 0.8867	5	Very Poor
F2	PEG	y = 3.2649x + 0.613 and R^2 = 0.9259	10	Poor
F3	PVP	y = 4.3167x + 7.5223 and R^2 = 0.9422	0.5	Good
F3	HPMC	y = 5.2817x + 4.4425 and R^2 = 0.9621	2	Good
F3	PEG	y = 5.4672x - 43.696 and R^2 = 0.8769	10	Excellent
F4	Lactose	y = 0.652x + 20.301 and R^2 = 0.9383	5	Passable
F4	Starch	y = 0.7415x + 8.4021 and R^2 = 0.8175	5	Good

Here, 'y' denotes Carr's Index and 'x' denotes the percentage of binders. Starch is usually used 5-25% w/w as a binder. According to Carr's index Chard described in USP29-1174, flow of a powder mixture can be described. Here, in this experiment we considered USP29-1174 as a reference. When 5% starch was used, there was a good flow of powders. Lactose is usually used 5-25% w/w as a binder. When 25% lactose was used, there was a very poor flow of powders. PVP is usually used 0.5-5% w/w as a binder. Using 0.5% PVP as a binder gave a very poor flow of powders. HPMC is usually used 2-5% w/w as a binder. When 5% HPMC was used, there was powder flow better than that of others. PEG is usually used 10-15% w/w as a binder. When 10% PEG was used, there was a poor flow of powders. PVP is usually used 0.5-5% w/w as a binder. When 0.5% PVP was used, there was a good flow of powders and better than that of others. HPMC is usually used 2-5% w/w as a binder. Using 2% HPMC gave a good flow of powders. PEG is usually used 10-15% w/w as a binder. When 10% PEG was used, there was an excellent flow of powders and better than that of any others percentages. Lactose is usually used 5-25% w/w as a binder. Using 5% lactose gave a passable flow of powders. Starch is usually used 5-25% w/w as a binder. When 5% starch was used, there was a good flow of powders and better than that of others.

***Table 5.2*: Hausner Ratio Equations and best percentages with flow property**

Mixture				**Flow**
Formulation	**Binder**	**Equation and Regression value**	**Best % of Binder**	**property According to USP29**
F1	Starch	y = 0.0079x + 1.252 and R^2 = 0.8235	5	Good
F1	Lactose	y = -0.0071x + 1.774 and R^2 = 0.8369	25	Very Poor
F2	PVP	y = 0.1219x + 1.3446 and R^2 = 0.9617	0.5	Very Poor
F2	HPMC	y = -0.0708x + 1.8021 and R^2 = 0.8796	5	Very Poor
F2	PEG	y = 0.0949x + 0.5379 and R^2 = 0.9535	10	Poor
F3	PVP	y = 0.0699x + 1.058 and R^2 = 0.9003	0.5	Good
F3	HPMC	y = 0.0894x + 0.9925 and R^2 = 0.9622	2	Good
F3	PEG	y = 0.0946x + 0.167 and R^2 = 0.9124	10	Excellent
F4	Lactose	y = 0.0137x + 1.2314 and R^2 = 0.9248	5	Passable
F4	Starch	y = 0.0121x + 1.0674 and R^2 = 0.7999	5	Good

Here, ‘y’ denotes Hausner Ratio and ‘x’ denotes the percentage of binders. According to the Hausner Ratio, USP29-1174, when 25% lactose was used, the flow property was very very poor and better than that of other percentages. Using 0.5% PVP gave a very poor flow of powders. When 5% HPMC was used, the flow property was very poor and better than that of other percentages. Using 10% PEG gave a poor powder flow. When 0.5% PVP was used, the flow property was good. When 2% HPMC was used, the flow property was better than that of other percentages. Using 10% PEG gave an excellent flow of powder. When 5% lactose was used, the flow property was passable. When 5% starch was used, the flow property was good and better than that of other percentages.

***Table 5.3*: Angle of Repose Equations and best percentages with flow property**

Mixture		**Equation and Regression value**	**Best % of Binder**	**Flow property According to USP29**
Formulation	**Binder**			
F1	Starch	$y = -0.463x + 43.207$ and $R^2 = 0.8378$	25	Passable
F1	Lactose	$y = -0.2416x + 48.382$ and $R^2 = 0.8273$	25	Very Very Poor
F2	PVP	$y = 2.5837x + 29.024$ and $R^2 = 0.9706$	0.5	Passable
F2	HPMC	$y = 3.1854x + 31.288$ and $R^2 = 0.885$	2	Passable
F2	PEG	$y = 2.1172x + 17.65$ and $R^2 = 0.8237$	10	Passable
F3	PVP	$y = -1.9085x + 37.437$ and $R^2 = 0.9831$	5	Good
F3	HPMC	$y = -4.4519x + 48.697$ and $R^2 = 0.9761$	5	Good
F3	PEG	$y = 0.3584x + 32.663$ and $R^2 = 0.7881$	10	Very Poor
F4	Lactose	$y = 0.3498x + 33.821$ and $R^2 = 0.9984$	5	Good
F4	Starch	$y = 0.4867x + 29.879$ and $R^2 = 0.9471$	5	Passable

Here, 'y' denotes Angle of repose and 'x' denotes the percentage of binders. According to the Angle of repose, USP29-1174, when 25% starch was used, the flow property was passable and better than that of other percentages. Using 25% lactose gave a very very poor flow of powder mixture. When 0.5% PVP was used, the flow property was passable and better than that of other percentages. When 2% HPMC was used, the flow property was passable and better than that of other percentages. Using 10% PEG gave a passable flow of powder. When 5% PVP was used, the flow property was good and better than that of other percentages. Using 5% HPMC gave a good flow of powder. When 10% PEG was used, the flow property was very poor and better than that of other percentages. Using 5% lactose gave a passable flow of powder. When 5% starch was used, the flow property was passable but better than that of other percentages.

CHAPTER SIX

CONCLUSION

6.1 Conclusion

Flow property of pharmaceutical solid dosage forms has particular interest from the pharmaceutical industries. Improved or faster flowability will increase the production of solid dosage forms. As excipients are used as a major portion of a solid dosage form, its flow property is of particular interest. This experiment was done to isolate several equation of some pharmaceutical binders. These equations will help the future researchers and pharmaceutical personnel to predict and determine the flowability of mixtures for adding the above mentioned binders. This research will not only help to save money but also to save time for further research projects on powder mixture flow property and new formulation determination.

CHAPTER SEVEN

REFERENCE

7.1 Reference

Abdullah, E. C. and Geldart, D., 1999. The use of bulk density measurements as flowability indicators, *Science Direct*, [online] Available at: http://www.sciencedirect.com/science/article/pii/S0032591098002083. [Accessed 11 February 2013].

Albert, C. and Briens, L., 2013. The Effect of Moisture on the Flowability, *Pub Med*, [online] Available at: http://www.ncbi.nlm.nih.gov/pubmed/24092523. [Accessed 15 March 2013].

Bagster, D.F. and Crooks, M. J., 2006. An Error Occurred Setting Your User Cookie, *Informa Health Care*, [online] Available at: http://informahealthcare.com/doi/abs/10.3109/03639047709055626. [Accessed 15 March 2013].

Crouter, A. and Timothy, L., 2013. The Effect of Moisture on the Flowability of Pharmaceutical Excipients, *Pharma Gate Way*, [online] Available at: http://www.pharmagateway.net/ArticlePage.aspx?doi=10.1208/s12249-013-0036-0. [Accessed 15 March 2013].

Emerya, E., Olivera, J., Pugsleya, T., Sharmab, T. and Zhou, J., 2009. Flowability of moist pharmaceutical powders. *Science Direct*, [online] Available at: http://www.sciencedirect.com/science/article/pii/S0032591008003562. [Accessed 11 February 2013].

Garett, M. and Lauren, B., 2013. The Effect of Lubricants on Powder Flowability for Pharmaceutical Application, *Pharma Gate Way*, [online] Available at: http://www.pharmagateway.net/ArticlePage.aspx?doi=10.1208/s12249-013-0007-5. [Accessed 15 February 2013].

Geldart, D., 2004. Particle & Particle Systems Characterization, *Wiley Online Library*, [online] Available at: http://onlinelibrary.wiley.com/doi/10.1002/ppsc.19960130408/abstract. [Accessed 11 February 2013].

Gold, G., Ronald, N. D., Blaze, T. P. and James, G. S., 1996. Powder flow studies II. Effect of glidants on flow rate and angle of repose, *Wiley Online Library*, [online] Available at: http://onlinelibrary.wiley.com/doi/10.1002/jps.2600551125/abstract. [Accessed 15 March 2013].

Hassan, M.S. and Raymond, W. L., 2009. Effect of Particle Shape on Dry Particle Inhalation: Study of Flowability, Aerosolization, and Deposition Properties, *Pharma Gate Way*, [online] Available at: http://www.pharmagateway.net/ArticlePage.aspx?doi=10.1208/s12249-009-9313-3. [Accessed 15 February 2013].

Morin, G. and Briens, L, 2013. The effect of lubricants on powder flowability, *PubMed*, [online] Available at: http://www.ncbi.nlm.nih.gov/pubmed/23897035. [Accessed 15 March 2013].

Nelson, E. 1995. Measurement of the repose angle of a tablet granulation, Journal of the American Pharmaceutical Association. *Wiley Online Library,* [online] Available at: http://onlinelibrary.wiley.com/doi/10.1002/jps.3030440714/abstract?deniedAccessCustomisedMessage=&userIsAuthenticated=false. [Accessed 11 February 2013].

Patel, R. and Podczeck, F., 1996. Investigation of the effect of type and source of microcrystalline cellulose on capsule filling, *Science Direct*, [online] Available at:http://www.sciencedirect.com/science/article/pii/0378517395042318. [Accessed 15 March 2013].

Podczeck, F. and Newton, J.M., 2000. Powder and capsule filling properties of lubricated granulated cellulose powder, *Science Direct*, [online] Available at: http://www.sciencedirect.com/science/article/pii/S0939641100001004. [Accessed 15 February 2013].

Rowe, R. C., Sheskey, P. J. and Quinn, M. E., 2009. *TheHand book of Pharmaceutical Excipients.* 7th ed. London: Pharmaceutical Press.

Shah, R. B., Tawakkul, M. A. and Khan,M. A., 2008. Comparative Evaluation of Flow for Pharmaceutical Powders and Granules, *Springer Link*, [online] Available at: http://link.springer.com/article/10.1208%2Fs12249-008-9046-8. [Accessed 11 February 2013].

Silva, J. P. S., Splendor, D., Gonçalves, I. M. B., Costa P. and Lobo J. M. S., 2013. Note on the Measurement of Bulk Density and Tapped Density of Powders According to the European Pharmacopeia. *Pharma Gate Way*, [online] Available at: http://www.pharmagateway.net/ArticlePage.aspx?doi=10.1208/s12249-013-9994-5. [Accessed 11 February 2013].

Tan, S.B. and Newton, J.M., 1990. Powder flowability as an indication of capsule filling performance, *Science Direct*, [online] Available at: http://www.sciencedirect.com/science/article/pii/0378517390900537. [Accessed 15 February 2013].

Tawakkul, M. A., Shah, R. B. and Khan, M. A., 2008. Comparative Evaluation of Flow for Pharmaceutical Powders and Granules, *Pharma Gate Way*, [ONLINE] Available at: http://www.pharmagateway.net/ArticlePage.aspx?doi=10.1208/s12249-008-9046-8. [Accessed 15 February 2013].

Taylor, M. K., Ginsburg, J., Hickey A.J. and Gheyas F., 2000. Composite method to quantify powder flow as a screening method in early tablet or capsule formulation development, *Pharma Gateway*, [online] Available at: http://www.pharmagateway.net/ArticlePage.aspx?doi=10.1208/pt010318. [Accessed 11 February 2013].

Thalberg, K., Lindholm, D. and Axelsson, A., 2004. Comparison of different flowability tests for powders for inhalation, Lund University Publications, [online] Available at: https://lup.lub.lu.se/search/publication/3918133. [Accessed 15 March 2013].

Trainaa, K. Clootsb, R., Bontempia, S., Lumayc, G., Vandewallec, N. and Boschini F., 2013. Flow abilities of powders and granular materials evidenced from dynamical tap density measurement, *Science Direct*, [online] Available at: http://www.sciencedirect.com/science/article/pii/S0032591012007887. [Accessed 11 February 2013].

U.S. Pharmacopeial Convention, 2013. USP29-NF24 1174. Powder Flow. Maryland: UPC. [online] Available at: http://www.pharmacopeia.cn/v29240/usp29nf24s0_c1174.html. [Accessed 15 February 2013].

Wong, A. C., 2002. Use of angle of repose and bulk densities for powder characterization and the prediction of minimum fluidization and minimum bubbling velocities, *Science Direct*, [online] Available at: http://www.sciencedirect.com/science/article/pii/S0009250902001501. [Accessed 11 February 2013].

Wouters, M. F. and Geldart, P.D., 1996. Characterising Semi-Cohesive Powders using angle of repose, *Science Direct*, [online] Available at: http://onlinelibrary.wiley.com/doi/10.1002/ppsc.19960130407/abstract. [Accessed 11 February 2013].

Yang, J., Ales Sliva, A., Amit Banerjee, A. and Dave, R. N., 2005. Dry particle coating for improving the flowability of cohesive powders, *Science Direct*, [online] Available at: http://www.sciencedirect.com/science/article/pii/S0032591005001531. [Accessed 15 March 2013].

Zhang, Y., Law, Y. and Chakrabarti, S., 2003. Physical properties and compact analysis of commonly used direct compression binders, *Pharma Gate Way*, [online] Available at: http://www.pharmagateway.net/ArticlePage.aspx?doi=10.1208/pt040462. [Accessed 15 March 2013].