Determination of Variation in Flow Property of Different Sets of PVP along with Amlodipine and Propranolol

Submitted by

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

Bachelor of Pharmacy

Under The Guidance of

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January, 2016

DECLARATION BY THE RESEARCH CANDIDATE

I, Mehedi Hasan Munna, hereby declare that the dissertation entitled "Determination of Variation in Flow Property of Different Sets of PVP along with Amlodipine and Propranolol" 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 record of original research work carried out by me during 2015 (January —December) under the supervision and guidance of Md. Anisur Rahman, Senior Lecturer Dept. of Pharmacy, East West University.

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CERTIFICATE BY THE SUPERVISOR

This is to certify that the dissertation " Determination of Variation in Flow Property of Different Sets of PVP along with Amlodipine and Propranolol" submitted to the department of pharmacy, East West University was carried out by Mehedi Hasan Munna (ID: 2012-3-70-012) in partial fulfillment of the requirements of the degree of Bachelor of Pharmacy.

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DEDICATION

This Research Paper Is Dedicated to

My Late Father

ABSTRACT

Flow property is very important in the pharmaceutical industry for the manufacturing process such as blending, tablet compression, capsule filling, transportation, and in scale-up operation. The purpose of this research work was to find out the ratio of pharmaceutical excipients in a mixture that will provide different types of desired flow property. We measured several parameters, such as, bulk volume, tapped volume, Carr's index, Hausner's ratio and angle of repose for different mixture of same pharmaceutical excipients. We did this for different ratios of PVP to determine different equations. We evaluated the laboratory experimental data to determine several specific equations (y= mx + c) for particular mixtures of specific pharmaceutical excipients. For a new solid drug formulations flow property of pharmaceutical excipients can be predicted and measured by these equations.

Keywords: PVP, Flowability, Bulk Volume, Tapped Volume, Carr's index, Hausner ratio and Angle of Repose.

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Chapter-I

Introduction

1.1 INTRODUCTION

The aim of this research project was to determine the flow characteristics of Polyvinyl Pyrrolidone (PVP) used in different ratio in pharmaceutical preparation. In this research PVP was mixed with mixture of exicipients in variying ratio and different formulation were made. After that active pharmaceutical ingredient was added to these mixture and flow characteristics of different formulations were observed and measured using different parameters such as angle of repose, Carr's index or Hausner ratio.

Particle size and size distribution is one of the main factors that has vast impacts on the flow ability of powder during handling, processing and tableting. For efficient and effective transport, storage and handling of powder in the industries flow ability is a vital parameter. It is the ability of the powder to flow in desired manner in a given processing or handling piece of equipment. Flow ability affects the design and processing of powder in handling equipment such as hoppers, silos, filling and packaging operations, conveying, etc. Sticking or caking during storage, prone to cohesion, ratholing, arching, poor content uniformity and poor solubility can be caused by poor flow ability. (Hart, 2015)

Because powders exhibit properties similar to both solids and liquids powder handling and processing tends to be problematic. The way of the powder behaves can be affected by surrounded air and degree of aeration. The common manufacturing problems of powder flow, includes non-uniformity (segregation) in blending, under- or over-dosage, inaccurate filling, obstructions and stoppages. These can resulted in rejected material, machine downtime and defective end-products. By common powder flow problems storage, handling, production, packing, distribution and end use can all be negatively affected. (Young, 2015)

The powder flow determining parameter, angle of repose is measured by using a funnel attached with a stand. The individual powder excipients or mixture of powder excipients are freely passed over the funnel onto a horizontal surface and the angle of the resulting pyramid are measured. Following this we used a equation to determine the value of angle of repose which indicates the respective flow characteristics of individual powder excipient or mixture of powder excipients. (Young, 2015)

Hausner Ratio and Carr's Index:

Into a graduated glass cylinder a volume of powder is filled and repeatedly tapped for a specific time. After tapping the volume of powder is measured and by using a equation the Hausner Ratio or the Carr's Index (%) are measured. High Hausner Ratio and Carr's Index are yield by cohesive powders. (Young, 2015)

In this research the flow characteristics of the excipients mixture with varying amount of PVP was determined. In a solid dosage form like tablets, capsules manufacturing process single exicipients is not used alone. Different classes of excipients mixture is used in manufacturing process. So it is important to determine the changes in flow characteristics of different exicipents mixture containing varying amount of PVP. So we can easily determine how much PVP should be used into an excipients mixture to get best flow property of the mixture.

1.2 PHARMACEUTICAL EXCIPIENTS

1.2.1 Definition

The word excipient is derived from the Latin excipere, meaning 'to except', which is simply explained as 'other than'. Pharmaceutical excipients are basically everything other than the active pharmaceutical ingredient. Ideally, excipients should be inert, however, recent reports of adverse reactions have suggested otherwise. (Haywood and Glass, 2011)

1.2.2 Function of excipients

The best new therapeutic entity in the world is of little value without an appropriate delivery system.today, medicines are available in many dosage forms including tablets, capsules, oral liquids, topical creams and gels, transdermal patches, injectable products, implants, eye products, nasal products, inhalers and suppositories. Pharmaceutical excipients are substances that are included in a pharmaceutical dosage form not for their direct therapeutic action, but to aid the manufacturing process, to protect, support or enhance stability, or for bioavailability or patient acceptability. They may also assist in product identification and enhance the overall safety or function of the product during storage or use.

Thousands of different excipients are used in medicines and make up, on average, about 90% of each product. They represent a market value of €3 billion (almost $4 billion) accounting for 0.5% of the total pharmaceutical market according to industry experts. (Haywood and Glass, 2011)

1.2.3 Types (Haywood and Glass, 2011)

Common excipients used in pharmaceutical industries are_

- Fillers and Diluents
- Binders and Adhesives
- Glidants
- Lubricants
- Antiadherents
- Disintegrants
- Coatings
- Flavours
- Sweeteners
- Preservatives
- Sorbents

1.2.3.1 Diluents

Diluent/filler for tablet must meet the following criteria. They are as follows:

- Diluent should not react with the drug substance and moreover it should not have any effect on the functions of other excipients
- It should preferably be colourless or nearly so.
- It should not have any physiological or pharmacological activity of its own
- It should have consistent physical and chemical characteristics
- It should neither promote nor contribute to segregation of the granulation or powder blend to which they are added
- It should neither support microbiological growth in the dosage form nor contribute to any microbiological load

- It should neither adversely affect the dissolution of the product nor interfere with the bioavailability of active pharmaceutical ingredient
- It should be able to be milled (size reduced) if necessary in order to match the particle size distribution of the active pharmaceutical ingredient. (Patel, Shah and Upadhyay, 2015)

1.2.3.1.1 Classification of Tablet Diluents/Filler (Patel, Shah and Upadhyay, 2015)

Tablet diluents or fillers can be divided into three categories.

- **Organic materials**:

  Carbohydrate and modified carbohydrates:

  A-lactose monohydrate, spray dried lactose and anhydrous lactose

  Starch and Pregelatinized starch.

  Sucrose, Manitol, Sorbitol.

  Powdered Cellulose, Microcrystalline Cellulose.

- **Inorganic materials:**

  Calcium phosphates : Anhydrous Dibasic Calcium Phosphate, Dibasic Calcium

  Phosphate, Tribasic Calcium Phosphate.

- **Co-processed Diluents:**

  Carbohydrate substances such as sugars, starches and celluloses may also function as binders during wet granulation process. When used in direct compression system, they serve as diluent. The inorganic diluents, do not exhibit binding properties when used in wet granulation and direct compression.

1.2.3.1.2 Classification of Diluents (Gohel, 2015)

Table-1: Classifications of diluents based on solubility (Gohel, 2015)

Insoluble Tablet Filler or Diluents	Soluble Tablet Filler or Diluent
Starch	Lactose
Powdered Cellulose	Sucrose
Microcrystalline Cellulose	Manitol
Calcium Phosphate	Sorbitol

Selection of diluent should be done after considering properties of diluent such as:

- Compactibility
- Hygroscopicity
- Flow ability
- Solubility
- Stability
- Disintegration qualities
- Lubricity

1.2.3.2 Binders (Gohel, 2015)

Binders are agents employed to impart cohesiveness to the granules. This ensures the tablet remains intact after compression. The development of new excipients for potential use as binding agent in tablet formulations continues to be of interest. This is because different binding agents can be useful in achieving various tablet mechanical strength and drug release properties for different pharmaceutical purpose. Natural polysaccharides are widely used in the pharmaceutical and food industry as excipients and additives due to their low toxicity, biodegradable, availability and low cost. Natural binders like different starches, gums, mucilage dried fruits

possess binding capacity as well as some other properties like disintegrant, filler, sustain release, and these natural polymers are much safer and economical than polymers like PVP. Different starches like rice, potato, maize, corn, wheat, tapioca starch and gums like ferula gummosa boiss, gum olibanum, beilschmiedia seed gum, okro gum, aegle marmelod gum, gum cordial, okra gum and cassia roxburghii seeds gum and plant fruit like date palm fruit and orange peel pectin shows good potency as a binding agent.

1.2.3.2.1 Types of Binders (Gohel, 2015)

1.2.3.2.1.1 Classification on the basis of their source

- **Natural polymers:** starch, pregelatinized starch, gelatin, acacia, tragacanth and gums.
- **Synthetic polymer:** PVC, HPMC, methyl cellulose, ethyl cellulose, PEG.
- **Sugar:** glucose, sucrose, sorbitol.

1.2.3.2.1.2 Classification on the basis of their application

- **Solution binders:** 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, polyvinyl pyrrolidone, starch, sucrose and polyethylene glycol.
- **Dry binders:** Dry binders are added to the powder blend, either after a wet granulation step, or as part of a direct powder compression (DC) formula. Examples include cellulose, methyl cellulose, polyvinylpyrrolidone, and polyethylene glycol.

1.2.3.2.2 Advantages of Natural binder (Gohel, 2015)

- Natural polysaccharides are widely used in the pharmaceutical and food industry as excipients and additives due to their low toxicity, biodegradable, availability and low cost.
- They can also be used to modify the release of drug, thereby, influencing the absorption and subsequent bioavailability of the incorporated drug.
- They act as vehicles which transport the incorporated drug to the site of absorption and are expected to guarantee the stability of the incorporated drug, the precision and accuracy of the dosage, and also improve the organoleptic properties of the drugs where necessary in order to enhance patient adherence .

- They should optimize the performances of dosage forms during manufacturing as well as when patients ingest them.

1.2.3.2.3 Disadvantage of Polymer binders

- Polymer binders can lead to processing difficulties such as rapid over granulation. Over time they occasionally lead to tablet hardening and a decrease in dissolution performance.
- When polymer binders are chosen, the addition of strong disintegrants such as super disintegrants is typically required but these are considerably expensive and have a negative effect on product stability as well as film coating appearance of the finished products. (Gohel, 2015)

1.2.3.3 Glidants

To improve the flow properties of the formulation glidants are added which is to be fed into the die cavity and aid in particle rearrangement within the die during the early stages of compression. Glidants are ineffective and consideration of force free mechanisms may be necessary if the flow properties are extremely poor. Starch is a popular glidant because it has additional value of disintegrant. Concentration of starch is common up to 10%, but should be limited otherwise it will worsen the flow of material. Talc concentration should be limited because it has retardant effect on dissolution-disintegration profile. It is superior to starch. Silaceous material like colloidal silica i.e. syloid, pyrogenic silica (0.25%), hydrated sodium silioaluminate (0.75%) are also successfully used to induce flow.

Glidants functions by interposing their particles between those of material and lower the overall interparticulate friction of the system by virtue of their reduced adhesive tendencies. Like lubricants, they are necessary at the surface of feed particles and they must be in fine state of division and appropriately incorporated in the mixture. (Gohel, 2015)

1.2.3.4 Lubricants (Gohel, 2015)

Lubricants acts by reducing friction by interposing an intermediate layer between the tablet constituents and the die wall during compression and ejection. Solid lubricants, act by boundary mechanism, results from the adherence of the polar portions of molecules with long carbon

chains to the metal surfaces to the die wall. Magnesium stearate is an example of boundary lubricant. Other is hydrodynamic mechanism i.e. fluid lubrication where two moving surfaces are separated by a finite and continuous layer of fluid lubricant. Since adherence of solid lubricants to the die wall is more than that of fluid lubricants, solid lubricants are more effective and more frequently used.

Lack of adequate lubrication produces binding which can results in tablet machine strain and can lead to damage of lower punch heads, lower cam track, die seats and the tooling itself. And it may also yield tablets with scratched edges and are often fractured at the top edges. With excessive binding the tablet may be cracked and fragmented by ejection.

1.2.3.4.1 Classification of lubricants (Gohel, 2015)

Lubricant are classified according to their water solubility i.e. water insoluble and water soluble. Selection of lubricant is depends partly on mode of administration, type of tablet, desired disintegration and dissolution properties, physicochemical properties of granules or powder and cost.

- **Water Insoluble Lubricants**

  Water insoluble lubricants are most effective and used at reduced concentration than water soluble lubricants. Since these lubricants function by coating, their effectiveness is related with their surface area.

Table-2: List Of Insoluble Lubricants (Gohel, 2015)

Insoluble lubricants	Concentration	Comments
Stearates (Magnesium Stearate, Calcium Stearate, Sodium stearate)	0.25 -1	Reduce tablet strength; prolong disintegration; widely used.
Talc	1 -2	Insoluble but not hydrophobic; moderately effective.
Sterotex	0.25 - 1	-
Waxes	1 - 5	-
Stearowet	1 - 5	-
Glyceryl behapate	1 - 5	Both lubricant and binder;
Liquid paraffin	Up to 5	Dispersion problem; inferior to stearates

- **Water Soluble Lubricants**

Water Soluble Lubricants are used when a tablet is completely soluble or when unique disintegration and dissolution characteristics are required. Tablet containing soluble lubricant shows higher dissolution rate than tablet with insoluble lubricants. Physical mixture of this lubricant i.e. SLS or MLS with stearates can lead to the best compromise in terms of lubricity, tablet strength and disintegration.

Table-3: List Of Soluble Lubricants (Gohel, 2015)

Water soluble lubricants	Concentration range %(w/w)
Boric acid	1
Sodium benzoate	5
Sodium oleate	5
Sodium acetate	5
Sodium Lauryl sulfate (SLS)	1 - 5
Magnesium lauryl sulfate (MLS)	1 - 2

1.2.3.5 Anti adherents

Some material have strong adhesive properties towards the metal of punches and dies or the tablet formulation containing excessive moisture which has tendency to result in picking and sticking problem. Therefore antiadherents are added, which prevent sticking to punches and die walls.

Talc, magnesium stearate and corn starch have excellent antiadherent properties. Vegan had suggested that silicon oil can be used as antiadherent. (Gohel, 2015)

Table-4: Examples of antiadherents (Gohel, 2015)

Antiadherents	Range %(w/w)	Comments
Talc	1 - 5	Lubricant with excellent antiadherents properties
Cornstarch	3 - 10	Lubricant with excellent antiadherents properties
Colloidal silica	0.1 - 0.5	Does not give satisfactory results due to small surface area.
DL-Leucine	3 - 10	Water soluble lubricant; excellent antiadherents properties
Sodium lauryl sulfate	<1	Antiadherents with water soluble lubricant
Stearates	<1	Antiadherents with water insoluble lubricant

1.2.3.6 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 methyl paraben and propyl paraben. (Patel, Shah and Upadhyay, 2015)

1.2.3.7 Sorbents

Sorbents are used for tablet/capsule moisture-proofing by limited fluid sorbing (taking up of a liquid or a gas either by adsorption or by absorption in a dry state. (Patel, Shah and Upadhyay, 2015)

1.2.3.8 Sweeteners

Sweeteners are two types shown in the table below.

Table-5: Types of sweeteners (Patel, Shah and Upadhyay, 2015)

Natural Sweetener	Artificial Sweetener
Mannitol	Saccharin
Lactose	Cyclamate
Sucrose	Aspartame
Dextrose	

Aspartame is about 180 times sweeter than sucrose. The primary disadvantage of aspartame is its lack of stability in the presence of moisture. When aspartame is used with hygroscopic components, it will be necessary to determine its stability under conditions in which the product can adsorb atmospheric moisture. Saccharin is 500 times sweeter than sucrose. Its major disadvantages are that it has a bitter aftertaste and is carcinogenic. Even cyclamate is carcinogenic. (Patel, Shah and Upadhyay, 2015)

1.2.3.9 Colourants:

Colourants do not have therapeutic activity. They do not improve product bioavailability or stability but are incorporated into tablets for purposes like to facilitate identification of similar looking products within a product line to avoid mix ups, to facilitate identification of products of similar appearance that exist in the lines of different manufacturers, to overcome colour change on aging, disguising of off-colour drugs, for brand image in the market, to enhance the aesthetic appearance of the product to have better patient acceptance. Most widely used colourants are dyes and lakes which are FD & C and D & C approved. Dyes are generally applied as solution especially in the granulating agent. Lakes are usually employed as dry powders for colouring. In general, direct compression tablets are coloured with lakes because no granulation step is used. Natural colourants can be used and generally they do not require the FDA certification before use in drug products. One of the important advantage in using lakes is reduced risk of interaction

between the drug and other ingredients as well as colour development is rapid which reduces processing time .While employing wet granulation , care should be taken to prevent colour migration during drying . In any coloured tablet, the formulation should be checked for resistance to colour changes on exposure to light. Reflectance Spectrophotometry, Tristimulus Colourimetric Measurements and Microreflectance Photometer used to measure the colour uniformity and gloss on a tablet surface. (Gohel, 2015)

Table-6: Types of colourants (Gohel, 2015)

FD & C COLOUR	COMMON NAME
Red 3	Erythrosine
Red 40	Allura red AC
Yellow 5	Tartrazine
Yellow 6	Sunset Yellow
Blue 1	Brilliant Blue
Blue 2	Indigotine
Green 3	Fast Green

1.3 EXIPIENTS USED IN PHARMACEUTICALS INDUSTRIES

1.3.1 Polyvinylpyrrolidone (PVP)

PVP is a very widely used excipient for the preparation of solid dosage forms. Main application is it´s function as a binder in wet granulation. It is also useful for the preparation of effervescent tablets or in direct compression applications. Many other uses, including non-parenteral applications, have been described in the very long history of this polymer. As a plasma volume expander for trauma victims, it was used since 1950s. Cross povidone contributes to pulmonary vascular injury in substance abusers who have injected pharmaceutical tablets prepared oral absorption. Povidone-iodine is a complex of povidone and iodine which is used as disinfectant. In pleurodesis (fusion of pleura because of in cessantpleural effusions), it is used because of its easy availability and low cost. (Brook, 2015)

1.3.1.2 Structural Formual of PVP

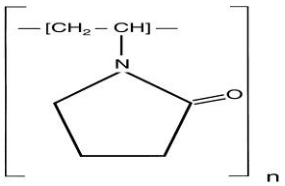

Fig-1.1: Structure of PVP

1.3.1.3 General Propertise of PVP

- Amphiphilic
- Compatible with a variety of resins and electrolytes
- Soluble in water and polar solvents, insoluble in esters, ethers, ketones and hydrocarbons
- Hard, glossy, transparent, oxygen permeable films which adhere to a variety of substrates
- Adhesive and cohesive properties
- Cross-linkable
- Linear nonionic polymer
- High polarity/proton acceptor
- Physiologically inert
- Unsuitable for thermoplastic processing
- Hygroscopic (Brook, 2015)

1.3.1.4 Physical properties:

1.3.1.4.1 Molecular Weight Determination:

Many studies are available based on measuring sedimentation, light scattering, osmometry, NMR spectroscopy, ebullimometry, and size exclusion chromatograph to determination of the molecular weight of PVP polymer. Narrower distribution curves of molecular entities are shown by the low molecular weight polymers than the high molecular weight compounds. By the use of these methods, any one of three molecular weight parameters can be measured, namely the number average (Mn), viscosity average (Mv), and weight average (Mw).

For the same polymer each of these characteristics can yield a different answer such as-

Number average (Mn) – 10,000

Viscosity average (Mv) – 40,000

Weight average (Mw) – 55,000

Therefore one must know which molecular average is cited in any review of the literature Conventionally, by their K-values molecular weights are expressed which are derived from relative viscosity measurements. (Brook, 2015)

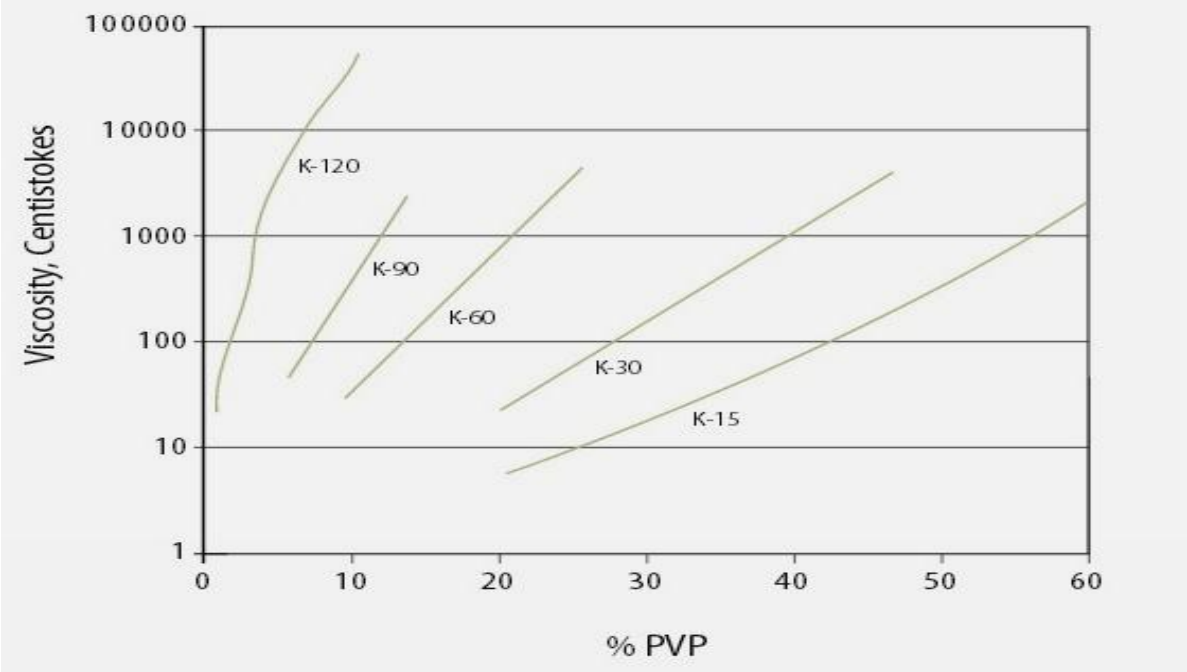

Fig-1.2: Viscosity vs % PVP (Brook, 2015)

Table-8: Viscosities of PVP K-30 polymers in Various Organic Solvents (Brook, 2015)

Kinematic Viscosities (in centistokes)		
Solvent	2% PVP	10% PVP
Acetic Acid (glacial)	2	12
1,4-Butanediol	101	425
Butyrolactone	2	8
Cyclohexanol	80	376
Diacetone Alcohol	5	22
Diethylene Glycol	39	165
Ethanol (absolute)	2	6
Ethyl Lactate	4	18
Ethylene Glycol	24	95
Ethylene Glycol Monoethyl Ether	3	12

Kinematic Viscosities (in centistokes)		
Solvent	2% PVP	10% PVP
Glycerin	480	2,046
Isopropanol	4	12
Methyl Cyclohexanone	3	10
N-Methyi-2-Pyrrolidone	2	8
Methylene Chloride	1	3
Monoethanolamine	27	83
Nitroethane	1	3
Nonylphenol	3,300	-
Propylene Glycol	66	261
Triethanolamine	156	666

Fig-1.3: Viscosity of PVP in various organic solvents (Brook, 2015)

Table-9: Effect of pH on Viscosity of 5% Aqueous PVP K-30 at 25°C (Brook, 2015)

pH	10	9	7	4	2	1	0.1	Conc HCl
Viscosity	2.4	2.4	2.4	2.4	2.3	2.3	2.4	4.96

Over a wide pH range PVP polymer solution viscosity does not change appreciably, but enhance in concentrated HCI. Strong caustic solutions precipitate the polymer but this precipitate solution redissolves on dilution with water.

Table-10: Effect of PVP K-30 polymer Concentration on Density in Water (Brook, 2015)

PVP Concentration	10	20	30	40	50
Density (g/ml)	1.02	1.04	1.07	1.09	1.12

Despite a significant increase in the concentration of PVPK-30 polymer the densities of PVP polymer water solutions are only slightly changed. (Brook, 2015)

1.3.1.5 Solubility (Brook, 2015)

In cold water, PVP polymer is readily soluble. The concentration of PVP is limited only by viscosity. Free-flowing solutions of PVP K-30 polymer are possible to prepare in concentrations up to 60% with only moderate effect on density. As 45 and 20 percent aqueous solutions, respectively PVP K-60 and K-90 polymer are available commercially. PVP K-30 polymer is also freely soluble in many organic solvents, including alcohols, some chlorinated compounds such as chloroform, methylene chloride and ethylene dichloride.

1.3.1.6 Compatibility

Both in solution and film form, PVP polymer exert a high degree of compatibility, with most inorganic salt solutions and with many natural and synthetic resins, as well as with other chemicals. (Brook, 2015)

1.3.1.7 Stability

PVP powder is hygroscopic so proper precautions should be taken to prevent excessive moisture pickup. PVP polymer powder can be stored under ordinary conditions without undergoing decomposition or degradation. In tied polyethylene bags enclosed in fiber packs, bulk polymer is supplied. The polyethylene bag should be kept closed at all times in the covered container when not in use. Moisture acts as a plasticizer on PVP polymer films. These films are otherwise chemically stable. With relative humidity the equilibrium water content of PVP polymer solid or films varies in a linear fashion and is equal to approximately one-third the relative humidity. Samples of dried, powdered PVP polymer, subjected to 20, 52, and 80 percent relative humidity until equilibrium is reached, show a 10, 19, and 31 percent moisture weight gain, respectively. Though PVP polymer powder are quite stable when heated exposure to extreme elevated temperatures should be avoided. At 150°C some darkening in color and decreased water solubility are evident on heating in air. However, PVP polymer appears to be quite stable when heated repeatedly at 110-130°C for relatively short intervals. If protected from molds aqueous PVP polymer is stable for extended periods. However, appropriate tests should be made with finished products containing PVP polymer before deciding on a preservative. Steam sterilization (15 lb. pressure for 15 min.) does not change the properties of the solutions. (Brook, 2015)

1.3.1.8 Applications

Table-11: Applications of PVP (Brook, 2015)

Area	Advantages
Ceramics (As a binder in high temperature fire-prepared products) .	➢ In the firing process binder is completely combustible. ➢ Exerts no influence on the ceramic end product

	➢ Compatible with inorganic materials.
Glass and Glass Fibers (Works as a lubricant ,binder and coating agent)	➢ Helps in processing as well as prevent abrasion of glass
Coatings/lnks (In digital printing coating, ball-point inks)	➢ Promotes flow in inks, better gloss, high tinctorial strength. ➢ Nonthixotropic. ➢ Antiblack agent. ➢ Grease resistant. ➢ Inkjet dye fixative.

Adhesives (pressure-sensitive and water-remoistenable)	➢ Best adhesive for glass, metal, plastics. ➢ Gives high initial strength, hardness. ➢ Specially suitable for remoistenable adhesive applications. ➢ Produce grease-resistant films. ➢ From water or organic solvents films can be cast. ➢ Change viscosity of polymer-based adhesives. ➢ Increases cold-flow temperature. ➢ Increases softening point of thermoplastics.
Polymerizations (As a substrate for graft polymerization, template in acrylic polymerization)	➢ Works as particle-size regulator, suspending agent and viscosity modifier of emulsion polymers. ➢ Improves strength, clarity, color receptivity in polymerization products.

	➢ To improve dye ability and stability of latices works as Post-polymerization additive. ➢ Pigment dispersant.
Detergents	➢ Inhibits dye transfer and Stabilizes enzyme
Electrical Applications Work as an expander in cadmium-type electrodes, binder in sintered-nickel powder plates.	➢ Hydrophilic material in electrode separators of microporous film types. ➢ To improve uniformity used as compatible dispersant in printed circuits. ➢ Protects light sensitive material in the CRT. ➢ For gold, nickel, copper and zinc plating baths and cathode ray tubes works as compatible dispersant for solar collection heat transfer liquids.

Lithography and Photography (In foil emulsions, etch coatings)	➢ Offers uniform viscosity, temperature stability. ➢ Nonthixotropic. . ➢ Grease-proof and water receptive. ➢ To ink ingredients, Chemically inert. ➢ Improves adhesion for light absorber, binder, dispersant carrier dyes and antistick agent.. ➢ Defoggant
Fibers and Textiles Used as synthetic fibers, dyeing and printing. Widely used as dye dispersant and to disperse titanium dioxide.	➢ Backbone for grafting monomers. ➢ For hydrophobic fibers as polyolefins, improves dye receptivity. ➢ Dye fixation improver and dye vehicle in wool transfer printing. ➢ For heat activated textile adhesives, textile finishes and print parts for various types of fabrics works as thickener.

	➢ Through dye complexion textile dye stripping and strike rate are controlled. ➢ Acts as a dye scavenger in print washing. ➢ Enhanced adhesives to glass-fiber sizes.
Coatings /Inks	➢ Viscosity control, suspension stabilization, flow control
Membranes (Used in liquid ultrafiltration, hemodialysis, selective permeability types of membranes)	➢ Good compatibility and crosslinking properties. ➢ Ability to complex with a broad variety of compounds. ➢ Strong polar character and hydrophilicity improves selective ➢ material separation properties.

Paper (as a paper adhesives)	➢ Improves strength and stability. ➢ Prevents sliding. ➢ Works as fluorescent whitening agent carrier. ➢ Improves luster, binding, absorbency, whitening and gloss. ➢ For coloring, dye stripping, Solubilizes dyes. ➢ Fiber and pigment dispersant. ➢ Complexing agent for modifying resins. ➢ For inorganic flakes and fibers works as binder
Suspensions / Dispersions	➢ Adsorbed on the surface of the colloid particles. ➢ Prevents them from coagulating.

Water and Waste Treatment, and Hygiene (Used in clogging of reverse osmosis membranes, water treatment in fish hatchery ponds, removal of oil, flocculants in waste water treatment)	➢ Complexes and gels in water to react with undesired water products.
Tableting	➢ Binder agent

1.3.2 Sodium lauryl sulfate

Sodium lauryl sulfate is used as a lubricant to eliminate friction during tablet compression and drawing out the mold. In tablet formulation Sodium lauryl sulfate act as lubricant in a range of 1-5%. Sodium lauryl sulphate increased absorption of water by starch or had a variable effect on water penetration in tablets. It is also a surfactant which is recommended to decrease the hydrophobicity of the drugs because the more hydrophobic the tablet the greater the disintegration time (Alibaba, 2013).

1.3.3 Starch

Starch is one of the earliest known binding agents to be used in tablet manufacturing process. It is a white powder without any odor or taste. Native starches are available from a wide variety of plant sources such as corn, potato and wheat. However, these varieties tend to be highly viscous, to agglomerate, and have poor flow properties, making their handling difficult during the tablet manufacturing process. Newer varieties such as pregelatinized starch help to overcome these drawbacks because they are pre-cooked and partly hydrolyzed during the production stage. Such varieties lend themselves well to wet Variation of flow property of different set of ratio of

excipients granulation as well as direct compression methods of tablet manufacture. Besides, it is directly compressible diluents. It possesses good binding properties and disintegrant activity. (Alibaba, 2013)

1.3.4 Microcrystalline Cellulose

MCC is useful in the preparation of tablets prepared by direct compression as well as wet granulation methods. Plant fibers contain alpha cellulose which can be chemically modified by controlled hydrolysis. This yields a partially depolymerized form of cellulose called microcrystalline cellulose (MCC). Generally, this product has a polymerization degree less than 400. Unlike other traditional binders that slow down the process of tablet disintegration, MCC acts as a binding and disintegrating agent. Tablets containing MCC should not be exposed to high humidity conditions, which tend to soften the tablets. (Alibaba, 2013)

1.3.5 Talc

Talc is not particularly effective on its own as a tablet lubricant or glidant but very effective with lubricants in the role of an anti-adherent in that it effectively prevents sticking to surfaces. When using talc, it should always be blended into the formulation first followed by the lubricant (i.e. magnesium stearate). The usable concentration of talc is in a range of 1-10%. Talc incompatible with quaternary ammonium compounds. It is not soluble in water. (Alibaba, 2013)

1.3.6 Calcium phosphates

They are granular insoluble materials. They are widely used both as wet granulation and direct compression diluents in tablet formulation. Bulk density of calcium phosphates is higher than that of organic fillers. They are directly compressible and are characterized by brittle fracture on compression during tableting process. Hard tablets are produced when calcium phosphates are used as diluents. They exhibit good flow properties. They are non hygroscopic and inexpensive. (Alibaba, 2013)

1.4 POWDER FLOW ABILITY

1.4.1 Definition

The ability of a powder to flow is referred as powder flow ability. Flow ability is a one-dimensional characteristic of a powder, whereby powders can be ranked from free-flowing to no flowing. But this simplistic view is insufficient to address common problems encountered by the formulator and equipment designer and the production personnel. (K. Presco and A. Barnum, 2015)

Flow ability is the result of the combination of material physical properties that affect material 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. (K. Presco and A. Barnum, 2015)

No flow problems (flow obstructions, segregation, irregular flow, flooding, etc.) occur if personel have enough knowledge about the flow properties of a powder or a bulk solid is necessary to design silos and other bulk solid handling equipment. Again quantitative information of flow ability of bulk products is required, e.g. as part of comparative tests (e.g. effect of flow agents or other additions on flow behavior) and quality control. The flow properties depend on some parameters, e.g,

- Particle size distribution,
- Particle shape,
- Chemical composition of the particles,
- Moisture,
- Temperature.

There are theoretical possibilities to determine the flow behavior of bulk solids in dependence of all of these parameters. The expense for the determination of all parameters of influence would be very high. So use of appropriate testing devices is necessary and also simpler to determine the flow properties. (K. Presco and A. Barnum, 2015).

1.4.2 Types of powder flow (Pharmacopeia.cn, 2015)

Principally there are two different flow patterns that can occur. They are

- **Core-flow:** Core flow can be considered the default flow pattern and is characterized by powder discharge through a preferential flow channel above the draw down point of the outlet. Powder is drawn into the flow channel from the top free surface of the inventory. This gives a first-in last-out discharge regime and, if operated on a continuous (rather than batch) mode, the powder around the walls in the lower section will remain static in the vessel until the time that it is drained down to empty.

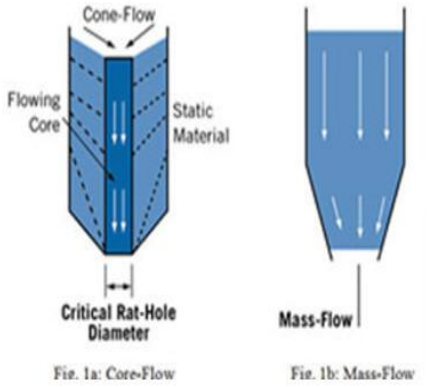

Fig-1.4: Flow types (Pharmacopeia.cn, 2015)

- **Mass-flow:** Mass flow is the desirable flow pattern for powders that are poor flowing or time sensitive, but must be specifically designed for. Here the entire contents of the vessel are 'live', giving a first-in first-out discharge regime. To achieve this, the hopper walls must be sufficiently steep and smooth. For a given wall material/converging angle, the powder wall friction must be below a critical value. Also, the product discharge must be controlled by a valve or feeder that allows powder to flow through the entire cross sectional area of the outlet. (It is this final point that prevents many vessels from operating in mass-flow.)

1.4.3 PARAMETERS OF MEASURING FLOW PROPERTIES OF POWDERS

Pharmaceutical industries widely use powder to manufacture tablet products. They have generated a wide variety of method for determining powder flow. But it is khown to all that no single or simple test method cano properly characterized the flow properties of pharmaceutical powders. (Pharmacopeia.cn, 2015)

Three commonly used methods for powder flow characterizations are_

- Angle of repose.
- Carr's index or compressibility index and
- Hausner ratio.

1.4.3.1 Angle of repose (AOR)

This method is widely used to determine the flow characteristics of powder. Angle of repose has a characteristic related to inter particulate friction or resistance to movement between particles. Results of the angle of repose test are dependent upon the method used. As a result of the segregation of material and consolidation or aeration of the powder experimental difficulties are arise as the cone is formed. Although this method has some difficulties, it is widely used in pharmaceutical industries.

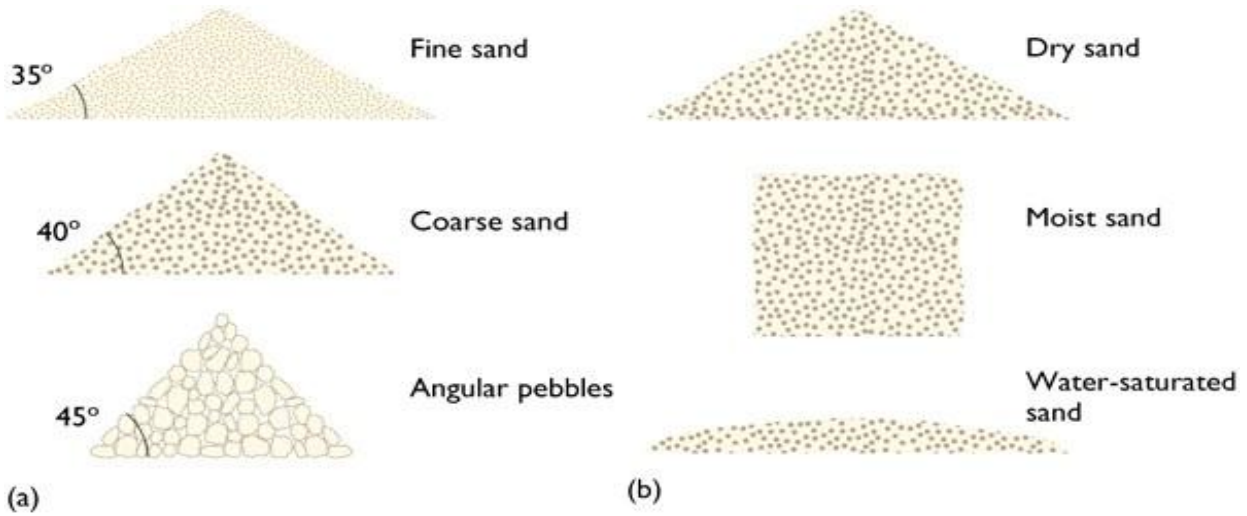

Fig-1.5: AOR of different powder forms (Pharmacopeia.cn, 2015)

The AOR is the constant, three-dimensional angle (relative to the horizontal base) assumed by a cone-like pile of material formed by any of several different methods. The most common methods for determining the static angle of repose can be classified on the basis of the following two important experimental variables.

They are_

1. Relative to the base, the "funnel" height (through which the powder passes) may be fixed, or the height may be varied as the pile forms.
2. The pile forms upon the base which may be of fixed diameter or the diameter of the powder cone may be allowed to vary as the pile forms. (Pharmacopeia.cn, 2015)

In the literature of formulations there are examples 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-12: Flow Properties and Corresponding Angles of Repose (Pharmacopeia.cn, 2015)

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

1.4.3.1.1 Experimental Considerations for Angle of Repose:

AOR 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. Important considerations in the following are raised in the existing literature. (Pharmacopeia.cn, 2015)

- By the impact of powder from above, the peak of the cone of powder can be modified. The distortion caused by impact can be minimized by careful building of the powder cone.
- The powder cone is formed upon the base (nature of the base) influences the AOR. So the powder cone must be formed on a common base. By forming the cone of powder on a layer of powder which can be achieved. It is possible to 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. (Pharmacopeia.cn, 2015)

1.4.3.1.2 Recommended Procedure for Angle of Repose

The base should be vibration free. The funnel height is varied 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. This method is not appropriate if a symmetrical cone of powder cannot be properly and reproducibly prepared. From the following equation the AOR can be determined by measuring the height of the cone of powder and measuring the diameter of the base. The angle of repose is denoted by α.

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

1.4.3.2 Compressibility Index and Hausner Ratio

The simple, fast, and popular method of predicting powder flow characteristics is Hausner ratio. 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. By measuring both the bulk volume and the tapped volume of a powder the compressibility index and the Hausner ratio are determined. (Pharmacopeia.cn, 2015)

Although there are some variations in the method of determining the compressibility index and Hausner ratio, the basic procedure is to measure the unsettled apparent volume, V_O, and 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 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 may be calculated using measured values for bulk density (ρ bulk) and tapped density (ρ tapped) as follows:

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

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

For the compressibility index and the Hausner ratio, the generally accepted scale of flow ability is given in the following table. (Pharmacopeia.cn, 2015)

Table-13: Scale of Flow ability (Pharmacopeia.cn, 2015)

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	1.46–1.59
>38	Very, very poor	>1.60

1.4.3.2.1 Experimental Considerations for the Compressibility Index and Hausner Ratio:

Compressibility index and Hausner ratio depend on the methodology used. In the existing literature, there are discussions of the following important considerations affecting the determination of the unsettled apparent volume (Vo), the final tapped volume (Vf), the bulk density (ρ bulk) and the tapped density(ρ tapped).

- 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. (Pharmacopeia.cn, 2015)

1.4.3.2.2 Recommended Procedure for Compressibility Index and Hausner Ratio:

Use a 250-mL volumetric cylinder with a test sample weight of 100g. Smaller weights and volumes may be used, but variations in the method should be described with the results. An average of three determinations is recommended. (Pharmacopeia.cn, 2015)

Chapter-II

Literature Review

Better flow property of powder is very important for the manufacture of direct compressible tablets in the pharmaceutical industries. So to know the flow characteristics of powder and to improve the flow characteristics of powder is necessary for the powder which has poor flow characteristics. In nineteenth century many method were developed to determine the powder flow property and to improve the flow property of powder. During this century several works of the scientist of many countries played a very important role to determine the flow characteristics of powders.

In the nineteenth century, at firth Gold and Palermo (Gold and Palermo, 1965) took an attempt to study the antistatic properties of tablet lubricants such as magnesium stearate, polyethylene glycol 4000, sodium lauryl sulfate and talc. The data indicates that these lubricants have the ability to lower the accumulation of static charges which results the flow of material through a tablet hopper. The study showed that different highly static materials influence the antistatic properties of these lubricants. If the concentration of lubricant gets lower, the antistatic effectiveness is decreased.

Kristensen HG and Jensen VG studied in 1969 on the reproducibility of granulation flow into dies during tableting, evaluated from the uniformity of tablet weights, has been compared with the flow properties of the granulations. The angle of repose, the flow rate and the internal angle of friction were used as measures of the flow properties. Under different conditions the granulations were prepared. The granule consists of 3 parts of lactose to 7 parts of potato starch granulated by an aqueous solution of gelatin. As a glidant (lubricant) various concentrations of talc were used. It had been shown that, for all of the methods of measurement, the flow properties have an optimum in the same glidant concentration range. Between flow properties and weight variations of tablets no correlation lets was observed. (HG and VG, 1969)

In the same year, Kristensen in his study of the preparation of tablets shown that, when the flow properties of the tablet granulations are optimized, the variations in the content of the tablets can be so high that the tablets are unacceptable. As a model tablets containing 50 mg. of ascorbic acid and 120 mg. of granulatum simplex added tablet as, with added varying amounts of glidants (lubricants), were used. He concluded that in the evaluation of a glidant and in the selection of its

concentration in the tablet formulation, the powder mixture's homogeneity and the possibility of segregation during preparation must be considered. (HG, 1969)

In 1976, by Marshall and Sixsmith, with and without the addition of spray dried lactose, the flow properties of 4 tableting grades of microcrystalline cellulose, Avicel PH 101 (I), Avicel PH 102 (II), Avicel PH 103 (III) and Avicel PH 105 (IV), were studied by 3 different techniques. None of the Avicels were free flowing powders, and the differences between the 4 grades were related to particle size and moisture content. Glidant properties was showed when added to spray dried lactose only at concentrations below 4% w/w. (Sixsmith, 1976)

In the year 1979, Bolhuis and his research fellows (Boihuis,Lerk,Moes, 1979) studied on the flow and the lubrication properties of a high dosage range drug,acetyl salicylic acid with different particle size distributions which was formulated with directly compressible excipients and compressed into tablets.The weight variation,drug content, friability,disintegration time and dissolution rate of the drug and stability after storage for eight weeks at 20‡C and 50% or 85% relative humidity were investigated by them.The knowledge of the properties and the interaction of drug,directly compressible exicipients and other tablet vehicle made the formulation possible and compression of different particle size acetylsalicylic acid powders into good quality tablets.

In the year of 1994, Schmidt and his research fellows (Schmidt et al 1994) evaluated and compared powder characteristics and tableting properties of ludipress, afree flowing granule containing povidone and crospovidone. Flow ability,bulk volume, tapped density, Hausner ratio, angle of repose and particle size distribution of Ludipress were evaluated.By using the scanningelectron microscopy (SEM) they examined the particle morphology. They found that Ludipress sample revealed a good batch-to-batch uniformity and flow charrateristics compared to the physical blend and other exicipients investigated.

The effect of eleven pharmaceutical excipients with Avicel PHI02 SCG was investigated by two scientists, Flemming and Mielck (Flemming and Mielck, 1995) in the next year. Physical characteristics like particle size distribution, true and bulk densities and flow rates had been evaluated. The study yields, for microtableting purpose flow rates were calculated on modern high speed rotary tableting machine, and also from very narrow orifices.

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).

After a year later, a comparative investigation has been performed by Talukdar and other scientists (Talukdar etal., 1996) between xanthan gum and HPMC which act as hydrophilic matrix-forming agents. They observed the compaction characteristics and drug release behavior of these materials. Though the compaction characteristics were found similar but the flow characteristics were different. HPMC is less flowable than xanthan gum which significantly affects the drug release profiles of these potential excipients.

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 the same year, 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).

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).

In year of 2000, Taylor and his research fellows (taylor et al 2000) worked on flow property of typical tablet and capsule formulation exicipents, active compound andrepresentative

formulation blend. They had followed novel flow measurement techniques to identify reliable bench test tomeasure powder flow as ascreening method in early tablet and capsule formulation development. They used test method that was vibrating spatula critical orifice and angle of repose, compressibility index and avalanching analysis. Emprical composite index was established by them and they ranked powder flow in accordance with formulator experience. They found data were not reproducible from vibrating spatula and avalanching method.

In 2002, a Chinese scientist, Anthony Chi-Ying Wong did an experiment on the angle 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).

In 2003 Mullarney and his research fellows (Mullamey et al, 2003) studied on the physical, flow, and mechanical properties of four common pharmaceutical sweeteners to assess their relative manufacturability in solid dosage formulations. To determine significant differences in particle shape, size distribution, and true density Sucrose, acesulfame potassium (Sunett), saccharin sodium, and aspartame were evaluated. Powder flow and cohesivity as well as compact mechanical properties such as ductility, elasticity, and tensile strength were measured and noticeably found different. Sucrose and acesulfame potassium demonstrated excellent flow ability and marginal mechanical property performance relative to over 100 commonly used pharmaceutical excipients evaluated in the authors' laboratory. Poor flow ability and superior compact strength were demonstrated by saccharin sodium and aspartame relative to sucrose and acesulfame, despite their noticeably higher brittleness. So careful selection of an appropriate sweetener is warranted in obtaining desirable process and tableting robustness, particularly if sweetener loading is high.

The effect of pharmaceutical excipients on properties affecting tablet production was evaluated by Nagel and Peck in the same year (Nagel and Peck, 2003). They discovered that pharmaceutical excipients have great impact on the tableting properties. They also took an attempt to establish the use of theophylline anhydrous in formulation so that it can be easily tableted. They examined Carr's's index to measure flow ability. Besides, the active ingredient, theophylline anhydrous, the formulation contains hydrous lactose and dicalcium phosphate as diluents, PVP as binder, fumed silica as flow promoter and the powder flow for each component was evaluated effectively.

In the same year, Zhang and his research fellows (Zhang, Law and Chakrabarti, 2003) investigated the basic physico-chemical property and binding functionality of commonly used commercial direct compression binders/fillers. The compressibility of these materials was also analyzed using compression parameters derived from the Heckel, Kawakita, and Cooper-Eaton equations. 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 content followed by MCC, DCP, lactose, and finally sugars; DCP displayed the highest density, followed by sugar, lactose, starch, and MCC; the material particle size is highly processing dependent. The data also demonstrated that MCC had moderate flow ability, excellent compressibility, and extremely good compact hardness; with some exceptions, starch, lactose, and sugar generally exhibited moderate flow ability, compressibility, and hardness; DCP had excellent flow ability, but poor compressibility and hardness. This research additionally confirmed the binding mechanism that had been well documented: MCC performs as binder because of its plastic deformation under pressure; fragmentation is the predominant mechanism in the case of lactose and DCP; starch and sugar perform by both mechanism.

In the following year 2004 Lindberg and his research team (Lindberg et al., 2004) evaluated flow properties of four different tablet formulation having poor flow ability for direct compression using five different techniques. The tableting parameters were Hausnerratio, powder rheometer and other flow behavior. The behavior of three of the formulation out of four was observed. The result was compared with the value of the flow ability measurements. The correlated rank order of the formulations was considered the same with all the techniques. The measured flow

properties directly reflect the behavior of the tablet formulation during powder mixture procedure.

The same year Bhattachar and his fellow scientists (Bhattachar et al., 2004) introduced the statement that in the development of dosage form, the flow properties of pharmaceutical powders in solid oral dosage forms is a fundamental phenomena. In this case, the vibratoryfeeder method was considered as the flow measurement technique to measure flow properties of common pharmaceutical powders in solid oral dosage forms. In these experiment, seventeen various powders were evaluated with the instrument to measure the flow properties and the result was included in the powder flow index (PFI). On the other hand, the powder flow was evaluated with another commonly used alalanche instrument and similarly the data was included in MTA as mean time. The results obtained from the twodifferent instrumental method having different algorithms, were compared with nonparametric statistical assessment of the data and proved as a reliable document. Afterwards, vibratory feeder method was recommended for measuring powder flow.

In the same year, Kachrimanis, Petrides, and Malamataris (Kachrimanis et al., 2005) 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 Variation of flow property of different set of ratio of excipients 30 diameter and particle size, followed by the bulk density, the difference between bulk and tapped densities and the particle convexity.

After a year later, Davies, C.E, Tallon S.J and Brown N Studied on Both bulk density and particie siz. Bulk density is an elusive parameter, but can be measured directly, and with

considerable precision, with an instrument consisting principally of a vertically mounted vessel attached to a load cell. The test material flows in at the top and leaves through an orifice which chokes the flow and keeps the sensing vessel full at all times; bulk density is obtained from the (known) active volume of the sensing vessel and the weight of material in it as measured by the load cell. As well as defining and maintaining a constant volume of product for continuous density measurement, the sensing vessel effectively maintains uniform flow conditions within the flowing powder mass, and so is an ideal location for taking measurements of powder properties. Accordingly, our apparatus was designed to include a capacitance probe, responsive to changes in moisture content and sensors for mean size determination from sound velocity measurements (the velocity of an audio-frequency acoustic wave traversing a particulate medium correlates well with mean particle size). (Davies, Tallon. and Brown, 2005)

In a year later, Abhaykumar Bodhmage studied on Flow ability on six different powders: Aspartame, Respitose, Alpha-D-Lactose monohydrate, Methocel, Hydroxypropyl methylcellulose- HPMC, a placebo pharmaceutical granulate, and common pastry flour. For particle shape and size analysis scanning electron microscopy (SEM) and stereomicroscopy were used. Using the laser light scattering technique particle size distribution was determined. Powder flow ability was measured using shear strength, angle of repose, and tapped-to-bulk density measurements. A novel method of measuring the dynamic angle of repose using electrical capacitance tomography (ECT) was developed. Analysis of the images from microscopy revealed that the particles of aspartame and HPMC powders were elongated, the particles of ML001, pastry flour and lactose iiimonohydrate powders were irregular, and the particles of placebo granulate were nearly spherical. Particle size was found to be the most reliable indicator of powder flow ability, with decreasing particle size corresponding to lower flow ability; however other parameters such as particle elongation and irregularity were also found to have an influence on powder flow ability. Although HPMCand pastry flour had similar particle sizes, they exhibited differences in flow ability. This can be explained by the greater irregularity of the flour particles. Particle irregularity may cause mechanical interlocking between the particles, thus reducing powder flow ability. ECT was found to be a promising non-intrusive tool for the measurement of the dynamic angle of repose. Unlike other methods for the measurement of dynamic angle of repose, the results obtained from ECT were not influenced by the effect of end

caps. The present technique could be used by pharmaceutical industries in process analytical technology (PAT) for the detection and elimination of potential flow problems early inthe manufacturing process. (Bodhmage, 2006)

In 2006, Bagster and Crooks evaluated a number of methods of estimating flow ability 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 a year later, Jacob and his research fellows (Jacob et al., 2007) 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 flow ability 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.

In the next year, Hou and Sun (Hou and Sun, 2008) investigated the effects of particle size, morphology, density on flow properties using a ring shear tester under the parameter of flow function. The study showed that smaller particles exhibit poor powder flow properties. Reduction of particle size had an effect on flow properties. If the powder has different density but similar particle size, shape and surface area, they have similar flow properties. In contrast, better flow property achieved by higher particle density

In the next year, V. P. Pandey, K. venkateswara Reddy and R. Amarnath studied with Lactose monohydrate, dibasic calcium phosphate (DCP) and microcrystalline cellulose phosphate

(MCCP) as diluents in the same quantity for manufacture of chloroquine phosphate tablet using polyvinyl pyrrolidone K-30 (PVP K-30) as binding agent and sodium starch glycolate (S.S.G.) as disintegrating agent. In the present study, it wasfound that lactose monohydrate was suitable diluent for chloroquine phosphate tablets considering hardness and disintegration time. There were not much variations in other parameters like Hausner ratio, compressibility index, angle of repose and friability for all the three diluents. (PANDEY, REDDY and AMARNATH, 2009)

After a year later, the one and only scientist Sun (Sun, 2010) discovered that in tablet manufacturing process an inadequate powder flow leads to a great problem. Besides, a minimum knowledge of flow properties for efficient pharmaceutical tablet development is required for successful tableting result. The finding was achieved in order to discover a powder exhibiting minimum acceptable flow properties on a high speed tablet press and the variation in flow property of different sets of excipients. Experiment showed that microcrystalline cellulose lies in the borderline between acceptable and poor powder flow area during the tableting process. This data also can serve as a reference value for comparing with other prototype formulation. The research concluded that a poor flowing powder exhibit flow problems should be avoided and further implementation of this approach can minimize the problem associated with flow measurement during large scale production.

In the same year, Sarraguca and his co-workers (Sarraguca et al., 2010) determined the flow properties of pharmaceutical powders by near infrared spectroscopy. They illustrated that physical properties of pharmaceutical powders are of topmost importance in the pharmaceutical industry. They examined the critical significance of flow properties on processes like blending, tablet compression, capsule filling and transportation using angle of repose, Carr's's index and Hausnerratio. They used near infrared spectroscopy which is a fast and low-cost analytical technique to determine the parameters of flow properties of pharmaceutical powders based on active ingredient paracetamol. The spectra were recorded on a Fourier-transform near infrared spectrometer in which the parameters were the angle of repose, true and tapped density. The comparison was made between near infrared based properties and reference methods results. The result showed that the physical properties affect the flow ability of pharmaceutical powders.

A year later, Zhou and his research fellows (Zhou et al., 2011) investigated that if the coating extent created by a mechanofusion process corresponded with observed changes in bulk powder properties. A fine lactose powder (approximate median diameter 20μm) was dry coated with magnesium stearate using from 0.1 to 5% (w/w) content. An ultra-thin coating layer of magnesium stearate was anticipated. In this study, using the state-of-the-art XPS and ToF-SIMS systems the surface coating was examined. by Carr index and shear cell testing the powder flow was characterized. XPS was successfully applied to demonstrate variations in surface coverage, as a function of additive levels, and indicated near complete coating coverage at additive levels of 1% (w/w) and above. ToF-SIMS results supported such coating coverage assessment, and indicated coating uniformly across the fine particle surfaces. The flow metrics employed could then be related to the coating coverage metrics. By SEM and BET the mechanofusion process also modified the apparent surface roughness observed. It was suggested that the changes in the surface chemical composition exerted a more evident and direct impact on the powder cohesion and flow characteristics than the changes in the surface morphological properties after the mechanofusion in this study.

In the same year, Chattoraj, Shi and Sun (Chattorajet al, 2011) demonstrated that poor flow properties hinder the easy handling of powders during industrial-scale processing. In their experiment, they showed that powder flow can be considerably improved by reducing the cohesion of powders by coating them with nanosized guest particles. They analytically investigated the effects of the flow behavior of a highly cohesive and poorly flowing grade of microcrystalline cellulose powder (Avicel PH105). Optimum flow enhancement has been made with specified preparation at vigorous mixtures. The flow properties of nanocoated Avicel PH105 are comparable to those of Avicel PH102, which exhibits adequate flow ability for processing on a high-speed tablet press. The result showed that Variation of flow property of different set of ratio of excipients. The technique proved as a potential source for addressing industrial powder handling problems caused by poor powder flow properties.

Two years later, Morin and Briens investigated the effect of lubricants on powder flow ability as flow ability 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 flow ability most (Morin and Briens, 2013).

In the same year, 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 the same year, Crouter and Briens investigated the flow ability of MCC, HPMC, CMC, PVP, corn starch, and potato starch. Flow ability of MCC, CMC and PVP decreased after a critical moisture content and for corn starch, it was increased. Flow ability of HPMC was not changed that much. The moisture decreased flow ability by forming stronger interparticle liquid bridges and increased flow ability 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 the same year, Vanarase and his reaearch fellows (Vanarase et al, 2013) focused on two aspects of continuous powder mixing, namely characterizing the effects of material properties on the bulk powder flow behavior and developing continuous blending strategies suitable for cohesive materials. On the bulk powder flow behavior, relative effects of process parameters and material properties were analyzed by performing a PLS analysis of the output parameters, including mean residence time, and axial dispersion coefficient as a function of input parameters (impeller speed, flow rate, bulk density and cohesion). By the bulk density and impeller speed, the mean residence time was primarily affected whereas By impeller speed and cohesion the axial dispersion coefficient was affected.. Impeller speed and cohesion showed a significant interacting effect on the axial dispersion coefficient. At higher impeller speeds, increase in cohesion leads to increase in the axial dispersion coefficient, whereas at lower impeller speeds a negligible effect of cohesion on the axial dispersion coefficient was observed. In the second part

of the paper, For blending cohesive materials a continuous blending methodology was demonstrated. A combination of high shear and low shear mixing with high-shear mixing as a first step exhibited an optimal mixing strategy, considering the feeding limitations of cohesive materials, and limitations in the application of shear in the bladed continuous mixer.

In 2015, Bruni developed a rheological model for the flow ability of aerated fine powders. An investigation by a mechanically stirred fluid-bed rheometer (msFBR) of the effect of the interparticle forces on the fluidization behavior of fine powders linked with rheological studies was carried out. The use of aeration below fluidization allowed to carry out experiments with powders at very low consolidation levels. Based on the Janssen approach to evaluate stresses in powder containers two mathematical models were developed in order to relate the torque measurements in the Fluidized Bed Rheometer to the flow properties of the powders measured with standard powder flow testers. The models were able to satisfactorily predict the torque measured by the msFBR. To justify its use Walker's (1966) and Walter's (1973) larger complexity of the stress analysis was adopted in one of the two models did not introduce significant improvements in the evaluation of the stress distribution to justify its use. From msFBR data a procedure for the inverse application of the model was developed and applied to estimate the powder flow properties starting. In terms of effective angle of internal friction application of this procedure provided good results and is promising for the ability of the system to explore powder flow at very low consolidation states. (Bruni, 2015)

In same year, with and without the addition of various concentrations of magnesium stearate granulated powdered cellulose was studied by Podczeck and Newton in terms of powder bulk properties and capsule filling performance on a tamp-filling machine. Carr's compressibility reached its minimum value at 0.4% magnesium stearate compared to the unlubricated material suggesting an improvement of powder flow. However, shear cell measurements and the use of a powder rheometer indicated that the addition of 0.2% magnesium stearate and more impairs powder flow and does not reduce interparticulate friction. The fill weight and plug density could be predicted from Carr's compressibility index and from the maximum bulk density when capsules were filled into hard gelatine capsules at a zero-compression setting. With increasing magnesium stearate concentration, the decrease in one and simultaneous increase in the other

bulk property caused both fill weight and plug density to go through a minimum at a lubricant concentration of 0.4%. When the capsules were filled at maximum compression, however, the addition of lubricant increased the coefficient of fill weight variation significantly. For any added concentration of magnesium stearate the plug density remained constant. However, the optimum lubricant concentration was found to be 0.8% magnesium stearate which was not an optimal concentration for the powder bulk properties. (JM, 2015)

In the same year, Dr.Gabriel Tardos worked focused on the study of Powder Mechanics. The ultimate goal of his work was to develop a quantitative description of flows for a wide variety of powders using a continuous model. The study was centered on the "intermediate" regime of flow where both frictional and inertial effects were important. He used a larger ange of materials of different shape and physical properties such as density, elasticity, etc. and several flow geometries to gain meaningful insight. He reported on a series of materials from simple (round beds) to complex (fine, odd-shaped, elastic and/or compressible), used in a shear cell of the Jenike type, an axial-flow Couette and a centripetal geometry characteristic of a "spheronizer". The stresses and porosity (void fraction), and their fluctuations was measured as a function of geometry and shear rate and generate a constitutive equation that was used in modeling. (Tardos, 2015)

In the same year, Ganesan, Rosentrater, Muthukumarappan had an experiment on handling and storage characteristics of bulk solids. In their resulting storage and flow behavior, physical properties of granular solids play a significant role, and are therefore essential to design appropriate, efficient and economic bulk solids handling and storage equipment and structures. Distillers Dried Grains with Solubles (DDGS) is a bulk material that has been widely used as a protein source for ruminants and non-ruminants for more than two decades. Distillers grains are energy and nutrient dense and are often used as a replacement for corn inanimal diets. Large quantities of distiller's grains are now being produced with the exponential growth of the fuel ethanol industry in the last few years. DDGS flow is problematic.Because by caking and bridging which occurs during transportation and storage it is often become restricted. This issue probably results from a number of factors including storage moisture, temperature, relative humidity, particle size, time, or temperature variations, to name a few. The aim of this study was

to review the primary factors affecting flow ability, handling, and storage of granular solids and powders and appropriate testing methodologies for these materials. (JK, Cook and L, 2015)

Chapter-III

Materials and Method

3.1 MATERIALS

3.2 Excipients Collection:

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

3.3 Excipients:

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

Table-14 : List of excipients through this research work.

SL no.	Name of Excipients	Source (Supplier Name)
1.	Calcium Phosphate	MERK, Germany
2.	Polyvinyl Pyrrolidone	MERK, Germany
3.	CMC	MERK, Germany
4.	Zn Stearate	MERK, Germany
5.	Talc	MERK, Germany

3.4 Equipments and Instruments:

Table-15 : 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

Fig-3.1: Electronic balance

Fig-3.2: Rough balance

Fig-3.3: Powder mixer

3.5 Apparatus:

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

Table-16 : 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
9.	Black Marker
10.	Conical Flask
11	White Paper
12	Desiccant
13	Scale

3.6 METHODS

3.6.1 Preparation of various set of formulas:

Several number of same type formulas of a combination of excipients which includes lubricants, disintegrants, binders and antiadherents were made. In all set of formulas PVP ratio were varied In some set amlodipine or Propranolol HCl was added. In the amlodipine containing sets all ratios contain same amount of amlodipine. In the Propranolol HCl containing sets all ratios contain same amount of Propranolol HCl. In these ways various formulas were made of 3g.

3.6.2 Flow property measurement

3.6.2.1 Determination of bulk volume:

- At first the mixture of materials in a test tube was transferred to a dry measuring cylinder.
- The volume was measured after manually tapping the cylinder about 2 times on a flat table top surface.
- The achieved volume is the bulk volume which was documented.

3.6.2.2 Determination of tapped volume:

After measuring the bulk volume, the mixture of materials in the measuring cylinder was tapped manually 50 times and above until little further volume change is observed. The tapping is achieved by raising the cylinder and allowing it to drop under a specified distance.The measured volume was documented.

3.6.2.3 Calculation of Carr'sindex and Hausnerratio:

The compressibility index and Hausner ratio were calculated by the given formula

$$\text{Compressibility index} = \frac{100 \times (V_0 - V_f)}{V_0}$$

$$\text{Hausner's ratio} = \frac{V_0}{V_f}$$

Where, Vo= Bulk volume, Vf = Tapped volume

3.6.2.4 Measurement of Angle of repose:

In this research project fixed funnel method was used.

3.6.2.4.1 Procedure:

First of all, funnel made of plastic, glass or stainless steel was set with the holding stand tightly. The funnel was fixed in a place, 4 cm above the bench surface. On the bench surface, a piece of paper was placed. The mixture of the running test tube was poured through the funnel without incorporating external pressure or stress.The powder mixture formed a cone on the paper. After the cone from 5g of sample was built, height of the granules forming the cone (h) in cm and the radius (r) of the base in cm were measured. The angle of repose was calculated by the given formula and documented.

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

Where, h = height of the powder cone from the base;

r = radius of the conical pile.

3.6.3 Preparation of Formulas:

3.6.3.1 Preparation of Formula, F:

By choosing different excipients from different classes except PVP, formula (F) was prepared. Here the selected excipient from a particular class will serve the properties of itself in that range of amount not the others.

Table-17 : The following amounts of excipients (given with their use) were taken for the preparation of Formula (F)10g.

Ingredients Name	Purpose of Use	Percentage	Quantity (in g)
Calcium Phosphate	Lubricant	45%	4.5
PVP	Disintegrant	25%	2.5
Zinc Stearate	Antiadherent	15%	1.5
CMC	Binder	25%	2.5
Talc	Diluents	15%	1.5
		Total=100%	Total=10g

3.6.4 Preparation of Different Sets:

3.6.4.1 Preparation of Set-1:

After preparing 10g of F, specific binder was mixed with it in different fixed and justified ratio. For this formula, PVP was used. The required amount of both PVP and F was calculated for preparing each 3g of mixture in five different ratios. A total of five of sample mixture of 3g were set up for further procedure that is the determination of flow property.

Table-18 : The amount of PVP and F in different ratios (Set-1) in 3g.

Ratio	PVP : F	Amount of PVP : F (in g)
1	13% : 87%	0.39 : 2.61
2	17% : 83%	0.51 : 2.49
3	21% : 79%	0.63 : 2.37
4	29% : 71%	0.87 : 2.13
5	33% : 67%	0.99 : 2.01

3.6.4.2 Preparation of Set-2:

After preparing 10g of F, specific binder was mixed with it in different fixed and justified ratio. For this formula, PVP was used. The required amount of both PVP and F was calculated for preparing each 3g of mixture in five different ratios. A total of five of sample mixture of 3g were set up for further procedure that is the determination of flow property.

Table-19 : The amount of PVP and F in different ratios (Set-2) in 3g.

Ratio	PVP : F	Amount of PVP : F (in g)
1	5% : 95%	0.15 : 2.85
2	10% : 90%	0.30 : 2.70
3	15% : 85%	0.45 : 2.55
4	20% : 70%	0.60 : 2.40
5	25% : 75%	0.75 : 2.25

3.6.4.3 Preparation of Set-3:

After preparing 10g of F, specific binder was mixed with it in different fixed and justified ratio. For this formula, PVP was used. The required amount of both PVP and F was calculated for preparing each 3g of mixture in five different ratios. A total of five of sample mixture of 3g were set up for further procedure that is the determination of flow property.

Table-20: The Amount of PVP and F in Different Ratios (Set-3) in 3g.

Ratio	PVP : F	Amount of PVP : F (in g)
1	7% : 95%	0.21 : 2.79
2	27% : 73%	0.81 : 2.19
3	30% : 70%	0.90 : 2.10
4	35% : 65%	1.05 : 1.95
5	40% : 60%	1.22 : 1.80

3.6.4.4 Preparation of Amlodipine Set-1:

Each ratio of the set-1 was divided to two equal portions. Each portion contains about 1.5 g of mixture. Amlodipine was added to each ratio of set-1. It is assumed that 80 mg of amlodipine tablet contain 5 mg of amlodipine. 1.4 g or 1400 mg contain 87.5 mg or .0875 g of amlodipine.

Table-21: Amlodipine Containing Different Ratios (Amlodipine Set-1) in 3g.

Ratio	PVP : F	Amount of PVP : F (in g)	Amlodipine added (in g)
1	13% : 87%	0.39 : 2.61	0.0875
2	17% : 83%	0.51 : 2.49	0.0875
3	21% : 79%	0.63 : 2.37	0.0875
4	29% : 71%	0.87 : 2.13	0.0875
5	33% : 67%	0.99 : 2.01	0.0875

3.6.4.5 Preparation of Amlodipine Set-2:

Each ratio of the set-2 was divided to two equal portions. Each portion contains about 1.5 g of mixture. Amlodipine was added to each ratio of set-2. It is assumed that 80 mg of amlodipine tablet contain 5 mg of amlodipine. 1.4 g or 1400 mg contain 87.5 mg or .0875 g of amlodipine.

Table-22: Amlodipine Containing Different Ratios (Amlodipine Set-2) in 3g.

Ratio	PVP : F	Amount of PVP : F (in g)	Amlodipine added (in g)
1	5% : 95%	0.15 : 2.85	0.0875
2	10% : 90%	0.30 : 2.70	0.0875
3	15% : 85%	0.45 : 2.55	0.0875
4	20% : 70%	0.60 : 2.40	0.0875
5	25% : 75%	0.75 : 2.25	0.0875

3.6.4.6 Preparation of Amlodipine Set-3:

Each ratio of the set-3 was divided to two equal portions. Each portion contains about 1.5 g of mixture. Amlodipine was added to each ratio of set-3. It is assumed that 80 mg of amlodipine tablet contain 5 mg of amlodipine. 1.4 g or 1400 mg contain 87.5 mg or .0875 g of amlodipine.

Table-23: Amlodipine Containing Different Ratios (Amlodipine Set-3) in 3g.

Ratio	PVP : F	Amount of PVP : F (in g)	Amlodipine added (in g)
1	7% : 95%	0.21 : 2.79	0.0875
2	27% : 73%	0.81 : 2.19	0.0875
3	30% : 70%	0.90 : 2.10	0.0875
4	35% : 65%	1.05 : 1.95	0.0875
5	40% : 60%	1.22 : 1.80	0.0875

3.6.4.7 Preparation of Propanolol Set-1:

Propanolol HCl was added to remaining ratio of set-1. It was assumed that 80 mg of Propanolol HCl tablet contain 5 mg of Propanolol HCl. 1.4 g or 1400 mg contain 87.5 mg or 0.0875 g of Propanolol HCl.

Table-24: Propranolol Containing Different Ratios (Propanolol Set-1) in 3g.

Ratio	PVP : F	Amount of PVP : F (in g)	Propanolol HCl added (in g)
1	13% : 87%	0.39 : 2.61	0.0875
2	17% : 83%	0.51 : 2.49	0.0875
3	21% : 79%	0.63 : 2.37	0.0875
4	29% : 71%	0.87 : 2.13	0.0875
5	33% : 67%	0.99 : 2.01	0.0875

3.6.4.8 Preparation of Propanolol Set-2:

Each ratio of the set-2 was divided to two equal portions. Each portion contains about 1.5 g of mixture. Propranolol HCl was added to each ratio of set-2. It was assumed that 80 mg of Propanolol HCl tablet contain 5 mg of Propanolol HCl . 1.4 g or 1400 mg contain 87.5 mg or 0.0875 g of Propanolol HCl

Table-25: Amlodipine Containing Different Ratios (Propanolol Set-2) in 3g.

Ratio	PVP : F	Amount of PVP : F (in g)	Propanolol HCl added (in g)
1	5% : 95%	0.15 : 2.85	0.0875
2	10% : 90%	0.30 : 2.70	0.0875
3	15% : 85%	0.45 : 2.55	0.0875
4	20% : 70%	0.60 : 2.40	0.0875
5	25% : 75%	0.75 : 2.25	0.0875

3.6.4.9 Preparation of Propanolol Set-3:

Each ratio of the set-3 was divided to two equal portions. Each portion contains about 1.5 g of mixture. Propanolol HCl was added to each ratio of set-3. It was assumed that 80 mg of Propanolol HCl tablet contain 5 mg of Propanolol HCl . 1.4 g or 1400 mg contain 87.5 mg or 0.0875 g of Propanolol HCl.

Table-25: Amlodipine Containing Different Ratios (Propanolol Set-3) in 3g

Ratio	PVP : F	Amount of PVP : F (in g)	Propanolol HCl added (in g)
1	7% : 95%	0.21 : 2.79	0.0875
2	27% : 73%	0.81 : 2.19	0.0875
3	30% : 70%	0.90 : 2.10	0.0875
4	35% : 65%	1.05 : 1.95	0.0875
5	40% : 60%	1.22 : 1.80	0.0875

Chapter-IV

Results

4. 1 RESULTS

4.1.1 Calculation of individual excipients flow properties:

The flow property of individual excipients was measured by calculating their Carr's index, Hausner ratio and angle of repose. For calculating Carr's index and Hausner ratio, their individual bulk volume and tapped volume were measured three times and the average value was taken. The observed value is given below:

4.1.1.1 Result of The Ratios of The Set-1:

4.1.1.1.1 Carr's index and Hausner ratio measurement for set-1:

Table-26: Carr's index and Hausner ratio measured for set-1.

Ratio	Bulk Volume, Vo (ml)	Most Acceptable Value of Vo (ml)	Tapped Volume, Vr (ml)	Most Acceptable value of Vr	Hausner Ratio	Compressibility index (%)
1 (13% : 87%)	7	7.00	4.80	4.80	1.45	31
	7		4.80			
	7		4.80			
2 (17% : 83%)	7.5	7.16	4.90	5.13	1.38	28
	7		5.50			
	7		5.00			

3 (21% : 79%)	7.5 7.5 7	7.33	5.50 5.50 5.50	5.50	1.33	24.96
4 (29% : 71%)	7.8 7.5 7.5	7.43	6 6.00 6.00	6.00	1.23	19.24
5 (33% : 67%)	7.8 7.8 7.5	7.70	6.80 6.50 6.80	6.70	1.14	12.98

4.1.1.1.2 Angle of Repose measurement for the ratios of Set-1:

Table-27: Angle of Repose measured for the ratios of Set-1.

Ratio	Height (h)	Avr Height (h)	Diameter (2r)	Avr Diameter (2r)	Radius (r)	Angle of Repose (o)
1	1.7	1.73	3.2	3.13	1.56	47.95

(13% : 87%)	1.8 1.7		3.2 3.0			
2 (17% : 83%)	1.8 1.7 1.8	1.76	3.2 3.2 3.2	3.20	1.60	47.47
3 (21% : 79%)	1.7 1.7 1.7	1.70	3.2 3.5 3.2	3.20	1.6	45.85
4 (29% : 71%)	1.5 1.6 1.6	1.56	3.8 3.8 4.0	3.86	1.93	38.94
5 (33% : 67%)	1.5 1.5 1.3	1.50	4.0 4.2 4.2	4.13	2.06	36.06

4.1.1.2 Results of The Ratios of Set-2:

4.1.1.2.1 Carr's index and Hausner ratio measurement for the ratios of Set-2.

Table-28 : Carr's index and Hausner ratio measured for set-2.

Ratios	Bulk Volume, Vo (ml)	Most Acceptable Value of Vo (ml)	Tapped Volume, Vr (ml)	Most Acceptable value of Vr	Hausner Ratio	Compressibility index (%)
1 (5% : 95%)	6.5 6.5 7.	6.66	4.50 4.50 4.50	4.50	1.48	32.43
2 (10% : 90%)	6.5 7 7	6.83	4.50 4.50 4.50	4.50	1.45	34.11
3 (15% : 85%)	7 7.5 7	7.16	5 5 5	5.00	1.43	30.16
4 (20% : 80%)	7 7.5 7.5	7.33	5.50 5.50 5.00	5.33	1.37	27.28

5 (25% : 75%)	7.5 7 7.5	7.33	6 5.5 6.	5.83	1.25	20.46

4.1.1.2.2 Angle of Repose measurement for the ratios of Set-2:

Table-29: Angle of Repose measured for the ratios of Set-2.

Ratios	Height (h)	Avr Height (h)	Diameter (2r)	Avr Diameter (2r)	Radius (r)	Angle of Repose (o)
1 (5% : 95%)	1.8 1.8 1.8	1.80	2.8 2.8 3.0	2.86	1.43	51.53
2 (10% : 90%)	1.8 1.8 1.7	1.76	2.8 3.0 3.0	2.93	1.46	50.32
	1.7		3.00			

3 (15% : 85%)	1.7 1.7	1.7	3.00 3.00	3.00	1.50	48.57
4 (20% : 80%)	1.7 1.6 1.6	1.66	3.00 3.20 3.20	3.13	1.56	46.77
5 (25% : 75%)	1.6 1.6 1.6	1.6	3.2 3.5 3.5	3.40	1.70	43.26

4.1.1.3 Results of The Ratios of The Set-3:

4.1.1.3.1 Carr's index and Hausner ratio measurement for the ratios of Set-3:

Table-30: Carr's index and Hausner ratio measured for set-3.

Ratio	Bulk Volume, Vo (ml)	Most Acceptable Value of Vo (ml)	Tapped Volume, Vr (ml)	Most Acceptable value of Vr	Hausner Ratio	Compressibility index (%)
1	6.5 7	6.83	4.50 4.80	4.60	1.48	32.65

(7% : 93%)	7.		4.50			
2 (27% : 73%)	7.5 7.5 7	7.40	6.00 6.00 5.50	5.83	1.26	21.21
3 (30% : 70%)	7.8 7 7.5	7.43	6.00 6.50 6.50	6.33	1.17	14.80
4 (35% : 65%)	7.8 7.5 7.5	7.60	6.50 6.80 6.80	6.70	1.13	11.84
5 (40% : 60%)	7.8 7.8 7.5	7.70	6.80 6.80 7.00	6.86	1.12	10.90

4.1.1.3.2 Angle of Repose measurement for the ratios of Set-3:

Table-31: Angle of Repose measured for the ratios of Set-3.

Ratio	Height (h)	Avr Height (h)	Diameter (2r)	Avr Diameter (2r)	Radius (r)	Angle of Repose (o)
1 (7% : 93%)	1.8 1.8 1.8	1.80	2.8 3.0 3.0	2.93	1.46	50.95
2 (27% : 73%)	1.6 1.5 1.5	1.53	3.7 3.7 3.7	3.7	1.85	39.59
3 (30% : 70%)	1.5 1.5 1.3	1.43	3.7 4.0 4.0	3.93	1.95	36.25
4 (35% : 65%)	1.3 1.3 1.3	1.30	4.0 4.0 4.2	4.06	2.03	32.63

5 (40% : 60%)	1.3 1.2 1.2	1.26	4.2 4.5 4.5	4.40	2.20	29.80

4.1.1.4 Results of The Ratios of Amlodipine Set-1:

4.1.1.4.1 Carr's index and Hausner ratio measurement for the ratios of amlodipine Set-1.

Table-32: Carr's index and Hausner ratio measured for amlodipine Set-1.

Ratio	Bulk Volume, Vo (ml)	Most Acceptable Value of Vo (ml)	Tapped Volume, Vr (ml)	Most Acceptable value of Vr	Hausner Ratio	Compressibility index (%)
1 (13% : 87%)	3.5 3.7 3.5	3.56	2.50 2.30 2.50	2.43	1.46	31.74
2 (17% : 83%)	3.8 3.5 3.5	3.60	2.50 2.50 2.50	2.50	1.44	30.55
	3.8		2.80			

3 (21% : 79%)	3.8 3.3	3.63	2.80 2.80	2.80	1.29	22.86
4 (29% : 71%)	3.8 3.8 3.5	3.70	3.00 3.00 3.00	3.00	1.23	18.91
5 (33% : 67%)	3.8 3.8 3.8	3.80	3.30 3.30 3.50	3.36	1.14	12.95

4.1.1.4.2 Angle of Repose measurement for the ratios of amlodipine Set-1.

Table-33: Angle of repose measured for the ratios of amlodipine Set-1.

Ratio (containing amlodipine)	Height (h)	Avr Height (h)	Diameter (2r)	Avr Diameter (2r)	Radius (r)	Angle of Repose (o)
1	1.3 1.2	1.23	2.4 2.4	2.33	1.16	46.67

(13% : 87%)	1.2		2.2			
2 (17% : 83%)	1.2 1.2 1.2	1.20	2.5 2.5 2.5	2.50	1.25	43.83
3 (21% : 79%)	1.2 1.2 1.1	1.16	2.5 2.8 2.8	2.70	1.35	40.67
4 (29% : 71%)	1.1 1.1 1.1	1.10	2.8 2.8 3.0	2.93	1.46	36.99
5 (33% : 67%)	1.0 1.0 1.0	1.0	3.0 3.0 3.0	3.00	1.50	33.69

4.1.1.5 Results of The Ratios of The Amlodipine Set-2:

4.1.1.5.1 Carr's index and Hausner ratio measurement for the ratios of amlodipine Set-2.

Table-34 : Carr's index and Hausner ratio measured for amlodipine Set-2.

Ratio With Amlodipine	Bulk Volume, Vo (ml)	Most Acceptable Value of Vo (ml)	Tapped Volume, Vr (ml)	Most Acceptable value of Vr	Hausner Ratio	Compressibility index (%)
1 (5% : 95%)	3.5 3.3 3.3	3.36	2.30 2.30 2.30	2.30	1.46	31.54
2 (10% : 90%)	3.3 3.5 3.5	3.36	2.30 2.50 2.3	2.36	1.42	29.76
3 (15% : 85%)	3.5 3.5 3.8	3.60	2.5 2.5 2.7	2.56	1.40	28.88
4 (20% : 80%)	3.5 3.8 3.8	3.7	2.8 2.8 2.5	2.7	1.37	27.02

5 (25% : 75%)	3.8 3.5 3.8	3.7	3.0 2.8 3.0	2.93	1.26	20.81

4.1.1.5.2 Angle of Repose measurement for the ratios of amlodipine Set-2.

Table-35: Angle of repose measured for the ratios of amlodipine Set-2.

Ratio (containing amlodipine)	Height (h)	Avr Height (h)	Diameter (2r)	Avr Diameter (2r)	Radius (r)	Angle of Repose (o)
1 (05% : 95%)	1.4 1.3 1.3	1.33	2.4 2.4 2.2	2.33	1.16	48.90
2 (10% : 90%)	1.2 1.2 1.2	1.20	2.5 2.5 2.5	2.50	1.25	43.83
	1.2		2.4			

3 (15% : 85%)	1.2 1.1	1.20	2.4 2.2	2.70	1.35	41.63
4 (20% : 80%)	1.2 1.1 1.1	1.13	2.5 2.5 2.8	2.60	1.30	40.99
5 (25% : 67%)	1.2 1.1 1.0	1.10	2.6 2.6 2.8	2.66	1.33	39.59

4.1.1.6 Results of The Ratios of The Amlodipine Set-3:

4.1.1.6.1 Carr's index and Hausner ratio measurement for the ratios of amlodipine Set-3.

Table-36 : Carr's index and Hausner ratio measured for amlodipine Set-3.

Ratios With Amlodipine	Bulk Volume, Vo (ml)	Most Acceptable Value of Vo (ml)	Tapped Volume, Vr (ml)	Most Acceptable value of Vr	Hausner Ratio	Compressibility index
1	3.5 3.5	3.43	2.3 2.3	2.30	1.48	32.94

(7% : 93%)	3.3		2.3			
2 (27% : 73%)	3.8 3.8 3.7	3.76	3.00 3.00 2.8	2.93	1.28	22.07
3 (30% : 70%)	3.8 3.5 3.8	3.70	3.00 3.30 3.20	3.17	1.17	14.59
4 (35% : 65%)	3.8 3.8 3.8	3.80	3.30 3.30 3.30	3.30	1.15	13.15
5 (40% : 60%)	3.8 3.8 4.0	3.86	3.40 3.40 3.50	3.43	1.12	11.13

4.1.1.6.2 Angle of Repose measurement for the ratios of amlodipine Set-3.

Table-37: Angle of repose measured for the ratios of amlodipine Set-3.

Ratio (containing amlodipine)	Height (h)	Avr Height (h)	Diameter (2r)	Avr Diameter (2r)	Radius (r)	Angle of Repose (o)
1 (7% : 93%)	1.3 1.3 1.3	1.30	2.4 2.4 2.2	2.33	1.16	48.25
2 (27% : 73%)	1.2 1.1 1.0	1.10	2.8 2.6 2.8	2.73	1.36	38.96
3 (30% : 70%)	1.0 1.2 1.0	1.06	2.8 2.8 2.8	2.80	1.40	37.13
4 (35% : 65%)	1.0 1.0 1.0	1.00	3.0 3.0 2.8	2.93	1.46	34.40
	1.0		3.0			

5 (40% : 60%)	0.9 0.9	0.93	3.0 3.0	3.00	1.50	31.79

4.1.1.7 Results of The Ratios of Propanolol Set-1:

4.1.1.7.1 Carr's index and Hausner ratio measurement for the ratios propanolol Set-1.

Table-38: Carr's index and Hausner ratio measured for propanolol Set-1.

Ratio (Containing Propranolol HcCl)	Bulk Volume, Vo (ml)	Most Acceptable Value of Vo (ml)	Tapped Volume, Vr (ml)	Most Acceptable value of Vr	Hausner Ratio	Compressibility index
1 (13% : 87%)	3.5 3.7 3.5	3.56	2.50 2.30 2.50	2.43	1.46	31.74
2 (17% : 83%)	3.8 3.5 3.5	3.60	2.30 2.50 2.50	2.43	1.48	32.50
3	3.7 3.7	3.70	2.50 2.80	2.70	1.37	27.02

(21% : 79%)	3.7		2.80			
4 (29% : 71%)	3.8 3.8 3.5	3.70	3.00 3.00 3.00	3.00	1.23	18.91
5 (33% : 67%)	3.8 3.8 3.8	3.80	3.30 3.30 3.30	3.30	1.15	13.15

4.1.1.7.2 Angle of Repose measurement for the ratios of propanolol Set-1.

Table-39: Angle of repose measured for the ratios of propanolol Set-1.

Ratio (containing Propranolol HCl)	Height (h)	Avr Height (h)	Diameter (2r)	Avr Diameter (2r)	Radius (r)	Angle of Repose (o)
1 (13% : 87%)	1.3 1.3 1.3	1.30	2.4 2.4 2.4	2.40	1.20	47.29

2 (17% : 83%)	1.3 1.2 1.2	1.23	2.5 2.4 2.5	2.46	1.23	45.00
3 (21% : 79%)	11 1.1 1.1	1.10	2.5 2.8 2.8	2.70	1.35	39.17
4 (29% : 71%)	1.0 1.0 0.9	0.96	3.0 3.0 2.8	2.93	1.46	33.32
5 (33% : 67%)	1.0 1.0 1.0	1.00	3.0 3.0 2.8	2.93	1.46	34.40

4.1.1.8 Results of The Ratios of The Propanolol Set-2:

4.1.1.8.1 Carr's Index and Hausner ratio measurement for the ratios of propanolol Set-2.

Table-40: Carr's index and Hausner ratio measured for propanolol Set-2.

Ratio With Amlodipine	Bulk Volume, Vo (ml)	Most Acceptable Value of Vo (ml)	Tapped Volume, Vr (ml)	Most Acceptable value of Vr	Hausner Ratio	Compressibility index
1 (5% : 95%)	3.5	3.43	2.30	2.30	1.49	32.94
	3.5		2.30			
	3.3		2.30			
2 (10% : 90%)	3.3	3.36	2.30	2.36	1.42	29.76
	3.5		2.50			
	3.5		2.3			
3 (15% : 85%)	3.5	3.60	2.4	2.40	1.50	33.33
	3.5		2.5			
	3.8		2.3			
4 (20% : 80%)	3.5	3.70	2.8	2.7	1.37	27.02
	3.8		2.8			
	3.8		2.5			
	3.7					

5 (25% : 75%)		3.70	3.0	3.00	1.23	18.91
	3.7		3.0			
	3.7		3.0			

4.1.1.8.2 Angle of Repose measurement for the ratios of propanolol Set-2.

Table-41: Angle of repose measured for the ratios of propanolol Set-2.

Ratio (containing amlodipine)	Height (h)	Avr Height (h)	Diameter (2r)	Avr Diameter (2r)	Radius (r)	Angle of Repose (o)
1 (05% : 95%)	1.4	1.40	2.4	2.33	1.16	50.35
	1.4		2.4			
	1.4		2.2			
2 (10% : 90%)	1.3	1.30	2.5	2.50	1.25	46.12
	1.3		2.5			
	1.3		2.5			
3	1.3	1.23	2.4	2.33	1.16	46.67
	1.2		2.4			

(15% : 85%)	1.2		2.2			
4 (20% : 80%)	1.2 1.2 1.2	1.20	2.5 2.5 2.8	2.60	1.30	42.70
5 (25% : 67%)	1.1 1.1 1.1	1.10	2.5 2.5 2.8	2.60	1.30	40.23

4.1.1.9 Results of The Ratios of The Propanolol Set-3:

4.1.1.9.1 Carr's index and Hausner ratio measurement for the ratios of propanolol Set-3.

Table-42: Carr's index and Hausner ratio measured for propanolol Set-3.

Ratios With Propranolol HCl	Bulk Volume, Vo (ml)	Most Acceptable Value of Vo (ml)	Tapped Volume, Vr (ml)	Most Acceptable value of Vr	Hausner Ratio	Compressibility index
1	3.3 3.5	3.36	2.30 2.50	2.36	1.42	29.76

(7% : 93%)	3.5		2.30			
2 (27% : 73%)	3.7 3.8 3.8	3.76	3.00 3.00 3.00	3.00	1.25	20.21
3 (30% : 70%)	3.7 3.7 3.7	3.70	3.30 3.00 3.00	3.10	1.19	16.21
4 (35% : 65%)	3.7 3.6 4.0	3.76	3.30 3.30 3.30	3.30	1.13	12.23
5 (40% : 60%)	3.8 3.8 3.8	3.80	3.50 3.50 3.50	3.50	1.09	7.89

4.1.1.9.2 Angle of Repose measurement for the ratios of propanolol Set-3.

Table-43: Angle of Repose measured for the ratios of propanolol Set-3.

Ratio (containing amlodipine)	Height (h)	Avr Height (h)	Diameter (2r)	Avr Diameter (2r)	Radius (r)	Angle of Repose (o)
1 (7% : 93%)	1.4 1.4 1.3	1.36	2.4 2.4 2.4	2.40	1.20	48.57
2 (27% : 73%)	1.1 1.1 1.0	1.06	2.8 2.6 2.8	2.73	1.36	37.93
3 (30% : 70%)	1.0 1.0 1.0	1.00	2.8 2.8 2.8	2.80	1.40	35.53
4 (35% : 65%)	1.0 1.0 0.9	0.93	3.0 2.8 2.8	2.86	1.43	33.03
	0.9		3.0			

5 (40% : 60%)	0.9 0.9	0.90	3.0 2.8	2.93	1.46	31.65

4.2 Comparison shown using graph among 3 types (excipients, amlodipine, propranolol) of Sets (Set-1, Set-2, Set-3) on the basis of Carr's Index, Hausner Ratio and Angle of Repose

By plotting percentage ratio of PVP in X-axis and respected Carr's index in Y-axis, a graph is plotted by which an equation and regression value was established. Using these equations, Carr's Index of any set of excipients and APIs can be achieved.

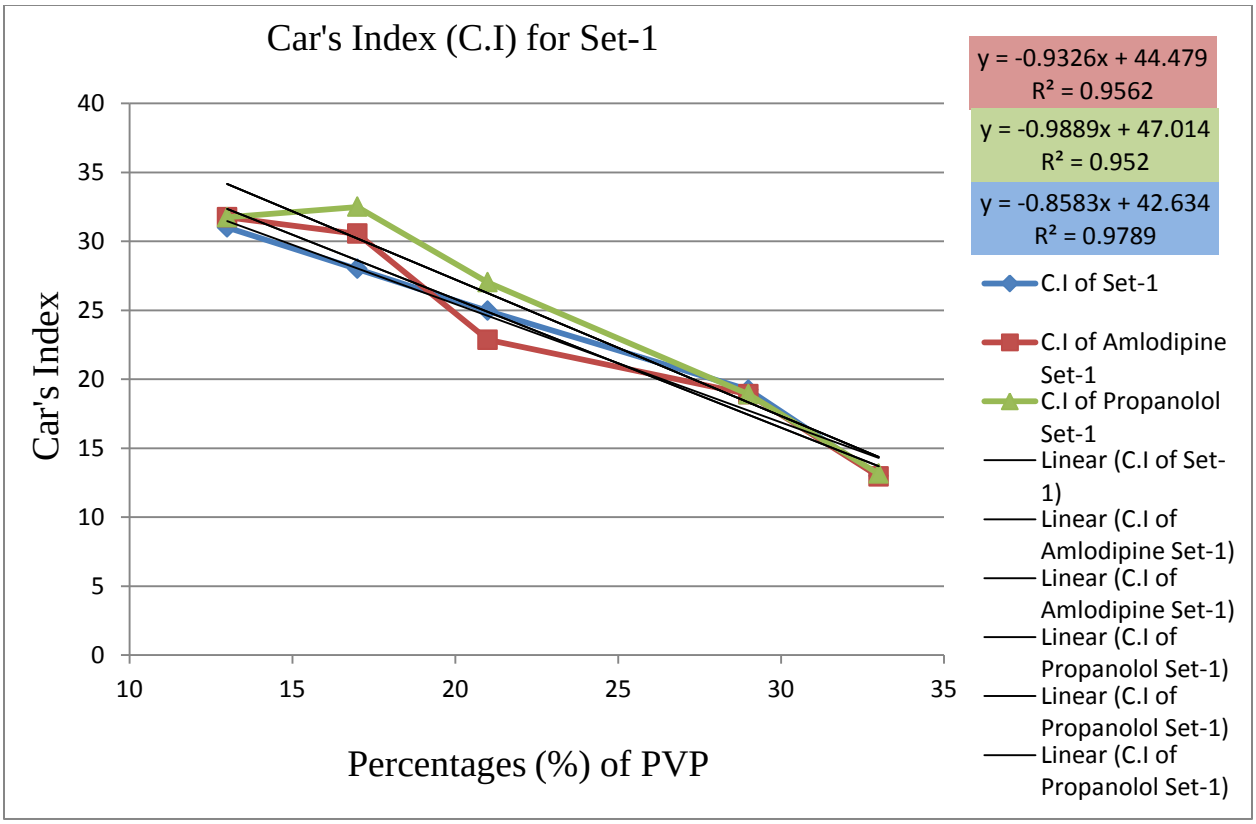

Fig-4.1: A percentage ratio of PVP versus Carr's Index graph

By plotting percentage ratio of PVP in X-axis and respected Hausner ratio in Y-axis, a graph is plotted by which an equation and regression value was established. Using these equations, Hausner ratio of any set of excipients and APIs can be achieved.

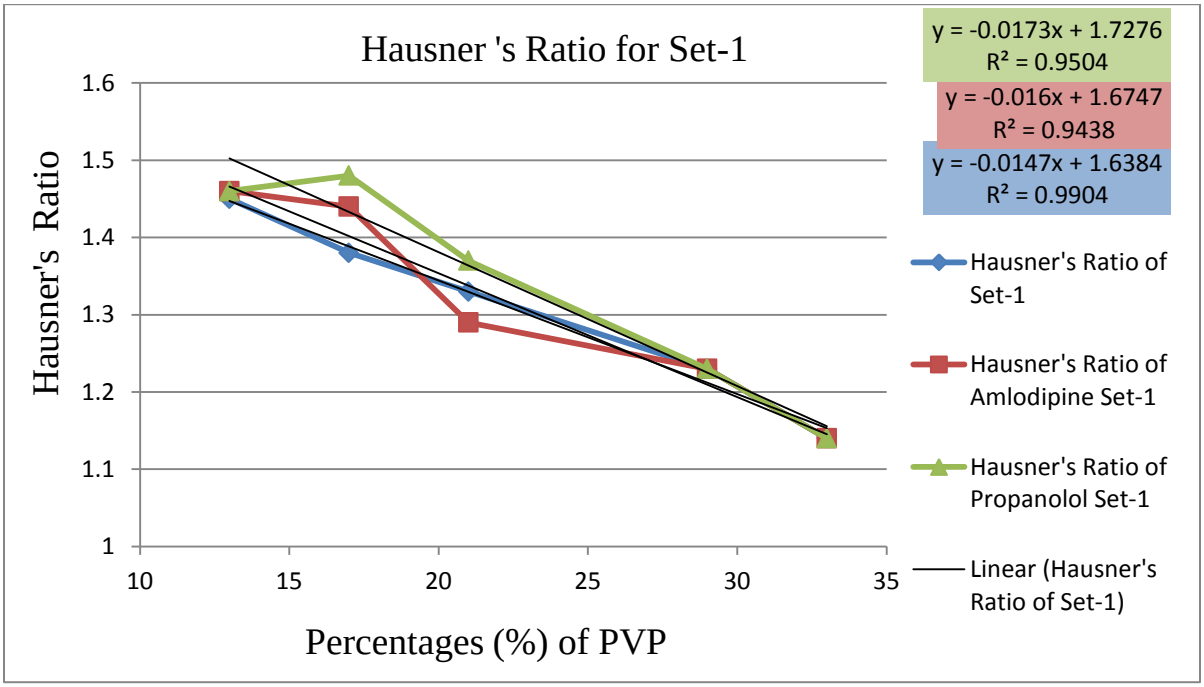

Fig-4.2: A percentage ratio of PVP versus Hausner's ratio graph

By plotting percentage ratio of PVP in X-axis and respected angle of repose in Y-axis, a graph is plotted by which an equation and regression value was established. Using these equations, angle of repose of any set of excipients and APIs can be achieved.

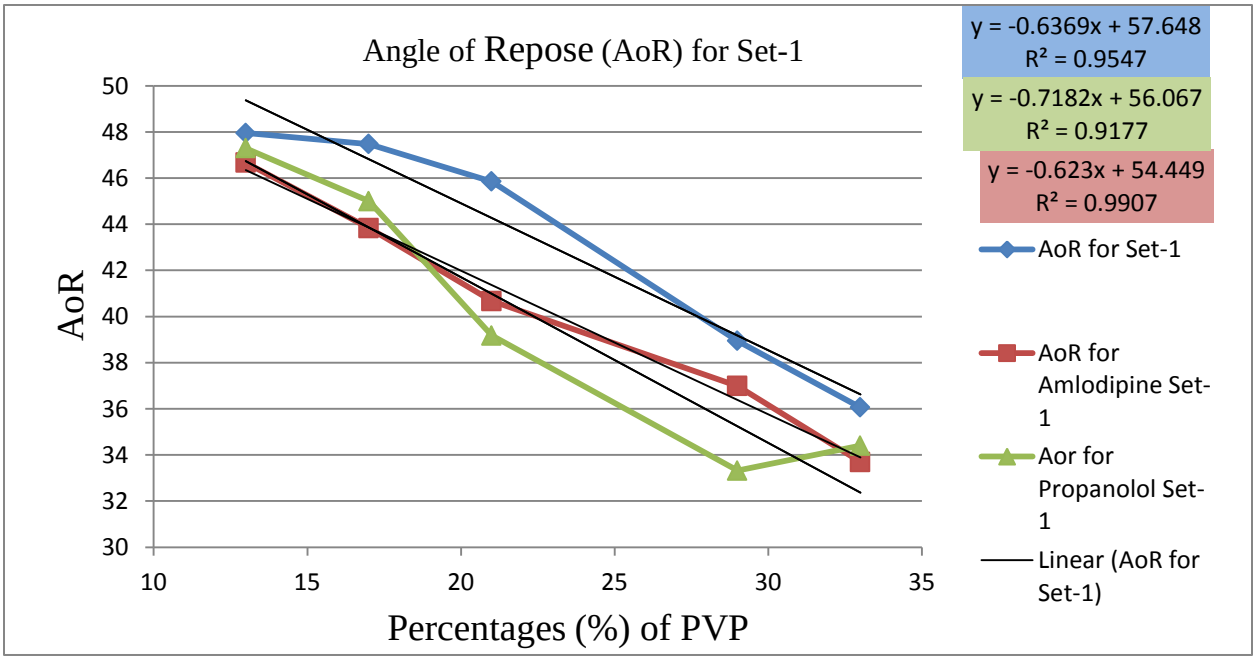

Fig-4.3: Angle of Repose (AoR) for Set-1

By plotting percentage ratio of PVP in X-axis and respected Carr's index in Y-axis, a graph is plotted by which an equation and regression value was established. Using these equations, Carr's Index of any set of excipients and APIs can be achieved.

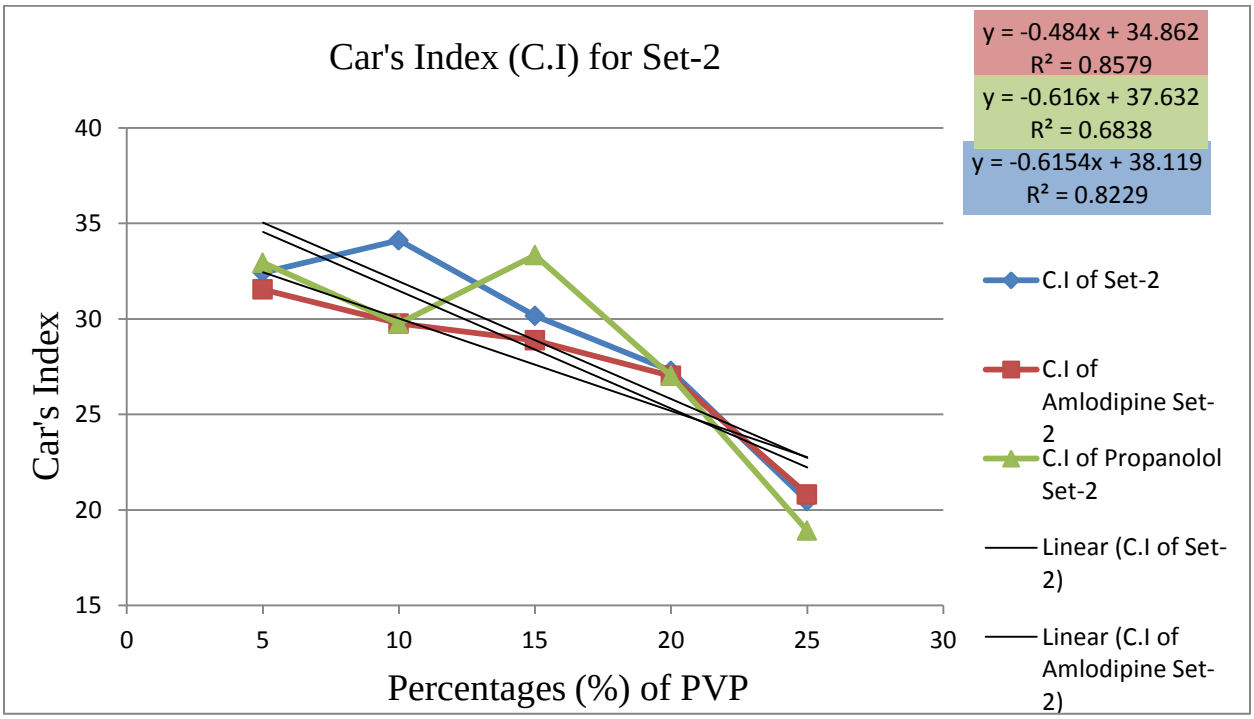

Fig-4.4: A percentage ratio of PVP versus Carr's Index graph

By plotting percentage ratio of PVP in X-axis and respected Hausner ratio in Y-axis, a graph is plotted by which an equation and regression value was established. Using these equations, Hausner ratio of any set of excipients and APIs can be achieved.

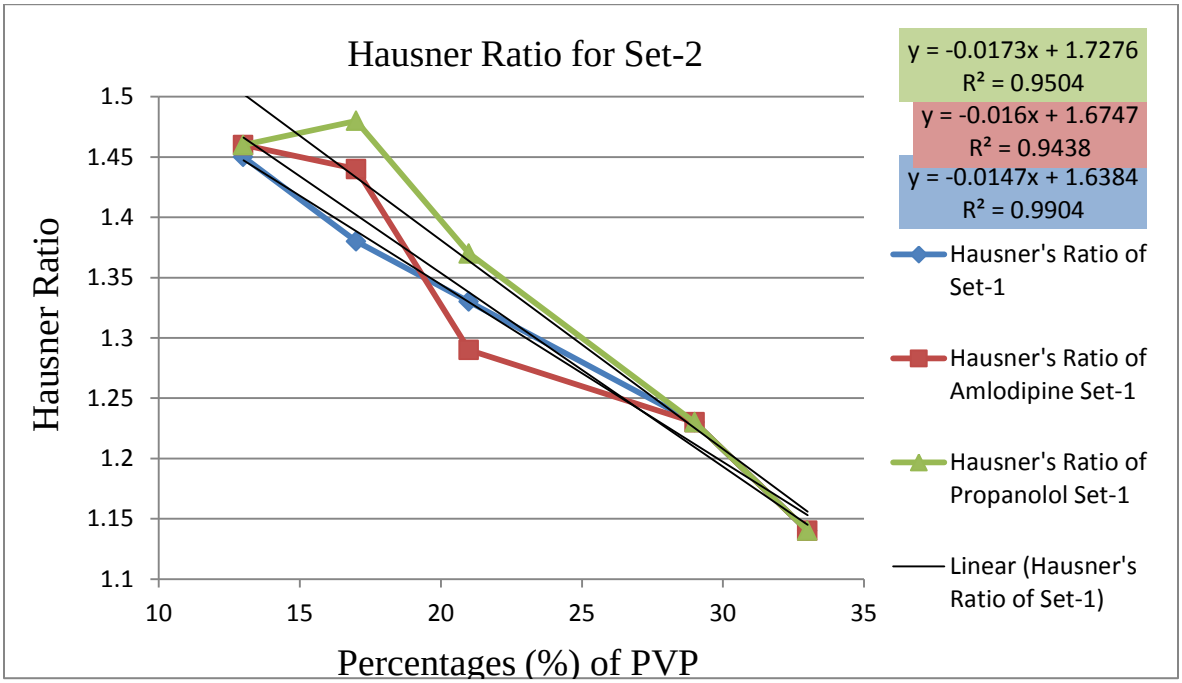

Fig-4.5: A percentage ratio of PVP versus Hausner's ratio graph

By plotting percentage ratio of PVP in X-axis and respected angle of repose in Y-axis, a graph is plotted by which an equation and regression value was established. Using these equations, angle of repose of any set of excipients and APIs can be achieved.

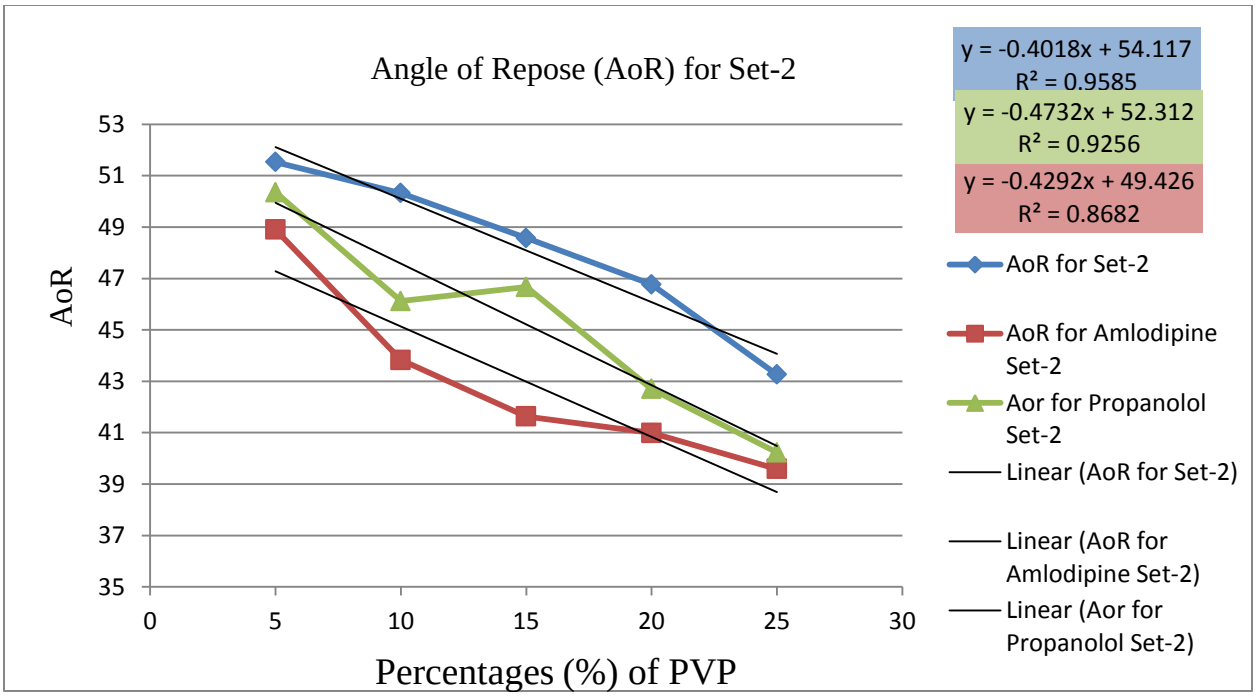

Fig-4.6: Angle of Repose (AoR) for Set-2

By plotting percentage ratio of PVP in X-axis and respected Carr's index in Y-axis, a graph is plotted by which an equation and regression value was established. Using these equations, Carr's Index of any set of excipients and APIs can be achieved.

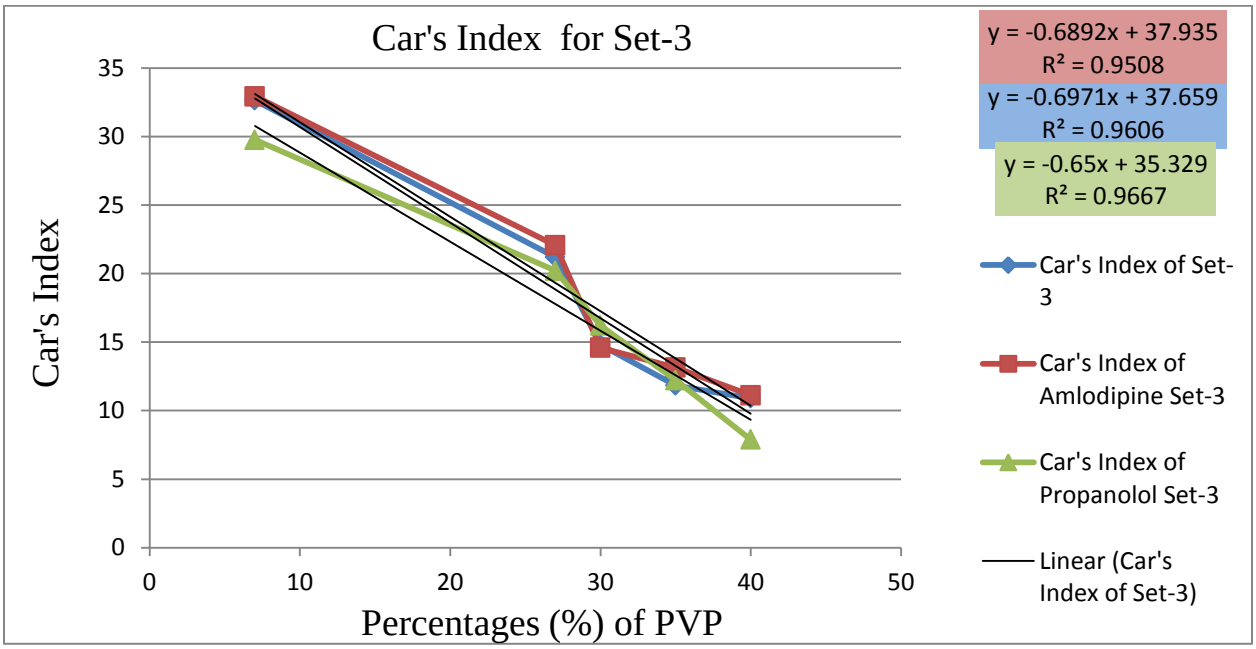

Fig 4.7: A percentage ratio of PVP versus Carr's Index graph

By plotting percentage ratio of PVP in X-axis and respected Hausner ratio in Y-axis, a graph is plotted by which an equation and regression value was established. Using these equations, Hausner ratio of any set of excipients and APIs can be achieved.

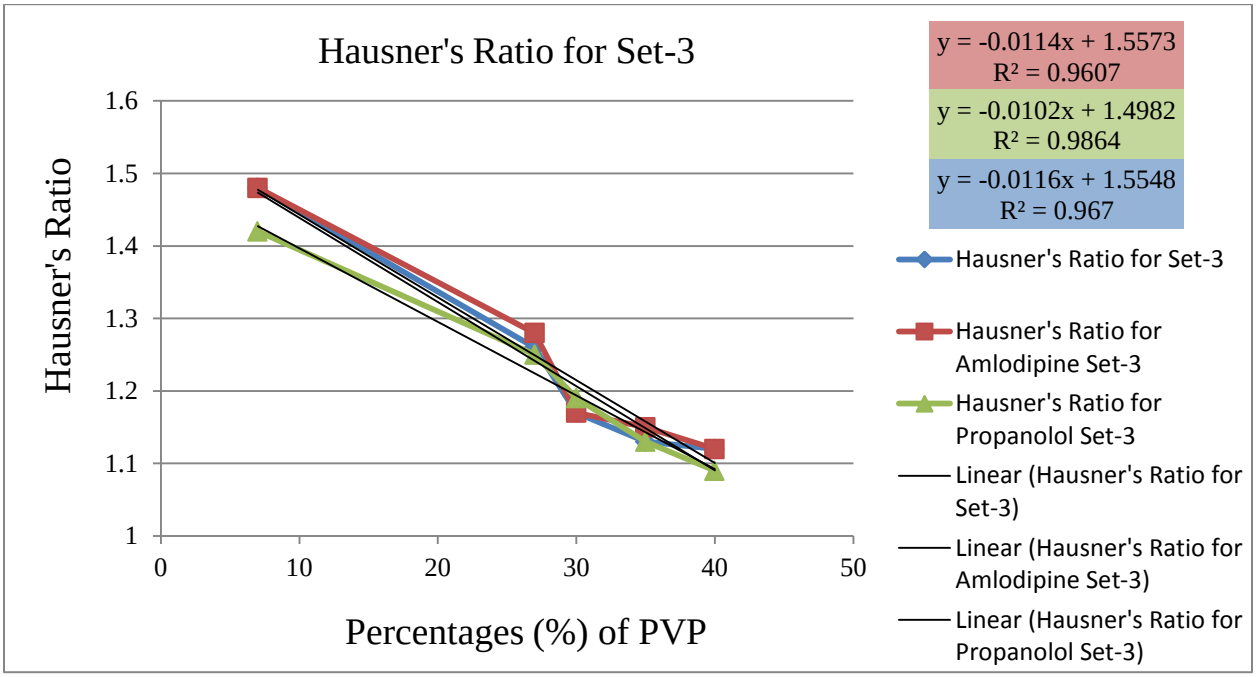

Fig-4.8: A percentage ratio of PVP versus Hausner's ratio graph

By plotting percentage ratio of PVP in X-axis and respected Hausner ratio in Y-axis, a graph is plotted by which an equation and regression value was established. Using these equations, Hausner ratio of any set of excipients and APIs can be achieved.

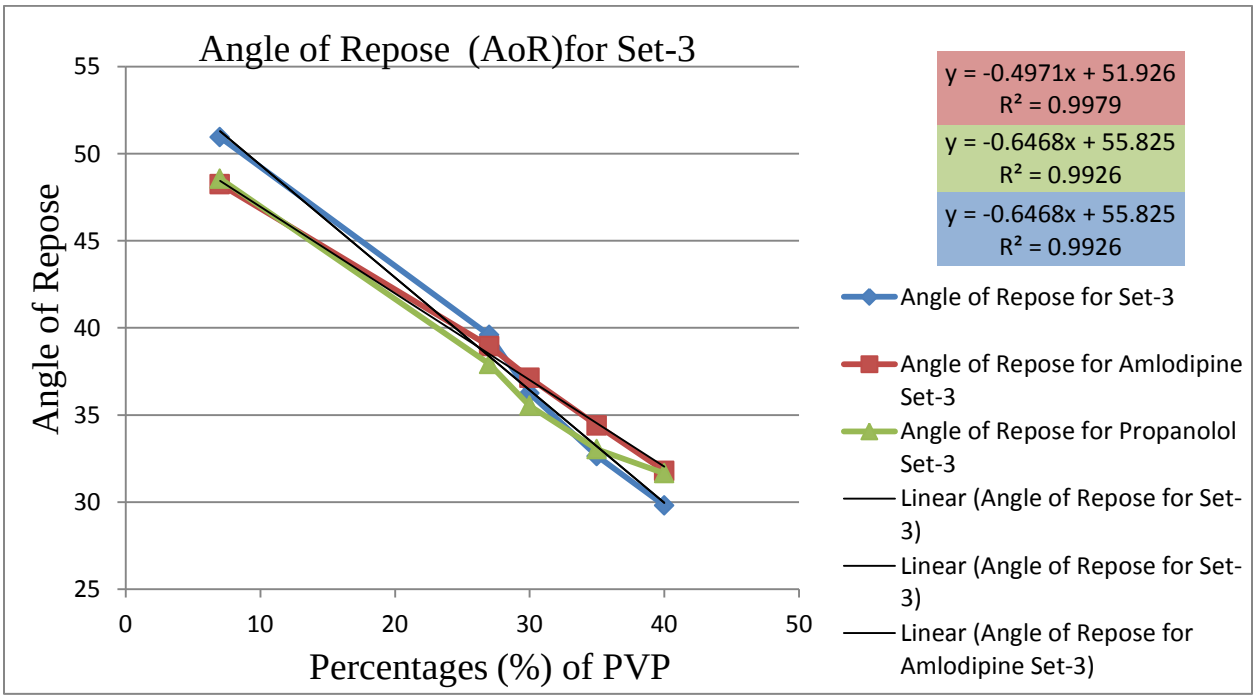

Fig-4.9: Angle of Repose (AoR) for Set-3

4.3 Equations And Regression Values:

This experiment was done to isolate several equation. For the ratios of PVP which helps to determine the flow property of the powder mixture. At which percentage the flow property will be maximum or minimum can be determined by those equations.

Table-44: Carr's Index Equations and Regression Values

Sets	Equations and Regression values
Set-01	$y = -0.593x + 38.04$…….(1) $R^2 = 0.943$
Set-02	$y = -0.586x + 37.38$…….(2) $R^2 = 0.846$
Set-03	$y = -0.697x + 37.65$…….(3) $R^2 = 0.960$
Amlodipine Set-01	$y = -0.932x + 44.47$…….(4) $R^2 = 0.956$
Amlodipine Set-02	$y = -0.615x + 38.11$…….(5) $R^2 = 0.822$
Amlodipine Set-03	$y = -0.689x + 37.93$…….(6) $R^2 = 0.950$
Propanolol Set-01	$y = -0.988x + 47.01$…….(7) $R^2 = 0.952$
Propanolol Set-02	$y = -1.015x + 39.89$…….(8) $R^2 = 0.911$
Propanolol Set-03	$y = -0.65x + 35.32$……...(9) $R^2 = 0.966$

Table-45: Hausner Ratio Equations and Regression Values

Sets	Equations and Regression values
Set-01	$y = -0.013x + 1.618$…….(1) $R^2 = 0.996$
Set-02	$y = -0.011x + 1.573$…….(2) $R^2 = 0.876$
Set-03	$y = -0.011x + 1.554$…….(3) $R^2 = 0.967$
Amlodipine Set-01	$y = -0.016x + 1.674$…….(4) $R^2 = 0.943$
Amlodipine Set-02	$y = -0.009x + 1.517$…….(5) $R^2 = 0.885$
Amlodipine Set-03	$y = -0.016x + 1.721$…….(6) $R^2 = 0.951$
Propanolol Set-01	$y = -0.016x + 1.721$…….(7) $R^2 = 0.951$
Propanolol Set-02	$y = -0.011x + 1.573$…….(8) $R^2 = 0.672$
Propanolol Set-03	$y = -0.010x + 1.498$…….(9) $R^2 = 0.986$

Table-46: Angle of Repose Equations and Regression Values

Sets	Equations and Regression values
Set-01	$y = -0.698x + 58.62$…….(1) $R^2 = 0.918$
Set-02	$y = -0.401x + 54.11$…….(2) $R^2 = 0.958$
Set-03	$y = -0.646x + 55.82$…….(3) $R^2 = 0.992$
Amlodipine Set-01	$y = -0.623x + 54.44$…….(4) $R^2 = 0.990$
Amlodipine Set-02	$y = -0.429x + 49.42$…….(5) $R^2 = 0.868$
Amlodipine Set-03	$y = -0.429x + 49.42$…….(6) $R^2 = 0.868$
Propanolol Set-01	$y = -0.718x + 56.06$…….(7) $R^2 = 0.917$
Propanolol Set-02	$y = -0.473x + 52.31$…….(8) $R^2 = 0.925$
Propanolol Set-03	$y = -0.529x + 52.07$…….(9) $R^2 = 0.992$

Chapter-V

Discussion

5.1 Discussion

The equations in the table-44, 'y' denotes Carr's index and 'x' denotes the percentage of PVP. According to Carr's index Chart described in USP29-1174, flow of a powder mixture can be described. Here, in this experiment USP29-1174 is considered as a reference. From the equations in the table-44, it was seen that increased amount of PVP improve flow property of powder mixture and when we used along with amlodipine and propanolol flow property is further slightly increased. For example, Carr's index equation III described that when 40% (x=40) PVP was used, there was a excellent flow of powders (y=10.9) due to granule formation. When 7% (x=7) PVP was used, there was a very poor flow of powder (y=32.65) because fine powder tends to aggregate. Carr's index equation IV-VI and VII-IX described that flow property is slightly improved when amlodipine or propanolol is added because of better granule formation. In the equation II derived from the set-2 straight line, slight variation observed in the Carr's index value when 10% PVP is used with amlodipine (abrupt fall in the Car's Index value) and when 15% PVP was used with propanolol (abrupt rise in the Car's Index value) respectively due to environmental interference.

In the same way the equations in the table-45, 'y' denotes Hausner ratio and 'x' denotes the percentage of PVP. According to Hausner ratio Chart described in USP29-1174, flow of a powder mixture can be described. Here, in this experiment USP29-1174 is considered as a reference. From the equations (table-45), it was seen that increased amount of PVP improve flow property of powder mixture and flow property is further slightly increased when used along with amlodipine and propanolol. For example, Hausner ratio equation III described that when 40% (x=40) PVP was used, there was a excellent flow of powder (y=1.12) due to granule formation. When 7% (x=7) PVP was used, there was a very poor flow of powder (y=1.48) because fine powder tends to aggregate. Equation IV-VI and VII-IX described that flow property is slightly improved when amlodipine or propanolol is added because of better granule formation. . In the equation II derived from the set-2 straight line, slight variation observed in the Hausner ratio value when 10% PVP is used with amlodipine (abrupt fall in the Hausner ratio value) and when 15% PVP was used with propanolol (abrupt rise in the Hausner ratio value) respectively due to environmental interference.

In the same way the equations in the table-46, 'y' denotes angle of repose and 'x' denotes the percentage of PVP. According to angle of repose Chart described in USP29-1174, flow of a powder mixture can be described. Here, in this experiment USP29-1174 is considered as a reference. From the equations in the table-46, it was seen that increased amount of PVP improve flow property of powder mixture and when we used along with amlodipine and propanolol flow property is further slightly increased. For example, angle of repose equation III (table-46) described that when 40% (x=40) PVP was used, there was a excellent flow of powder (y=29.8) due to granule formation. When 7% (x=7) PVP was used, there was a very poor flow of powder (y=50.95) because fine powder tends to aggregate. Equation IV-VI and VII-IX described that flow property is slightly improved when amlodipine or propanolol is added because of better granule formation. In the equation II derived from the set-2 straight line, slight variation observed in the angle of repose value when 10% PVP is used with amlodipine (abrupt fall in the angle of repose value) and when 15% PVP was used with propanolol (abrupt rise in the angle of repose value) respectively due to environmental interference.

Chapter-VI

Conclusion

6.1 Conclusion

The flow of powder during manufacturing indicates the quality of product. Flow of powder also affects the manufacturing efficiency. During formulation developments the flow of blend may affects the exicipients selection and determine whether the direct compression method can be used or not. So the knowledge of flow property of pharmaceutical solid dosage forms is very important for the pharmaceutical industries. Improved or faster flow ability will increase the production of solid dosage forms. As excipients are used as a major portion of a solid dosage form. This experiment was done to find out several equations for various ratios of PVP used. These equations will help the future researchers and pharmaceutical personnel to predict and determine the flow ability of mixtures for adding the PVP. For further research projects on powder mixture flow property and new formulation determination, this research will help to save money and time.

Chapter-VII

References

6.1 References

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