IJPSR (2016), Vol. 7, Issue 8 **(Review Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 22 March, 2016; received in revised form, 05 July, 2016; accepted, 13 July, 2016; published 01 August, 2016

FUNCTIONALITY TESTING OF EXCIPIENTS: A REVIEW

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Keywords:

Excipients, Lubrication, Preformulation, Physical Characterization,

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ABSTRACT: The quality of medicines depends not only on the active principles and production processes, but also the performance of the excipients, hence we say' Excipients are Cindrellas of Formulation'. The traditional concept of the excipient as any component other than the active substance has undergone a substantial evolution from an 'inert' and cheap vehicle to an essential constituent of the formulation. The rapid evolution of scientific, regulatory and economic factors, the introduction of delivery systems and the advance in biopharmaceutics have led to a new interest in the role and functionality of the excipients. There are number of raw materials available from a multitude of sources used in pharmaceutical industry where their chemical structures vary from small polymer to long chain polymer. Excipients are now chosen to perform a variety of functions which guarantee the stability and bioavailability of the drug substance and its manufacturability on a large production scale. Beyond the dosage form necessities, excipients particularly in the case of solid dosage forms are used. As a consequence, their characterisation must go beyond the simple tests for identity, purity and strength as prescribed in general by the Pharmacopoeia monographs. Full physical characterisation of solid materials is now made possible with the help of high resolution analytical techniques on the molecular, particulate and bulk levels, this approach now has become necessary to guarantee the behaviour of the excipient during the formulation and production phases of all solid and liquid dosage forms. Excipient harmonisation, standardised functionality tests, preformulation data bases will contribute to change the conventional trial-and-error formulation approach into a far more scientific and technological development. Hence study of excipient has now gained importance which would lead to develop new formulation.

INTRODUCTION: Evolution of concept of excipients: [8] From the standpoint, the excipient is no longer to be considered an inert product but an essential and functional component of a modern pharmaceutical dosage form which indeed uses a pharmaceutical excipient. What are the external factors that have contributed to this evolution, not only in the concept but also in the regulations governing excipients?

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.7(8).3208-17

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.7 (8).3208-17

The globalisation of demand and economies of scale of various industries are the consequences of an industrial philosophy that gives partnerships and links a bridge between pharmaceutical companies with the formation of some important multinational companies enjoying considerable financial reserves from regulatories. This enables them to support the basic and applied research activities necessary to innovate their range of products in the future.

The organisation undergoes transformation because of its scattered location of the production plants and hence it reduces the time required for development of products and hence marketing of same products from time to time increases. As a reflection of this, even the machinery, such as ampoule fillers, tabletting and encapsulating machines, coating

machines has to be re-designed so as to work at high speeds and give proper results of same. It is necessary that new excipients are compatible with all the new production machinery (eg-rotating tablettting machines, granulators, coaters) but also with innovative and active principles coming, that is, from biotechnologies, genetics and modern peptide synthesis. Moreover, the interest in and wide-spread use of new therapeutic systems and modified-release forms is another factor that spurs the demand for more sophisticated excipients that can fulfil specific functions within the formulation. These innovative formulations permit the optimisation of plasmatic concentrations of the active principle, thus increasing efficacy, the patient's compliance and the added value of the medicinal product.

In the past, excipients were taken from materials of natural origin and were used commonly in the chemical and agricultural food-stuffs sectors and employed in the pharmaceutical field, without purification so as to improve the assay or their chemical or physical characteristics. Analytical tests were conducted for most of the materials within the Pharmaceutical Industry and not by the supplier of the raw material. The tests were often limited as the expertise tested for specific tests of the material or excipients and these were not sufficient to characterize the excipients quality, much less their functionality. For example, only one type of 'spray-dried' lactose was available for the production of tablets and capsules by direct compression.

It was found latter that secondary amines react with spray dried lactose known as' Maillard Reaction' .Magnesium Stearate was widely employed as a lubricant, even though there was skimp knowledge of its structure and lubricating capacity and its functionality. Since 1970, the situation has evolved swiftly under the pressure of new knowledge of the solid state of materials and the ever more stringent qualitative requirements demanded by the Regulatory Authorities. In 1970 the US National Formulary included over a hundred monographs on excipients and the publication of two editions of the 'Handbook of Pharmaceutical Excipients', which contains monographs that meet pharmaceutical technologists and helps for evaluation of same. Furthermore, at the beginning of 1990, the Secretaries of the three most important Pharmacopoeias, the USP, the Eur. Ph. and the J. Ph., agreed on the importance of harmonising the standards and the testing methods regarding excipients, so as to satisfy the requirements of the industry and their own respective Regulatory Agencies.

The monograph on lactose monohydrate has reached the last stage of publication and those on Magnesium Stearate, saccharose, polyvinylpyrrolidone as well as powdered and microcrystallised cellulose are at advanced stages in the procedure of publication .Some testing methods on the physical state, such as particle size, specific surface area, bulk and tapped density are also in an advanced phase of joint compilation for publication. The change in modified release dosage forms, new therapeutic systems, new production technologies have lead to development of new research material along with development of new functional excipient.

All these factors and more have changed the traditional concept of an excipient and lead to the development of new concept and new function of excipient where it can fulfil several functions of pharmaceutical formulation and serve as a best formulation stage for researchers. They have also contributed to focusing the researchers or technologists attention to the quality of Excipient which directly links to the efficacy and safety use of medicinal product along with its active principles present in it.

Regulatory guidance:

According to current regulatory guidelines, for example ICH Q8 Pharmaceutical Development, the marketing authorisation application should discuss the Excipients chosen and their concentration, and demonstrate the characteristics that can influence the medicinal product performance and manufacturability relative to the respective function of each excipient. Excipient provide them with their intended functionality. The information on excipient performance can be used as appropriate to justify the choice and quality attributes of the excipient.

Functionality-Related Characteristics Section:

In monographs: [23] Monographs on excipients may have a section entitled 'Functionality-related characteristics'. This section includes information for the user or researcher and is not a mandatory part of the given monograph. The section gives statement of characteristics that are known to be relevant for certain uses of the excipient. For functionality the statement may be relevant but for characteristics it may be irrelevant as the structure and the chemical form varies in terms of temperature, heat, light.etc.. For this reason, the section should not be seen simply as a supplement to the monograph. It is the responsibility of the manufacturer of the medicinal product that how he decides that the information on FRCs are applied to manufacturing processes and how the data is used for pharmaceutical development. The manufacturer may release this data for the testing of raw excipient when they are not extracted from medicinal plants. The information on the functionality-related characteristics may be given in different ways such as:

- Name of the FRC;
- Name of the FRC and a recommended method for its determination or evaluation referring wherever possible to a general chapter of the Pharmacopoeia;
- Name of the FRC with a recommended method for its determination and where it can be accepted according to the monograph present in Pharmacopoeia. The given characteristics of the subject may be of great importance that has to be mentioned in FRC section. The degree of polymerisation is used in the mandatory.

Lubrication: [1, 12]

Most pharmaceutical tablet formulations require the addition of a lubricant to reduce friction at the die wall. Some of the lubricants used are Magnesium Stearate, talc.etc. Lubricants are of two types Boundary lubricant sand Fluid lubricants. Die wall lubricants function by interposing a film of low shear strength at the interface between the tableting mass and the die wall. There is some chemical bonding between this boundary lubricant and the surface of the die wall and the edge of the tablet during tabletting. The best lubricants are those with low shear strength but strong cohesive tendencies in direction at right angles to the plane of shear. By utilizing materials with low shear strength as lubricants, shear failure occurs in the lubricant layers and not at the compressed powder or resultant wall interfaces.

Lubricants are intended to prevent adhesion of the tablet materials to the surface of dies and punches or die wall and to reduce inter particle friction that may improve the rate of flow of the tablet granulation. Lubricants are the materials that act by reducing friction by forming an intermediate layer between the tablet ingredients 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.

In the pharmaceutical industry, fluid lubricants are not used widely. However liquid paraffin may be used indeed. Boundary lubrication is the most common mechanism for tabletting. A Boundary lubricant typically forms layers/film between surfaces or at interfaces which reduces friction, where the penetration of the lubricant into surface of tablet occurs. Structurally, the boundary lubricants are long chain molecules with active end-groups such as stearic acid and its metallic salts typical end-groups which includes : 1) –OH (long chain alcohol); 2) –NH2 (long chain amine); 3) COOH (long chain fatty acids); and 4) metal ions such as Mg2+. Lubricants containing these molecules with these end-groups can be readily adsorbed on the surfaces of metals or other particles to form an oriented monolayer.

These layers prevent further contact between the intended surfaces and powder particles of the tablet. The efficiency of a boundary lubricant is measured by the extent which can mask the tablet surface. In other words, a lubricant film such as the film of Magnesium Stearate needs to be sufficiently thick to cover the surface of the tablet. In addition, the breaking down of the lubricant film plays a significant role so that the motion of lubricated surface is facilitated. The dihydrate of Magnesium

Stearate, which gives the best lubrication efficiency,due to its layered structure and chemical structure.

Magnesium Stearate is the most widely used lubricant in tablet manufacturing. However, its lubrication properties vary from batch to batch, even though when the material is obtained from the same producer. This results in change in their functionality and change in the testing of Magnesium Stearate. For this reason, Magnesium Stearate is frequently studied. Current United States Pharmacopeial—National Formulary (USP 30-NF 25) requirements include chemical analysis of stearic acid and palmitic acid content and physical tests for specific surface area (SSA) and loss on drying (moisture contents).

The manufacturer's certificate of analysis(COA) often supplements the pharmacopeial methods with additional physical tests, such as particle size, and apparent (bulk) and tapped density. However, these tests are not direct measures of the lubrication efficiency of the Magnesium Stearate powder but add to the efficacy of the material. Magnesium Stearate contains stearate salts which leads to the calculation of various state salt content.

This study was designed to independently evaluate the equivalence of the Magnesium Stearate powders and to assess the impact of changes in the Magnesium Stearate on the finished product quality. An additional goal was to identify material characteristics that may be root causes for differences in the functionality of the Magnesium Stearate powders resulting in the difference in the final product performance and differentiating for various physical and chemical characteristics.

Lubricant effect on flow: [4]

Powder flow is critical during tableting as it must flow easily and uniformly into the tablet dies which ensure tablet weight uniformity and production of tablets with consistent and same weight. Powder flow is seen when gravitational forces becomes higher than the friction and cohesion forces which influences particle-particle interactions. Cohesive forces are particles-particles interaction/ attraction and includes Van der Waals forces, capillary forces and electrostatic forces. Cohesive forces are affected by the surface properties of the particles. As boundary layer lubricants forms a film around particles affecting the cohesive forces which indirectly affects the powder flow. Friction acts at contact points between particles and thus, surface morphology of lubricant affects friction forces. If the contact area is increased, then potential contact points are increased which directly increases friction. Boundary layer lubricants acts by decreasing friction.

Although lubricants are necessary and added to help tableting, their impact upon tablet properties and manufacturing cannot be ignored.

In the mixing process during the direct tabletting procedure, small lubricant particles would be dispersed between other large ingredient particles. When shear stress acts over all the particles in the subsequent compression process, the lubricant powder particles disintegrate, like mica, leading to a decrease in the friction force.

What causes these problems?

The hydrophobic coating of the lubricant interferes with "wetting" which leads to increase in the time required for the tablets to disintegrate and the drug to become dissolved.

However a complete coating of lubricant may affect tablet hardness by interfering with the interparticle bonding of it .In formulations the tablets are formed with components that bond by plastic deformation.

Tablets formed by brittle fracture are less affected because brittle fracture produces clean "unlubricated" sites where bonding can occur during compression.

Physical Characterization of Lubricant: [2, 6, 7]

Specific Surface Area:

The specific surface area of powder is determined by physical adsorption of gas on the surface of solid and by calculating the amount of adsorbate gas corresponding to monomolecular layer on the surface. Physical adsorption results from relatively weak forces (Van der Waal forces) between the adsorbate gas molecules and adsorbent surface of the test powder. The determination is usually

carried out at the temperature of liquid nitrogen. The amount of gas adsorbed can be measured by volumetric or continues flow procedure. A more precise measurement of surface area is made by Brunauer, Emmett, and Teller (BET) nitrogen adsorption, in which a layer of nitrogen molecules is adsorbed to the sample surface at -196°C. Once surface adsorption has reached equilibrium the sample is heated to room temperature, the nitrogen gas is desorbed and its volume is measured and converted to number of adsorbed molecules via the ideal gas low. Since each nitrogen molecule (N2) occupies an area of 16A2, one may readily compute the surface area per gram for each preweighed sample. By determining the surface area at several particle pressure of nitrogen (5% to 35% N2 in He), extrapolation to zero nitrogen partial pressure yields the true monolayer surface area.

Particle size determination:

Particle size is often considered one of the most important parameters, however, as particle size reduces, the surface area increases significantly in comparison with the volume, so surface properties increasingly determine the dispersions characteristics. Particle size determination is carried out by Malvern Masterizer, Laser Diffraction, or Wet Method.

True density:

True density of a solid particle is the average mass per unit volume, exclusive of all voids that are not fundamental part of molecular packing arrangement. It is a property of particulate material, and hence should be independent of the method of determination. There are three methods to measure the true density: Helium pycnometer, Mercury porosimeter, and air pycnometry. In gas pycnometer, the volume occupied by a known mass of powder is determined by measuring the volume of gas displaced by the powder. The quotient of the mass and volume is the pycnometric density. The pycnometric density equals the true density unless the material contains impenetrable voids, or sealed pores that are inaccessible to the gas used in the pycnometer .

True Density is an important parameter to be measured. It is defined as the mass to the volume occupied by that mass. Therefore, contribution to the volume made by pores or internal voids must be excluded when measuring the true density. For non-porous material, it can be measured by fluid displacement method but for porous materials, where it is difficult to penetrate the fluid into the pores, gas displacement method is useful. The apparatus used to measure sample volume of such material is well known as 'pyknometers' or 'pycnometers' where 'pycnos' means 'thickness' or 'density'.

Zeta potential:

One of the significant surface properties is the surface charge. This is an important factor in determining the interactions between particles, and hence dispersion characteristics such as dispersion stability, flocculation, viscosity, film forming characteristics. etc. The surface charge cannot be measured directly. Instead the charge at a distance from the particle, called the zeta potential is measured. This potential is usually more of interest because particles interact according to the magnitude of this value, rather than the potential at the surface of the particle.

A higher absolute zeta potential implies greater Coulombic repulsion between the particles and higher absolute zeta potential should have a lesser tendency to aggregate.

Angle of repose:

The angle of repose has been used in several branches of science to characterize the flow property of solid. An angle of repose is characteristic related to interparticulate friction or resistance to movement between particles. Angle of test results reported to very depend upon the method used.

Bulk density and tapped density:

Bulk density of solid is often difficult to measure since the slightest disturbance of the bed may result in a new bulk density. Moreover it is clear that bulking properties of powder are dependent on the history of the powder, and that it can be packed to have range of bulk densities. Thus it is essential to specify how the determination made. Because the interparticulate interaction that influence the bulking properties of the powder are also the

interaction that interfere with powder flow, a comparison of bulk and tapped densities can give relative importance of these interaction in given powder.

Bulk density often is bulk density of the powder 'as poured' or as passively filled in measuring cylinder. The tapped density is limiting density attained after 'tapping down'.

Carr's index is a one-point determination and does not always reflect the ease or speed with which the powder consolidates. Indeed, some materials have a high index (suggesting poor flow) but may consolidate rapidly. Rapid consolidation is essential for uniform filling on tablet machines.

Moisture content:
Moisture content is determined using a Karl–Fischer Titrator according to USP method.

Direct titration:
The titrimetric determination of water is based upon the quantitative reaction of water with an anhydrous solution of sulfur dioxide and iodine in the presence of a buffer that reacts with hydrogen ions. In the original titrimetric solution known as Karl Fischer Reagent, the sulfur dioxide and iodine are dissolved in pyridine and methanol.

The test specimen may be titrated with the reagent directly or the analysis may be carried by a residual titration procedure.

The stoichometry of the reaction is not exact and the reproducibility of a determination depends upon such factors as the relative concentration of the reagent ingredients, the nature of the inert solvent used to dissolve the test specimen and the technique used in the particular determination. Therefore an empirically standardized technique is used in order to achieve the desired accuracy. Precision in the method is governed largely by the extent to which atmospheric moisture is excluded from the system.

The titration of water is usually carried out with the use of anhydrous methanol as the solvent may be used for special or unusual test specimen.

Wettability (Contact angle measurement):
Contact angle measurements on pharmaceutical solids give useful information on wettability. Most pharmaceutical solids occur as powders, and it is generally recognized that contact angle determinations on such systems must be made indirectly. Several methods are available Washburn, Bartell and Osterhof, Kossen and Heertjes. Measurements have also been made by compressing the powder into a compact, and measuring the angle of a drop of liquid formed directly on the compact, a technique analogous to the methods used for determining contact angles on smooth surfaces. The success of this method must depend on whether a smooth surface is formed by the act of compressing the powder. As the roughness and heterogeneous nature (e.g. pores) of a surface are known to affect the contact angle, it may be expected that factors such as compression pressure and particle size of the powder may influence the final result.

The wetting of solid materials usually implies the replacement of air on the surface of a solid by a liquid. In addition to the components of the system, the type of wetting is also important. Osterh of and Bartell distinguished between three types of wetting, namely those of adhesion, immersion, and spreading.

The wettability of powders is an important property, because wetting is often the first step of dispersion or dissolution. Quick and homogeneous dispersion of a solid in a liquid, and fast dissolution, can only occur when a sufficient wetting is achieved. Thus wettability is a value that should be measured in a quantitative manner in order to appreciate exactly the properties of powders. Wetting of a solid by a liquid is a surface phenomenon. When a drop of liquid is poured on a solid surface, the wetting of the solid can be appreciated by the contact angle (Ɵ) between the solid and the liquid drop. Wetting is also an important factor in the rate of penetration of a liquid into a powder bed.

Chemical Characterization: [11]
Gas Chromatography:
The free fatty acids contained in a one gram sample of commercial Magnesium Stearate were isolated,

by extraction into 25mL of acetone, and quantified, by analyzing 5-mL aliquots of the resulting solution as described below. The solid remaining following the extraction was dried, and 100 mg of the dried material was decomposed by boiling with a small amount of concentrated hydrochloric acid. The liberated soap fatty acids were extracted into four 10-mL portions of chloroform, the extracts were combined, and the solvent was evaporated under reduced pressure by an aspirator. The residue remaining after evaporation of the solvent was redissolved in 25 mL of acetone, and 1-mL aliquots of the resulting solution were analyzed as described below.

Functionality Testing of Excipients: [1, 8]

During the course of drug development, considerable amount of attention is given to the physical and chemical properties of the drug entity. After addition of Functionality test in April 2007 for USP, it has become hot button issue. Once a decision is made regarding the drugs and the mode of delivery, appropriate excipients are chosen for the dosage form and formulated. In the ideal case, these excipients are chosen only for their ability to increase the drugs administration to the patient, promote (control) drug release, promote bioavailability, increase therapeutic index and protect the drug from degradation during various environmental conditions.

The limited physical characterization or chemical characterization that is performing on excipients reflects functionality only indirectly. Worldwide harmonization of excipient monographs is already being discussed and developments in this area would certainly require detailed functionality testing of excipient material. Excipient functionality is a broad, qualitative and descriptive term for the purpose or role and excipients serves in formulation.

USP released a general information chapter on excipient performance in December 2007. According to this chapter, the excipients monograph that includes its functionality tests requires the mechanism of action of excipient described in it. Hence the demand for functionality has increased.

Functionality Evaluation of Lubricant: [12, 14]

Tablet ejection force:

Tablet ejection force is currently considered an estimator of lubricating capacity. Radial die-wall forces and die wall friction affects the ease with which the compressed tablet can be removed from the die easily. The force necessary to eject a finished tablet follows some pattern. They are divided in three:-

1. The distinctive peak force required for initiating ejection, by breaking of tablet/die wall adhesions,

2. A smaller force usually required to push the tablet to the die wall,

3. Decrease in the force of ejection as tablet emerges from the die. Variations on this patterns are also found when there is less/inadequate amount of lubrication and/or when there is sticky conditions between the tablet and the die wall adhesions. A direct connection is to be expected between die wall frictional forces and the force required to eject the tablet from die.

The ejection force is monitored while maintaining a constant compression force. However, difficulty is seen to maintain the constant compression force on tabletting mass/instruments. The compression force also includes variables of tabletting mass: - manufacturing methods which are used to prepare blends by physical mixture or slugging or chemical mixture, lubricant concentration, weight control setting, hardness control setting, hopper placement (distance from bottom of hopper to the surface of the turret), and height of pharmaceutical bed inside the hopper. Even if the variables are hold constant some of the variations are seen in compression forces.

There is a correlation between the compression force, ejection force, weight, hardness, amount of feed in die, compactibility of powder and concentration of lubricant. A general decrease in compression force, ejection force, weight and hardness, amount of feed in die, compactibility of powder occurred with an increase in the lubricant

concentration because of its property. Hence there is avdecrease in the tablet weight with increasing lubricant concentration, it is clear that a decreased amount of blend flowed into the die as it passed beneath the feed-frame on the tablet press.

Compressibility:
Practically all the widely used compression equations describe the relationship between relative density or porosity of the compact and the applied pressure. The most frequently utilized is the Heckel equation, which is based on the assumption that the densification of the bulk powder column follows the first order kinetics. Compression behaviour of both the plain materials and their powder mixtures was evaluated using the Heckel equation.

Effect on Tablet Properties: [20]
Besides reducing friction and cohesion, lubricants may cause undesirable changes in the properties of the tablet. The presence of lubricant in a powder is thought to interfere in a destructive way with the bonding between particles during compaction, thus reducing final tablet strength. Lubricant type, concentration, method of lubrication, and the manner of incorporating the lubricant all affect the tablet compression. It is generally accepted that Magnesium Stearate has more negative effect on the hardness and tensile strength of the tablets with more deformable materials than brittle ones conducted study using dibasic calcium phosphate as an example of a material that is susceptible to brittle fracture during compaction. Results showed that the tablet strength showed no change when Magnesium Stearate up to 3%wt was present. The adverse impact of Magnesium Stearate on lactose and starch, excipients that also deform plastically, was also observed.

Because many lubricants are hydrophobic, tablet disintegration and dissolution are often retarded by the addition of lubricant. Multiple studies have led to the theoretical conclusion that the deleterious effects observed are a cause of the combination of the large surface area and hydrophobicity of the lubricant. Many research showed that the powder form of Magnesium Stearate have more adverse effects on tablet hardness and disintegration than the granular form.

Tablet Compression: [3]
All tablets are made by a process of compression. Solid, in the form of relatively small particles, is contained in a die and a compressing force of several tones is applied to it by means of punches. The shape of the die governs the cross-sectional shape of the tablet, and the distance between the punch tips at the point of maximum compression governs its thickness. The conformation of the tablet faces, usually flat or convex, is a reflection of those of the punches. The tip of the lower punch moves up and down within the die, but never actually leaves it. The upper punch descends to penetrate the die and apply the compressive force. It is then withdrawn to permit ejection of the tablet, brought about by an upward movement of the lower punch.

Stage 1.Filling
The lower punch falls within the die, leaving a cavity into which particulate matter flows under the Influence of gravity from a hopper. Though tablets are usually described in terms of weight, the die is filled by a volumetric process. The volume is determined by the depth to which the lower punch descends in the die. Unless this volume is filled reproducibly on each occasion, then the mass of the tablet will vary, and with it the drug content of each tablet. Therefore, uniform filling is essential. However, it must be borne in mind that the die cavity has a cross-section of only a few millimeters, and only a fraction of a second is available for filling each die. It therefore follows that the particles must flow easily and reproducibly.

Stage 2.Compression
The upper punch descends, and its tip enters the die, confining the particles. The distance separating the punch faces decreases, either by movement of the upper punch alone (as in eccentric presses) or by movement of both punches (as happens in rotary presses). The porosity of the contents of the die is progressively reduced, and the particles are forced into ever closer proximity to each other. This process is facilitated by the particles fragmenting and/or deforming. Once the particles are close enough together, interparticulate forces then cause the individual particles to aggregate, forming a tablet. The magnitude of the force is governed by the minimum distance separating the punch faces.

Therefore, a second essential property of the particles is that they cohere under the influence of a compressive force. It is also essential that this coherence be maintained when the compressing force is removed.

Stage 3.Ejection

The upper punch is withdrawn from the die, and so the force being applied to the tablet is removed. The effect of this might be to cause the deformed particles to return to their former shape, which would result in a decrease in interparticulate contact and hence tablet strength. It is essential that this does not occur. As the upper punch leaves the die, the lower punch moves upwards, pushing the tablet before it. During the compression stage, the particles are forced into intimate contact with the interior die wall. It follows that attempts to remove the tablet will be opposed by frictional forces and so successful ejection demands lack of adhesion between the tablet and the die wall.

Few powders possess all these essentials and some possess none of them. Thus, before successful tabletting can take place, some preliminary treatment with the addition of one or more excipients is almost invariably needed. Few powders possess all these essentials and some possess none of them. Thus, before successful tabletting can take place, some preliminary treatment with the addition of one or more excipients is almost invariably needed.

Fundamentals of Lubrication: [4]

Commercial Magnesium Stearate is used extensively in the pharmaceutical industry as a powder lubricant in tablet manufacture. It is a variable material with respect to chemical composition, often containing a large proportion of magnesium palmitate, and physical character and hence may have an unpredictable effect on formulations.

The action of lubricant powders will depend essentially on three factors:

1. The concentration or degree of lubricant presence at the tablet-die wall interface,
2. The inherent frictional character of the lubricant powder at the interface;
3. The breakdown or wear of the lubricant layer during the lubrication process.

$$\mu = F/W = As/W$$

Where μ is the coefficient of friction, F is the frictional force, *A* is the real contact area, and s is the shear strength of the softer material and W is the normal load.

Instrumented punch and die assembles have been employed to measure friction coefficients during powder compression and ejection. Such an approach is difficult for Magnesium Stearate and palmitate powders, as their high compressibility results in thin compacts for which radial force measurements may be unreliable and ejection forces small. Also, a tableting technique produces a frictional result which is an average of the gradation of particle movements at the die wall drug compression

CONCLUSION: This study highlights the importance of the functionality testing of Lubricants, in addition to testing for the compendial requirements. It also demonstrates that the lubricant functionality testing is important in terms of formulations. The process parameters such as specific surface area, zeta potential, dissolution. etc. demonstrates the function of lubricant. The requirement of the monograph and the testing of the lubricant follows the USP NF procedure.

ACKNOWLEDGEMENT: First and foremost I offer my sincerest gratitude to my Guide, Dr. Mrudula H. Bele, who has supported me throughout my thesis with his patience and knowledge whilst allowing me the room to work in my own way.

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How to cite this article:
Derle ND, Derle DV, Bele MH and Khatale SB: Functionality Testing of Excipients: A Review. Int J Pharm Sci Res 2016; 7(8): 3208-17.doi: 10.13040/IJPSR.0975-8232.7(8).3208-17.