ScienSage

Journal of Advanced Scientific Research

Available online through http://www.sciensage.info/jasr

ISSN
0976-9595
Research Article

Development of Directly Compressible Ascorbic Acid Tablet Using Novel Excipients

Seema Jagtap, Dr. Bajaj Amrita, Maskare Rina, Darshana Jain*

C.U. Shah College of Pharmacy, SNDT women's University, Juhu Tara Road, Santacruz (west), Mumbai -400049.

**Corresponding author: darshanaj_cup@yahoo.com*

ABSTRACT

Ascorbic acid is a high dose drug, degrading in presence of moisture because of an oxidative process leading to biologically inactive substances. Physical properties of ascorbic acid indicate that it is unsuitable for direct compression at concentrations above 60% in a tabletting mixture. Pharmaceutical excipients contribute unique functionalities to tablet formulations thereby largely determining their quality, compressibility and ease of processing. The objective of the study was to evaluate and compare performance of directly compressible excipient blends for their suitability in ascorbic acid tablet manufacture and to investigate effect of compression pressure on tablet characteristics and assess lubricant sensitivity of compressible excipients and modified hydrogenated fat bleds. These excipients blends were evaluated for particle size, shape, flow properties, % compressibility, Hausner's ratio and elastic recovery. Tablets comprising of drug: excipients (70:30) ratios were compressed using single stroke tablet compression machine. Comparative evaluation of excipients was carried out by investigating effect of compression pressure on hardness and disintegration time of tablets. Lubricant concentration and critical mixing time were optimized using 3^2 factorial designs. Friedman's test was applied for statistical analysis of experimental data thus selection of suitable excipients. Blends comprising of modified hydrogenated fat, microcrystalline cellulose and aerosil was found to be most suitable combination. Hard, fast disintegrating and stable tablets containing 70% of ascorbic acid with excipients blends were obtained having Friedman's test score of 64.5. Using functionality related testing performance, criteria for selection of directly compressible excipients was developed to facilitate industrial scale-up operations.

Keywords: Ascorbic acid, Tablets, Modified Hydrogenated Fat

1. INTRODUCTION

Tablets can be manufactured by wet granulation, dry granulation, or direct compression [1]. Most of the pharmaceutical manufacturers are opting for direct compression tabletting since it involves fewer processing steps, simplified validation, elimination of heat and moisture, economic, and also improves drug stability compared with wet granulation [2]. With dry granulation, reproducibility of the product is difficult to achieve. Hence, the current trend in the pharmaceutical industry is to adopt direct compression technology. Although simple in terms; the direct compression process is highly influenced by powder characteristics such as flowability, compressibility and dilution potential [3-6]. The other attributes that directly compressible excipients should possess high compatibility, good flowability, good blending properties, low lubricant sensitivity, good stability and inertness [7-9]. No single material is likely to exhibit all the ideal characteristics. The physicochemical properties of excipients that ensure a robust and successful process, good flowability, good compressibility, low or no moisture sensitivity, low lubricant sensitivity, and good machine ability even in high speed tabletting machines with reduced dwell times is required. Excipients with improved functionality can be obtained by developing new chemical excipients, new grades of existing materials and new combinations of same. New combinations of existing excipients are an interesting option for improving excipients functionality because all formulations contain multiple excipients. A much broader platform for the manipulation of excipients functionality is provided by combination of two or more excipients. Combination of two or more excipients in various ratios is simple and effective process, the objective of which is to provide a synergy of functionality improvement as well as increasing the concentration of active ingredient in tablet.

Ascorbic Acid is a water-soluble vitamin, needed for the growth and repair of tissues in all parts of body [10]. It helps the body make collagen, an important protein used to make skin, cartilage, tendons, ligaments, and blood vessels [11, 12]. Ascorbic Acid is essential for healing wounds, and for repairing and maintaining bones and teeth. Low levels of Ascorbic Acid have been associated with a number of conditions, including high blood pressure, gallbladder disease, stroke, some cancers, and atherosclerosis (the build-up plaque in blood vessels that can lead to heart attack and stroke). Getting enough Ascorbic Acid from your diet may help reduce the risk of developing some of these conditions.

Powdered form of ascorbic acid lacks good flow and lubrication properties. Satisfactory tablets have been prepared

using crystalline ascorbic acid. Although medium size crystals were best from compression point of view, reflection from the relatively large crystals on the tablet surfaces was distracting and gave the impression of mottling.

Ascorbic acid is a high dose drug. It limits the quantity of the added excipients. Hence excipients selection for direct compression of ascorbic acid is a critical factor. Unfortunately, the physical properties of ascorbic acid indicate that it is unsuitable for direct tabletting at concentration above 60% in tabletting mixture [13-15]. Combination of excipients leads to the formation of mixtures that granulates with superior properties compared with physical mixtures of components or individual components [16-20]. Usually a combination of plastic and brittle materials is used for co-processing. This combination prevents storage of too much elastic energy during the compression, which results in a small amount of stress relaxation and a reduced tendency of capping and lamination thereby optimum tabletting performance [21-24]. Micro Crystalline Cellulose (MCC) is well known as a tablet diluent, binder and disintegrant. Cellulose exhibits disintegration property due to capillary action; it has a self lubricating quality and thus, it requires less lubrication than other excipients [25, 26]. In addition, it exhibits inherent compatibility because of plastic deformation and limited elastic recovery. However, one of the few problems associated with cellulose is its very poor flowability, which can lead to variability of the drug content in the finished dosage form. Hence, it needs to be modified into large particle with improved flow properties or it needs to be substituted with some other excipients. Modified hydrogenated fat (MHF) was evaluated to provide a cost effective alternative for MCC. MHF was mixed with other excipients like aerosil, primogel, calcium carbonate and starch to improve compressibility and other powder characteristics. These attributes may improve the binding of the tablet, avoid addition of water and thereby decrease the disintegration time of the tablets. In the present investigation MHF was combined with other excipients of tablets. The powder and tabletting characteristics of these blends were compared with avicel PH 200 blends which are most widely used directly compressible excipients.

2. MATERIAL AND METHODS

Ascorbic acid was purchased from FINE-CHEM LTD (Mumbai), modified hydrogenated fat (MHF), primogel, aerosil, calcium carbonate, MCC (Avicel PH 200) and starch from SIGNET CHEMICAL CORPORATION (Mumbai).

2.1. Composition and Evaluation of Directely Compressible Excipient Blends

2.1.1. Composition of excipient blend

For, tablets, where the drug constitutes a major portion of the total weight, suitable directly compressible excipients are employed to facilitate direct compression process.

Various studies were carried out to provide directly compressible excipients blend with improved compressibility and flow characteristics.

The blends were prepared with excipients indicated in table 1 and were encoded as A1, A2, A3, A4, A5, A6, A7 and A8. A newly designed modified hydrogenated fat (MHF) was evaluated to provide a cost effective alternative for avicel (MCC). MHF was mixed with other excipients like aerosil, primogel, calcium carbonate and starch to improve compressibility and flow characteristics. These blends were compared Avicel PH 200 which is most widely used directly compressible excipients. The performance of this blend was compared with those of MCC (Avicel)

Table 1: The composition of tablet blend

Blend no.	Excipients name	Percentage (%)
A 1	Modified hydrogenated fat: primogel: aerosil	99.0:0.5:0.5
A 2	Modified hydrogenated fat: primogel: aerosil	94.0:5.5:0.5
A 3	Modified hydrogenated fat: microcrystalline cellulose: aerosil	70:29.5:0.5
A 4	Modified hydrogenated fat: microcrystalline cellulose: aerosil	50.0:49.5:0.5
A 5	Modified hydrogenated fat: microcrystalline cellulose: aerosol	29.5:70:0.5
A 6	Modified hydrogenated fat: calcium carbonate: primogel: aerosil	49.0:49.0:1.5:0.5
A 7	Modified hydrogenated fat: calcium carbonate: primogel	16.0:81.0:3.0
A 8	Avicel PH 200 (MCC)	100

2.1.2. Evaluation of excipient blends

Investigations of physicochemical properties of the excipients alone and when combined with the drug were performed. The excipients blend were evaluated for particle size, shape, moisture content, density and flow properties.

2.1.2.1. Particle size and shape determination

The dimensions of particulate solids are of importance in achieving optimum production of tablet formulation. It was found that particle size and shape have effect on flow properties, packing properties, volume reduction mechanism, dustability, degree of segregation, lubricant sensitivity, % compressibility and compact strength. Hence size and shape of

the excipients was determined and influence on the subsequent physical performance of tablets was studied.

2.1.2.2. Bulk density determination

Moisture plays a significant role not only in determination of stability but also in compressibility of blends.

Some direct compression excipients contain apparently high levels of moisture; this moisture in most cases is lightly bound either as water of hydration (lactose monohydrate) or by hydrogen degradation. The loose water causes degradation of actives.

2.1.2.3. Flow properties

Fluidity is required in order to transport the material through hopper of tabletting machine to die cavity. Inadequate fluidity gives rise to arching, bridging or rat holing. Fluidity is also essential so that adequate filling of dies occurs in the tabletting machine to produce tablets of constant weight. If the powder formulation dose not flow satisfactorily, variable die filling will produce tablets that vary strength and in weight. Flow properties can be determined directly by measuring the flow through orifice or by indirect methods like angle of repose, % compressibility and Hausner's ratio.

Angle of Repose (θ) = $\tan^{-1}$ h/r
Coefficient of friction = $\tan\theta$
Where, h = height of pile; r = radius of pile

2.1.2.4. Compatibility

Compatibility of the excipients contributes to the strength of the compact formed.

2.2. Compression and Evaluation of Tablets

Ascorbic acid tablets were prepared using different directly compressible excipients in 70:30 (drug: excipients) ratio. The blends are encoded as T1, T2, T3, T4, T5, T6, T7 and T8 were mixed with ascorbic acid cube mixer.

Premix was directly compressed using ' single stroke tablet compression machine' with standard concave punches 7.5 mm diameter. The amount of blend equivalent to 500 mg of ascorbic acid was placed in the die cavity. All the blends were tabletted with constant weight at same compression pressure. The compositions of tablets formulations T1-T8 are in Table 2.

Table 2: Composition of tablets formulations

Formulation/ Ingredient(mg)	T1	T2	T3	T4	T5	T6	T7	T8
Ascorbic acid	500	500	500	500	500	500	500	500
MHF	213	202	150.5	107.5	63.5	105.5	34.5	-
Primogel	1	12	-	-	-	3	6.5	-
MCC	-	-	63.5	106.5	150.5	-	-	-
$CaCO_3$	-	-	-	-	-	105.5	174	-
Aerosil	1	1	1	1	1	1	-	-
Avicel PH 200	-	-	-	-	-		-	215
Total	715	715	715	715	715	715	715	715

All the manufactured tablets were evaluated for uniformity of weight, uniformity of thickness, hardness, friability, lubricant sensitivity and disintegration time. The results are given in Table 4 & Figure 2 and3.

2.2.1. Uniformity of drug content

Weight variation usually is observed due to improper flow properties, demixing of the blend or improper tooling. Twenty tablets from each batch were individually assayed for its drug content. The mean drug content and the standard deviation are given in Table 6.

2.2.2. Dissolution Rate

The dissolution rate was determined in 900 ml of purified water equilibrated at 37±0.5°C, stirred at 50 r.p.m. The tablets were placed in dissolution medium and 10 ml of the sample was withdrawn at regular intervals. It was mixed with 100 ml of freshly boiled and cooled distilled water and 250 ml of 1 M sulphuric acid. It was titrated with 0.01 M iodine solution using starch solution as indicator, until persistent blue violet colour is produced. The quantity of ascorbic acid equivalent to iodine was calculated from factor given below.
Each ml of 0.01 M iodine solution equivalent to 0.0017612 gms of ascorbic acid. The results are given in Table 6 and fig 4.

2.2.3. Lubricant Sensitivity testing

Lubricants are excipients that, when present in small amounts between two contacting, rubbing surfaces reduce interfacial friction. The duration of mixing time and lubricant concentration significantly affect apparent bulk volume of the mix, flow properties, % compressibility, ejection force during tableting, hardness, disintegration time and dissolution properties of the tablets. These finding provide some rational for the changes in processing characteristics and properties of

finished drug products often encountered in the scale-up of solid dosage formulation [5].

It has been observed that some excipients in binary drug excipient mixtures have better compatibility when used without lubricants, as shown by the higher values excipient in single punch machine with no lubricant added. If the same system is augmented with magnesium stearate significant reduction of hardness is achieved with the same compacting pressure. Such change is due to diminution in adhesion and cohesively caused by the lubricant action. The absolute reduction in cohesitivity is a function of lubricant efficiency, but the same Lubricant can affect diverse excipients in different manners. Some of them are more subscripting materials were hardly influenced by lubrication. On the other hand, a maximum effect of deformation without fragmentation under compression.

Hence lubricant sensitivity of all excipient blends was evaluated to determine the less lubricant susceptible excipient blend. The effect of lubricant on tablet characteristics is described below.

2.3. Determination of critical lubricant concentration

Magnesium stearate was passed through 120#. Drugs were mixed with the excipients in 70:30 ratio in Erweka cube mixer.

Each mixture was blended with variable proportions of magnesium stearate ranging from 0.25, 0.5 to 1% for the period of 2 min. Each blend was tested for compactibility by compressibility by compressing tablets at a weight equivalent to 500 mg of drug. The tablets obtained were tested for appearance, hardness, disintegration time and dissolution time.

2.4. Determination of critical mixing time

In a second serious of experiment drug and excipients (70:30) blend was mixed with 0.5% magnesium stearate for different mixing time raging from 2-8 min. The tablet obtained using single stroke tablet compression machine was tested for appearance, hardness and D.T. Directly compressible mixures were mixed with increased concentration (0.25, 0.5 and 1.0%) of magnesium stearate.

2.5. Effect of lubricant concentration on tablets hardness and disintegration time

The effect of increased concentration of magnesium stearate on tablet performance characteristic was studied. The results are shown on table 4. The maximum concentration of lubricant, which maintained tablet hardness at 4kg/cm^2 was noted as critical lubricant concentration. The maximum time of mixing which mainted tblet hardness at 4kg/cm^2 was noted as critical mixing time.

Lubricant sensitivity ratio (LSR) was calculated from the formula given below.

LSR= Tablet hardness without lubricant- Tablet hardness with lubricant/Tablet hardness without lubricant

2.6. Effect of mixing time on tablets hardness and disintegration time

The preblandes were mixed with 0.25% Magnasium Sterate and mixing time was varied from 2 to 8 min. Effect of mixing time on tablets hardness and disintegration time was assessed and shown in table 5.

3. RESULTS AND DISCUSSIONS

3.1. Evaluation of precompression mixture

A series of precompressed blends (Table1) were systematically designed. In this study it was found that all the formulated batches containing drug: excipients ratio (70:30) were successfully prepared. The characterization of mixed blends was done for determination of mass-volume relationship parameters. The evaluated parameters are bulk density, tapped density, Hausner's ratio, Angle of repose, % compressibility and Compatability. Results for the same are indicated in table 3.

The dimensions of particulate solids are of importance in achieving optimum production of tablet formulation. It was found that particle size and shape have effect on flow properties, packing properties, volume reduction mechanism, dustability, degree of segregation, lubricant sensitivity, % compressibility and compact strength. Hence size and shape of the excipients was determined and influence on the subsequent physical performance of tablets was also studied. In the shape determination analysis we found that mixed blend undergoes a series of subtle changes with different combination and excipient blends. A4 containing modified hydrogenated Fat, MCC and Aerosil with maximum concentration of modified hydrogenated fat (50.0%) exhibited highest diameter figure 1 indicates photomicrograph of ascorbic acid and excipient. Blends A3, A4 and A5 containing microcrystalline cellulose were found to contain fibrous particles. The presence of primogel in the excipient blend showed irregular shape of particles. In the size distribution analysis we found that blends had a narrow size distribution and 85.71 % blends were within range of 48.72-68.46 μm. There is no notable difference in the prepared excipient blends.

Table 3: Characterization of mixed blends

Blend no.	Formulation parameters Particle shape	Average particle size (μ)	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Hausner's ratio	Angle of repose (degree)	% compressibility
A 1	Spherical Irregular particles	54.72 114.1	0.656	0.792	1.207	22.72	17.17
A 2	Spherical Few irregular particles	49.56 121.3	0.665	0.831	1.249	28.41	19.97
A 3	Spherical Fibres	48.72 69.57	0.674	0.832	1.233	18.67	15.70
A 4	Spherical Fibres	68.46 86.7	0.693	0.832	1.2005	19.23	16.67
A 5	Spherical Fibres	52.42 71.54	0.689	0.827	1.2012	20.58	16.66
A 6	Spherical Few irregular particles	62.94 96.83	0.829	0.995	0.2009	29.08	16.59
A 7	Spherical Irregular particles	65.74 102.7	1.061	1.226	1.0938	32.05	17.00
A 8	Spherical	194.8	0.594	0.734	1.2353	14.61	19.05

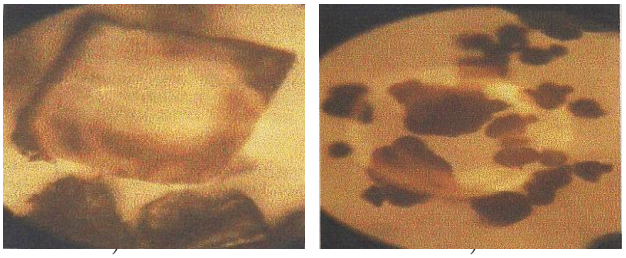

Figure 1: Photomicrograph of A) Ascorbic acid and B) excipients

Bulk density helps in evaluating the flowability of a powder blends by comparing the loose density, tapped density and the rate at which it is packed down the directly compressible blends. The result of bulk density and tapped density for all the batches indicates that the mixed blends have good packability.
Fluidity is required in order to transport the material through hopper of tableting machine to die cavity. Inadequate fluidity gives rise to arching, bridging or rat holing. Fluidity is also essential so that adequate filling of dies occurs in the tableting machine to produce tablets of constant weight. If the powder formulation dose not flow satisfactorily, variable die filling will produce tablets that vary strength and in weight. Flow properties can be determined directly by measuring the flow through orifice or by indirect methods like angle of repose, % compressibility and Hausner's ratio.

The flow behavior of the prepared blends was determined by angle of repose. Ascorbic acid has good flow characteristics. This was considered due to high density (0.77gm/ml) of ascorbic acid. When mixed excipients, it showed excellent flow properties. Blends containing calcium carbonate showed highest flow rates. Mixing of ascorbic acid with excipients improved the overall flow of the excipient itself. Blends containing MHF, MCC and aerosil also showed very good flow characteristics in comparison to other blends.

The % compressibility of all batches was determined and it was found to be 17.805-25.029. It was observed that among the directly compressible excipients used, MHF, MCC and Aerosil has highest % of compressibility 25.029, which may contribute to its fast release when compared with other excipients.

3.2. Effect of lubricant concentration on tablets hardness

All the excipients blends were found to be susceptible to the lubricant concentration. The extent of lubricant action was different for all the excipients as seen from table 4 and 5.
Magnesium stearate forms an adsorbed lubricant film around host particles during mixing process. This lubricants film interferes with the bonding properties of the host particles by acting as a physical barrier. In case of magnesium stearate, lubricant- excipient interaction (adhesion) is higher than lubricant-lubricant (cohesion) interactions. The strong adhesive interactions explain the formation of monomolecular

magnesium stearate film over excipient. This will decrease the number of strong cohesive interactions between the excipient particles causing a decrease in tablet strength.

Avicel PH 200 was found to have greater lubricant sensitivity ratio (0.5). This results due to large reduction in the tablet strength. This was considered due to biggest particle size (188μm) of Avicel, which indicates low surface area. Hence low concentration of magnesium stearate is needed for effective surface coverage and subsequent reduction in the bonding strength. With addition of magnesium stearate the number of cohesive interactions will reduce which which result in subsequent reduction in the compact strength. Avicel frgments by plastic deformation. Hence no new lubricant free surfaces are created under compression, which decrease drug-excipients interaction.

The critical lubricant concentration was found to be highest (0.5%) for Avicel, which is due to very good initial compact strength of the tablets.

Excipients blends A3, A4 and A5 showed minimum lubricant sensitivity ratio. It was observed from table 4 that blend A3 composed of 21% MHF and 9% MCC have critical lubricant concentration of 0.5%. While blend A4 and A5 have lower lubricant sensitivity ratio in comparison to Avicel PH 200. This blend consists of MCC with fibrous particles, which make mechanical interlocking possible. Hence it maintained the compact strength to optimum level even after addition of magnesium stearate. Also particle size of MHF is smaller in comparison to Avicel PH 200. Hence more lubricant is needed for monomolecular film formation on MHF particles. Hence these blends showed less lubricant sensitivity as compared to Avicel 200.

Excipient blends A1 and A2 containing MHF and primogel also showed lubricant sensitivity ratio of 0.25%. Addition of lubricant caused reduction of compact strength below optimum value.

3.3. Effect of lubricant concentration on disintegration time

All the tablet formulations showed rise in the disintegration time with increase in magnesium stearate concentration. Magnesium stearate forms hydrophobic lubricant film around the particles and hence prevents the penetration of water resulting in increase in disintegration time.

Table 4. Effect of lubricant concentration on tablets hardness and disintegration time

Formulation no.	Lubricant conc.(%)	Hardness ($kg/cm^{2)}$	L.S.R.	D.T. (min.)	C.L.C. (%)
A1	0	4	-	23.35	0
	0.25	3	0.25	23.39	
	0.5	2	0.33	23.38	
	1.0	2	0	27.07	
A 2	0	4	-	19.23	0
	0.25	3	0.25	19.20	
	0.5	3	0	19.17	
	1.0	2	0.33	23.09	
A3	0	5.0	-	10.21	0.5
	0.25	4	0.2	11.13	
	0.5	4	0	13.39	
	1.0	2	0.5	14.57	
A4	0	5	-	4.34	0.25
	0.25	4	0.2	5.5	
	0.5	3	0.25	7.55	
	1.0	3	0	8.22	
A5	0	5	-	4.34	0.25
	0.25	4	0.2	4.40	
	0.5	3	0.25	4.51	
	1.0	3	0	4.56	
A6	0	3.0	-	15.31	--
	0.25	2.5	0.1666	17.14	
	0.5	2.0	0.2	18.57	
	1.0	2.0	0	21.06	
A7	0	2	-	5.25	--
	0.25	1.5	0.25	6.02	
	0.5	1	0.5	7.04	
	1.0	Nil	-	7.14	
A8	0	9	-	0.57	0.25
	0.25	4.5	0.5	1.05	
	0.5	3	0.333	1.17	
	1.0	3	0	1.24	

LSR value of zero indicates no reduction in tablet strength

3.4. Effect of lubricant mixing time on hardness

The mixing time affects the extent of lubricity as well other tablet parameters. Magnesium stearate forms a uniform surface-adsorb on the host surface and then delaminate or deaglomerate on host particles. Such process results in greater coverage of the excipients surface by the lubricant thereby producing a greater interfacial surface between the lubricant and excipient.

The effect of mixing time on hardness is shown in table 4. It was found that the hardness continued to decrease mixing time, but the extent of negative effect is different for all the excipients. The formation A8 containing Avicel was drastically affected by change in the mixing time. The hardness was found

to be reduced from 9 kg/cm^2 to 2 kg/cm^2. The blends A3, A4 and A5 had C.M.T. of 2 min. this was attributed to the fibrous particle shape of MCC, which make mechanical possible.

3.5. Effect of lubricant mixing time on disintegration time

The duration of mixing had a major effect upon the tablet disintegration. The mixture blended for a longer time produced tablets with a slow disintegration. The observed effect upon tablet disintegration may be attributed to the formation A3, A4, A5 and A8 showed no significant effect on disintegration time this may be probably due to presence of strong disintegrant in the formulation which is due to presence of MCC.

Table 5. Effect of lubricant mixing time on hardness and disintegration time

Formulation no.	Mixing time (min)	hardness (kg/cm$^{2)}$	L.S.R.	D.T. (min.)	C.M.T (min.)
A1	Initial	4.0	-	23.35	
	2	3.0	0.25	23.39	0
	5	2.0	0.33	24.35	
	8	0	1.0	27.23	
A 2	Initial	4.0	-	19.23	
	2	3.0	0.25	19.20	0
	5	2.0	0.33	20.43	
	8	0	1.0	22.54	
A3	Initial	5.0	-	10.21	
	2	4.0	0.2	11.19	2
	5	3.0	0.25	11.43	
	8	2.0	0.33	12.03	
A4	Initial	5.0	-	4.34	
	2	4.0	0.2	5.55	
	5	2.5	0.375	6.12	2
	8	1.5	0.4	6.43	
A5	Initial	5.0	-	4.34	
	2	4.0	0.2	4.40	
	5	3.0	0.25	4.56	2
	8	2.0	0.33	5.17	
A6	Initial	3.0	-	15.31	
	2	2.5	0.166	17.14	--
	5	1.5	0.4	18.54	
	8	0	1.0	20.32	
A7	Initial	2.0	-	5.25	
	2	1.5	0.25	6.02	0
	5	0	1.1	7.47	
	8	0	-	9.36	
A8	Initial	9	-	0.57	
	2	4	0.5	1.05	
	5	3	0.2	1.14	2
	8	2	0.33	1.28	

3.6. Compression and Evaluation of tablets

A tablet is designed to contain a specific amount of drug in a specific amount of tablet being made is routinely measured to ensure that contains the proper amount of drug. The diameter of tablet was found to be 7.5 mm. The thickness of the tablet was found between 5.4-6.02 and average weight of tablet between 0.708-0.734. So, it was predicted that all the tablets exhibited uniform weight with low standard deviation values within the acceptable variation as per IP (Table 6).

The hardness of the prepared tablet varied from 2.5-8.5cm^2(Table 6), which has satisfactory strength to withstand the applied mechanical shocks. The excipients blends T8 (Avicel PH 200) showed maximum compatibility of Avicel PH 200, which was considered due to plastic deformation of excipient. The friability of all the formulations was found to be less than 1.0%, which shows the durability of prepared tablets; resistance to lose weight indicates the tablets ability to withstand abrasion in handling, packaging and shipment (Table 6).

In the formulation of ascorbic acid tablets, the tablets containing higher concentration disintegrating agent shows excellent disintegration properties when compared with the other formulation. Formulation containing no disintegrating agent or less concentration of disintegrating agent shows poor disintegration properties. The disintegrating time varied from 0.57-23.25 minutes (Table 6).

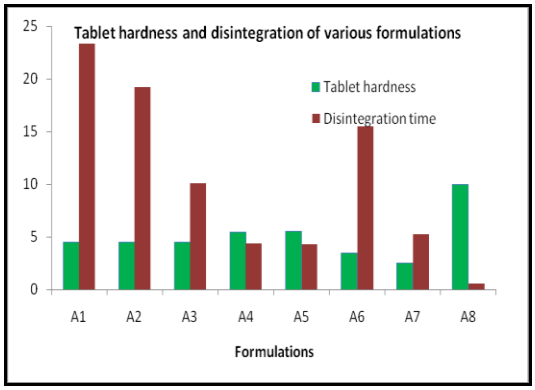

Figure 2: Tablet hardness and disintegration

Lubricants are excipients, present in small amounts between contacting, rubbing surfaces reduces interfacial friction. The duration of mixing time and lubricant concentration significantly affects apparent bulk volume of the mix, flow properties, % compressibility, and ejection force during tableting, hardness, disintegration time and dissolution properties of the tablets. These finding provide some rationale for changes in processing characteristics and properties of finished drug products often encountered in the scale-up of solid dosage formulations.

Table 6. Characterization of ascorbic acid tablets

Blend no.	Formulation parameters						
	Diameter (mm)	Thickness (mm)	Weight (mg)	Hardness (kg/cm^2)	Friability (%)	Disintegration time (minutes)	Drug Content
T 1	7.5	6.02	0.727	4.5	0.85	23.35	100.43
T 2	7.5	6.05	0.721	4.5	0.78	19.23	101.48
T 3	7.5	6.08	0.714	4.5	0.87	10.21	103.11
T 4	7.5	5.88	0.708	5.5	0.8	4.34	101.96
T 5	7.5	5.98	0.708	5.5	0.73	4.30	100.47
T 6	7.5	5.78	0.731	3.5	1.01	15.31	102.19
T 7	7.5	5.93	0.734	2.5	>1.0	5.25	100.57
T 8	7.5	5.89	0.710	8.5	0.38	0.57	98.98

All the excipients blends were found to be susceptible to the lubricant concentration. The extent of lubricant action was different from all the excipients as seen from table 5.

Magnesium stearate forms an adsorbed lubricant film around host particle during mixing process. This lubricant film interferes with the bonding properties of the host particles by acting as a physical barrier. In case of magnesium stearate, lubricant- excipient interaction (adhesion) is higher than lubricant-lubricant (cohesion) interactions. The strong adhesive interactions explain the formation of monomolecular magnesium stearate film over excipient. This will decrease the number in tablet strength.

Hardness of tablets decreases with increase in the concentration of lubricant, the reason behind this result could be due to reduction of compact strength below value. But vice-versa in case of disintegration; it increases with increase in lubricant concentration. Magnesium stearate form hydrophobic lubricant film around the particles and hence prevents the penetration of water resulting in increase in disintegration time. The effect of mixing of magnesium stearate on disintegration time was found in contrast to the tablet strength. The tablets showed an increase in disintegration time after 5 min of mixing of the preblends with magnesium stearate. Formulation A5 and A8 containing MCC which is a strong swelling disintegrant were less prone to lubricant susceptibility.

The hardness continued to decrease with increased mixing time, but extent of negative effect is different for all the excipients. The blends A3, A4 and A5 had critical mixing time of 2 min. this was attributed to the fibrous particle shape of MCC, which make mechanical interlocking possible.

Formulation A3,A4, A5 and A8 showed no significant effect on disintegration time this may be probably due to presence of strong disintegrant in the formulation which is due to presence of MCC.

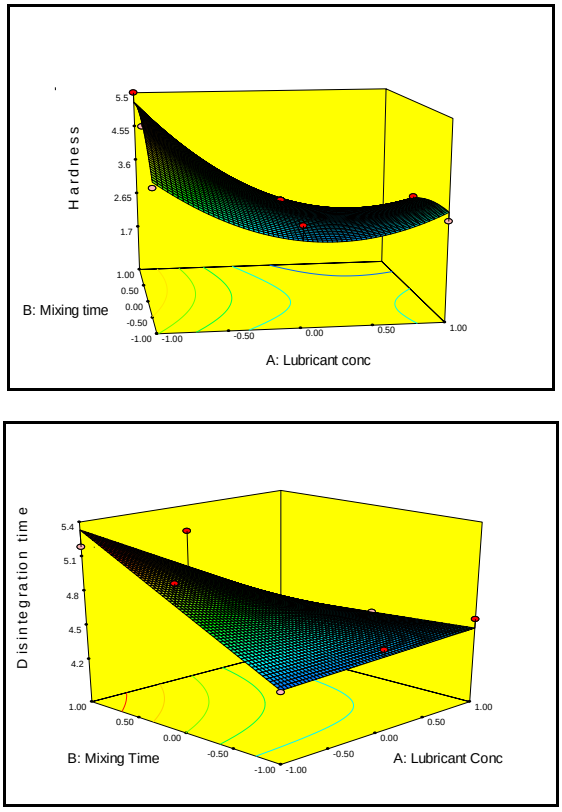

Figure 3: Effect of mixing time and lubricant concentration on a) Hardness; b) Disintegration time

3.7. Dissolution time

Dissolution rate of the drug from the primary particles of the tablet is the important factor in drug absorption and for many formulations is the rate-limiting step. Dissolution rate is indicative of the availability of a drug from tablet. The result of dissolution showed that as the presence of primogel, increase the rate of dissolution rate and also the drug was released faster. The maximum drug release was found in formulation T5 (98.50%). Table 7 and figure 4 gives comparative evaluation of dissolution profile.

Table 7: Comparative evaluation dissolution profile

Time interval (min)	T1	T2	T3	T4	T5	T6	T7	T8
	%Drug released							
5	17.73	20.72	31.76	89.00	98.50	15.84	88.66	99.80
10	30.82	33.70	57.53	98.24	99.60	33.45	96.08	99.30
15	42.45	46.82	99.43	99.30	99.00	40.16	100.34	98.80
30	81.35	99.92	99.92	99.49	99.62	86.49	99.83	98.34
45	99.96	99.97	99.82	99.37	99.68	99.85	99.27	97.83

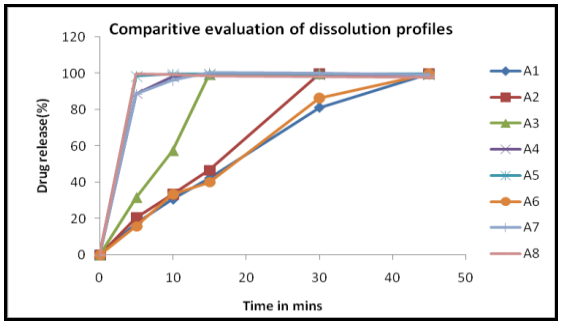

Figure 4: Dissolution profile of various formulation

3.8. Statistical evaluation

The friedmann's test is a nonparametric test applied to the data which is at least ranked and which is in the form of two-way ANOVA design.

The test is applied for the selection of most suitable excipient blend. It is used to test the performance of all the excipients, with regard to critical and secondary parameters. The critical parameters for purpose of evaluation included flow properties, effect on hardness, friability, disintegration time and dissolution rate.

Whereas secondary parameters assessed were appearance, lubricant sensitivity, processing problems, critical lubricant concentration and critical mixing time. Each parameter was given a score ranging from (1-8) in increasing order of performance. Excipient blend with best performance was given a minimum score of 1. The excipient blends with same values were given average score. The excipient blends with the highest total score was selected as most suitable excipients (Table 8 and 9).

Table 8: Friedman's test as applied to various parameters

	Excipient blend/functionality specification	T1	T2	T3	T4	T5	T6	T7	T8
		Secondary parameters							
1	Lubricant sensitivity ratio	0.25 (3)	0.25 (3)	0.2 (5.5)	0.166 (7.5)	0.2 (5.5)	0.166 (7.5)	0.25 (3)	0.5 (1)
2	Processing problems	Picking, sticking (1.5)	Picking, sticking (1.5)	Self lubricating (6.5)	Some ejection pressure (1.5)	Self lubricating (6.5)	Self lubricating (6.5)	Self lubricating (6.5)	High ejection pressure (8)
3	Critical mixing time	0 (3.5)	0 (3.5)	5 (7)	5 (7)	2 (7)	- (1.5)	- (1.5)	5 (7)
	Score	8	8	19	16	19	15	10.5	16
	Tablet excipient with decreasing order of performance	**T3, T5 > T3>T4> T6 > T8 >T1 >T2**							

Table 9: Friedmann's test as applied to ascorbic acid formulations

Excipient blend/functionality specification		A1	A2	A3	A4	A5	A6	A7	A8
Critical parameter									
1	Flow properties(gm/cm^2)	22.72 (5)	28.41 (6)	18.67 (4)	19.23 (3)	20.58 (2)	29.08 (7)	32.05 (8)	14.61 (1)
2	Hardness (kg/ cm^2)	4.5 (4)	4.5 (4)	4.5 (4)	5.5 (6)	5.55 (7)	3.5 (2)	2.5 (1)	10 (8)
3	Friability (%)	0.85 (4)	078 (6)	0.87 (3)	0.8 (5)	0.73 (7)	1.01 (2)	>1 (1)	0.38 (8)
4	Disintegration (min)	23.35 (1)	19.23 (2)	10.21 (4)	4.34 (6)	4.30 (7)	15.31 (3)	5.25 (5)	0.57 (8)
5	Content uniformity	100.43 (5)	101.48 (5)	103.11 (5)	101.96 (5)	100.47 (6)	102.19 (5)	100.57 (5)	98.98 (3)
Score		19	23	20	25	29	19	20	28
Tablet excipient with decreasing order of performance		**A5> A8>A4>A3 > A2 >A1,A6**							

4. CONCLUSION

Hence, on the basis of above results it was concluded that use of directly compressible excipients in ratio of drug:excipients (70:30) decrease in disintegration time due to swelling. Dissolution time for T-5 is shortest among other formulation.

5. REFERENCES

1. Aulton ME. Pharmaceutics, the Science of Dosage Forms Design, International Student Edition, Churchill Livingstone, 304, 1988.
2. Steinberg M, Blecher I. *Pharm Tech*, 2001; 62-65.
3. Jon Gabrielsson Nystrom. *Drug Dev Ind Pharm*, 2000; **26(3):**175-296,
4. Karhill PG, Sherif Badaway. *Drug Dev Ind Pharm*, 1990; **64:**27-34
5. Alderborn G, *Int J Pharm*, 1991; **73:**249-258.
6. Rang Kanchan, Sherif Badaway, *Drug Dev Ind Pharm*, 1995; **21(3):**361-368
7. Sitton E, Lewis CJ. *J Pharma Pharmaol*, 1964;**16(Suppl.):**111T,
8. Levy G, Gumtow RH. *J Pharm Sci,* 1963; **52:**1139.
9. Shah C, Mlodozniec AR. *J Pharm Sci*, 1977; **66:**1377.
10. Drug And Nutrients, The Interactive Effect,Roe D.A.,Campbell T.C. Marcel And Dekker Series, Vol- 21, 225.
11. Ascorbic Acid (Vitamie C), Manual By Sarabhai Marck Ltd.
12. Vademecum For Vitamin Formulations, Volker B., Wissenschaftliche Verlagsgesellschoff Mbtt Stultgart, 1988,90,128
13. Nystrom C, Glazer M, *Int J Pharm*, 1985; **23:**255.
14. Alderborn G, Pasanen K. *Int J Pharm*, 1985; **23:**79.
15. Nystrom C, Mazur J. *Int J Pharm*, 1982; **10:**209.
16. Alderborn Goran And Nystrom Chister," Pharmaceutical Powder Compaction Technology ,"Marcel And Dekker Series , 419-487-,1996
17. Hans Leuenberger. *European J Pharmaceutics And Biopharm*, 2000; **49:**151-159.
18. Picker KM. *Europian J Pharmaceutics and Biopharm*, 1999; **48:**27-36.
19. Kenta Goto. *Drug Dev Ind Pharm,* 1999; **25(8):**869-878.
20. Tsuimin Tsai, Jen-Sen Wu. *J Pharm Sci*, 1992; **31:**576
21. Leuenberger H, Bonny JD, Lerk CF. *Int J Pharm*, 1982; **12:**41-55.
22. Garr JSM. *Int J Pharm*, 1991; **73:** 75-80.
23. Coffin-Beach DP, Hollenbeck PG. *Int J Pharm*, 1983; **17:**313.
24. Asa Adolfsson, Nystrom C. *Int J Pharm*, 1996; **132:**95-106,
25. Reuy-Ching Husang, Gretchen R. Peck, *Pharmtech*, 2001; 112-122.
26. Doelker, Massuelle D, Veuillez F. *Drug Dev Ind Pharm*, 1995; **21(6):** 643-661.