Research Article

Affect of Aqueous Film Coating Formulations on Ascorbic Acid Tablets under Specified Process Parameters

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ABSTRACT

Ascorbic acid tablets were produced by standard procedure and tested for the suitability of the coating process. The uncoated tablets were then coated by using two coating formulations, when the coating variables were specified during the coating process. To achieve the specified weight gain, the formulation containing HPMC E6, Propylene glycol, FD&C Yellow # 5 and deionised water was found taking more time than another one containing HPMC E50, PEG 6000, FD&C Yellow # 5 and deionised water. The disintegration time of the coated tablets was also found different for the specified formulations, and higher than the uncoated tablets.

INTRODUCTION

Due to the ease of manufacturing, convenience in administration, accurate dosing, and stability compared to oral liquids, tamper-proofness compared to capsules, and safety compared to parenteral dosage forms, tablets are the most popular dosage form in use today.[1] In order to mask unpleasant taste or odour, enhance stability against light and moisture, produce an elegant product, or impart a functional purpose such as the modification of drug release profiles, provide identity to products, improve swallowability, and allow higher packaging speeds by reducing friction as well as reducing dust generation, tablets are usually coated by using coating material.[2,3] The coating material is applied to the exterior of a tablet with the intention of conferring benefits and properties the dosage form over the uncoated variety. In film coating, spraying of a solution of polymer, pigments and plasticizers on to a rotated, mixed tablet bed forms a thin, uniform film on tablet surface.[4,5] Film coating is performed by two types: aqueous film coating (generally water is used as a solvent) and non aqueous film coating (generally organic solvents are used), out of which, the first one is more preferable as the second one is associated with safety, atmospheric pollution, etc.[4,5] Aqueous film coating is applied as a thin polymeric film to the surface of a tablet.[4] Three primary components are involved in tablet coating which are tablet properties, coating process and coating formulation.[4-6] The quality of the final coated product depends mainly upon these components.[4-14] The tablets that are to be coated must possess the proper physical characteristics.[4-6] By careful selection of uncoated tablets that to be coated, quality of the final coating tablets can partially be controlled. The variable inputs to a film coating process derived from differences in equipment installations include but are not limited to inlet air volume, temperature and humidity, coating pan dimensions and rotating speed, numbers and distance between spray guns, distance between spray guns and tablet bed, atomizing air pressure, spray rate of the coating solution, , nozzle orifice size, etc.[6-14] Therefore, these variables, relevant to the coating process, should carefully be controlled for acceptable quality of the final coating tablets. The coating formulation, however, should select carefully which requires extensive effort to apply, and is, therefore, time consuming. Coating formulation typically comprises polymer, plasticizer, colorants and solvents.[4,5] Because of a number of key features and advantages, hydroxypropylmethylcellulose (HPMC), which are cellulose ethers, swellable and hydrophilic polymers, have been identified as the most popular film formers, and are used as viscosity enhancing agents.[15] They may be used as the basic for hydrophilic matrices for controlled release oral delivery.[16] The manufacture of tablets requires numerous excipients with different functions, several of them covered by polyglycols (PEGs).[17] Solid PEGs are also frequently used as plasticizers in tablet coatings.[18] Propylene glycol, which is a clear, colorless and hygroscopic liquid, may also be

used as a plasticizer in tablet formulations.[19] Ascorbic acid, which is best known by its antioxidant activity and the free radical scavenging, is a poorly compressible water-soluble and moisture sensitive essential vitamin.[20-22] Many physiological and mental disturbances can be occurred due to its lacking in the human body.[22] This complex nature of Ascorbic acid is made it to choice as a model of study. In the present study, Ascorbic acid tablets are produced and coated by using two aqueous film coating formulations to test the affect of the formulations on the coated tablets at specified tablet and coating process variables.

MATERIALS AND METHODS

MATERIALS

All chemicals, used in the present study, were approved only for training purposes. Granules were produced by using Ascorbic acid (Honson Ingredients; TIPT* Lot # 13A0101), Lactose Monohydrate (Flowlac 100 [Wyndale; TIPT Lot # 07B0511]), Microcrystaline Cellulose (MCC 101 [Mingtai Chemical Co. Ltd.; TIPT Lot # 12B0108]), Polyplasdone–XL (International Specialty Products, Inc.; TIPT Lot # 00B0411) and Plasdone K90 (International Specialty Products, Inc.; TIPT Lot # 05B0502) at 25%, 50% 18%, 3% and 3.5%, respectively. After granulation, magnesium stearate (MgSt) [Bärlocher] was used to lubricate the granules. Two formulations, i.e. FORMULATION1 (HPMC E50 [The Dow Chemical Co., Midland; TIPT Lot # 07B0109], 2.5%; PEG 6000 [Stepan Company, Northfield; TIPT Lot # T97B103], 1.0%; FD&C Yellow # 5 [Warner Jenkinson Ltd., Canada; TIPT Lot # AM2645], 0.2%, deionised water, 96.3%) and FORMULATION2 (HPMC E6 [The Dow Chemical Co., Midland; TIPT Lot # 07B0107], 4.0%; Propylene glycol [Van Waters & Rogers Ltd.; TIPT Lot # 00B0911], 2.0%; FD&C Yellow # 5, 0.4%, deionised water, 93.6%) were used to obtain the coating solutions.

METHODS

All methods were performed according to the Good Manufacturing Practices (GMP).[23] During the tablet production (granulation, lubrication and compression) and coating process (coating solution preparation and coating), the temperature, relative humidity and air pressure of the station were maintained at 20°±2°C, 20% – 40%, and >5 Pascal, respectively.

Granulation

Except the lubricant (MgSt), all other ingredients (Ascorbic acid, Flowlac 100, MCC 101, Polyplasdone–XL and Plasdone K90) were firstly dry blended by using a twin shell V-blender (The Patterson – Kelley Co. Inc., USA; TIPT ID # PE95002) for 20 minutes. 40% of the binder (Plasdone K90) was used in this blend. The resulting dry blend was then used for low shear wet granulation by using a Hobart Planetary Granulator (TIPT ID # PE9600). The calculated 60% void volume of the dry blend was used as the volume of deionised water to prepare binder solution with the rest of the 60% of the binder (Plasdone K90). The concentration of the binder solution was calculated as 10.9%. 35ml deionised water was used as extra during the wet massing to reach the capillary stage. After reaching the capillary stage in the wet granulation, the granules were then passed through a Mesh 10 screen of Manesty Rotogram Granulator 184 TBS (Mark III, England; TIPT ID # PE00002). The screened granules were then transferred into a dryer (Gruenberg, Gruenberg Oven Co., Inc., USA; TIPT ID # PE94001), and dried until the moisture content was reached at 2 – 3%. The dry granules were sieved with a Ro-Tap shaker (W.S. TYLER, USA; TIPT ID # TE97001) and collected separately from mesh 14 (1410µm), 18 (1000µm), 30 (590µm), 40 (420µm) and 60 (250µm) (USA Standard Testing Sieve, A.S.T.M. E – 11 Specification, VWR Scientific, USA).

Lubrication

Granules of Mesh 14, 18, 30, 40 and 60 were mixed together properly and blended with 0.5% MgSt by using the twin shell V-blender for 3 minutes.

Compression

A Stokes B2 round tablet press (Manesty Betapress, F.J. Stokes Corporation, USA; TIPT ID # PE9500) with 16 stations and 9mm round standard concave tooling was used for the compression process. 50g of the granule was used for set-up, i.e. manual run without feed frame, manual run with feed frame and automatic run with feed frame. Then, the final tablet production was carried out. During the final tablet production, the following tablet parameters were followed: tablet weight: 324 ± 10.5mg, tablet hardness: 8 Strong-Cobb Units (SCU) ± 3.0% and tablet dimension: 9mm diameter. Compression pressure was kept fixed (1.5 – 2.2 tons) for the whole period of the final tablet production. The lot of the produced tablets was collected in three bins at

a time interval of 1.0 minute. To remove excess powder on the surface, the produced tablets were dedusted by using a deduster (KEY Industries, USA). With 10 tablets for each collected randomly during the final tablet production, In-Line Tests were done for the tablet weight by using an electronic digital balance (Precisa Instruments Ltd., Switzerland; TIPT ID # WS04003), tablet thickness, and hardness by using a hardness tester (Pharma Test, Germany; TIPT ID # TE0901).

After the final production, visual inspection was performed to find out and remove defective tablets. To pass the produced tablets for further processing, friability test[24] was performed for each of the three bins by using a friability tester (Scepter, Canada; TIPT ID # QC95/008). Six tablets were also collected from each of the three bins to determine the disintegration time[25] by using a tablet disintegration tester (HAAKE W13, Vankel, USA; TIPT ID # 94001). The tablets of the three bins were then mixed together and divided into two parts of 450g each for coating with FORMULATION1 and FORMULATION2.

Coating solution preparation

FORMULATION1: Out of 96.3%, ≈60% of deionised (DI) water of the formulation was heated to 70°C – 80°C. 2.5% HPMC E50 of the formulation was dispersed in it gradually by using a Starrier (Heidolph, Germany; TIPT ID # PE95014) at low to medium speed. The resulting solution was then cooled down at ≈50°C and 1.0% PEG 6000 of the formulation was added by the ease of the Starrier. The solution was cooled down at room temperature (≈20°C) and 0.2% FD&C Yellow # 5 of the formulation was added by using the Starrier. The rest of ≈40% of DI water of the formulation was then added, and the solution was kept in the In-Process area for 24 hours with proper labelling.

FORMULATION2: ≈60% of DI water out of 93.6% of the formulation was heated to 70°C – 80°C, and 4.0% HPMC E6 of the formulation was dispersed in it gradually by using the Starrier accordingly. 0.4% FD&C Yellow # 5 of the formulation was added to the solution after cooling it down at room temperature (≈20°C). 2.0% Propylene glycol of the formulation was then added to the resulting solution slowly. The rest of ≈40% of DI water of the formulation was heated to ≈50°C and then added to the solution gradually. The prepared coating solution was kept in the In-Process area for 24 hours with proper labelling.

Coating process

During the coating process, the following specifications were maintained: inlet air (Campbell Housfeld AN95001, TIPT ID # AN96003) temperature: 65°C – 75°C, inlet air velocity: 0.5 – 2.0 m/s, inlet air relative humidity: >40%; exhaust setting (HEPA filter, Ereweka ER5002, TIPT ID # PD964006): medium; tablet bed temperature: 55°C – 65°C; coating pan (Ereweka AR400; TIPT ID # PE95004) speed: 3 – 10 RPM; atomizing air (Campbell Housfeld AN9500, TIPT ID # PE95005) pressure: 30 – 40 psi; spray rate of spray gun (Campbell Housfeld DH5800-F0510, TIPT ID # PE95009): 2 – 6g/min., distance between spray gun nozzle and tablet bed: 20 – 30 cm, coating efficiency: 70%, and weight gain: 3%,.

Uncoated tablets, selected for coating with FORMULATION1 and FORMULATION2 (450g uncoated tablets for each), were preheated firstly in the coating pan at ≈50°C, and then 10 tablets were collected randomly to get the initial weight for determining % weight gain per 15 min. time interval during the coating process. The whole system of the coating process and parameter was specified and maintained accordingly, and then, the coating process was started, and finished when the % weight gain reached at ≈3%. By continuing the rotation of the coating pan, the coated tablets were cooled down at room temperature gradually to avoid defects of the coated tablets. Six tablets were collected randomly and separately from the tablets coated with FORMULATION1 and FORMULATION2 to perform the disintegration test.[25]

RESULTS AND DISCUSSION

The weight, thickness and hardness of the uncoated Ascorbic acid tablets, along with the average value ($\bar{x}$) are presented in **Table 1**. Along with the $\bar{x}$ values, **Table 2** and **Table 3** represent the friability and disintegration time of the uncoated tablets, respectively. % Weight gain at a time interval of 15 min. during the coating process for FORMULATION1 and FORMULATION2 is presented in **Table 4**. The disintegration time, along with the $\bar{x}$ values, for the coated tablets are presented in **Table 5**.

It is obvious from **Table 1** and **Table 2** that the produced Ascorbic acid tablets are suitable for the coating process. The acceptable tablet weight loss during the friability test is ≥1%.[24] Tablet disintegration is the first step for a drug to become bioavailable.[23,25] The tablet must first disintegrate and discharge the drug to the body fluids. The drug in the disintegrated tablets must be dissolved in the fluid to be absorbed into the blood stream. Some drugs

are intended to be used locally in the gastrointestinal tract (GIT). In these instances, tablet disintegration provides drug particles with a greater surface area for increased localized activity. From **Table 3** and **Table 5**, it is found that the disintegration time of uncoated tablets increases by applying the coating formulations. The disintegration time is increased more for FORMULATION2 than FORMULATION1. The increase in disintegration time for FORMULATION1 and FORMULATION2 are found as ≈38.9% and ≈53.9%, respectively. This may due to the difference between formulation ingredients. Therefore, both of the formulations can be used for delayed drug release and FORMULATION2 will be more efficient than FORMULATION1 in this case. **Table 4** indicates that the coating process takes more time to achieve the specific weight gain for FORMULATION2 than FORMULATION1. The total time required to complete the coating process with FORMULATION1 and FORMULATION2 are 120 min. and 210 min., respectively. This may be due to the presence of Propylene glycol in FORMULATION2, which may take more time to spread and evaporate than PEG 6000. HPMC E6 of FORMULATION1 and HPMC E50 of FORMULATION2 may have some impact on this aspect. Moreover, FORMULATION1 contains more DI water than FORMULATION2, which may have an intense affect on the coating process due to the ease of evaporation. Profound data on these aspects are still unavailable, and therefore, it is difficult to explain. Furthermore, the time required for completing the coating process also depends on batch size or load of tablets.

CONCLUSION

Ascorbic acid tablets, produced and used in the present study, have been found as disintegrated gradually when coated with FORMULATION1 involving HPMC E50, PEG 6000, FD&C Yellow # 5 and deionised water. The disintegration time increases more for coating with FORMULATION2 involving HPMC E6, Propylene glycol, FD&C Yellow # 5 and deionised water. Therefore, FORMULATION2 is assumed more efficient than FORMULATION1 for delayed drug release. Film coating technology has become very important, particularly in formulation development. Many factors must be well thought-out during film coating process. However, sufficient information on these factors, especially affect of coating formulation on coating properties, are still not available, resulting lacking of proper understanding of the process. Further studies are, therefore, required to find out proper explanation about the affect of various factors on coating process. The findings, presented in this paper, will be helpful to design further studies for the production of eminence coated tablets with specificity to overcome disadvantages of conventional uncoated tablets.

Table 1: Tablet weight, thickness and hardness of the uncoated Ascorbic acid tablets

Tablet no.	Weight (mg)			Thickness (mm)			Hardness (SCU)		
	Bin 1	Bin 2	Bin 3	Bin 1	Bin 2	Bin 3	Bin 1	Bin 2	Bin 3
1	326	325	323	4.57	4.48	4.53	8.3	8.1	7.7
2	324	328	325	4.51	4.55	4.50	7.1	8.6	7.9
3	327	331	321	4.55	4.58	4.48	8.0	7.9	7.8
4	327	324	329	4.51	4.60	4.59	8.5	7.7	8.3
5	324	331	331	4.52	4.48	4.51	7.8	8.3	8.1
6	321	330	330	4.58	4.55	4.59	8.1	8.0	7.9
7	324	324	324	4.52	4.55	4.48	8.2	8.1	8.0
8	328	330	328	4.48	4.53	4.56	7.8	8.1	8.4
9	330	324	327	4.53	4.48	4.52	7.9	7.9	8.3
10	321	323	323	4.51	4.54	4.47	7.9	8.2	8.0
$\bar{x}$	325.2	327	326.1	4.528	4.534	4.523	7.96	8.09	8.04

Table 2: Friability of the uncoated Ascorbic acid tablets

Bin #	Initial sample weight (g)	Final sample weight (g)	Weight variation (%)	$\bar{x}$
1	6.666	6.654	0.18	0.115
2	6.635	6.634	0.015	
3	6.717	6.707	0.15	

Table 3: Disintegration time (min.) of the uncoated Ascorbic acid tablets

Tablet #	Bin 1	Bin 2	Bin 3
1	16	15	10
2	12	11	13
3	14	10	13
4	15	10	11
5	10	14	15
6	13	15	14
$\bar{x}$	13.3	12.5	12.6

Table 4: % Weight gain at a time interval of 15 min. during the coating process

	FORMULATION 1	FORMULATION 1
1	0.054	0.037
2	0.71	0.43
3	1.06	0.57
4	1.48	0.78
5	1.92	0.96
6	2.49	1.04
7	2.86	1.33
8	3.02	1.66
9	–	1.90
10	–	2.39
11	–	2.61
12	–	2.86
13	–	2.94
14	–	3.05

Table 5: Disintegration time (min.) of the coated Ascorbic acid tablets

Tablet #	FORMULATION 1	FORMULATION 2
1	18	22
2	18	18
3	21	20
4	17	21
5	15	19
6	17	18
$\bar{x}$	17.7	19.7

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