Journal of Applied Pharmaceutical Science Vol. 3 (08), pp. 057-063, August, 2013
Available online at http://www.japsonline.com
DOI: 10.7324/JAPS.2013.3810
ISSN 2231-3354

Enteric coating of hard gelatin capsules by the spouted bed process

H.V.A. Oliveira, M.P.G. Peixoto, L.A. Tacon & L.A.P.Freitas*
Faculdade de Ciências Farmacêuticas de Ribeirão Preto Núcleo de Apoio à Pesquisa em Produtos Naturais e Sintéticos Universidade de São Paulo, Brazil.

ARTICLE INFO

Article history:
Received on: 28/12/2012
Revised on: 27/01/2013
Accepted on: 24/05/2013
Available online: 30/08/2013

Key words:
Eudragit® L30 D55, weight gain, sodium diclofenac, viscosity, disintegration, dissolution profile.

ABSTRACT

The aim of this work was to study the aqueous enteric film coating of hard gelatin capsules in a single step, with no sub coats. A lab scale spouted bed coater with bottom spray feed was employed to coat capsules using gastric resistant methacrylic polymer Eudragit® L30D55. Preliminary experiments were carried out to determine an appropriate coating suspension formulation and to characterize the fluidization behavior of the capsules. Process factor effects, such as the coating time, coating solution viscosity and substrate load on capsule weight gain were studied using a full factorial 2^3 design. Coating efficiencies ranged from 69.5 to 84.9% and weight gain from 10.8 to 33.2%. The suspension viscosity did not affect significantly the efficiencies. The percentages of gastric resistant capsules increased linearly with weight gains. 100% of the capsules were shown to be gastric-resistant when coated with a minimum of 17% mass increase and their dissolution profiles showed less than 5% drug release after 2 h in HCl solution.

INTRODUCTION

The film coating of pharmaceutical forms has been widely applied to prevent active pharmaceutical ingredient (API) denaturation and deterioration by environmental factors and also to provide these pharmaceutical forms specific release qualities, such as sustained and pH dependent release (Jones, 1985; 1988). The pH dependent coating is commonly applied to solid dosage forms when APIs are sensitive to the stomach environment or when they may cause significant gastric irritation. In these cases, the polymeric film resists the acidic gastric medium and API release occurs at enteric pH. Several studies have dealt with enteric film coating of tablets (Felton *et al.,* 1997; Lehmann and Dreher, 1981), microgranules (Swift *et al.,* 1992) and pellets (Bodea and Leceuta, 1996). Hard gelatin capsules (HGC), one of the most important oral dosage forms, are considered an alternative to many problems associated with tableting, including poor compaction, actives content or weight uniformity (Bussemer and Bodmeier, 2003). HGC are usually filled with solids but can also be filled with semisolids and liquids (Bussemer and Bodmeier, 2003; Burns *et al.,* 1994).

* *Corresponding Author*
Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo, Via do Café s/n, Campus USP, 14040-903, Ribeirão Preto, SP, Brazil, Phone: 55 16 3602 4225; Fax: 55 16 3602 4879,

However, HGC cannot be applied to enteric systems due to their high solubility in both acid and alkaline environments. Although enteric coating is the best alternative to overcome this limitation, great care should be exercised when coating HGC, since the two piece design is associated with sealing problems (Porter, 1997) and shell flexibility tends to cause the film to crack during coating (Felton *et al.,* 1995). A few attempts have been made to add gastric resistant properties to soft (Felton *et al.,* 1995; 1996; Bussemer and Bodmeier, 2003) and hard gelatin capsules (Murthy *et al.,* 1986; 1988; Kalala *et al.,* 1996). In a study of HGC enteric coating conducted by Murthy *et al.,* (1986), the authors compared the release properties of HGC coated with Eudragit L 30 D, Aquateric and Coateric and found no significant difference using either diethyl phthalate or triethyl citrate as plasticizers. However, the gastric resistance of Eudragit L 30 D coated HGCs showed good ageing stability.

In a subsequent work, Murthy *et al.,* (1988) reported an investigation into the effect of hydroxypropyl cellulose (HPC) subcoats and overcoats on organic and aqueous based enteric polymers. The authors indicated that smooth and homogeneous films were obtained in all cases and the use of HPC pre-treatment resulted in no difference in enteric release profiles. Kalala *et al.,* (1996) determined *in vitro* ibuprofen release from HGC coated with a mixture of poly (ether-ester) azo polymers and Eudragit SR100.

Release profiles depended on film thickness and only polyethylene glycol (PEG) coated capsules were shown to be adequate for colon specific drug delivery.

However, in the studies reported (Kalala *et al.,* 1996), HGC film coating was performed manually by dipping them into the polymer solution, followed by a drying step. Coating thickness, one the most important factors for gastric resistance, cannot be fully controlled with this technique; an alternative is the fluid bed coating technique (Jones, 1985; Parikh *et al.,* 1993; Christensen and Bertelsen, 1997; Murthy *et al.,* 1986; 1988).

A study on the fluid bed enteric coating of HGC was reported by Thoma & Bechtold (1999). Aqueous spray coating formulations caused problems like the softening of HGC shells and stickiness due to gelatin solubilization. The authors were able to overcome the problem by applying cellulose subcoats, although they admitted the methodology significantly increased capsule brittleness. Although an appropriate component balance in a given coating formulation and the control of the critical operational process variables (Parikh *et al.,* 1993; Porter, 1997) could achieve the desired HGC release properties, published papers on this subject are lacking.

The aim of this work was to study the process conditions for the enteric coating of HGC without the application of subcoats, and to determine the influence of process factors on the spouted bed coating and enteric characteristics of sodium diclofenac HGC. Coating formulation and process conditions, along with HGC fluidization properties, were evaluated in preliminary runs and their roles in coating were discussed. The effects of HGC load, coating formulation viscosity and coating time on coating weight gain and percentage of gastric-resistant HGC were studied using a 2^3 full factorial design. The surface response equation obtained was used to set experimental conditions to determine the relationship between weight gain and percentage of gastric resistant HGC. The dissolution profiles of HGC capsules were also determined.

MATERIALS AND METHODS

Materials

Hard gelatin capsules, sizes 0, 1 and 3 were obtained from RP Sherer do Brasil Ltda (Rio de Janeiro, Brazil). Sodium diclofenac was purchased from Purifarma Ltda (São Paulo, Brazil); lactose, magnesium stearate, titanium dioxide, sodium carboxy methyl cellulose and talc from Henrifarma Ltda (São Paulo, Brazil); and PEG 400/6000 from Synth (São Paulo, Brazil). Simethicone was obtained from Dow Co and Eudragit® L 30 D 55 was kindly supplied by Almapal Ltda (São Paulo, Brazil).

Methods

Capsule preparation

Gelatin capsules (HGC) # 0, 1 and 3 were filled with 500, 400 and 200 mg, respectively, of a homogenized mixture of 1% (w/w) magnesium stearate, sodium diclofenac 25% (w/w) and spray dried lactose 74% (w/w). A manual capsule filling device (Multilabor, Brazil) was used. After filling, capsule weight uniformity was determined by individually weighing 100 capsules. The maximum relative standard deviation found in mass distribution was ±5%. The filled capsule weights are shown in Table 2.

Coating preparations and procedure

Polymer suspensions were prepared by adding Eudragit® L 30 D 55 to a previously prepared mixture of plasticizer, opacifier, dye and anti-foaming in water. The combination of all ingredients was submitted to vigorous agitation using a high shear mixer (Diax 600, Heidolph).

The HGCs were coated in Wurster type equipment model LM FBC 1.0 (Labmaq Ltd., Brazil) with bottom spray. The operational conditions chosen after preliminary coating runs were: polymer suspension feed rate 1.5 ml/min, inlet spouting air temperature at 45^{o}C, air flow rate 40% above the minimum spouting velocity and spray nozzle air flow rate and pressure of 50 l/min and 2 kgf/cm^2, respectively. Other operational conditions, like equipment capsule load, coating time and polymer suspension viscosity were varied according to the experimental design.

Disintegration test

In order to evaluate the percentage of gastric resistant on coated HGCs, disintegration tests were performed according to the United States Pharmacopoeia (USP XXIII, 1995). In each test, samples of six coated capsules were placed in each of three baskets and immersed in 0.1 M HCl solution at 37^{o}C in the disintegration apparatus for 1 hour. For each coating condition, the test was performed with 1 replicate, resulting in a total of 36 capsules tested. During the test, the capsules showing swelling, moisturizing, crackling or disintegration were considered not approved. Those that passed the test were then transferred to a phosphate buffer solution (pH =6.8) at 37 ^{o}C. The percentage of gastric resistant capsules obtained in each operational condition was calculated.

Dissolution test

Dissolution tests were performed according to the United States Pharmacopoeia (USP XXIII, 1995). The HGCs were immersed in HCl 0.1 M for 2 hours at 37 ^{o}C, using USP apparatus 2 at 50 rpm. At the end of the 2 hour period the capsules were transferred to a phosphate buffer solution (pH = 6.8) and samples were taken after 10, 20, 30, 45 and 60 minutes to determine diclofenac content and the dissolution profile. Spectrophotometric determination of diclofenac was carried out according to the United States Pharmacopoeia on Hitachi U-2001 equipment (USP XXIII, 1995).

Experimental design

The coating experiments followed a full 2^3 factorial design (Box *et al.,* 1978). The process variables analyzed were capsule load, coating time and suspension viscosity. The levels of the three factors studied are shown in Table 1. The linear and cross

effects of the factors studied may be determined by this design. In order to follow the levels adopted in the design, the factors should be decoded by the following formula:

$$Coded \cdot Variable = \frac{(uncoded \cdot value - 0.5 \times (high \cdot value + low \cdot value))}{0.5 \times (high \cdot value - low \cdot value)}$$

The response function applied was a linear equation, as given below:

$$Y_i = A_0 + A_1X_1 + A_2X_2 + A_3X_3 + A_4X_1X_2 + A_5X_1X_3 + A_6X_2X_3 + A_7X_1X_2X_3$$

where, Y_i = dependent variable = weight gain; X_1 = coded substrate load; X_2 = coded suspension viscosity; X_3 = coded coating time and A_i = polynomial coefficients.

The data on weight gain was analyzed by factorial regression using the module Visual General Linear Model (VGLM) from the software Statistica ´99 Edition (Statsoft, Inc.).

Table. 1: Factor levels for coating experiments.

Factors	Levels	
	-1	+1
1. Substrate load, W (g)	100	180
2. Suspension viscosity, μ (P)	0.02	0.10
3. Coating duration, T (min.)	60	120

RESULTS AND DISCUSSION

The spouting of HGC

Before coating could be carried out, many aspects related to the spouting of the pharmaceutical forms had to be addressed (Jones, 1985; Mehta *et al.*, 1997). Thoma and Bechtold (1999) reported problems with the two-piece HGC design, resulting in the separation of HGC pieces during fluidization. Also, an insufficient level of coat drying may lead to bubble formation or non uniformity in the film (Felton *et al.*, 1995; Jones, 1985; Thoma and Bechtold, 1999). In spouted bed coating, care must be exercised in the flow regime characterization and spouting quality, as well as in heat and mass transfer rates during film layer drying. These phenomena are directly related to air flow rate, inlet air temperature, polymer solution feed rate, substrate loads, coating time and atomization quality (Jones *et al.*, 1985; Parikh *et al.*, 1993; Freitas and Freire, 1997; Christensen and Bertelsen, 1997; Shelukar *et al.*, 2000).

Some characteristics of the size 0, 1, and 3 capsules filled with sodium diclofenac and lactose are presented in Table 2. HGC sizes and shapes are not typical for spouting (Geldart, 1973; Kunii and Levenspiel, 1991), thus requiring preliminary evaluation to determine some of the bed dynamic and stability aspects prior to the onset of the coating study. The lab scale equipment used is adequate for particle charges of up to 1.0 kg (FBC 1.0, Labmaq do Brazil Ltd.). Some very important HGC bed dynamic features were determined following the procedures recommended in the specialized literature (Kunii and Levenspiel, 1991; Epstein and Grace, 1997).

Flow regimes were classified by visual observation and evaluation of constructed curves of the pressure drop, Δ P, versus fluidizing air flow rate, V (Kunii and Levenspiel, 1991). During the experiments, when fluidizing air was fed to the bottom of the chamber, a fountain of particles was formed above the top surface of the bed and typical Δ P x V curves, like that shown in Figure 1, proved that the flow regime was that of a conventional spouted bed. Spouting is a fluidization regime derived when the ratio of column diameter to the inlet air orifice diameter is reduced to a certain limit, which causes the channeling of the gas stream and the cyclic motion of the solids, as opposed to the random movement found in fluidized beds. The descriptions of the spouting regime as compared to fluidization are well posed in the literature, and it is considered equivalent to the regime obtained in a Wurster apparatus (Epstein and Grace, 1997). This regime is recommended for large particles, classified as Geldart´s group D (Geldart, 1973), which agree well with the sizes and specific mass of the HGCs described in Table 2.

Table. 2: Capsule characteristics.

Size	M_c (mg)	D_c (cm)	L_c (cm)	V_c (cm^3)
00	585	0.73	1.85	0.68
01	460	0.66	1.67	0.50
03	268	0.56	1.36	0.30

Dc – capsule diameter; Lc – capsulelength; Mc – capsule weight; Vc – capsule volume.

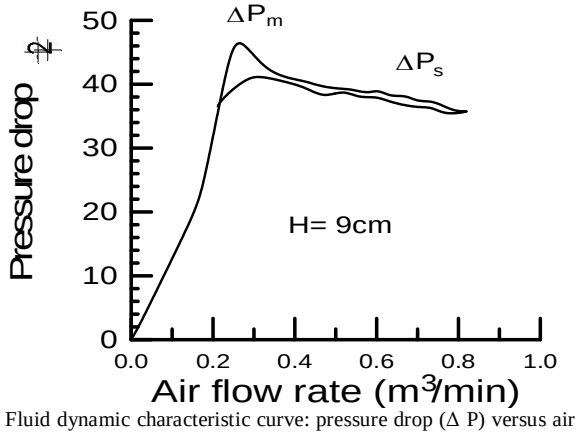

Fig. 1: Fluid dynamic characteristic curve: pressure drop (Δ P) versus air flow rate for HGC fluid beds. (ΔP_M –maximum pressure drop; ΔP_S –spouting pressure drop).

Spouting stability was visually observed by the fountain behavior, according to its shape and height throughout the experiments. The results showed an unstable flow for size 0 HGC, resembling the slugging fluidization regime (Kunii and Levenspiel, 1991), while size 1 presented some degree of instability, with irregular movements in the equipment, like those previously described for HGC spouting (Oliveira *et al.*, 2005). Size 3 HGC presented good stability during spouting, with smooth cyclic movements and a steady fountain height. The results in spouting stability show the importance of flow regime characterization before any further coating processing is conducted in spouted beds. Fluidization quality or stability depends not only on the properties of the solid dosage form, but also on equipment

design and capacity (Mehta *et al.,* 1997). On a larger scale, the design may be improved to provide better spouting qualities for all HGC sizes. Considering the purpose of the present work, only size 3 HGCs were used.

The coating solution formulae

Besides the equipment conditions, polymeric film formulae are decisive for successful coating. The type and content of plasticizer in the formulae may be related to film brittleness, flexibility, flow, toughness, strength, tear resistance and ageing stability (Banker, 1966). The effects of plasticizers on disintegration times of Eudragit® L 30 D 55 coated soft gelatin capsules were investigated by Felton *et al.,* (1995) and significant differences in film coatings using triethyl citrate (TEC) or tributyl citrate (TBC) were found. The polymer concentration in the solution can also affect many of the coating properties, principally solution rheology. The coating suspension viscosity is expected to affect droplet size and atomization quality (Aulton *et al.,* 1997). Polymer droplets hitting the substrate should be able to spread evenly over its surface and coalesce to form a smooth continuous film of even thickness. Inadequate control of atomization may result in film coat defects such as picking, sticking and greater roughness. Preliminary coating experiments were made with five different polymer suspensions, containing different quantities of each component, based on recommendations from the product technical catalogue (Eudragit® L30 D55). Table 3 shows the evaluated polymeric formulae containing different quantities of polymer, plasticizer and opacifier. All the formulae studied contained 0.5% of anti-foaming agent (Simethicone).

Table. 3: Coating formulae investigated.

Formulae	Components (W/W, %)					Solid Contents (%)
	Eudragit L 30 D 55	PEG 400	PEG 6000	Talc	TiO_2	
1	16.7	1.0	0.5	3.0	1.5	12.01
2	15.0	1.5	0.5	3.0	2.0	12.5
3	25.0	1.5	0.5	4.0	2.0	16.5
4	35.0	2.0	1.0	4.0	2.0	20.5
5	43.0	2.0	1.0	4.0	2.0	22.9

Formula number 5 did not present problems during coating and in the HGC visual inspection. Several problems were detected with the other preparations: latex precipitation in preparation 1 caused frequent clogging in the spray nozzle and peristaltic pump tubing, as well as film coating brittleness and a high tendency for HGC agglomeration. This was due to the low polymer content and consequently lower viscosity, accelerating solids precipitation. The same problems were observed in preparation 2. Total polymer and other ingredient contents in the preparations were increased in order to solve these problems. Thus, increased plasticizers content improved film flexibility in preparations 3 and 4, but some tendency for agglomeration was still observed. Preparation 5 was the one chosen to carry out the study, since the film coating showed good quality.

During these preliminary experiments, it was observed that inlet air temperatures above 50°C caused spray nozzle clogging, which is probably related to the polymer glass transition temperature. Also, with polymer preparation feed rates above 2 ml/min, HGC tended to result in bed agglomeration, due to limited drying capacity at low temperatures. For these reasons, the following coating experiments were conducted at the operational conditions shown in Table 4.

Table. 4: Operational conditions for HGC fluid bed coating.

Factors	
HGC	Size 3
Coating preparation	Nr 5 (Table 3)
Coating suspension feed rate	1.5 ml/min
Spray nozzle air rate	50 l/min
Spray nozzle air pressure	2 kgf/cm^2
Fluidizing air temperature	45°C
Fluidizing air flowrate	40% above MS*

* MS – minimum spouting velocity, determined for each substrate load (Epstein and Grace, 1997).

Coating experiments

After the preliminary coating tests, experiments were planned based on the processing factors that were shown to be critical for high efficiency and uniform (HGC joint sealing) coating. The first factor, the load of capsules in the equipment, is directly related to the process condition, e.g., spouting behavior and quality, as well as to the efficiency of the drying process. The spouting behavior is expected to affect capsules cyclic motion and residence time in each section of the spouted bed, which reflects in the coating efficiency.

The coating time or process duration, which was the second factor chosen, is indirectly related to HGC mass gain, e.g., the film coating thickness. During coating time the capsules weight increase and this alters the spouting behavior, which may lead to changes in coating efficiency. The third factor, coating suspension viscosity affects aspects related to the coating efficiency and film properties, like spray droplets size and uniformity. The size affects the efficiency of droplets collection by the capsules. Also, the viscosity of the wet film of polymer suspension on substrate (HGC) surface may affect capsules movement in the down comer section of the bed and cause efficiency changes.

Table. 5: Actual factorial design and respective results for weight gain and efficiency.

Treatment nr.	Coded factors			WG (%)	E (%)
	X1	X2	X3		
1	+1	+1	+1	17.5	69.5
2	-1	+1	+1	33.2	81.6
3	+1	-1	+1	17.2	70.9
4	-1	-1	+1	31.9	80.4
5	+1	+1	-1	11.1	70.9
6	-1	+1	-1	18.9	84.9
7	+1	-1	-1	10.8	72.3
8	-1	-1	-1	18.4	80.6

WG – weight gain; E – efficiency.

In earlier reports, solution viscosities were always studied by altering formulae total solid or polymer content (Parikh *et al.,* 1993; Aulton *et al.,* 1997; Porter, 1997), but in this study, solution viscosity was varied by adding a thickening agent, sodium carboxy

methyl cellulose (NaCMC), in differing amounts. As seen in Table 5, the coating trials resulted in good efficiencies, ranging from 69.5 to 84.9%. The efficiency values were calculated by the ratio of capsule weight gain to the total non-volatile content in the coating formula applied during the process. The efficiency could be much higher at a larger scale, since in lab scale coaters, like the one used herein, the strong effect of the wall may diminish efficiency. The effects of processing factors on HGC weight gain (WG) are shown in Figures 2, 3 and 4. Figure 2 presents percentage weight gain as a function of substrate load and suspension viscosity, indicating that substrate load affects the weight gain, while suspension viscosity appears not to affect it. The reasons for the variation in coating efficiency with the substrate load include changes in capsule recirculation rates and concentration in the central region of the bed. It was previously reported that substrate load affects the gas-solid flow in spouted beds (Epstein & Grace, 1997). Figure 3 presents %WG as a function of substrate load and coating time. In this Figure, %WG is shown to decrease with increasing substrate load and decreasing coating time. Both factors were expected to affect %WG directly, considering that the coating suspension composition was the same in all experiments. As the efficiencies were affected by the factors studied, it was expected that this would also affect weight gain.

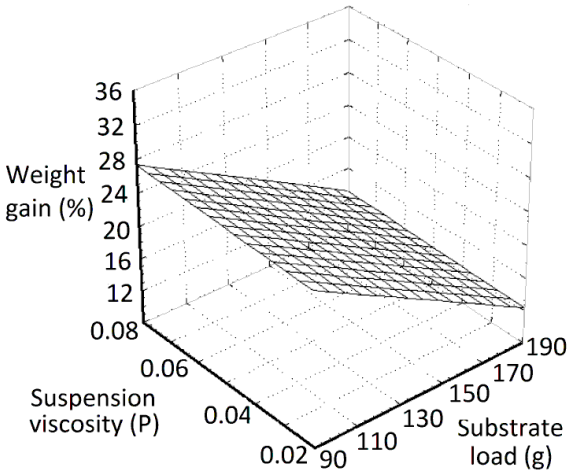

Fig. 2: Weight gain as a function of substrate load and suspension viscosity.

Figure 4 presents %WG as a function of suspension viscosity and coating time. The surface plot confirms the effects shown in Figures 2 and 3, i.e. %WG increases with coating time and is not affected by suspension viscosity. Suspension viscosity is expected to affect the quality of nozzle atomization and droplet size, as well as suspension spreading on the substrate surface. Spray droplet size may affect efficiencies considerably, due to droplet-air drag forces in the bed. This has usually been studied based on changes in solid content in coating suspensions (Mehta, 1997), which may incur mistaken conclusions, since the effects of these two factors cannot be isolated; namely viscosity and solid content. In this work, the viscosity was altered by the addition of a thickening agent (NaCMC) in small concentrations to make the changes in solid content negligible. This was successfully attained, as shown in Table 1. However, the data showed that this factor did not significantly affect coating efficiency. Also, the quality of the coating (smoothness), evaluated by visual observation, was not affected by the suspension viscosity. The resulting variance analysis and respective significant effects on HGC weight gain (%) are shown in Table 6.

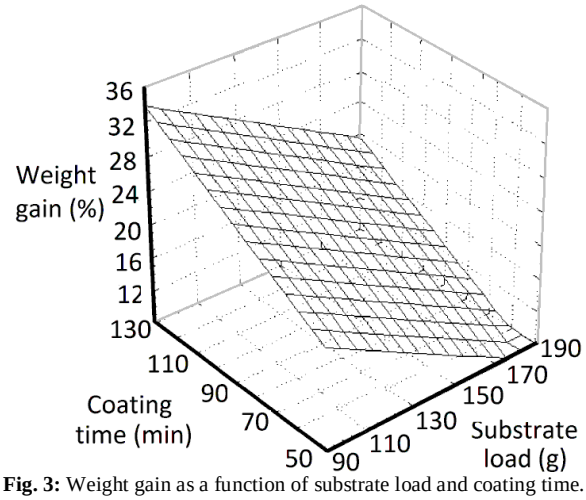

Fig. 3: Weight gain as a function of substrate load and coating time.

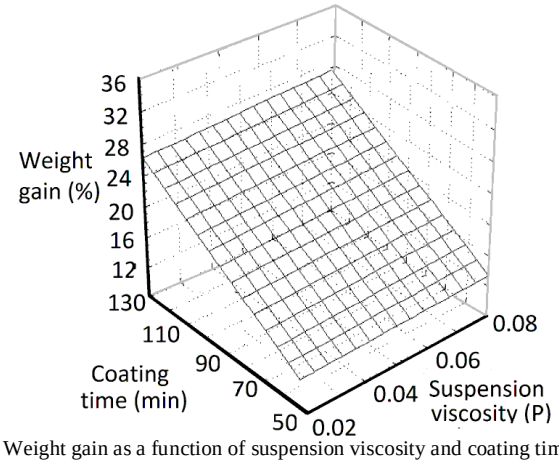

Fig. 4: Weight gain as a function of suspension viscosity and coating time.

Table. 6: Variance analysis on weight gain data.

Factor	Sum of squares	Degrees of freedom	Mean square	Fcalc
W	262.205	1	262.205	3277.56*
□	0.720	1	0.720	9.00
T	206.045	1	206.045	2575.56*
Interactions				
W x □	0.180	1	0.180	2.25
W x T	28.125	1	28.125	351.56*
□ x T	0.080	1	0.080	1.00
Error	0.080	1	0.080	
Total	497.434	7		

Significant at: * 5% level.

As this table shows, substrate load and coating time affected weight gain at a 5% significance level. The interaction between these two factors was also significant at a 5% level. Other factors, like suspension viscosity and other cross or interaction effects were not significant even at a 20% level. An equation was fitted to the experimental data, taking into account only the three

significant terms. The multiple linear fit resulted in a correlation index of $R^2 = 0.9998$ and the following equation:

$$\%WG = 19.9 - 5.7\left(\frac{W-0.14}{0.04}\right) + 5.1\left(\frac{T-90}{30}\right) - 1.8\left(\frac{W-0.14}{0.04}\right)\left(\frac{T-90}{30}\right)$$

where, W = substrate load and T = coating duration

Gastric resistance evaluation

Disintegration tests

Disintegration tests on HGC coated under different operational conditions (Table 5) indicate that there was a minimum %WG to achieve gastric resistance in 100% of the HGCs. Additional data was obtained by analyzing HGC with several coating levels. The operational conditions to obtain the desired %WG were determined with the aid of Equation 3, setting the coating duration at 80 minutes and determining the substrate load.

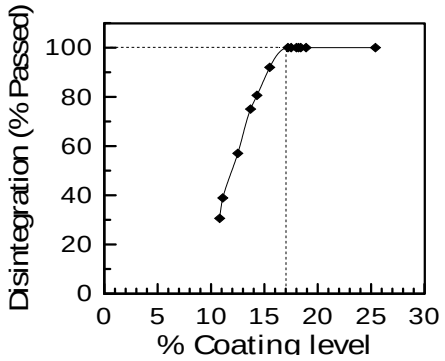

Fig. 5: Percentage of gastric resistance as a function of HGC weight gain.

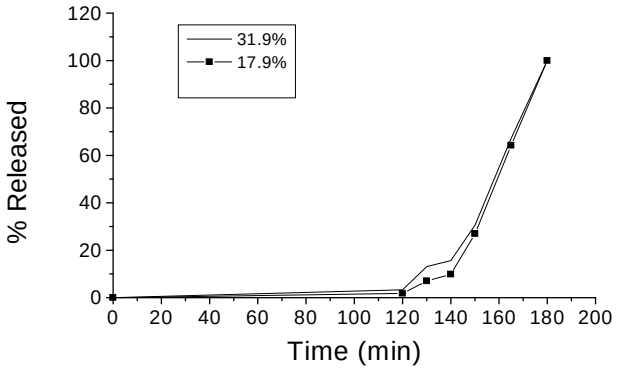

Fig. 6: Dissolution profiles for HGC coated with 17.0% and 31.9% weight gain.

The disintegration tests were then performed for HGC coated with %WGs varying from 11 to 30%. For validation of the enteric coating HGC process it is important to ensure that all the capsules present gastric resistance after coating. The percentage of HGCs that passed in the disintegration tests as a function of the coating level or %WG, are shown in Figure 5. This Figure shows that the percentage of gastric resistant HGCs increases linearly with coating level and reaches full resistance (100%) for weight gains above 17%. The result shows that it is very important to carry out disintegration tests on large HGC samples, since it is also possible that only a partial number of HGCs attain gastric resistance. In this work, disintegration tests were realized with samples of 36 capsules. The minimum weight gain to assure gastric resistance, 17%, is much higher than the coating levels indicated for tablets. This is probably related to the joint in the two piece HGC, since it requires a thicker coating film with adequate mechanical resistance. Mehta et al (1986) evaluated the enteric coating of HGC, sizes 1 and 4, with Eudragit L 30 and found adequate gastric resistance for coating levels of 20 mg/cm^2, which corresponded to 20.5 and 24.7% weight increase, respectively.

The minimum weight gain for homogeneous enteric properties may depend on HGC quality, since joint specification depends on the supplier and on polymer preparation. This means that the figure obtained in this study of 17% cannot be generalized and the procedure shown here should be reproduced for new developments.

Dissolution tests

To verify release profiles, the capsules approved in the disintegration tests were submitted to the dissolution test. Capsules with 17.0 and 31.9% weight gain were submitted to the test according to the Pharmacopoeia (USP XXIII, 1995). The profiles are shown in Figure 6.

Sodium diclofenac release was nearly zero in the HCl media, i.e., less than 5% after 120 min, however, the capsules readily disintegrated and released 75% of the drug in 45 minutes when transferred to phosphate buffer. No difference occurred in the behavior of HGCs coated to 17.0 or 31.9% weight gain. The performance shows the perfect pH dependant effect of the HGC coatings obtained in the spouted bed process. The release profiles shown are in accordance with USP requirements.

CONCLUSIONS

Due to their hygroscopic character and two piece design, HGC coating with aqueous polymeric solutions requires high aeration/drying capacity and excellent solid mixing/movement. The results showed that the spouted bed process is an adequate choice for coating this versatile pharmaceutical form, allowing enteric properties with a single coating layer. However, the coating operation demands evaluation of both the polymeric formulation and processing conditions. The results herein showed that substrate load and coating time, as well as their interaction, affect HGC weight gain, which in turn affects the percentage of gastric resistant capsules. The data obtained showed that full gastric resistance is attained with a minimum of 17% weight gain, which is a high level when compared to that recommended for tablets, but is lower than figures reported in previous studies regarding HGCs. In addition, adequate dissolution profiles were obtained.

ACKNOWLEDGEMENTS

Financial support from FAPESP (99/10183-6 and 02/00291-0 and CNPq (PQ-2) is gratefully acknowledged. The

authors would also like to thank Rohm Gmb and Almapal Ltda (São Paulo, Brazil) for providing Eudragit® L30 D55.

REFERENCES

Aulton, M.E.; Hogan, J.E.; Twitchell, A.M. Physical Properties of HPMC Solutions and their Role in the Film Coating Process and the Quality of Coated Product. In Aqueous Polymeric Coatings for Pharmaceutical Dosage Forms, Marcel Dekker, New York, NY, 227-266, 1997.

Banker, G. S. Film coating theory and practice. J. Pharm. Sci. 1966. 55 (1), 81-89.

Bodea, A.; Leucuta, S.E. Optimization of Propranolol Hydrochloride Sustained Release Pellets using a Factorial Design. Int. J. Pharm., 1997, 154(1), 49-57.

Box, M.; Hunter, W.G.; Hunter, J.S. *Statistics for Experimenters*. John Wiley & Sons, New York, 1978.

Burns, S.J.; Higginbottom, S.; Corness, D.; Hay, G.; Whelan, I.; Atwood, D.; Barnwell, S.G.. A Study of Enteric-Coated Liquid Filled Hard Gelatin Capsules with Biphasic Release Characteristics. Int. J. Pharm., 1994, 110(3), 291-296.

Bussemer, T.; Bodmeier R. R. Formulation Parameters affecting the Performance of Coated Gelatin Capsules with Pulsatile Release Profiles. Int. J. Pharm., 2003, 267 (1-2), 59-68.

Christensen, F.N.; Bertelsen, P. Qualitative Description of the Wurster Based Fluid Bed Coating Process. Drug Dev Ind Pharm., 1997, 23(5), 451-463.

Epstein, N.; Grace, J.R. Spouting of Particulate Solids. In Fayed, M.E.; Otten, L., eds. Handbook of Powder Science and Technology, Van Nostrand Reinhold Co: New York, NY, 509-536, 1997.

Felton, L.A.; Haase, M.M.; Shah, N.H.; Zhang, G.; Infeld, M.H; Malick, A.W.; McGinity, J.W. Physical and Enteric Properties of Soft Gelatin Capsules Coated with Eudragit L30 D55. Int. J. Pharm., 1995, 113(1),17-24.

Felton, L.A.; McGinity, J.W. Influence of Plasticizers on the Adhesive Properties of an Acrylic Resin Copolymer to Hydrophilic and Hydrophobic Tablet Compact. Int. J. Pharm., 1997, 154 (2), 167-178.

Felton, L.A.; Shah, N.H.; Zhang, G.; Infeld, M.H., Malick, A.W.; McGinity, J.W. Physical Mechanical Properties of Film Coated Soft Gelatin Capsules. Int. J. Pharm., 1996, 127(2), 203-211.

Freitas, L.A.P.; Freire, J.T. Development of a Spouted Bed Coater for Tablets. Proceedings of the II Congres Europeen sur la Fluidisation. Univeridad del Pais Vasco, Bilbao, Spain, ed. M. Olazar, 1997.

Geldart, D. Types of gas fluidization. Powder Technol., 1973, 7(5), 285-292.

Jones, D.M. Factors to Consider in Fluid Bed Processing. Pharm. Tech., 1985, 9(4), 50-62.

Jones, D.M. 1988. Air Suspension Coating. In J. Swarbrick & JC Boylan, eds. Encyclopedia of Pharmaceutical Technology; Marcel Dekker, New York, pp.189-216.

Kalala, W.; Kinget, R.; Mooter G. V.; Samyn C. Colonic drug-targeting: In vitro release of ibuprofen from capsules coated with poly(ether-ester) azopolymers. Int. J. Pharm.,1996, 139 (1-2),187-195.

Kunii, D.; Levenspiel, O. Fluidization Engineering. Butterworth-Heinemann: Boston, 1991.

Lehmann, K.; Dreher, D. Coating of Tablets and Small Particles with Acrylic Resin by Fluid Bed Technology. Int. J. Pharm. Tech. and Prod. Manuf., 1981, 2(4), 31-43.

Mehta, A. Processing and Equipment Considerations for Aqueous Coatings. In Aqueous Polymeric Coatings for Pharmaceutical Dosage Forms; Marcel Dekker, New York, 287-326, 1997.

Mehta, A.H.; Valazza, M.J.; Abele, S.E. Evaluation of Fluid Bed Process for Enteric Coating Systems. Pharm. Tech., 1986, 10(4), 46-56.

Murthy, K.S.; Enders, N.A.; Mahjour, M.; Fawzi, M.B.A. Comparative Evaluation of Aqueous Enteric Polymers in Capsule Coatings. Pharm. Tech., 1986, 10(10), 36-46.

Murthy, K.S; Kubert, D. A; Fawzi M.B. In vitro release of hard shell capsule products coated with aqueous and organic based enteric polymers. J. Biomater. Appl., 1988, 3 (1), 52-79.

Oliveira, H.V.A.; Peixoto, M.P.G.; Freitas, L.A.P. Study on the efficiency of hard gelatin capsules coating in a spouted bed. Dry. Technol., 2005, (23), 2039-2053.

Parikh, N.H.; Porter, S.C.; Rohera, B.D. Aqueous Ethylcellulose Dispersion of Ethylcellulose. I. Evaluation of Coating Process Variables. Pharm. Res., 1993, 10(4), 525-534.

Passos, M.L.; Mujumdar, A.S.; Raghavan, V.G.S. 1987. Advances in Drying. pp 359,

Porter, S.C. Use of Opadry, Sureteric and Surelease for the Aqueous Film Coating of Pharmaceutical Oral Dosage Forms. In Aqueous Polymeric Coatings for Pharmaceutical Dosage Forms; Marcel Dekker, New York, pp. 327-372, 1997.

Shelukar, S.; Ho, J.; Zega, J.; Roland, E.; Yeh, N.; Quiram, D.; Nole, A.; Katalare, A.; Reynolds, S. Identification and Characterization of Factors Controlling Tablet Coating Uniformity in a Wurster Coating Process. Powder Technol., 2000, 110 (1-2), 29-36.

Swift, G.L.; Mills, C.H.; Rhodes, J.; Evans, B.K.; Bennett, A.; Tavares, I.A. A Pharmacokinetic Study of Sulfasalazine and 2 New Formulations of Mesalazine. Aliment Pharm. Therap., 1992, 6(2), 259-266.

Thoma K.; Bechtold K. Influence of aqueous coatings on stability of enteric coated pellets and tablets. Eur. J. Pharm. Biopharm., 1999, 47(1), 39-50.

U.S.P. 1995. XXXIII. United States Pharmacopeial Convention, Rockville, MD, pp. 1790-1791,

How to cite this article:

H.V.A. Oliveira, M.P.G. Peixoto, L.A. Tacon & L.A.P.Freitas. Enteric coating of hard gelatin capsules by the spouted bed process. J App Pharm Sci. 2013; 3 (08): 057-063.