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USP Disintegration Apparatus as a Potential Tool for Evaluating Drug Release from Controlled-Release Dosage Forms

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ABSTRACT

Official compendia lack in vitro dissolution guidelines for simulated fed conditions. The goal of this project was to compare disintegration times and drug release characteristics for Polygel CR tablets using USP dissolution Apparatus 1 and the USP disintegration apparatus. Calcium tablets plus vitamin D with different deaggregation properties were also used to study the food-weight effect on tablet disintegration. A USP disk, either flat or on its side, was placed on a tablet contained inside the USP disintegration apparatus to simulate the dosage form being in total contact with food after a heavy meal or in partial contact with food after a light meal, respectively. Drug release profiles for Polygel CR tablets in a simulated fasted state were not remarkably different whether the USP disintegration apparatus or USP dissolution Apparatus 1 was used (66.3 ± 2.1% versus 55.3 ± 1.3% in 6 h). Drug release, however, was observed to be higher in the simulated fed state when the USP disintegration apparatus with a disk was used (88.9 ± 5.9% versus 47.5 ± 0.8% in 6 h, $p < 0.05$). The data generated using calcium tablets plus vitamin D also suggest that food weight does not significantly accelerate the disintegration of tablets designed with rapid disintegration properties. However, the presence of a meal in the stomach may speed up the disintegration of slower disintegrating tablets.

INTRODUCTION

In 1968 Pernarowski et al. (*1*) developed the rotating basket dissolution apparatus, and shortly after that, Poole (*2*) invented the paddle dissolution method. These two designs have become USP Apparatus 1 and Apparatus 2, respectively, and are still the most commonly used instruments. In 1970 the first official dissolution test for a solid dosage form was published in *USP XVIII* (*3*). Since then, dissolution has become widely accepted as a useful tool to reduce development costs, a means to screen formulations, and a way to prepare the conduct of clinical trials and reduce their costs. The FDA has also considered dissolution as a test for the quality control of drug products that is separate and distinct from disintegration (*4*). In addition, dissolution testing provides information about how excipients chosen during research and development impact the dissolution profiles. Substantial debate on the use of dissolution as a quality control test has taken place, including arguments that a drug product could fail the dissolution test without showing an effect on bioavailability or efficacy (*3*). One of the reasons for this is that most dissolution scientists work in as simplified a fashion as possible; thus, what happens in a dissolution vessel is not a simulation of what happens in the body. The food-weight effect on a solid dosage form has not been investigated thoroughly in vitro. There is also lack of compendial guidelines.

To propose a new in vitro model for studying drug release from controlled-release (CR) tablets in both fasted and fed conditions, three different brands of over-the-counter calcium tablets and a Polygel CR niacin tablet were chosen as the model dosage forms for this project. Niacin ($C_6H_5NO_2$), which has a molecular weight of 123.11 g/mol, a solubility of 16.67 mg/mL (*5*), and a pK_a of 2.2 (*6*), is known as nicotinic acid or vitamin B_3. It is one of the essential components of the normal human diet and is important for metabolism. Advanced deficiency of niacin can lead to a condition called pellagra, in which individuals develop diarrhea, dermatitis, and dementia (*5*). Niacin is also used therapeutically to reduce cholesterol and triglyceride levels in the blood. Specifically, it reduces low density lipoprotein and increases high density lipoprotein. Therefore, the main medicinal use of niacin in the United States today is for its hypolipidemic response by lowering serum cholesterol by 10–15% and triglycerides by 20–30% (*7*).

The role of calcium in bone health is indisputable. Calcium is absorbed in the small intestine. The amount of calcium absorbed depends on a several factors such as the acidic condition in the intestines, vitamin D level, estrogen level, and the type of calcium supplement. The elemental calcium content is what is important to the consumer. For instance, a tablet containing 500 mg of calcium carbonate

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has 200 mg of elemental calcium. Hence, one tablet in this example only provides 200 mg of calcium, not 500 mg (*8*).

The current dissolution method listed in *USP 31/NF 26* for niacin tablets (*9*) suggests using 900 mL of 0.1 N HCl with the USP Apparatus 1 (basket) method; the tolerance is not less than 65% of the labeled amount of niacin dissolved in 60 min. These guidelines are not for niacin CR tablets. Since drug release from such formulations in the human gastrointestinal tract (GIT) involves passing through media of different pH levels, a dissolution method should include media changes from one stage to another.

Therefore, the overall purpose of this project was three-fold. First, it was to investigate how the media should be prepared and changed when the dissolution study was advanced from acid stage to buffer stage. Two medium change methods are available in the *USP* (*10*): add directly, and drain and add (*8*). However, the current method is written for an immediate-release dosage form and gives no instructions as to which method should be used for extended-release niacin tablets. The question is, Are both medium change methods applicable to the assessment of hydrogel dosage forms, or is one method superior to the other?

The second aim was to compare drug release from the Polygel model dosage form in both simulated fasted and simulated fed conditions by using USP dissolution Apparatus 1 and the USP disintegration apparatus. A USP disk (*11*) weighing 3.05 g would be placed on top of the tablet to simulate food-weight effect on drug release. To accomplish this, the dissolution media were prepared based on the physiological pH of a human stomach and small intestine when food was present or not, and the dissolution experimental time was made comparable to the retention time of each section in the GIT (Table 1).

The last purpose was to propose a model that allows the study of food weight effect upon a tablet by placing a USP disk on a tablet in different positions. The use of a disk laid flat simulated a tablet that was in total contact with food after a heavy meal, whereas a disk lying sideways simulates a tablet in partial contact with food after a light meal. Calcium tablets plus vitamin D from three different manufacturers were used to test this particular model.

MATERIALS AND METHODS

Materials

Reagents and standards

Niacin reference standard (Niacin RS, Supelco, MO), hydrochloric acid (36.5–38%), sodium hydroxide pellets, and HPLC grade acetonitrile were purchased from VWR International (Bridgeport, NJ). Tribasic sodium phosphate was obtained from PCCA (Houston, TX).

Dissolution Media

Three media, 0.1 N HCl, pH 2.2 hydrochloric acid buffer, and pH 6.8 phosphate buffer, were prepared according to the guidelines listed in the *USP* (*15*). Hydrochloric acid (0.1 N) was used as simulated fasted gastric fluid, pH 2.2 HCl buffer as simulated fed gastric medium, and pH 6.8 phosphate buffer as simulated small intestinal fluid in both fasted and fed states.

Instrumentation

A Hewlett Packard Model 8453 UV-vis spectrophotometer (New Brunswick, NJ) was used to analyze dissolution and disintegration samples. Dissolution studies were performed with a Distek Premier 5100 seven-vessel system. The USP disintegration apparatus consisted of a basket-rack assembly and a 1000-mL beaker with immersion fluid maintained at 39 ± 1 °C by a water bath (Precision Scientific, Model 183, Chicago, IL) to simulate body core temperature.

Commercial Tablet Model Dosage Forms

Polygel CR tablet

SloNiacin, an over-the-counter 500-mg Polygel CR tablet (Upsher-Smith Laboratories Inc., MN), was obtained from a local pharmacy. The excipients listed in

Table 1. Comparison of Different Parts of the Gastrointestinal Tract[a]

	Fasted State		Fed State		Ionic Concentration (nM)		
	pH	Residence Time	pH	Residence Time	Na^+	HCO_3^-	Cl^-
Esophagus	6.8	>30 sec					
Stomach	1–2	1–5 h	2–5*	*	70	<20	100
Duodenum	6.1 (5–6.5)	>5 min	4.5–5.5 (1 h)	1 h			
Jejunum	6.5 (6.0–7.0)	1–2 h	4.7 (2 h)	2 h	140	50–110	130
Ileum	6.5	2–3 h	6.5	*			
Colon	5.5–7.8	15–48 h	8.0	up to 72 h			

[a] Combined from ref *12–14*.
*Dependent on volume, pH, and buffer capacity of the food.

the Polygel CR product label were glycerol behenate, hydrogenated vegetable oil, hypromellose (hydroxypropyl methylcellulose), magnesium stearate, silicon dioxide, and Red 40 (*5*).

Calcium plus vitamin D tablets

Three different brands of 500-mg calcium tablets with vitamin D (Nature Made, CVS, and OsCal) were purchased from a local pharmacy. The ingredients of these commercial calcium tablet products are listed in Table 2.

Table 2. Excipients of Three Brands of 500-mg Calcium Tablets with Vitamin D

Excipient	Nature Made	CVS	OsCal
Acacia Gum		√	
Calcium Carbonate	√		√
Calcium Stearate			√
Carnauba Wax	√		
Cellulose Coating		√	
Cholecalciferol			√
Corn Starch			√
Corn Syrup Solids			√
Croscarmellose		√	
Gelatin			√
Glycerin	√		
Hydroxypropyl Methylcellulose	√		
Magnesium Stearate		√	
Maltodextrin	√	√	
Methylparaben			√
Mineral Oil	√		
Vegetable Oil		√	
Polyethylene Glycol	√		√
Polysorbate 80			√
Polyvinyl Alcohol			√
Propylparaben			√
Sodium Starch Glycolate			√
Sucrose			√
Talc			√
Titanium Dioxide		√	√
dl-alfa Tocopherol			√

Methods

Construction of Niacin Standard Curves

The absorbance maxima of niacin in 0.1 N HCl, pH 2.2 hydrochloric acid buffer, and pH 6.8 phosphate buffer were determined to be 261 nm, 261 nm, and 263 nm, respectively. One hundred milligrams of Niacin RS was dissolved in 100 mL of 0.1 N HCl, pH 2.2 HCl buffer, and pH 6.8 phosphate buffer to prepare stock solutions. To construct standard curves, the stock solutions were diluted to concentrations of 0.01, 0.02, 0.04, 0.1, 0.3, and 0.4 mg/mL for 0.1 N HCl and pH 2.2 HCl buffer, and 0.0016, 0.008, 0.04, 0.2, and 1 mg/mL for the pH 6.8 phosphate buffer. The lower concentration was included for the pH 6.8 phosphate buffer standard curve because release of niacin Polygel was lower in this pH. Standard curves for niacin in 0.1 N HCl, pH 2.2 HCl buffer, and pH 6.8 phosphate buffer had correlation coefficients (r^2) of 0.9998, 0.9993, and 0.9995, respectively. The linear range for niacin in 0.1 N HCl and pH 2.2 HCl buffer was 0.01 to 0.40 mg/mL, and in pH 6.8 phosphate buffer, 0.0016 to 1.00 mg/mL.

Investigation of Dissolution Medium-Change Methods

Method A: Add Directly

A Polygel CR tablet was placed in Apparatus 1 with 500 mL of deaerated 0.1 N HCl at 50 rpm. After two hours, 500 mL of deaerated 0.0375 M tribasic sodium phosphate (Na_3PO_4) preheated to 37 ± 0.5 °C was added. The deaeration was done by filtering the medium through a 0.25-µm porosity, 2.5-cm diameter PTFE membrane assembled in a suction flask. The resulting buffer solution was adjusted to pH 6.8 by addition of 2 N NaOH to mimic small intestinal fluid.

Method B: Drain and Add

For method B, the initial dissolution operating conditions were the same as for method A. At the end of two hours, the dissolution platform was lifted into the air for 10 min. The medium was drained from the dissolution vessel, then 1000 mL of preheated, deaerated pH 6.8 phosphate buffer was added. The platform was then lowered and stirring was resumed at 50 rpm for four hours. The sampling time points during the acid stage were 0.25, 0.5, 1, 1.5, and 2 h; those for the buffer stage were 0.25, 0.5, 1, 1.5, 2, and 4 h. The acid samples were quantified spectrophotometrically at 261 nm, and the phosphate buffer samples at 263 nm.

Drug Release from Polygel Formulation during Fasted and Fed State

The same media were prepared for both the dissolution and disintegration experiments. In the simulated fasted condition, a Polygel CR tablet was immersed in 0.1 N HCl for 2 h and then in pH 6.8 phosphate buffer for 4 h.

Disintegration study

The test apparatus was calibrated to ensure that the USP standard (*11*) had been met; that is, the basket was

raised and lowered in 800 mL of deionized water as the immersion fluid at 29–32 cycles per minute. The volume of fluid in the vessel was such that at the highest point of the upward stroke, the wire mesh remained at least 2.5 cm below the surface of the fluid and descended to not less than 2.5 cm from the bottom of the vessel on the downward stroke. Then 800 mL of preheated (39 ± 1 °C) deaerated 0.1 N HCl was used as the test immersion fluid to mimic a tablet in an empty stomach. At the end of two hours, the apparatus was paused. The basket containing the Polygel tablet was quickly switched to another beaker containing 800 mL of deaerated pH 6.8 phosphate buffer preheated to 39 °C to mimic the intestinal fluid. No disk was applied to a test tablet. Operation of the apparatus was resumed for four hours. Six milliliters of immersion fluid was collected with replenishment of an equal volume of fresh medium during each sampling point. The sampling schedule at the acid stage was 0.25, 0.5, 1, 1.5, and 2 h, and that of buffer stage was 0.25, 0.5, 1, 2, 3, and 4 h. Acidic samples were assayed spectrophotometrically at 261 nm, and buffer stage samples at 263 nm. A correction factor for these sampling volumes was implemented during data analysis. When the concentration of an undiluted sample was suspected to be outside the linear range of the standard curve, the sample solution was further diluted two-fold before assay.

Dissolution study

USP Apparatus 1 (*10, 16, 17*) was chosen for the dissolution study with 500 mL of preheated (39 ± 1 °C) deaerated 0.1 N HCl. The basket rotation speed was set at 50 rpm for 2 h to simulate the fasted gastric condition. Then medium change Method A, Add Directly, was used to bring the medium to 1000 mL at pH 6.8. The dissolution study continued at 50 rpm for another 4 h to simulate the fasted condition in the small intestine. The sampling schedule and assay method were the same as those for the disintegration study.

Drug Release from Polygel Formulation during Fed State

In the simulated fed study, a tablet was studied in pH 2.2 HCl buffer for 6 h in both dissolution and disintegration studies.

Disintegration study

The apparatus conditions were the same as described above with two exceptions; pH 2.2 HCl buffer was used, and a USP disk weighing 3.05 g was placed flat on the top of the tested tablet to mimic the effect of food weight in maximal contact with the test tablet after a heavy meal. Samples were collected at 0.25, 0.5, 1, 1.5, 2, 3, 4, and 6 h and quantified spectrophotometrically at 261 nm.

Dissolution study

Apparatus 1 was chosen for the dissolution study with 1000 mL of preheated pH 2.2 phosphate buffer and a basket rotation speed of 100 rpm for 6 h to simulate fed condition. Sampling schedule was the same as that for the disintegration study above.

Evaluation of Effect of Disk Position on the Disintegration Time of Calcium Tablets

Hardness testing (Schleuniger-2E, Vicotr Co., Marion, IA) of all three brands of calcium with vitamin D tablets (Nature Made, CVS, and OsCal) was performed to eliminate the concern of a formulation parameter that may bias the disintegration results. All brands had hardness greater than 20 kiloponds.

A USP disk was placed in different positions on a calcium tablet inside the tube of the disintegration basket to simulate light or heavy food weight. Disk laid flat was to mimic the tablet being compacted by a full meal, while disk laid upright with its side in contact with the test tablet was to simulate a calcium tablet being partially touched by a light meal in the stomach. The time when a calcium tablet was completely disintegrated inside the apparatus was then recorded.

Statistical Analysis

Excel 2000 (Microsoft) was used to manage raw data. Using SigmaStat 3.5 (SYSTAT Software Inc., San Jose, CA), independent *t*-test and one-way ANOVA were performed for two-group data and three-group data analysis when normality and equal variance met. All pairwise multiple comparison procedure (Tukey Test) was selected as the posthoc test (*18*). Rank Sum test and Kruskal–Wallis ANOVA on Ranks were chosen for two-group and three-group comparisons when unequal variance existed. Population differences are considered significant at $p < 0.05$ (*18*).

RESULTS

Medium Change Methods

The niacin released from the Polygel CR tablet in acid stage during simulated fasted condition was biphasic: curved in the acid stage (Figure 1A) and linear in the buffer stage (Figure 1B). The best-fit equation obtained for the release versus time profile in the acid stage is:

$$Y = 19.482\,X^3 - 88.033\,X^2 + 183.06\,X + 1.624$$

where X is time in hr and Y is the amount of niacin (mg) released into the medium. The correlation coefficient, r^2, is 0.9988.

When Method A (Add Directly) was used to change dissolution medium from acidic pH to pH 6.8, the 4-hr drug release from a Polygel CR tablet was linear, and the release rate during this buffer stage was 27.5 ± 1.5 mg/h. But when Method B (Drain and Add) was used to change medium, the release rate was significantly slowed. The computed average of the release rate was only 16.5 ± 5.8 mg/h ($n = 8$, $p < 0.001$, Table 3).

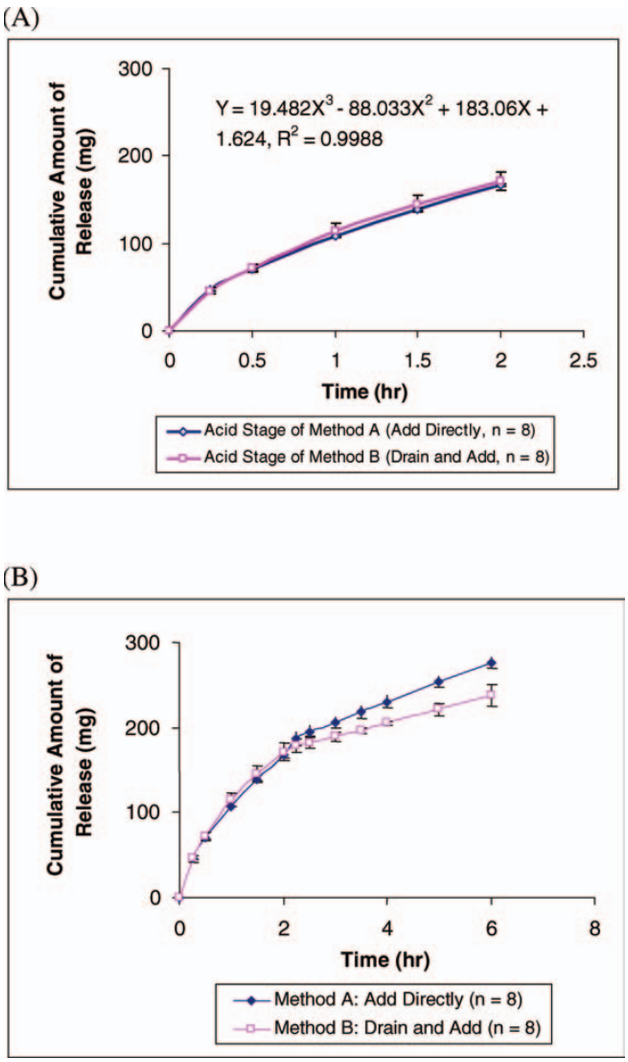

Figure 1. Niacin release from a Polygel CR tablet using Method A vs. Method B to change medium. Release in acid stage during simulated fasted condition was biphasic: (A) curved in the acid stage and (B) linear in the buffer stage.

Drug Release from the Polygel Formulation during Fasted and Fed States

Use of a disintegration apparatus or a dissolution apparatus did not seem to affect the cumulative percent niacin release from a Polygel CR tablet during simulated fasted condition at the end of 6-h experimental period (66.3 ± 2.1%, $n = 6$ versus 55.3 ± 1.3%, $n = 8$, Table 4). The cumulative percent of drug release in 6 h, however, was much higher in the simulated fed state when the USP disintegration apparatus with a disk of 3.05 g was applied to simulate the food-weight effect (Figure 2). The results were 88.9 ± 5.9%, $n = 6$ versus 47.5 ± 0.8%, $n = 5$ (Table 4).

The cumulative percent of niacin release from a Polygel CR tablet in simulated fasted and simulated fed states were plotted for USP dissolution Apparatus 1 and the USP disintegration apparatus. The correlation coefficient, r^2, was 0.9976 for simulated fasted state, which was 0.1 N HCl as test medium for 2 h, then pH 6.8 phosphate buffer for 4 h. No disk was added to the USP disintegration apparatus, and the basket spinning rate of the USP dissolution apparatus was 50 rpm. The r^2 value was 0.9955 for the simulated fed study (Figure 3). In this case, pH 2.2 HCl buffer was used as the test medium. A 3.05-g disk was added on top of the test tablet inside the disintegration apparatus. The basket rotation speed was 100 rpm. The r^2 values were similar, but the slope of the simulated fed state trend line was 1.7 times that of the simulated fasted state trend line (1.933 versus 1.143, Figure 3).

Table 3. Comparison of Medium Change Methods on Niacin Release Rates from Polygel CR Tablet during 4-h Buffer Stage (pH 6.8) Dissolution Study

	Release Rate	
Sample ID	**Method A** (mg/h)	**Method B** (mg/h)
1	25.21	11.04
2	26.52	11.29
3	25.86	11.44
4	26.99	11.04
5	29.20	22.95
6	28.74	20.25
7	28.45	22.88
8	28.81	21.49
Avg ± SD	27.5 ± 1.5	16.5 ± 5.8[a]

[a] $p < 0.001$

Table 4. Percentage Niacin Released from a Polygel CR Tablet in 6 h Using USP Apparatus 1 and Disintegration Apparatus

	Disintegration Apparatus	Dissolution Apparatus 1
Fasted	66.3 ± 2.1% ($n = 6$)	55.3 ± 1.3% ($n = 8$)
Fed	88.9 ± 5.9% ($n = 6$)	47.5 ± 0.8% ($n = 5$)

Calcium Tablet Disintegration Time with a USP Disk at Different Positions inside the Apparatus

Among the three brands of 500-mg calcium with vitamin D tablets tested with and without a USP disk and in different disk positions (laid flat vs. laid upright) to mimic different degrees of food weight effect on a tablet disintegration, neither the presence of a disk nor the position of a disk made a difference in the disintegration of the CVS and OsCal brands. Nature Made calcium and vitamin D tablets disintegrated faster with a disk laid flat on top than with a disk laid upright (9.88 ± 0.68 min versus

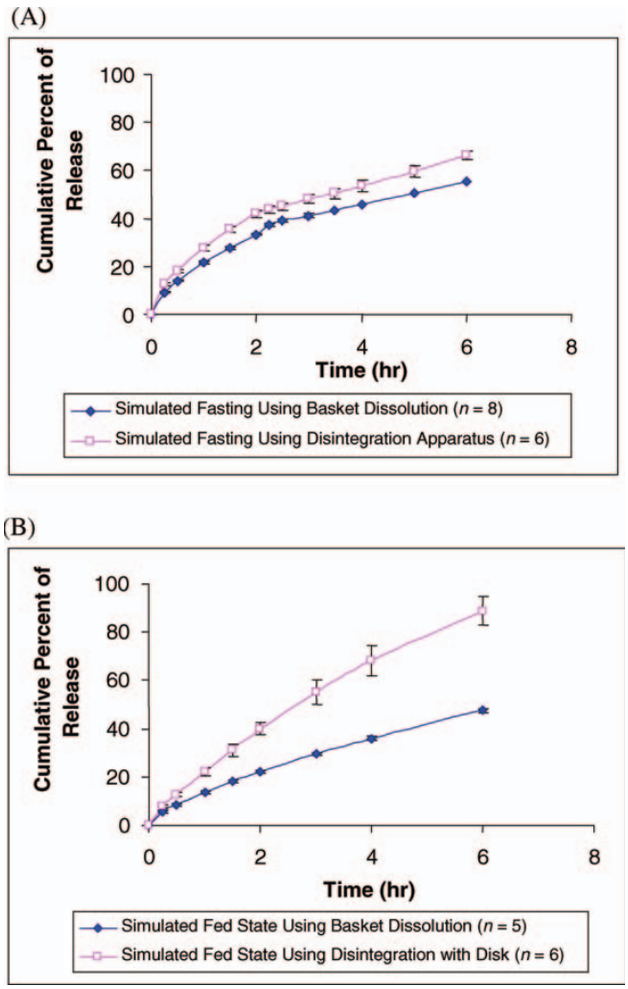

Figure 2. Niacin release from a Polygel CR tablet in (A) fasted and (B) fed conditions using USP dissolution Apparatus 1 and the USP disintegration apparatus.

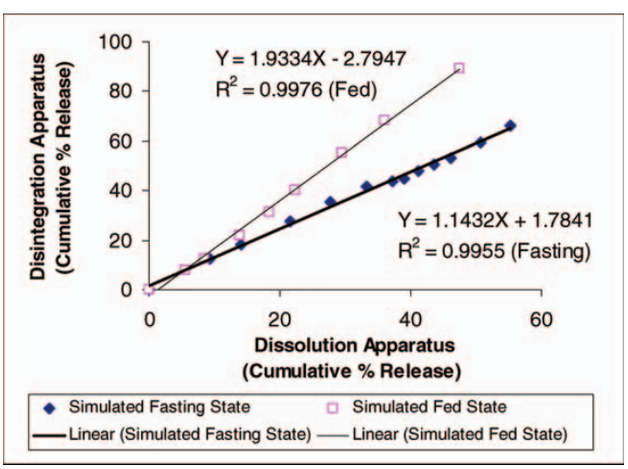

Figure 3. Comparison of correlation of niacin release from a Polygel CR tablet using USP dissolution Apparatus 1 and the USP disintegration apparatus for simulated fasted state (no disk added) and simulated fed states (disk on top of the test tablet).

14.7 ± 1.30 min, $n = 9$, $p < 0.05$, Table 5). The disintegration of Nature Made calcium and vitamin D tablets was slowest when no disk was applied (20.43 ± 0.93 min, $n = 9$, Table 5).

DISCUSSION

Method A (Add Directly) was superior to Method B (Drain and Add) during the dissolution test of a Polygel CR tablet for the following three reasons. First, after tablet exposure to an acidic medium for 2 h, the swollen scaffold of the Polygel tablet may deswell due to the lack of medium support when the dissolution platform is lifted to change dissolution medium as required in Method B. The air may also block the channels and affect the diffusion of drug molecules after the platform is returned to the system (Figure 4). Second, Method A simulates the physiological environment more closely as it is a continuous process for a tablet to travel in the medium from the stomach into the small intestine (Table 1). Third, data indicate that the errors between vessels and between run variations are smaller when Method A is employed (Figure 3B). Hence, Method A is recommended for the dissolution study of a Polygel CR tablet.

The niacin released from the Polygel CR tablet, a hydrogel and lipophilc matrix system, in acid stage during simulated fasted dissolution study was observed as biphasic: curved in the acid stage and linear in the buffer stage (Figure 1). The excipients controlling the niacin release from the Polygel CR product (e.g., glycerol behenate, hypromellose) are pH-independent. In the beginning of the dissolution study, which was in the acidic medium, the niacin molecules present on and near the surface of the tablets dissolved quickly. As time progressed, the release rate slowed due to the increased diffusion distance, which may explain why the release in acidic medium is a curve. But during the pH 6.8 phosphate buffer stage, the release profile became linear instead of moving upward as a curve (data not shown). Although the reason is unknown, we speculate that this observation may be linked to the charge interactions among niacin ions, hydrogen ions, chloride ions, sodium ions, and mono- and bi-basic phosphate ions present in the medium, making the release rate of niacin from the inner part of the tablet through gel material more constant (Figure 1, Table 3).

The correlation coefficients, r^2, using USP dissolution Apparatus 1 and the USP disintegration apparatus for niacin release from a Polygel CR tablet in simulated fasted state (no disk added) and simulated fed states (with a disk of 3.05 g on top of test tablet) were 0.9976 and 0.9955, respectively, implying that both apparatus performed precisely and reliably within the test period (6 h) under the proposed experimental conditions. But the slope of simulated fed state trend line was 1.7 times that of the simulated fasted state trend line (1.933 versus 1.143). This observation suggests that using a USP

Table 5. Disintegration Times of Three Brands of Calcium Tablets with and without a USP Disk

Disk Configuration	**OsCal** (min)	**CVS** (min)	**Nature Made** (min)
No Disk[a]	9.23 ± 2.73 (n = 16)	3.71 ± 0.25 (n = 5)	20.43 ± 0.93 (n = 9)
Disk Laid Flat[b]	7.26 ± 0.93 (n = 16)	2.86 ± 0.12 (n = 5)	9.88 ± 0.68[d] (n = 9)
Disk Laid Upright[c]	7.84 ± 1.10 (n = 16)	3.10 ± 0.25 (n = 5)	14.79 ± 1.30[d] (n = 9)

[a] Represents fasted state.
[b] Mimics a heavy meal in full contact with the tablet.
[c] Mimics a light meal partially contacted the tablet.
[d] $p < 0.05$.

Figure 4. Polygel CR Tablet after being in an acidic medium for 2 h.

disintegration apparatus would predict drug release in simulated fed state almost twice higher than using Apparatus 1, but the prediction of drug release in simulated fasted state using either apparatus is similar (Figure 3).

The disintegration of the CVS calcium supplement with vitamin D follows bulk disaggregation in a rapid pattern, which occurred in 3.71 ± 0.25 min (n = 5, Table 5). When the study was repeated placing a USP disk flat on the top of a tablet, its disintegration did not accelerate much, 2.86 ± 0.12 min (n = 5, Table 5). The Nature Made calcium supplement with vitamin D was apparently manufactured by dry compression without a protective coat. The disintegration of this tablet was observed as erosion from the surface and was the slowest of the three brands (20.43 ± 0.93 min, n = 9, Table 5). Because of its longer disintegration time, placement of a USP disk flat on its top accelerated disintegration, which is probably caused by the bumping movements of the disk while the basket was raised and lowered inside the beaker (9.88 ± 0.68 min, n = 9, Table 5).

CONCLUSIONS

Medium change Method A (Add Directly) is recommended when conducting the dissolution of a Polygel CR tablet. The niacin release from such a tablet was biphasic: curved in acid stage and linear in buffer stage (pH 6.8). There was no impact on drug release due to food weight and churning effect using USP dissolution Apparatus 1, while there may be an effect using USP disintegration apparatus with a disk. Disk adherence to a Polygel CR tablet affects medium buoyancy and leads to greater variation of drug release among samples in the simulated fed than in the simulated fasted study. The data from this simulation research also indicate that food weight does not accelerate disintegration remarkably in a tablet designed with rapid disintegration properties such as the calcium tablets studied. However, a meal in the stomach may speed up the disintegration of a slower disintegrating tablet.

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