In vitro Evaluation of Extemporaneously Compounded Immediate-release Capsules with Premixed Excipients, Based on the Biopharmaceutics Classification System (BCS) of the Drugs

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ACKNOWLEDGMENTS

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INTRODUCTION

Pharmaceutical compounding has grown significantly in recent years and represents an ever-expanding branch of pharmacy practice. By granting patients with individualized therapies and lower costs, compounding offers a solution to the recurring issues related to specific therapeutic regimes, therefore increasing patient adherence to prescribed treatment.

Among the many dosage forms compounded by pharmacists, hard capsules have proven to be particularly effective and have, therefore, played an important role in drug delivery within pharmaceutical applications. Factors such as limited selection of over-the-counter drugs and patient preferences can often be associated to their continuous rise in popularity. Deemed as versatile, this treatment method allows pharmacists to incorporate several compatible drugs within a single capsule, which minimizes the consumption of several dosage forms, enhances patient compliance, and, ultimately contributes to a more successful therapeutic outcome.

Upon consumption, the bioavailability of a particular drug is often dictated by its bioavailability of the drugs compounded in hard capsules is not always optimized and choosing the appropriate excipients is a key factor to improve the dissolution kinetics of active pharmaceutical ingredients. The Biopharmaceutical Classification System, which categorizes drugs regarding their solubility and permeability, is a unique tool which can be used to select the most compatible excipients for a particular drug when compounding immediate-release capsules. The aim of this study was to evaluate the efficiency of premixed excipient blends called CapsuBlend Excipients, based on the Biopharmaceutical Classification System concept, for drug dissolution rate and absorption enhancement. Drug assay and dissolution profiles were studied for three batches of metronidazole 250-mg, theophylline 100-mg, and levocarnitine 250-mg capsules, each respectively representing a highly soluble, poorly soluble, and hygroscopic drug. Methods followed the specifications set forth in the United States Pharmacopeia. Assay results demonstrated that each batch of metronidazole 250 mg, theophylline 100 mg, and levocarnitine 250 mg contained not less than 90.0% of and not more than 110.0% of the labeled amount of drug, which is in accordance with the United States Pharmacopeia requirements. Moreover, dissolution profile results for the aforementioned capsules depicted dissolution values meeting the Pharmacopeial criteria of acceptance. These results reinforce the fact that the Biopharmaceutical Classification System concept represents a valuable guideline for formulation chemists or pharmacists to assist them for capsule compounding. To ensure a high level of efficiency of compounded capsules, premixed excipient blends, carefully developed by taking into consideration the solubility and permeability of a drug, represent a significant formulation advantage to improve the dissolution of active pharmaceutical ingredients.

The authors are affiliated with MEDISCA, Montreal, Quebec, Canada.
dissolution kinetics which, in turn, is directly associated with its physicochemical properties. Such factors must be considered by compounding pharmacists when preparing encapsulated dosage forms. External factors, such as excipients used in conjunction with the drug, may also have an impact on the dissolution kinetics by either altering the medium in which the drug is dissolved or simply by reacting with the drug itself. For instance, when present in high concentrations, capsule lubricants such as magnesium stearate may repel water and ultimately reduce the drug dissolution rate. Similarly, high concentrations of surfactants such as sodium lauryl sulfate (SLS) can cause micelle formation and impede the rate of dissolution. Yet, when SLS is found in low concentrations, it increases the rate of drug dissolution by decreasing the surface tension. Taken as a whole, when used in appropriate concentrations and combinations, excipients may be added intentionally to the formulation to enhance the rate and level of drug absorption or, alternatively, to delay the rate of absorption.

In 1995, Amidon and other researchers introduced the concept of the Biopharmaceutical Classification System (BCS). This BCS was developed as a mean to provide a scientific approach for drug classification based on aqueous solubility and intestinal permeability. For instance, a drug is considered highly permeable when the extent of absorption in humans is more than 90% and highly soluble when the highest dose is soluble in 250 mL or less of buffer ranging between a pH of 1 and 7.5.

Knowledge of the BCS can help pharmacists or formulation chemists in the development of a dosage form based on mechanistic, rather than empirical approaches; serving as a valuable guideline when selecting capsule fillers and ultimately, aiding in the improvement of the dissolution rate, and absorption of a particular drug.

For example, Class I medications (high solubility and high permeability) normally have few bioavailability problems. As a result, a premixed blend offering desired flowability and disintegration without impeding dissolution would be most suitable. Class II medications (low solubility and high permeability) are limited in their absorption capabilities, and it is, therefore, recommended to employ excipients which aid in dissolution and act as wetting and disintegrating agents. Class III medications (high solubility and low permeability) have limited absorption due to their low permeability and require a combination of excipients which will enhance their absorption. Class IV medications (low solubility and low permeability) can present serious obstacles to oral bioavailability; they are commonly formulated in a solubilized form, such as in anhydrous liquids, for later encapsulation. However, if initially prepared with appropriate excipients which would allow for absorption increase, then their bioavailability can readily be improved.

To depict the effectiveness of class-specific excipient blends, the in vitro drug release of metronidazole 250-mg (Class III drug), theophylline 100-mg (Class IV drug), and levocarnitine 250-mg (Class I drug but hygroscopic) immediate-release capsules was investigated. Three batches of each of the aforementioned capsules were prepared and analyzed to ensure reproducibility of drug release.

The aim of this study was to evaluate the efficiency of premixed excipient blends called Capsublend (MEDISCA Pharmaceutique Inc., Saint-Laurent, Quebec), based on the BCS concept, for drug dissolution rate and absorption enhancement.

**MATERIALS AND METHODS**

**Chemical Substance of Reference**

Metronidazole USP (Lot 19810B), used as a reference standard, was obtained from Tianjin Zhongan Pharmaceutical Company (Xiqing District, Tianjin, China). Theophylline USP (Lot 07319), used as a reference standard, was obtained from Shandong Xinhua Pharmaceutical (Zibo, Shandong, China). Levocarnitine USP (Lot 29237A), used as a reference standard, was obtained from Hengtaichem (Kaiyuan City, Lianoning Province, China).

**Capsules Preparation**

Three batches of 35 capsules with 250 mg of metronidazole (F004197A, F004197B, F004197C), three batches of 35 capsules with 100 mg of theophylline (F004275A, F004275B, F004275C), and three batches of 35 capsules with 250 mg of levocarnitine (F004199A, F004199B, F004199C) were compounded and provided by MEDISCA Pharmaceutique Inc. For each batch, the necessary amount of active pharmaceutical ingredient (API) and corresponding premixed excipient blend “Capsublend” was calculated and mixed by geometric dilution. The Capsublends had been prepared beforehand according to the list of ingredients depicted in Tables 1, 2, and 3 (MEDISCA Pharmaceutique Inc.). Size #1 colorless hard gelatin capsules (Lot 35972/B; MEDISCA Pharmaceutique Inc.) and size #0 colorless hard gelatin capsules (Lot 29650/C; MEDISCA Pharmaceutique Inc.) were used depending on individual requirements. Finally, volumetric filling of the capsules was performed using a capsule machine (Model 120 Color Plus; Ideal, Arujá, Brazil).
Note: Metocarnitine is a Class I drug.

<table>
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<th>INGREDIENTS</th>
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<tr>
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<td>N94245F01</td>
</tr>
<tr>
<td>Colloidal silicon dioxide</td>
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<td>28448/D</td>
</tr>
<tr>
<td>Microcrystalline cellulose</td>
<td>QS 100.0</td>
<td>27688/B</td>
</tr>
</tbody>
</table>

Note: Theophylline is a Class IV drug.

<table>
<thead>
<tr>
<th>INGREDIENTS</th>
<th>PERCENTAGE</th>
<th>LOT NUMBER</th>
</tr>
</thead>
<tbody>
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<td>Sodium lauryl sulfate</td>
<td>&lt;2.0</td>
<td>28037/D</td>
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<tr>
<td>Sodium starch glycolate</td>
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<tr>
<td>Colloidal silicon dioxide</td>
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<tr>
<td>Microcrystalline cellulose</td>
<td>&lt;50.0</td>
<td>27688/B</td>
</tr>
<tr>
<td>Mannitol</td>
<td>QS 100.0</td>
<td>27567/A</td>
</tr>
</tbody>
</table>

Note: Levocarnitine is a Class I, hydroscopic drug.

**Assessment of Quality of Immediate-release Capsules**

All encapsulated batches underwent mean weight according to specifications of the Brazilian Pharmacopeia (BP) National Formulary,13 followed by assay testing of the APIs according to the United States Pharmacopeia (USP)14 specifications. Once the aforementioned criteria were met, dissolution testing was performed on the capsule batches, according to the method described in the USP.

**Mean Weight**

Ten capsules of each formulation were individually weighed and average, standard deviation, and coefficient of variation were calculated. The results were compared to the specifications of the BP, as there is no known USP standard for mean weight verification.13

**Assay**

**Metronidazole 250-mg capsules**

Initially, a mobile phase solution was prepared by filtering and degassing a 4:1 mixture of water (Serial #F6NM17935F; Milli-Q Plus TOC; Millipore, Molsheim, France) and high-performance liquid chromatographic (HPLC)-grade methanol (Lot 103561; Fisher Scientific, Trinidad), respectively. An assay stock solution was then prepared by emptying the contents of 20 capsules containing 100 mg of metronidazole (MEDISCA Pharmaceutique Inc.). A portion equivalent to 100 mg of metronidazole was weighed and transferred to a 100-mL volumetric flask, to which 80 mL of the mobile phase was added. The mixture was sonicated for 10 minutes and then shaken mechanically for 30 minutes. The latter was diluted to volume with mobile phase. A portion of the solution was centrifuged, resulting in a supernatant having a nominal concentration of 1 mg/mL of metronidazole. A standard solution was prepared by dissolving an accurately weighed amount of Metronidazole USP (Lot 19810/B; MEDISCA Pharmaceutique Inc.) in mobile phase to obtain a known concentration of 0.03 mg/mL. A portion of the latter was passed through a nylon membrane filter having a porosity of 0.45 mcm or finer. The first 10 mL of the filtrate was discarded and the remainder was used.

Equal volumes (30 mL) of the standard and assay preparations were injected into the liquid chromatograph (Model 710B WISP, Serial #71B-009453; Waters, Milford, Massachusetts) and were passed through a 4.6-mm × 15-cm column containing 5-mcm L7 packing. Samples were run at a flow rate of 1.0 mL/min. The system was equipped with a 319 nm detector (Lambda-Max 481, Serial #481-109896; Waters).

Chromatograms were recorded for twice the retention time of metronidazole followed by measurement of metronidazole response peaks. The quantity of metronidazole in capsules was calculated using the following formula:

\[
100(CS/CU)(rU/rS)
\]

where CS is the concentration, in mg/mL, of Metronidazole USP in the standard solution; CU is the nominal concentration, in mg/mL, based on the label claim of metronidazole in the assay preparation; and rU and rS are the peak responses obtained from the assay and the standard preparations, respectively.14

**Theophylline 100-mg Capsules**

An assay preparation was made by emptying the contents of 20 capsules containing 100 mg of theophylline (MEDISCA Pharmaceutique Inc.). A portion equivalent to 100 mg of anhydrous theophylline was weighed and transferred to a 250-mL volumetric flask and dissolved in 150 mL of HPLC-grade methanol (Lot 103561; Fisher Scientific). The latter was diluted to volume with HPLC-grade methanol and filtered using a membrane filter. A standard solution was prepared by dissolving an accurately weighed quantity of Theophylline USP (Lot 07319; MEDISCA Pharmaceutique Inc.) in HPLC-grade methanol to obtain a solution having a known concentration of 400 mcg/mL. The mobile phase was then prepared using a 64:35:1 mixture of water (Serial #F6NM17935F; Milli-Q Plus TOC; Millipore), methanol (Lot
103561; Fisher Scientific), and glacial acetic acid (Lot 10610MH; Sigma-Aldrich, St. Louis, Missouri).

Equal volumes (20 mcL) of the standard and assay preparations were injected into the liquid chromatograph (Model 710B WISP, Serial #71B-009453; Waters) and were passed through a 4-mm × 30-cm column containing L1 packing. Samples were ran at a flow rate of 2 mL/min. The system was equipped with a 254-nm detector (Model Lambda-Max 481, Serial #481-109896; Waters).

Three replicate injections of both preparations were performed to record the peak responses. The quantity of anhydrous theophylline in capsules was calculated using the following formula:

\[ \text{0.25C(}r_U/ r_S\text{)} \]

where \(C\) is the concentration, in mcg/mL, of Theophylline USP in the standard preparation, and \(r_U\) and \(r_S\) are the peak responses obtained from the assay preparation and the standard preparation, respectively.\(^\text{14}\)

**Levocarnitine 250-mg Capsules**

The assay test for levocarnitine capsules was based on the USP methodology for levocarnitine tablets.\(^\text{14}\)

Initially, a pH 4.5 phosphate buffer (0.05 M) was prepared by dissolving 6.805 g of monobasic potassium phosphate in 1000 mL of water (Serial # F6NM17935F; Milli-Q Plus TOC; Millipore). Subsequently, a mobile phase was prepared by filtering and degassing a 65:35 mixture of acetonitrile and pH 4.5 phosphate buffer (0.05 M), respectively. The pH was adjusted to 4.7 using phosphoric acid (Lot MKBB4759; Sigma-Aldrich). A standard solution was then prepared by accurately weighing a quantity of Levocarnitine USP (Lot 29237/A; MEDISCA Pharmaceutique Inc.), followed by dilution in water (Serial # F6NM17935F, Milli-Q Plus TOC; Millipore) to obtain a solution having a known concentration of about 3 mg/mL. A system suitability solution (resolution solution) was prepared by accurately weighing quantities of Levocarnitine Rs USP and Levocarnitine Related Compound A RS USP in water (Serial # F6NM17935F; Milli-Q Plus TOC; Millipore) to obtain a solution having concentrations of about 1.5 mg/mL and 0.007 mg/mL, respectively.

An assay solution was also required and prepared by transferring the contents of 10 levocarnitine 250-mg capsules, accurately weighed, to a 500-mL volumetric flask, and diluted with water to volume. Once completely disintegrated, the solution was passed through a filter having a 0.45-mcm porosity. The filtrate was diluted quantitatively with water to obtain a solution having a known concentration of 3 mg/mL of levocarnitine.

Separately, equal volumes (20 mcL) of the standard preparation, system suitability solution, and assay preparation were injected into the liquid chromatograph (Model 710B WISP, Serial #71B-009453; Waters) and were passed through a 3.9-mm × 30-cm column containing 10-mcm L8 packing. Samples were ran at a flow rate of 1.0 mL/min. The system was equipped with a 205-nm detector (Model Lambda-Max 481, Serial #481-109896; Waters). The chromatograph was programmed to initially elute 50 mL of acetonitrile then change the composition linearly over the next 20 minutes to a mixture of 65% acetonitrile and 35% water; 100 mL was eluted. Once completed, the following 20 minutes were ran with 100% mobile phase, and allowed the chromatography to proceed for about 3 hours.

Chromatograms for the system suitability solution, standard, and assay preparations were obtained and their corresponding peak responses were recorded. The system suitability parameters were met. The quantity of levocarnitine in capsules was calculated using the following formula:

\[ (L/D)(C(r_U/ r_S)) \]

where \(L\) is the labeled amount of levocarnitine in each tablet (mg); \(D\) is the concentration, in mg/mL, of levocarnitine in the assay preparation, based on the labeled quantity per tablet and the extent of dilution; \(C\) is the concentration, in mg/mL, of Levocarnitine RS USP in the system suitability preparation; and \(r_U\) and \(r_S\) are the peak responses obtained from the assay preparation and the standard preparation, respectively.\(^\text{14}\)

**Dissolution**

**Metronidazole 250-mg Capsules**

The in vitro dissolution test of the compounded metronidazole capsules was evaluated over 30 minutes using USP dissolution apparatus I with 100-rpm stirring at 37°C + 0.5°C (Model #47-200-01A, Serial #2330-44-1193; Hanson Research, Chatsworth, California). Each vessel was filled with 900 mL of dissolution medium consisting of 0.1N hydrochloric acid (Lot 207254; A&C Chemicals, Saint-Laurent, Quebec) at pH 1.2.\(^\text{14}\) Ten-milliliter samples were taken at 5, 10, 15, 20, and 30 minutes. The sample volumes were replaced with fresh dissolution medium at the appropriate pH to maintain a constant volume. The aliquots were then centrifuged, diluted, and the amount of metronidazole in the release samples was determined using a spectrophotometer at 278 nm (Model 552-0006, Serial #28185; Perkin-Elmer, Oak Brook, Illinois) and a standard solution with a known concentration of metronidazole in the same medium as reference.\(^\text{14}\)

**Theophylline 100-mg Capsules**

The in vitro dissolution test of the compounded theophylline capsules was evaluated over 60 minutes using USP dissolution apparatus II with 50-rpm stirring at 37°C + 0.5°C (Model 72-600-400, Serial #2330-44-1193; Hanson Research). Each vessel was filled with 900 mL of dissolution medium consisting of water (Serial # F6NM17935F, Milli-Q Plus TOC; Millipore). Ten-milliliter samples were taken at 10, 20, 30, 45, and 60 minutes. The sample volumes were replaced with fresh dissolution medium to maintain a constant volume. A small helicoidal anchor was used to keep the
capsules submerged in the dissolution medium, as described by Murphy et al. The aliquots were then centrifuged, diluted with 0.1 N hydrochloric acid (Lot 207254; A&C Chemicals) and the amount of theophylline in the release samples was determined using a spectrophotometer at 268 nm (Model 552-0006, Serial #28185; PerkinElmer) in comparison with a standard solution with a known concentration of theophylline in the same medium.

**Levocarnitine 250-mg Capsules**

The in vitro dissolution test of the levocarnitine capsules was based on the USP methodology for levocarnitine tablets. The compounded levocarnitine capsules were evaluated over 30 minutes using USP dissolution apparatus II with 75-rpm stirring at 37°C ± 0.5°C (Model 72-600-400, Serial #2330-44-1193; Hanson Research). Each vessel was filled with 900 mL of dissolution medium consisting of purified water (Serial # F6NM17935F, Milli-Q Plus TOC; Millipore). Ten-milliliter samples were taken at 5, 10, 15, 20, and 30 minutes. The sample volumes were replaced with fresh dissolution medium to maintain a constant volume. A small helicoidal anchor was used to keep the capsules submerged in the dissolution medium, as described by Murphy et al.

The amount of levocarnitine dissolved in the samples was determined by employing the procedure set forth in the assay for levocarnitine capsules, making any necessary modifications, based on the Levocarnitine Tablets USP monograph.

**RESULTS**

All compounded capsule batches were found to be in accordance with the mean weight tests. Official specifications establish that, for hard capsules up to 300.0 mg, the weight variation allowed is ± 10.0%; for capsules over 300.0 mg, the weight variation allowed is ± 7.5%.

Assay analysis demonstrated that each batch of metronidazole 250-mg, theophylline 100-mg, and levocarnitine 250-mg capsules were in accordance with the pharmacopeia criteria of acceptance, which states that not less than 90.0% and not more than 110.0% of the labeled amount should be found. Results are depicted in Tables 4, 5, and 6, respectively.

Dissolution profiles for metronidazole 250-mg, theophylline 100-mg, and levocarnitine 250-mg capsules are summarized in Figures 2, 3, and 4, respectively. All fall within their individually established USP specifications.

**DISCUSSION**

Although immediate-release capsules are considered a simple dosage form, they can most often pose a challenge to a formulation chemist and pharmacist, namely when selecting the right excipients to increase the bulk volume of a particular drug. However, their presence can have a significant effect on the dissolution rate of a drug; such is said of Lactose monohydrate. Although the latter is one

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**TABLE 4. Mean Weight and Assay Results for 250-mg Metronidazole Immediate-release Capsules.**

<table>
<thead>
<tr>
<th>BATCHES</th>
<th>MEAN WEIGHT (MG) (CV%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>ASSAY (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F004197A</td>
<td>353.70 (3.06)</td>
<td>94.80</td>
</tr>
<tr>
<td>F004197B</td>
<td>357.60 (2.69)</td>
<td>96.80</td>
</tr>
<tr>
<td>F004197C</td>
<td>371.30 (2.99)</td>
<td>93.60</td>
</tr>
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<sup>a</sup>CV = coefficient of variation
<sup>b</sup>CV = n = 10 determinations

**TABLE 5. Mean Weight and Assay Results for 100-mg Theophylline Immediate-release Capsules.**

<table>
<thead>
<tr>
<th>BATCHES</th>
<th>MEAN WEIGHT (MG) (CV%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>ASSAY (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F004275A</td>
<td>192.73 (3.15)</td>
<td>95.20</td>
</tr>
<tr>
<td>F004275B</td>
<td>171.88 (3.44)</td>
<td>96.90</td>
</tr>
<tr>
<td>F004275C</td>
<td>197.39 (2.31)</td>
<td>96.70</td>
</tr>
</tbody>
</table>

<sup>a</sup>CV = coefficient of variation
<sup>b</sup>CV = n = 10 determinations

**TABLE 6. Mean Weight and Assay Results for 250-mg Levocarnitine Immediate-release Capsules.**

<table>
<thead>
<tr>
<th>BATCHES</th>
<th>MEAN WEIGHT (MG) (CV%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>ASSAY (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F004199A</td>
<td>278.52 (2.45)</td>
<td>107.20</td>
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<tr>
<td>F004199B</td>
<td>299.13 (3.03)</td>
<td>102.40</td>
</tr>
<tr>
<td>F004199C</td>
<td>302.38 (3.30)</td>
<td>92.40</td>
</tr>
</tbody>
</table>

<sup>a</sup>CV = coefficient of variation
<sup>b</sup>CV = n = 10 determinations

**FIGURE 2. Dissolution profiles for metronidazole capsules with premixed excipient blend suggested for Class I and III drugs.**
of the most commonly used fillers, it provides poor powder flowabil-
ity and is shown to interact negatively with various drug actives.5
This example reinforces the fact that factors such as excipient blend
selection, powder homogeneity and flowability, as well as drug-
excipient compatibility need to be evaluated and taken into consid-
eration prior to capsule formulation.5

For any orally administered drug product, the two fundamental
properties controlling the extent and rate of absorption are its aque-
ous solubility and gastrointestinal permeability.17 Using this con-
cept to categorize drug actives into four different classes, the BCS
highlights their individual properties and, in turn, demonstrates
their varying excipient needs. Knowledge and comprehension of
this system can serve as a valuable tool when selecting excipients
for capsule formulations5; consequently, this system was selected
as the foundation for the three premixed excipient blends utilized in
this study.

A flowchart was developed to be used as a guide during the cap-
sule formulation design (Figure 5). The factors considered for
choosing the most appropriate excipient were:

- Stability of the active ingredient in the formulation (e.g., hygro-
scopicity)
- Interaction between the API and excipients used in the com-
position of premixed excipient blends
- Biopharmaceutical drug classification
- Flowability of the powder mixture to be encapsulated

However, the above criteria should not supersede other vali-
dated analysis or laboratory evaluation (e.g., testing the dissolu-
tion profile) demonstrating other appropriate excipients/active
combinations.

The three different compounded batches of metronidazole 250-mg
capsules (F004197A, F004197B, and F004197C) showed assay
results in accordance with the Pharmacopeial criteria of acceptance
(not less than 90.0% and not more than 110.0% of the labeled amount
of metronidazole).14 The compounded capsules showed a metronida-
zone amount between 93.60% to 96.80% (Table 4).

The three different compounded batches of theophylline 100-mg
capsules (F004275A, F004275B, and F004275C) also showed assay
results in accordance with the Pharmacopeial criteria of acceptance
(not less than 90.0% and not more than 110.0% of the labeled amount
of theophylline).14 The compounded capsules showed a theophylline
amount between 95.20% to 96.70% (Table 5).

At last, the three different compounded batches of levocarnitine
250-mg capsules (F004199A, F004199B, and F004199C) showed
assay results not less than 90.0% and not more than 110.0% of the
labeled amount of levocarnitine.14 The compounded capsules
showed a levocarnitine amount between 92.40% to 107.20% (Table
6). Although a monograph for levocarnitine capsules is not available,
these results are in accordance with the Pharmacopeial criteria of
acceptance found in the capsules’ monographs available in the USP–
National Formulary.14

According to the dissolution profiles results, the three compounded
batches of metronidazole 250-mg capsules showed dissolved values
greater than 85% of the labeled amount of metronidazole in 30 min-
utes, therefore meeting the Pharmacopeial criteria of acceptance.14
The three different compounded batches of theophylline 10-mg
capsules (F004275A, F004275B, and F004275C) showed dissolved
values greater than 80% of the labeled amount of theophylline in 60 minutes, therefore meeting the Pharmacopeial criteria of acceptance.¹⁴

The three different compounded batches of levocarnitine 250-mg capsules (F004199A, F004199B, and F004199C) showed dissolved values greater than 75% of the labeled amount of levocarnitine in 30 minutes, therefore meeting the Pharmacopeial criteria of acceptance.¹⁴

The dissolution profile results of each compounded capsule batch are in accordance with USP specifications, which suggest that the use of premixed excipient blends such as the CapsuBlend excipients are effective for compounding immediate release capsules.

CONCLUSION

The three different compounded batches of metronidazole 250-mg, theophylline 100-mg, and levocarnitine 250-mg capsules, respectively, met the USP requirements. Indeed, the results of the assay study depicted that not less than 90.0% and not more than 110.0% of the labeled amount of drugs was obtained, hence promoting chemical stability of the drug in the compounded dosage form. Furthermore, dissolution profiles of all capsules showed that the dissolved values met the Pharmacopeial criteria of acceptance.¹⁴

The three premixed excipient blends (CapsuBlend-S, CapsuBlend-P, and CapsuBlend-H) used, respectively, to formulate metronidazole 250-mg, theophylline 100-mg, and levocarnitine 250-mg capsules had a positive impact on the dissolution kinetics of the aforementioned drugs. The results showed that when the appropriate amount and combination of excipients is used to formulate hard capsules, the dissolution as well as the level and absorption rate of the drug can be also improved.

REFERENCES

6. Lennernäs H, Abrahamsson B. The use of biopharmaceutic classification of drugs in drug discovery and development:

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