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# Impact of Solvent Selection and Absorptivity on Dissolution Testing of Acetylsalicylic Acid Enteric-Coated Tablets

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## ABSTRACT

The objective of this study was to investigate the effect of physiological conditions on the dissolution rate of acetylsalicylic acid (ASA) from two commercial brands compared against compendial tests. All parameters of the analysis were chosen according to ICH (Q2(R1)) guidelines and were validated statistically. The maximum wavelength ($\lambda_{max}$) and absorptivity (ε) for ASA were determined in different solvents at different pH values (6.8 and 4.9) by a validated UV-Vis spectrophotometric method. When ethanol (EtOH) was used as co-solvent, ε was found to be 3.15, and when 0.1 N NaOH was used, ε was 18.50. Dissolution tests were conducted according to pharmacopeia specifications; however, the lack of a direct specification in determining ε in the pharmacopeia has permitted enormous probabilities of employing different solvents. Herein, when NaOH was used to dissolve ASA, ε was calculated to be 18.50, and upon conducting compendial dissolution tests for enteric-coated tablets, only 20% of ASA was released after 4 h. When analyzing the same data using ε of 3.15 (calculated from dissolving ASA in EtOH), the amount of released ASA was found to be 95% after 2 h. Furthermore, the effect of a fed and fasted state pH was not significant on the dissolution rate, and both brands met the compendial requirements.

**KEYWORDS:** Acetylsalicylic acid, solvent effect, spectrophotometric method, method validation, dissolution

## INTRODUCTION

Quality control (QC) tests are classified according to *United States Pharmacopeia* (USP) and *British Pharmacopeia* (BP) as official or compendial tests and non-official or non-compendial tests (*1*, *2*). Dissolution testing is an official test and a significant component of the drug development process (*3*, *4*).

The evolution of new pharmaceutical products strengthened the value of in vitro dissolution testing for the design and optimization of new formulations (*5*). Recently, the correlation between biopharmaceutical specifications and in vitro-in vivo data has received great consideration, where the dissolution test may be predictive for in vivo (clinical) performance (*6*, *7*). As a result, dissolution media needs to be carefully selected to simulate in vivo dissolution based on physiological variations across the gastrointestinal tract (GIT) (*8*). In particular, pH of the dissolution medium is a crucial element that dictates the dissolution behavior, as it directly affects solubility and ionization of weakly acidic and basic drugs (*9*–*11*). The pH varies considerably across the GIT; the highly acidic stomach pH of 1.2 in the fasted state rises to pH 4.9 in the fed state (*12*). The pH also varies from the ileum and small intestine to the colon, attributed to gland secretions and gastric emptying of stomach contents as well as the presence of diseases, drugs, and food (*8*, *13*). For example, pH of the duodenum reaches about 6.5 in both fasted and fed states, while that of the small intestine can increase to 7.4.

Acetylsalicylic acid (ASA, $C_9H_8O_4$) is a weak acid (pKa 3.5) that is commonly administered orally as enteric-coated tablets to address the documented problem of irritating the gastric mucosa (*14*). At pH greater than 5, ASA will ionize to its carboxylate form, resulting in a faster dissolution rate (*15*). However, the enteric-coated layer is usually an acidic polymer. Thus, the coating layer usually does not dissolve in the acidic medium (i.e., stomach)

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and shields the drug until reaching the site of higher pH (small intestine); consequently, the influence of pH on the dissolution rate of ASA is important.

The objective of this study was to investigate the effect of solvent and physiological conditions (fasted versus fed pH) on the dissolution rate of ASA from two commercial brands compared with compendial tests in addition to determining the maximum wavelength ($\lambda_{max}$) and absorptivity (ε) to understand the effect of simulated physiological media for the dissolution profile of ASA. To confirm the results, classical validation was also carried out according to ICH guidelines to ensure the suitability of the procedures applied (*16*, *17*).

## MATERIALS AND METHODS

### Chemicals and Reagents

ASA (purity 99.9%; USP standard) was purchased from A-Z Chem in Pretoria, South Africa. Sodium acetate anhydrous ($CH_3COONa$, 99%) was purchased from Guangdong Guangzhou Sci-Tech Co., Ltd (Guangzhou, China). Sodium hydroxide (NaOH, 99%) was purchased from EMD Millipore Corporation (Fairburn, Georgia). Ethanol ($CH_3CH_2OH$; EtOH), trisodium phosphate ($Na_3PO_4$, 98%) and potassium dihydrogen phosphate ($KH_2PO_4$, 99.9%) were purchased from Fisher (Shanghai, China). All chemicals were of analytical grade and were used without further purification. Two commercial ASA products (100-mg enteric-coated tablets) were purchased from the Jordanian market: "product A" was manufactured by Bayer, lot No. BTAKWR2 (Germany), and "product B" was manufactured by United Pharmaceuticals, lot No.: M508 (Jordan).

### Equipment

Spectroscopic analysis was carried out using a double beam spectrophotometer (UV-1800, Shimadzu, Japan) using a 1.0-cm path length quartz cell. Dissolution testing was carried out using a USP apparatus 2 (paddle) (Electrolab, India), and disintegration testing was carried out using a disintegration tester (1512120, Electrolab). The pH of the dissolution media was adjusted by a pH meter (Metter Toledo, Schweiz) with accuracy ± 0.1.

### Preparation of Acetylsalicylic Acid (ASA) Standard Stock Solutions in Different Solvents

Four solvents were prepared from the ASA standard stock solution. Solvent 1 was the ASA standard stock solution dissolved in ethanol (EtOH) and tri-sodium phosphate (TSP) buffer at pH 6.8. Solvent 2 was the ASA standard dissolved in 0.1 M NaOH/TSP buffer at pH 6.8. Solvent 3 was the ASA standard stock solution dissolved in EtOH/acetate buffer at pH 4.9. Solvent 4 was the ASA standard dissolved in 0.1 N NaOH/acetate buffer at pH 4.9.

#### *Preparation of Phosphate Buffer Solution, pH 6.8*

A 41.9-g sample of tri sodium phosphate was weighed and transferred to 500 mL volumetric flask and dissolved by water, the solution was sonicated for 5 min, then completed to 500 mL. The buffer solution at pH 6.8 was prepared according to USP by preparing a mixture of 0.1 N hydrochloric acid and 0.2 M tri sodium phosphate (1:3), then pH was adjusted to 6.8.

#### *Preparation of Acetate Buffer Solution, pH 4.9*

The solution was prepared according to USP (*1*). Sodium acetate was weighted and transferred to 1-L volumetric flask, the pH was adjusted to 4.9 by adding a specific volume of 2 N acetic acid, then water was added for completion of the volume to 1 L.

#### *ASA Standard Stock Solution in Tri-Sodium Phosphate (TSP) Buffer, pH 6.8*

Solvent 1 was prepared as follows. A standard stock solution of ASA (50 mg/100 mL) was prepared by dissolving 50 mg of ASA in 15 mL of EtOH as a co-solvent, sonicating for 5 min (*18*), then completing the volume to 100 mL using tri-sodium phosphate buffer solution (0.2 M) at pH 6.8. For solvent 2, the same procedure was repeated by dissolving 50 mg of ASA in 15 mL of 0.1 N NaOH as another co-solvent. The pH was adjusted to 6.8 ± 0.05.

#### *ASA Standard Stock Solution in Acetate Buffer, pH 4.9*

Solvent 3 was prepared as follows. A standard stock solution of ASA (50 mg/100 mL) was prepared by dissolving 50 mg of ASA in 15 mL of EtOH as a co-solvent, sonicating for 5 min, then completing the volume to 100 mL using acetate buffer solution (0.036 M) at pH 4.9 (*18*). For solvent 4, the same procedure was repeated by dissolving 50 mg of ASA in 15 mL 0.1 N NaOH as another co-solvent. The pH was adjusted to 4.9 ± 0.05.

### Determination of Maximum Wavelength for ASA Standard Stock Solutions in Different Solvents

A 10-mL sample from each ASA stock solution was transferred to a 50-mL volumetric flask, and the volume was completed to 50 mL using the appropriate buffer according to the assigned pH (final ASA concentration = 0.1 mg/mL). For each prepared solution, a UV-Vis scan was performed within the range 200–400 nm against a blank for each solvent, from which the maximum wavelength ($\lambda_{max}$) of ASA was determined (Table 1).

### Method Validation

The validation for the ASA determination included

*Table 1. Validation Parameters for ASA Determination in Different Solvents*

| | Solvent 1: ASA-EtOH-TSP, pH 6.8 | Solvent 2: ASA-NaOH-TSP, pH 6.8 | Solvent 3: ASA-EtOH-acetate buffer, pH 4.9 | Solvent 4: ASA-NaOH-acetate buffer, pH 4.9 |
|---|---|---|---|---|
| $\lambda_{max}$ (nm) | 267 | 296 | 267 | 296 |
| LOD (mg/mL) | 0.0003 | 0.0003 | 0.0050 | 0.0003 |
| LOQ (mg/mL) | 0.0090 | 0.0090 | 0.0150 | 0.0090 |
| Concentration range (mg/mL) | (0.003–0.5) | (0.0008–0.1) | (0.010–0.5) | (0.0008–0.1) |
| Linear equation | y = 3.15x + 0.008 | y = 18.55x + 0.005 | y = 3.24x + 0.014 | y = 18.87x + 0.003 |
| $R^2$ | 0.999 | 0.999 | 0.999 | 0.999 |
| Absorptivity (g/Lcm) | 3.15 | 18.55 | 3.24 | 18.87 |

*Data are the mean of three values (n = 3).*
*ASA, acetylsalicylic acid; EtOH, ethanol; TSP, tri-sodium phosphate buffer; NaOH, sodium hydroxide; LOD, lower limit of detection; LOQ, lower limit of quantitation.*

linearity and linear working range. Sensitivity of the proposed method was estimated in terms of the limit of detection (LOD) and limit of quantitation (LOQ). Robustness, precision (stability for inter- and intra-day), and accuracy (% recovery) were applied according to ICH guidelines (*17*).

### Calibration Curve and Standard Working Solutions of ASA

Calibration curves (*n* = 3) were constructed for ASA by preparing 10 different concentrations of each ASA standard stock solution by serial dilution. The concentration linear range (mg/mL) for each solvent was listed in Table 1. The absorbance of each standard solution was measured at its $\lambda_{max}$. The LOD and LOQ of ASA solutions in different solvents and different pH values were calculated depending on the standard deviation (SD) of the absorbance and absorptivity of calibration curve (*17*, *19*, *20*).

### Precision

The concentration of three QC samples including low ($QC_L$), medium ($QC_M$), and high ($QC_H$) (*n* = 3 for each) were used for calculating the recovery, precision, and accuracy of the optimized method for each solvent (*19*). The low, medium, and high QC samples were defined for each solvent as follows, respectively: 0.01, 0.1, and 0.5 mg/mL for solvent 1; 0.0025, 0.025, and 0.1 mg/mL for solvent 2; 0.015, 0.1, and 0.5 mg/mL for solvent 3; and 0.0025, 0.025, and 0.1 mg/mL for solvent 4.

Precision was measured for each solvent by conducting intra-day (different time on the same day) and inter-day (on different days) measurements. Intra-day measurements were repeated three times on the same day (*n* = 3 each time), and inter-day measurements were repeated on three consecutive days (*n* = 3 each day). The coefficient of variance (CV) and confidence intervals were calculated according to ICH guidelines (*20*).

### Accuracy

Accuracy was measured for each solvent by performing a recovery study of ASA as per ICH guidelines (*20*) at three concentration levels (50%, 100%, and 150%) by replicate analysis (*n* = 3). A known amount of the pure drug was added to a known concentration of the substances, and the percentage of drug recovered, CV, absolute error, and relative error were calculated (*17*, *20*).

### Robustness

Robustness was evaluated by measuring the absorbance of samples at three different concentrations (low, mid, high). The low, mid, and high concentrations for each solvent were, respectively, 0.05, 0.1, and 0.5 mg/mL for solvent 1; 0.0025, 0.025, and 0.1 mg/mL for solvent 2; 0.025, 0.1, and 0.5 mg/mL for solvent 3; and 0.0025, 0.025, and 0.1 mg/mL for solvent 4. The absorbance measurements were at three wavelengths within the range $\lambda_{max}$ ± 3 nm; these were 264, 267, and 270 nm for solvents 1 and 3 and 293, 296, and 299 nm for solvents 2 and 4.

### Dissolution Studies

The dissolution test was conducted according to USP specifications for products A and B in a 1-L vessel. Different dissolution media (pH 1.2 and 4.9) were employed in the acid stage (*21*). The temperature was maintained at 37 ± 0.5 °C using USP apparatus 2 (paddle) at a rotation speed of 100 rpm. Samples (3 mL) were manually withdrawn from the acid stage at 10, 20, 30, 45, 60, 90, and 120 min, then the media were drained and replaced with 1 L of fresh TSP pH 6.8 (buffer stage). The experiment continued for 4 additional hours, and samples (3 mL) were withdrawn at 10, 20, 30, 45, 60, 90, 120, 180, and 240 min. Fresh pre-warmed buffer was added after each sample withdrawal. At the end of the dissolution test, the change in pH after

dissolution was not significant (i.e., difference in pH before and after dissolution was less than 0.01).

All samples were filtered through a 0.45-µm syringe filter, and the released amount of ASA was determined by measuring the UV absorbance at 267 and 296 nm for the acid stage and at 267 and 296 nm for the buffer stage. The % ASA released was calculated for each time point using the following equation:

$$\frac{\text{Amount released at each time (mg)}}{\text{Amount of ASA in the tablet (mg)}} \times 100\%$$

### Disintegration Studies

Disintegration testing was conducted on products A and B by measuring the time required for tablet breakdown according to USP specifications. The test was carried out in a disintegration tester. Six tablets were placed in the chambers of the basket, in a 1-L beaker containing 600 mL of HCl pH 1.2 and 4.9 at 37 ± 0.5 °C for 2 h. Then the media was drained from the vessels and replaced with 600 mL of fresh TSP buffer pH 6.8. The time required for complete disintegration of the tablets was recorded and the average time was calculated (*1*, *4*, *22*).

### Statistical Analysis

One-way ANOVA was used to detect significant differences in the dissolution profile for products A and B followed by Tukey's HSD test. All statistical analyses were performed using SPSS (version 21.0, IBM Corp). The level of significance was set at $p < 0.05$.

## RESULTS AND DISCUSSION

### Method Validation for Determination of ASA

The determination of ASA by UV-Vis spectroscopy was validated in all solvents used and met the ICH acceptance criteria. The linearity and linear working range, LOD, LOQ, as well as $\lambda_{max}$ and calculated absorptivity (ε) are summarized in Table 1. For solvents containing NaOH, $\lambda_{max}$ was 296 nm, and for solvents containing ethanol, $\lambda_{max}$ was 276 nm; these findings were consistent with previous studies (*24*, *25*).

It has been reported that differences in solvent polarity and the type of solute-solvent interaction(s) have an impact on the physicochemical properties of molecules, attributing to interactions with the transition state of individual molecules. Therefore, differences in the stability and reactivity as well as the molecular spectrum of the molecule is expected (*23*–*26*).

The two pH values employed in this study provided media that is capable ionizing ASA with a percentage of ionization equal to 99.94% for the TSP buffer at pH 6.8 and 98.17% for acetate buffer at pH 4.9. Consequently, the ionized ASA was negatively charged on the oxygen atom (delocalization of the molecular electronic charge) after removing the acidic hydrogen from the carboxylic group in ASA molecule. As follows, the interaction increases between ASA molecules, making them more active. The more active molecule requires less energy for excitation, leading to absorption at greater wavelength. In addition, the greater polarity of water and ethanol compared to NaOH aqueous solution impacted the shift to a longer wavelength.

### Precision and Accuracy

For all solvents, the precision results were measured at three different concentrations (low, mid, high) for intra-day (at 1-h intervals) and inter-day (1-day intervals) variability. The CV values were within 15% in both intra-day and inter-day measurements. The average accuracy (% recovery) values were within the range of 93.03%–108.3%.

The absolute and relative error values were also calculated, and the results indicated that the method applied to determine ASA concentration was fit for the intended purpose (Table 2).

### Robustness

The robustness results for ASA in all solvents were within the normal limits according to the ICH guidelines, and the CV for each concentration at three wavelengths was within the accepted range (< 3%), indicating that the method used was robust.

### Dissolution Studies

#### *Product A*

Figure 1A depicts the dissolution studies of ASA product A using the two-phase compendial procedure, which states that initial 2 h should be conducted in an acidic stage of 0.1 N HCl (pH 1.2), followed by a second buffer stage representing TSP at pH 6.8 for another 4 h. There was a significant difference upon computing absorptivity using two different matrices. For example, when using NaOH as a co-solvent, ε was found to be 18.5. Using this value to determine the amount of ASA released showed a maximum release of 10% after 6 h (360 min). However, when using EtOH as a co-solvent, ε was found to be 3.15. When this value was used to calculate ASA released, it showed a complete release after 3 h (180 min).

USP specifications state that drug release in the acidic stage should not exceed 10% of total amount of ASA, and drug release in the buffer stage should not be less than 80% after 90 min. Figure 1A shows that ASA release

*Table 2. Precision and Accuracy of ASA Determination*

| Concentration (mg/mL) | 95% CI | Precision | | Accuracy | |
|---|---|---|---|---|---|
| | | SD | CV% | Abs. error | RE% |
| **Solvent 1: EtOH then TSP, pH 6.8** | | | | | |
| **0.01** | (0.0283, 0.0417) | 0.0059 | 17.135 | +0.001 | 9.371 |
| **0.1** | (0.2979, 0.3521) | 0.0240 | 9.512 | +0.003 | 1.059 |
| **0.5** | (1.5234, 1.6906) | 0.0739 | 7.365 | +0.009 | 2.244 |
| **Solvent 2: NaOH then TSP, pH 6.8** | | | | | |
| **0.0025** | (0.0.31, 0.062) | 0.0136 | 0.017 | 0.0000 | 0.025 |
| **0.025** | (0.457, 0.483) | 0.0117 | 2.484 | +0.0002 | 0.858 |
| **0.1** | (1.790, 1.938) | 0.0653 | 3.505 | +0.0001 | 0.076 |
| **Solvent 3: EtOH then acetate buffer, pH 4.9** | | | | | |
| **0.015** | (0.0326, 0.0486) | 0.0080 | 20.4215 | -0.0026 | 17.266 |
| **0.1** | (0.3037, 0.3217) | 0.0090 | 2.7201 | -0.0046 | 4.5124 |
| **0.5** | (1.6137, 1.6257) | 0.0060 | 0.3400 | -0.0044 | 0.8753 |
| **Solvent 4: NaOH then acetate buffer, pH 4.9** | | | | | |
| **0.0025** | (0.0443, 0.049) | 0.002 | 5.180 | 0.00003 | 1.198 |
| **0.025** | (0.469, 0.495) | 0.011 | 2.382 | 0.0005 | 1.971 |
| **0.1** | (1.857, 1.928) | 0.031 | 1.646 | 0.0001 | 0.131 |

*Data are the mean of three values (n = 3).*
*ASA, acetylsalicylic acid; CI, confidence interval; SD, standard deviation of the mean; CV, coefficient of variance; Abs, absolute; RE, relative error, EtOH, ethanol; TSP, tri-sodium phosphate buffer; NaOH, sodium hydroxide.*

from product A complied with these criteria when using EtOH as a co-solvent, and a statistically significant ($p < 0.05$) lower percentage of drug release was recorded when using NaOH as a solvent, which did not comply with compendial requirements. Therefore, these results indicate that an ε value of 3.15 is suitable for determining ASA.

The use of NaOH as a matrix for determining ε for ASA is commonly employed in the literature (*27*). Nevertheless, the ionization of ASA in NaOH leads to the presence of a negative charge in the structure of ASA, which increases the interaction with incident light and subsequently absorbance increases, leading to higher slope in the calibration curve. In ASA specifically, ε was six times higher with NaOH versus EtoH. This difference can lead to calculation errors and may confuse new researchers; however, the significant reduction in the actual amount of drug released in the dissolution medium reflects the need to specify the procedure and solvents used in constructing calibration curves and determining ε for ASA. The observed difference warrants that, upon developing new formulations containing ASA, instructions to compute ε should be specified in detail, which in turn influences the accuracy of measurements for content uniformity and drug release.

The procedure and results of compendial dissolution were set as a control for the investigated conditions in the following sections, thus ε was considered to be 3.15 based on using EtOH as a co-solvent.

Figure 1B represents the dissolution studies of ASA product A at two different media in the acidic stage: pH 1.2 (compendial) and pH 4.9 (simulating fed state during the first 2 h) (*21*). Then, the dissolution test continued for another 4 h for both experiments using TSP pH 6.8. Dissolution results were superimposed in the acidic stage ($p > 0.05$). For example, at 20 min, the release was 0 at pH 1.2 and pH 4.9. The mean percentage of drug release was significantly increased to 60.80 ± 10.90% in TSP stage at 140 min, when pH 4.9 acetate buffer was used in the acid stage, compared to 38.28 ± 13.13% when pH 1.2 was used ($p = 0.0013$). This could be attributed to partial dissolution of the enteric coating, which contains methacrylic acid residues ($pK_a = 4.65$), when ASA tablets were incubated in acetate buffer at pH 4.9, leading to faster drug release compared with the pH 1.2 medium (*28*). Nonetheless, the dissolution rate of product A at pH 1.2 and 4.9 was identical in the first stage of dissolution. Thus, pH did not play a significant role in dissolution at that stage.

### *Product B*

Figure 2A demonstrates the dissolution profile of ASA product B, representing the same two-phase compendial procedure as described for product A. Upon considering

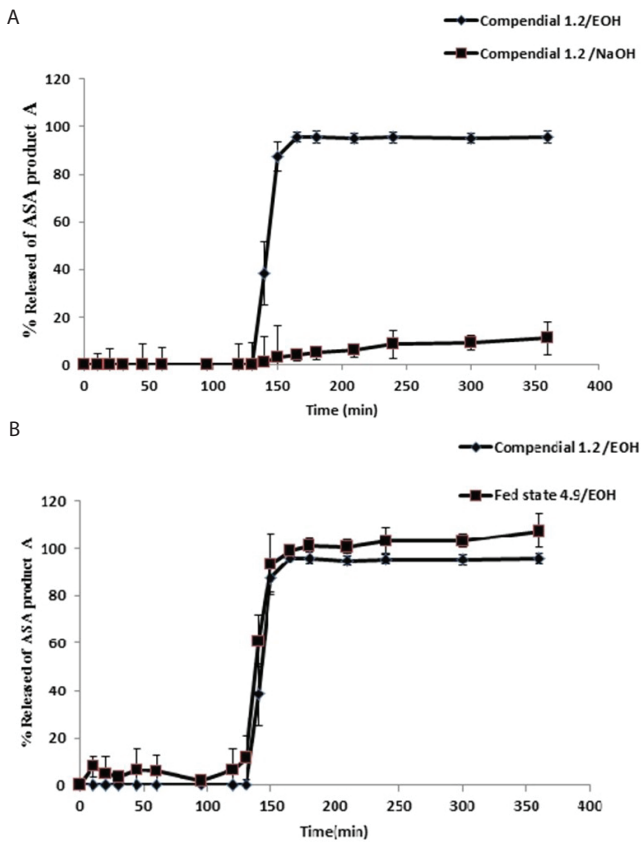


*Figure 1. Dissolution profile of ASA Product A (n = 6) at 37 °C, 100 rpm in (**A**) 0.1 N HCl pH 1.2 followed by TSP buffer stage, pH 6.8, when two different absorptivities are used to calculate ASA released, and in (**B**) 0.1 N HCl, pH 1.2 compendial and pH 4.9 acetate buffer followed by buffer stage pH 6.8.*
*ASA, acetylsalicylic acid; EtOH, ethanol; TSP, tri-sodium phosphate buffer; NaOH, sodium hydroxide; HCl: hydrochloric acid.*

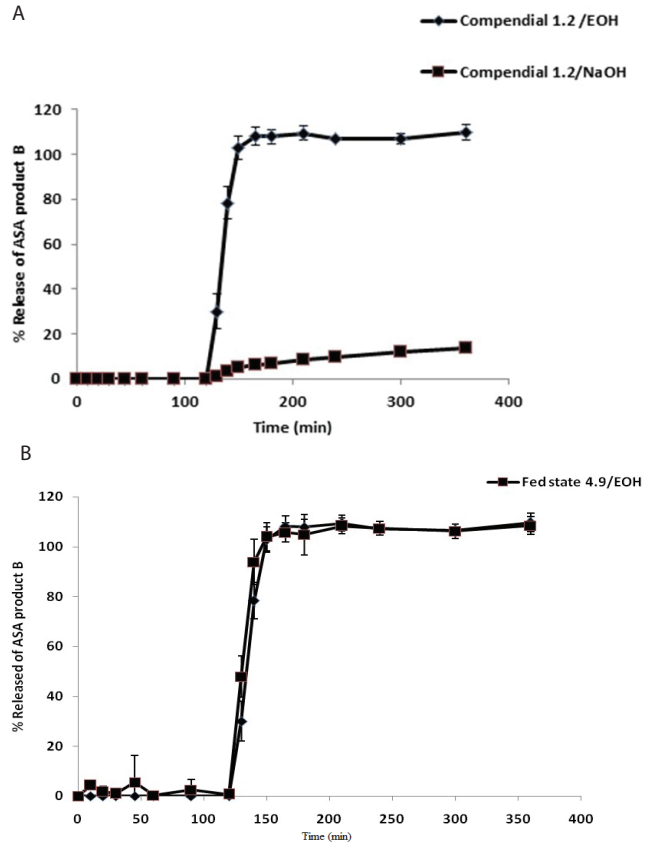


*Figure 2. Dissolution profile of ASA Product B (n = 6) at 37 °C, 100 rpm in (**A**) 0.1 N HCl pH 1.2 followed by TSP buffer stage, pH 6.8, when two different absorptivities are used to calculate ASA released, and (**B**) 0.1 N HCl, pH 1.2 compendial and pH 4.9 acetate buffer followed by buffer stage pH 6.8.*
*ASA, acetylsalicylic acid; EtOH, ethanol; TSP, tri-sodium phosphate buffer; NaOH, sodium hydroxide; HCl: hydrochloric acid.*

the ε value based on using NaOH as a co-solvent (18.5), the release did not exceed 20%, which did not meet compendial requirements. This result indicates that using NaOH as a solvent to compute ε may lead to inaccurate results.

Figure 2B shows the dissolution profile of product B in pH 1.2 during the initial 2 h, followed by pH 6.8 (TSP) for 4 h. The results were compared to ASA release in acetate buffer at pH 4.9 during the first 2 h to simulate the fed state, followed by TSP at pH 6.8 for an additional 4 h. The dissolution profiles were similar in all stages at all time intervals ($p > 0.05$). For example, at 140 min, drug release reached 93.85 ± 9.07% when acetate buffer at pH 4.9 was used in the acid stage, and it was 78.37 ± 7.39% when 0.1 N HCl at pH 1.2 was used in the acid stage ($p = 0.7$). According to this investigation, fed and fasted pH did not play a major role in the dissolution profile of product B.

## Disintegration Studies

### *Product A*

The results of disintegration studies for ASA product A are shown in Table 3. For the compendial (NaOH) and non-compendial (EtOH) media, there was no disintegration in the acidic stage (as expected because the layer is acidic), whereas in buffer stage, the average disintegration time was 11:39. The disintegration results are consistent with dissolution results because the percentage of drug release reached 90% after 20 min in the buffer stage.

For product A in acetate buffer at pH 4.9 followed by TSP, there was no disintegration in the acidic stage, whereas in the buffer stage the average disintegration time was 9:13. Shorter disintegration time was attributed to the higher pH to which the tablets were exposed before the second stage, leading to partial disruption of the enteric layer.

### *Product B*

The results of disintegration studies for ASA product B are shown in Table 3. Similar to Product A, no disintegration was observed in the first stage, whereas the disintegration time was quick after being transferred to buffer stage (4:40).

*Table 1. Disintegration Time for ASA Product A and B*

| Media | | Product A | | Product B | |
|---|---|---|---|---|---|
| | | Stage 1 | Stage 2 | Stage 1 | Stage 2 |
| **Compendial media** | 0.1 N HCl (pH 1.2) | No disintegration within 2 h | | No disintegration within 2 h | |
| | TSP (pH 6.8) | | 11 min 39 s | | 4 min 40 s |
| **Non-compendial media** | Acetate buffer (pH 4.9) | No disintegration within 2 hr | | No disintegration within 2 h | |
| | TSP (pH 6.8) | | 9 min 13 s | | 3 min 52 s |

*Data are the mean of six values (n = 6) at 37 °C.*
*ASA, acetylsalicylic acid; TSP, tri-sodium phosphate buffer; HCl, hydrochloric acid.*

## CONCLUSION

This study focuses on the significance of basic sciences and analytical chemistry and their impact on QC testing of commercially available drug products, using ASA as an example. The drug solvent interaction affected the drug's UV absorption spectrum and led to variation in maximum wavelength ($\lambda_{max}$). In the case of ASA, the variation in $\lambda_{max}$ had an impact on the calibration curve and determination of ε, which in turn influenced the accurate determination of drug dissolution rate. Using EtOH as a solvent for preparing ASA standard stock solutions led to more accurate results than those observed when NaOH was employed as a solvent as recommended by the USP. The results were confirmed by testing two commercial ASA enteric-coated tablets.


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## CONFLICT OF INTERESTS

The authors disclosed no conflicts of interest related to this article.

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