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Original Article

DEVELOPMENT AND STABILITY EVALUATION OF ATORVASTATIN EXTEMPORANEOUS ORAL SUSPENSION FOR ELDERLY PATIENTS

SIRIKANYA KAEWPRADIT[1,2], YUWAKORN SIRIPITHAYA[3], CHUTIMA JANTARAT[1,2*]

[1]Drug and Cosmetics Excellence Center, Walailak University, Thasala, Nakhon Si Thammarat-80160, Thailand. [2]School of Pharmacy, Walailak University, Thasala, Nakhon Si Thammarat-80160, Thailand. [3]The Center for Scientific and Technological Equipment, Walailak University, Nakhon Si Thammarat-80160, Thailand

[*]Corresponding author: Chutima Jantarat; [*]Email: chutima.ja@wu.ac.th

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ABSTRACT

Objective: This study aims to develop an extemporaneous oral suspension formulation of atorvastatin (ATV) and evaluate its stability.

Methods: ATV extemporaneous oral suspension was developed by preparation using different suspension vehicles. The developed formulation was stored at ambient temperature (30±2 °C) and refrigerated temperature (4±2 °C) to evaluate its physical and chemical stability. The formulation was also exposed to 3% hydrogen peroxide (H_2O_2), 1 M hydrochloric acid (HCl), and 1 M sodium hydroxide (NaOH) to evaluate its stability under stress conditions. ATV was analyzed using High-Performance Liquid Chromatography (HPLC), which was validated prior to use.

Results: A vehicle containing 0.6% sodium carboxymethyl cellulose (SCMC) was suitable for the preparation of ATV extemporaneous oral suspension. The HPLC method was found to have linearity covering the range of 10–100 µg/ml with a correlation coefficient (*r*) greater than 0.99. Accuracy and precision were in the range of 99–110% and below 11 %RSD, respectively. The pH and viscosity of the developed formulation stored under ambient and refrigerated temperatures did not differ over 7 d, while the re-dispersibility time of the formulation stored in refrigerator shifted to higher more slowly than the formulation stored at ambient temperature. The % ATV remaining over 7 d was 92.02–106.67% at 30±2 °C and 99.64–107.58% at 4±2 °C. After being subjected to stress conditions, ATV remained stable under oxidation and alkaline conditions, while it significantly degraded under acidic conditions, remaining 24.27%.

Conclusion: The developed ATV extemporaneous oral suspension using a suspension vehicle containing 0.6% SCMC was chemically stable for at least 7 d at 30±2 °C and 4±2 °C. However, this formulation should be preferably stored at refrigerator temperature for use within 7 d to maintain both chemical and physical stability. The formulation was not stable under acid-stress conditions.

Keywords: Atorvastatin, Extemporaneous, Formulation, Suspension, Stability

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INTRODUCTION

Atorvastatin (ATV) is a Hydroxymethylglutaryl-Coenzyme A (HMG-CoA) reductase inhibitor. To reduce lipid levels, statins are the first-line therapy [1] and ATV is one of the most prescribed cholesterol-lowering drugs from the statins groups [2]. The mechanism of action of statins is by inhibiting the enzyme HMG-CoA reductase, resulting in a reduction in the level of cholesterol synthesis in the liver. ATV can lower blood triglyceride levels, slightly increase High-Density Lipoprotein Cholesterol (HDL-C) levels [3], and reduce Low-Density Lipoprotein Cholesterol (LDL-C) by more than 50%. An important role of ATV in the elderly is to prevent Atherosclerotic Cardiovascular Disease (ASCVD) [4]. Elderly patients are a special category of patients. Physiological changes by aging might affect medication nonadherence, such as difficulty swallowing, physical limitations, and cognitive impairment from dementia. Extemporaneous formulations provide benefits by addressing the limitations of commercially available medications. For example, Amphotericin B extemporaneous ointments were prepared for non-dermatophyte onychomycosis and targeted treatment as non-commercial alternatives [5]. Furosemide suspensions for pediatric use address the challenge of administering accurate doses to children who cannot swallow tablets [6]. Additionally, the sildenafil oral suspension was prepared to ensure formulation stability and precision for pediatric patients [7]. Commercially available ATV tablets do not meet the requirements of the elderly patient group. Therefore, ATV in liquid preparations might solve this problem.

Due to the solubility properties of ATV, which is very slightly soluble in water and has a solubility of 1.23 mg/ml in a pH 6.0 aqueous solution [8], preparation in oral suspensions is suitable. The advantage of suspension is that it improves patient compliance because this dosage form can mask the taste by adding flavoring agents to make the formulation more palatable [9]. The lack of suspension dosage forms in hospitals might be one of the administrative problems for patients who have difficulty swallowing tablets. Prescribing suspension for pediatric patients or patients who are unable to swallow tablets or capsules can be solved by preparing the medication for immediate use or extemporaneous compounding. Suspension is the simple compounding type of extemporaneous. All pharmacists have training to prepare these product type, while complex compounding types of extemporaneous substances such as morphine in parenteral, cytotoxic, or hormones require training in the relevant competencies in a continuing professional development plan [10]. Extemporaneous suspension formulations are prepared by reducing the particle size of the Active Pharmaceutical Ingredient (API) and adding a wetting agent to moisten the API to aid particle dispersion in the suspension vehicle. Then, levigate, incorporation of suspending agent to volume, and gradually add vehicle to volume [11]. The vehicle is an important factor in extemporaneous suspensions due to its effects on compatibility with API and physical properties. Additionally, its effect on the preservative system spread ability and its ability for taste masking [12]. Important quality control tests of extemporaneous suspensions include pH, specific gravity, globule size range, pourability, color, clarity, mold growth, and drug contents [13]. The method for determining the content of ATV in the formulation would be validated according to the International Conference on Harmonisation (ICH) Q2(R1) to ensure that the analytical procedure is appropriate for quantifying the ATV content of the formulations [14]. Parameters that need to be checked include specificity, linearity and range, accuracy, precision, and robustness. The samples, after preparing as extemporaneous suspension, were evaluated under storage conditions to determine their stability by using a validated analytical method.

ATV in extemporaneous suspension dosage forms is generally prepared in hospitals and prescribed to elderly patients without monitoring the stability of ATV in the formulation. To ensure the stability of ATV extemporaneous suspension, including quality, safety, and efficacy, the stability study should be performed. The beyond-use date of non-preserved aqueous dosage forms should not be more than 14 d when stored in the refrigerator [15]. The drugs are specified to be controlled between 2 and 8 °C [16]. The storage conditions varied depending on the storage place, such as a hospital or a storage site in a patient's house. The stability study of ATV in an extemporaneous suspension dosage form should be conducted to ensure the quality of products covers beyond the use date. According to ASEAN guideline on stability study of drug product (R1), the stability parameters for oral suspensions are required to be established. This includes conducting chemical tests like assays and assessing physical stability aspects such as color, odor, pH, viscosity, and re-dispersibility. In addition, microbial limit tests should be performed [17].

The aim of this study was to develop an extemporaneous oral suspension formulation of atorvastatin (ATV) and evaluate its stability. ATV extemporaneous oral suspension formulations were prepared using suspension vehicles routinely used in hospitals. The conditions and duration of the stability study were chosen to cover typical storage times. To determine suitable storage conditions, samples were kept refrigerated and at ambient temperature to assess stability parameters. ATV in the formulations was analyzed using the High-Performance Liquid Chromatography (HPLC) method, which was validated prior to use.

MATERIALS AND METHODS

Materials and reagents

Standard atorvastatin was purchased from Sigma-Aldrich (Saint Louis, MO, USA). Oral vehicles were sourced from routine used in Queen Sirikit National Institute of Child Health and Angthong Hospital, Thailand, hereinafter referred to as vehicle A and B, respectively. Atorvastatin 40 mg tablets used were Sandoz® (Lek Pharmaceuticals, Slovenia). Acetonitrile HPLC grade was purchased from RCI Labscan Limited (Bangkok, Thailand). All chemicals and reagents employed in this study were of analytical grade from RCI Labscan Limited (Bangkok, Thailand).

Extemporaneous suspension preparation

The ATV extemporaneous suspension preparation was prepared at a concentration of 0.4% w/v, which is a concentration commonly used in hospitals [3]. The method for preparing the ATV extemporaneous suspension was adopted from a previous report [11] as follows. First, 15 ATV 40 mg tablets were crushed and ground to obtain a fine powder in a mortar to ensure the consistency of particles and the accuracy of the dose. The vehicle was then gradually added in geometric proportions to wet and disperse the powder. Thereafter, the suspension was poured into a cylinder, and the mortar was rinsed with a small portion of the vehicle. Additional vehicle was added to reach the desired volume (150 ml). To determine the appropriate vehicle to use with ATV, vehicles A and B, which have different compositions as indicated in table 1, were examined. Each ATV extemporaneous suspension formulation was prepared in three batches and then subjected to stability testing under two conditions: 30±2 °C (ambient temperature) and 4±2 °C (refrigerator temperature).

HPLC conditions and sample analysis

To analyze the amount of ATV in the extemporaneous suspension, the HPLC analytical method adopted from United State Pharmacopoeia (USP) was used [18]. The chromatographic analysis was performed on a C18, 4.6 × 100 mm, 3.5 µm column with an Agilent 1290 series HPLC system (Agilent Technologies, USA). The mobile phase consisted of acetonitrile and 0.1 M ammonium acetate buffer in a 50:50 (v/v) ratio. The mobile phase was supplied at a rate of 1 ml/min. The injection volume used was 5 µl. UV detection was conducted at 245 nm. The column temperature was 25 °C. The ATV extemporaneous suspension sampled for analysis was prepared by dissolving in HPLC mobile phase, adjusting the final volume to a concentration of 50 µg/ml, and centrifuging before analysis.

Table 1: Composition of the vehicles used for the preparation of ATV extemporaneous suspension

Ingredients	Vehicle A	Vehicle B
Carboxymethyl Cellulose (CMC) mucilage	14	-
Sodium Carboxymethyl Cellulose (SCMC)	-	0.6
70% Sorbitol	20	20
Glycerin	-	20
Citric acid	Adjust pH to 5–6	-
Paraben concentrate	1	10
Purified water	5	-
Simple syrup qs to	100	-
Purified water qs to	-	100

Method development and validation

Previous research has analyzed ATV extemporaneous suspensions by HPLC [3], and the linearity of the analytical method was presented within the range of 5-20 µg/ml. However, differences in excipients might affect the accuracy and precision of the analytical method. The vehicle used in this study was formulated from common compounds used in hospitals in Thailand. Hence, method validation is required to ensure that the analytical method can determine ATV in the prepared formulation. This work developed and validated a method for analyzing suspensions obtained from different vehicles with a fixed dose of ATV. According to the ICH Q2(R1) [14], analytical method on assay should be develop in importance parameters, including specificity, linearity and range, accuracy, and precision.

Specificity

To ensure that the method can analyze the sample without interference from excipients or impurities, specificity testing should be performed. The chromatogram of the sample, which was an ATV extemporaneous suspension, was compared with the chromatograms of the ATV standard and placebo. To meet the specificity acceptance criteria, the peaks of the placebo should not interfere with the ATV peak.

Linearity and range

To determine the direction between the concentration of analytes and peak area, a linearity test was carried out. The standard ATV was prepared to achieve five concentrations, including 10, 20, 50, 80, and 100 µg/ml. To justify the direction of proportion between concentration of analyses and peak area, the correlation coefficient (r) was determined. Limit of Detection (LOD) and Limit of Quantitation (LOQ) were calculated from Equations 1 and 2, respectively.

$$LOD = 3.3\,\sigma/s \quad \ldots (1)$$

$$LOQ = 10\,\sigma/s \quad \ldots (2)$$

Accuracy and precision

According to the ICH Q2(R1) guidelines, the accuracy is determined by the closeness of the values found and the true values [14]. The closeness of the test value to the true value was assessed using a

method similar to the one used for the sample [19]. The accuracy of the method was assessed using the standard addition technique. ATV standards were spiked into the sample matrices and diluted with the HPLC mobile phase to achieve concentrations of 40, 50, and 60 μg/ml, which correspond to test concentrations of 80, 100, and 120 %, respectively. Each concentration was analyzed three replicated. Accuracy results were reported in terms of %accuracy, and precision was determined and reported in terms of %RSD.

Stability determination

According to ASEAN Guidelines, stability testing of drug products should be carried out based on parameters covering various attributes, including chemical stability, physical stability, and microbiological stability [17]. This study determined the stability of ATV extemporaneous suspensions in two main conditions: long-term (30±2 °C/RH not specified) and accelerated (4±2 °C), as well as stress testing.

Physical stability

Appearance

The prepared extemporaneous suspension was observed for color and odor. The physical stability of the suspension dosage form was observed in terms of caking under two conditions, at 30±2 °C and 4±2 °C for one week.

pH

The pH of the samples was analyzed with a pH meter (3510 model, Jenway, UK) and observed under two conditions, at 30±2 °C and 4±2 °C for 7 d.

Viscosity

The viscosity of samples from three batches was measured using a viscometer (DV-III Ultra, Brookfield, USA) for 7 d at two conditions to evaluate the effect of the swelling polymer coating on the tablets.

Re-dispersibility determination

Re-dispersibility is a critical quality attribute for a suspension dosage form that describes the ability of the suspended particles in a formulation to re-disperse uniformly throughout the suspension. The re-dispersibility parameter was measured using a timer, starting from the moment the suspension was manually agitated. The endpoint was that the suspended particles were uniformly suspended throughout the suspension without visible aggregates or sediments [20].

Chemical stability

To determine the amount of ATV in the suspension dosage form at specific points in time, drug content was examined using HPLC. Products were stored at two conditions, including 30±2 °C/RH not specified and 4±2 °C. ATV 40 mg tablets were ground, wetted, and dispersed in the vehicle to achieve a concentration of 0.4% w/v in extemporaneous suspension as described in Extemporaneous suspension preparation section. The sample solution concentration was extracted and diluted with methanol to achieve a concentration of 50 μg/ml. Then, the samples were centrifuged at 13000 rpm for 5 min, and the supernatant was injected into HPLC.

Stress tests

To evaluate the stability of the prepared ATV extemporaneous suspension under stress conditions, forced degradation with oxidation and hydrolysis reactions that occurred from the parent drug were performed. The conditions used for the forced degradation study were adopted from a previous report [21] as follows.

Hydrolysis reaction

The hydrolysis reactions were determined under three conditions, including neutral, acid, and alkali conditions. For neutral conditions, ATV tablets, after prepared as extemporaneous suspension, were added with water and stored at 105 °C for 14 h, whereas samples treated with 1 M hydrochloric acid (HCl) were stored at room temperature for 14 h for acid conditions. For alkali condition, samples were treated with 1 M sodium hydroxide (NaOH) at room temperature for 14 h. Then, the stability of samples and degradation products was determined using HPLC.

Oxidation reaction

The samples were treated with 3% hydrogen peroxide (H_2O_2) and stored at room temperature for 14 h to determine the stability and degradation products of the extemporaneous suspension under oxidation conditions.

Assessment of greenness and applicability of the analytical method

To evaluate the greenness of the analytical method, Green Analytical Procedure Index (GAPI) and the Analytical GREEnness (AGREE) metric were used. The free software was obtained from https://mostwiedzy.pl/complexgapi [28] and https://mostwiedzy.pl/AGREE [27], respectively. To determine the applicability of the analytical method, this study was performed on Blue Applicability Grade Index (BAGI) from https://mostwiedzy.pl/bagi [26].

RESULTS AND DISCUSSION

Extemporaneous suspension preparation

The product formulated using vehicle. A provided unable re-dispersible suspension due to its high viscosity. This might be due to the high concentration of carboxymethyl cellulose (CMC) mucilage contained in the formulation. Therefore, vehicle B was chosen to formulate the ATV extemporaneous suspension for stability study.

Method development and validation

Specificity

As shown in fig. 1, the retention time (R_t) of ATV in the extemporaneous suspension (R_t = 3.4) corresponded to the retention time of ATV standard (R_t = 3.5) without any interference from the excipients. This ensures that the analytical method in this study met the acceptance criteria of the specificity parameter. The maximum absorption wavelength of ATV occurred at 245 nm.

Linearity and range

From 5 different concentrations of ATV standard, including 10, 20, 50, 80, and 100 μg/ml, the peak area of the signal increased as the concentration increased. Table 2 shows slope, y-intercept and correlation coefficient (*r*) of linearity equations. The correlation coefficient (*r*) of all curves was more than 0.999 [19]. The points could be well explained by the regression line as they were close to 1 with the ATV concentration range being 10–100 μg/ml. The LOD and LOQ of the analytical method were found to be lower than 10 μg/ml, which was the lowest concentration of the calibration curve. Therefore, the specified calibration range (10–100 μg/ml) should be considered appropriate for the analysis of ATV extemporaneous suspension.

Table 2: Slope, y-intercept, and correlation coefficient obtained from the linear equation of the ATV calibration curve on three different d

Day	Slope (×10³)	Y-Intercept (×10³)	Correlation coefficient (*r*)
1	22.816	-40.231	0.9992
2	22.945	-22.843	0.9996
3	25.063	38.407	0.9988

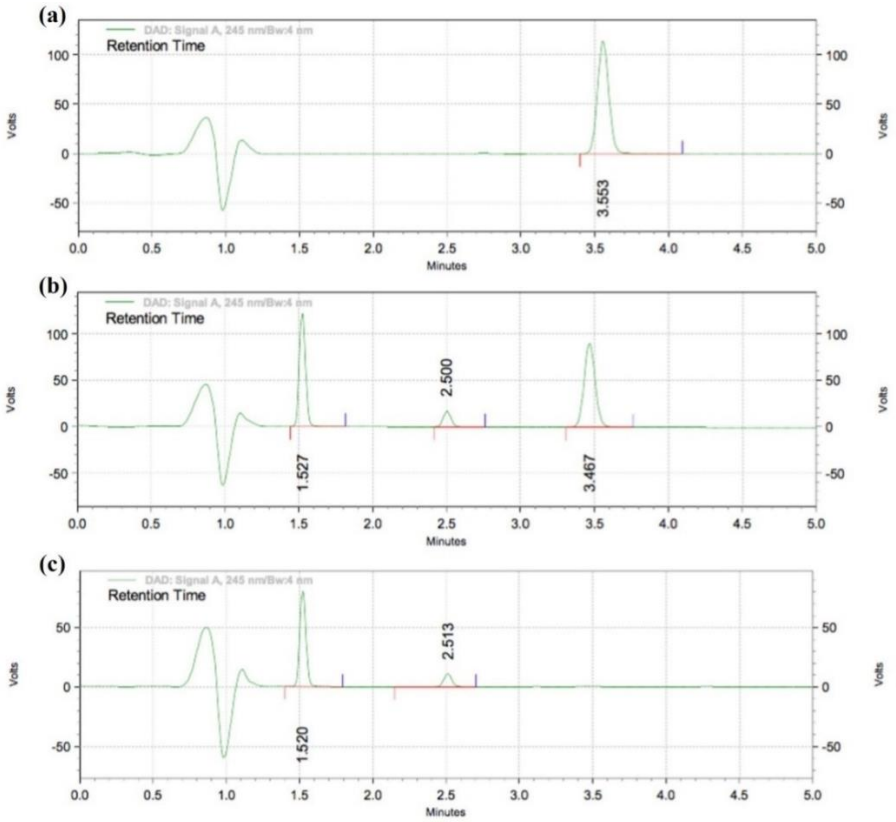

Fig. 1: HPLC chromatograms of (a) ATV standard, (b) ATV extemporaneous suspension, and (c) placebo, respectively

Accuracy and precision

Accuracy and precision were determined by spiking three concentrations of ATV standard to achieve concentrations of 40, 50, and 60 µg/ml in the sample matrices with three replicates at each concentration. The results are shown in table 3. The accuracy results were 109.7±7.8%, 99.2±1.2%, and 100.8±1.5% for three concentration levels of 80%, 100%, and 120% of the test concentration (40, 50, and 60 µg/ml), respectively. The precision of the three concentrations studied was below 8 %RSD for repeatability and below 11 %RSD for intermediate precision. The method achieved linearity in the concentration range of 10–100 µg/ml by using acetonitrile and 0.1 M ammonium acetate buffer in a 50:50 ratio as the mobile phase. These results demonstrate excellent reproducibility and accuracy within the studied range. In comparison to previous research [3], where ATV extemporaneous formulations were prepared using veegum and xanthan gum as suspending agents. The mobile phase consisting of acetonitrile, methanol, and 0.02 M potassium dihydrogen phosphate (45:45:10) was used, yielding accuracy values of 99.8±0.244%, 101.0±0.165%, and 100.3±0.596%. Linearity was observed in the range of 5–20 µg/ml. Although both studies achieved acceptable linearity and accuracy, the current method extended the concentration range to 100 µg/ml, suggesting improved applicability for higher-concentration formulations. Additionally, the solvent composition in this study offered a simplified approach while maintaining consistent accuracy, making this method potentially more efficient for routine analysis.

Table 3: Validation results of the HPLC method for the analysis of ATV extemporaneous suspension

Parameters	Obtained value
Specificity	No interference on analyte peak
Linearity[a]	$r \geq 0.999$
Range	10–100 µg/ml
Accuracy[b,c]	
at 80% assay level	109.7±7.8
at 100% assay level	99.2±1.2
at 120% assay level	100.8±1.5
Precision repeatability	
at 80% assay level	7.14
at 100% assay level	1.20
at 120% assay level	1.48
Intermediate	
at 80% assay level	5.29
at 100% assay level	10.55
at 120% assay level	2.77
LOD	0.12 µg/ml
LOQ	0.37 µg/ml

[a]Linearity determined on three different days, [b]Accuracy at the 80, 100, and 120% assay levels was 40, 50, and 60 µg/ml, respectively, [c]Reference of acceptance criteria from the United State Pharmacopoeia Convention, 2013

Physical stability

Appearance

The appearance of the ATV extemporaneous suspensions formulated from vehicle B after being stored under two conditions for one week was the same. The suspensions contained a cloudy white sediment with visible particles dispersed throughout. The odor was reminiscent of plastic.

pH

The molecular structure of ATV had basic properties. Therefore, the suspension should be formulated in the basic environment to prevent protonation of ATV. As shown in fig. 2a, the pH values of the formulation were in the range of 9.6–10.41 and 9.46–10.23 under 30±2 °C and 4±2 °C, respectively. This indicates that storing the product in ambient and refrigerated conditions did not affect the pH of the formulation.

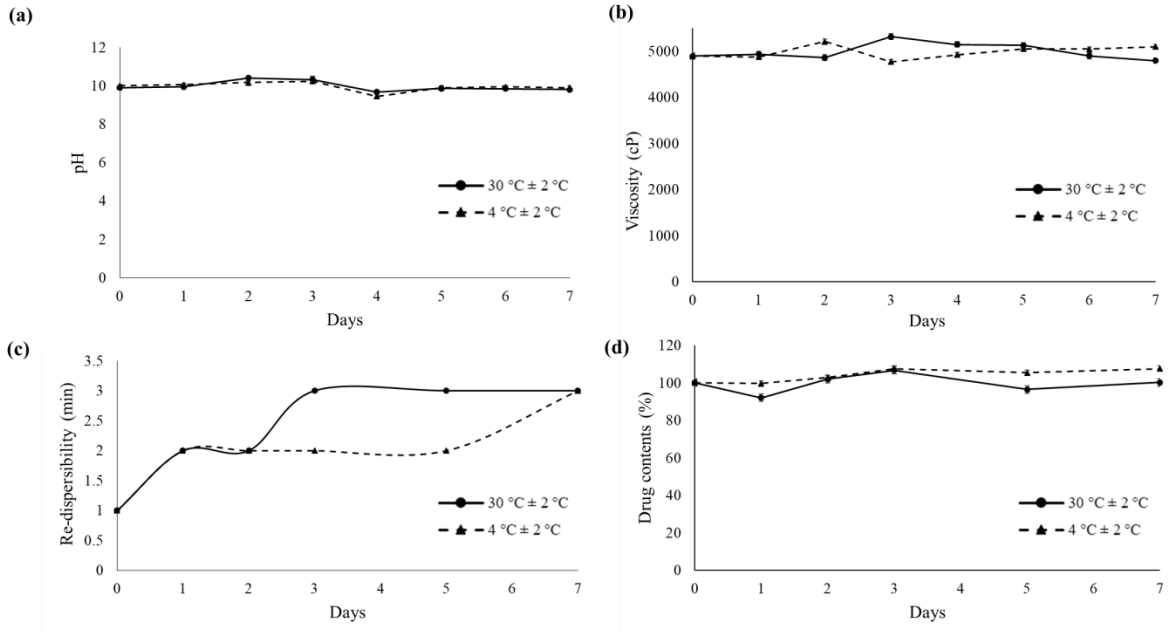

Fig. 2: Physicochemical properties of ATV extemporaneous suspensions storage at 30±2 °C and 4±2 °C from various tests include: (a) pH, (b) Viscosity, (c) Re-dispersibility, and (d) Drug contents over 7 d

Viscosity

The viscosity of the formulation was in the range 4864.33–5322.00 cP and 4772.33–5214.00 cP at 30±2 °C and 4±2 °C, respectively. As shown in fig. 2b, the viscosity of the formulation storage at 30±2 °C increased slightly on day 3. This might be due to swelling of the polymer coated on the tablet [22]. Temperature has a significant effect on the viscosity of a suspension. Higher temperature may facilitate molecular movement resulting in reduced molecular interactions, which results in lower viscosity compared to the formulation storage at 4 °C. However, the viscosity of the formulations stored at 30±2 °C and 4±2 °C showed no obvious difference during storage on day 0–3. This might be due to the relatively high viscosity of the prepared extemporaneous formulation. The trend of viscosity appeared to be different after day 3, where at 30±2 °C the viscosity tended to decrease, while at 4±2 °C the trend was opposite. However, overall, the change in viscosity of the formulation stored at both temperatures was very little.

Re-dispersibility determination

The formulation demonstrated good dispersibility properties, as the particles dispersed throughout the vehicle within 3 min, as shown in fig. 2c. At time 0 (immediately after preparation), the samples stored at both 30±2 °C and 4±2 °C dispersed within approximately 1 min. The re-dispersibility time significantly increased from day 0 to day 1, which corresponded to the viscosity result from the swelling of the polymer coating the tablet. As time progressed, the re-dispersibility time of the suspension stored at 30±2 °C gradually increased and reached a steady state on day 3, which was higher than the suspension stored at 4±2 °C. This indicates that the refrigerated temperature was able to maintain the physical properties better than the ambient temperature. At storage conditions of 4±2 °C, the re-dispersibility time increased on day 1 and remained constant until day 5, and it increased again on day 7. However, there was a smaller increase in the re-dispersibility time of the suspension stored at 4±2 °C compared to the re-dispersibility time of the suspension stored at 30±2 °C. This indicates that lower temperature is more favorable for the stability of this suspension. For practical application, the suspension should be stored at a temperature below 4 °C.

Chemical stabilities

The content of ATV was determined using the HPLC method as described in the HPLC conditions and sample analysis section. The method was validated and used to examine the content of ATV in the formulation over 7 d. From fig. 2d, the percentage remaining over 7 d was 92.02–106.67% at 30±2 °C and 99.64–107.58% at 4±2 °C. This indicates that the drug can be stored in these two conditions because the drug content remained within the acceptance criteria of 90–110% [18]. At 30±2 °C, the percentage of the remaining drug slightly decreased and more fluctuated than at the lower temperature. This might be due to higher temperatures accelerating chemical reactions leading to drug degradation [23].

Stress tests

ATV extemporaneous suspension was examined for stress testing in 2 reactions with 4 stress conditions. The remaining ATV was presented at a retention time of 3.507 as indicated in fig. 3. The unknown degradation product was presented at 2.513 min. After exposure to oxidative conditions using 3% H_2O_2, the remaining ATV was 98.6%, as shown in table 4. This indicates that the ATV extemporaneous suspension exhibited strong resistance to degradation due to oxidation. Likewise, the percentage remaining in basic conditions was 94.51%. This indicates that ATV was stable under basic conditions as described in previous research [24].

Additionally, ATV exhibited moderate stability in neutral aqueous conditions, with 78.76% of the drug remaining in water. Due to the water being able to form an acid and a base, a hydrolysis reaction occurred on the molecule. Conversely, ATV was significantly degraded under acidic conditions, as 24.27% of ATV remaining. Statins are unstable in acidic conditions, resulting in difficulties in preparing a stable suspension [3]. Because the molecule was alkaline, the drug was protonated under acidic conditions [25].

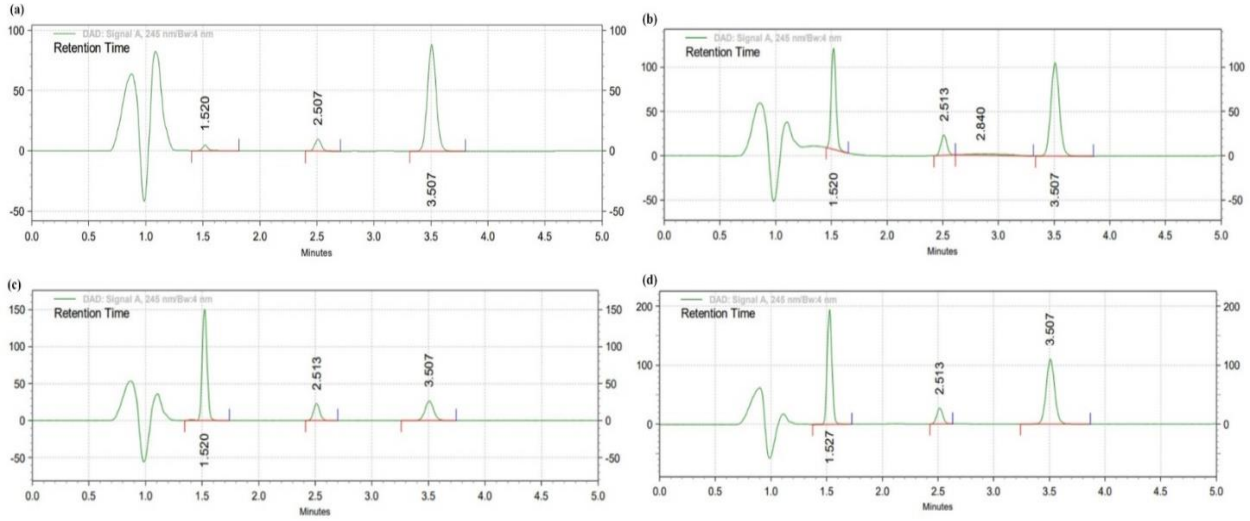

Fig. 3: HPLC chromatograms of ATV extemporaneous suspension after exposure to stress conditions include (a) neutral condition, (b) base hydrolysis, (c) acid hydrolysis, and (d) oxidation

Table 4: The remaining percentage of ATV in extemporaneous suspension after exposure to stress conditions

Condition	Oxidation	Hydrolysis		
	3% H_2O_2	1 M HCl	1 M NaOH	Water
% Remaining	98.6	24.27	94.51	78.76

Assessment of greenness and applicability of the analytical method

On the evaluation of the greenness of the analytical method, as shown in fig. 4a, the areas of sample handling (areas 2 and 3) and sample preparation (area 8) were presented in green due to the non-preservation of the sample, the lack of sample transportation, and the absence of the complex sample preparation step (area 5). The yellow area was caused by the reagents and solvent used (areas 9, 10, and 11). The red area of the instrument used was from the waste of acetonitrile as the mobile phase. Due to the injection time per analysis of 5 min with the mobile phase consisting of acetonitrile and 0.1 M ammonium acetate buffer in a 50:50 (v/v) ratio, the waste obtained from the analysis step was less than 100 ml. According to the GAPI results, the AGREE pictogram (fig. 4b) was present in a large green area except for the red area on the number 3 as from the off-line analytical method between sample setting and HPLC system and the orange area on the number 11 as from the use of acetonitrile. To assess the practicality of the analytical method in routine use, the BAGI pictogram in fig. 4c shows that the method had applicability in routine use. The large area was present in dark blue, and the score was 82.5, which was between 25 and 100 [26].

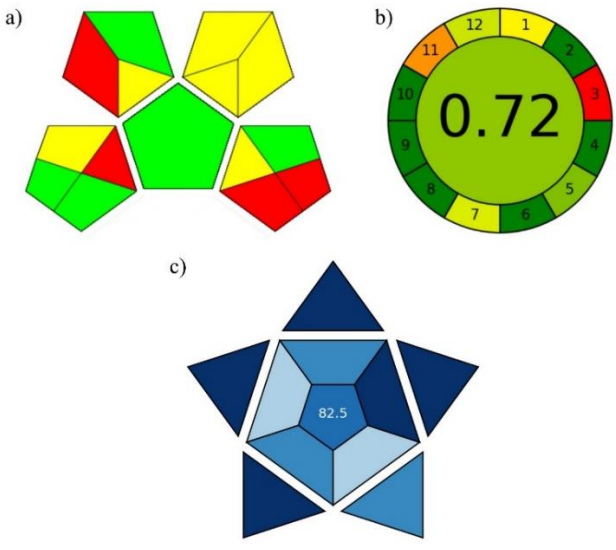

Fig. 4: Method evaluation includes: a) GAPI pictogram, b) AGREE pictogram, and c) BAGI pictogram

CONCLUSION

Vehicle B containing 0.6% SCMC was suitable to formulate ATV extemporaneous suspension. The product was chemically stable at 30±2 °C and 4±2 °C, which maintained stability for 7 d. However, storage in the refrigerator shifted the re-dispersibility time of the formulation to higher more slowly than storage in ambient temperature. Therefore, the developed formulation was preferable stored in refrigerator to be used within 7 d to maintain both chemical and physical stability. The formulation was not stable under acid-stress conditions.

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Nil

AUTHORS CONTRIBUTIONS

Sirikanya Kaewpradit: Methodology, Formal analysis, Visualization, Writing-original draft, Writing-review and editing. Yuwakorn Siripithaya: Methodology, Formal analysis, Visualization, Writing-review and editing. Chutima Jantarat: Conceptualization, Methodology, Investigation, Data curation, Formal analysis, Visualization, Writing-original draft, Writing-review and editing.

CONFLICT OF INTERESTS

Declared none

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