MULTISCIA
JOURNALS PUBLISHERS

FRONTIERS IN PHARMACEUTICS

ISSN: (3065- 1786)

editor.fpm1@gmail.com

https://multisciajournals.com/journals/index.php/fp

Frontiers in Pharmaceutics
Volume 1 Issue 2 2025

Comparison of Acyclovir Ointments' Physicochemical Properties and Usability

R Hazra, A Saha, SB Deb
Department of **Pharmaceutics**

Article Info

Received: 28-04-2025 Revised:08-05-2025 Accepted:14-05-2025 Published:25-05-2025

1. Introduction

Many prescription medications are now over-the-counter (OTC) medications, which can be purchased without a prescription with a pharmacist's guidance for self-medication [1, 2]. Terbinafine hydrochloride, an antifungal medication, and vidarabine, an antiviral medication, are switch over-the-counter medications for external medicine, while famotidine, an inhibitor of gastric acid secretion, and indomethacin, an anti-inflammatory medication, are switch over-the-counter medications for internal medicine. For certain medications, pharmacotherapy is necessary for patient care, either through counter service or a pharmacist's advice to undergo a medical evaluation [3]. Depending on the patient's needs, generic medications may also be prescribed as prescription medications [4]. However, patients' experiences with brand-name, generic, and over-the-counter medications vary due to the chemicals they include. For instance, brand-name, generic, and over-the-counter medications were used to assess the physicochemical characteristics of vidarabine. Variations in viscosity among formulations resulting from variations in formulation additives were documented [5]. Because brand-name, generic, and over-the-counter medications have varying components, it is important to take into account the emotions that come with using various drug formulations. Therefore, by understanding the physicochemical characteristics of each formulation, pharmacists may advise patients on self-medication. But as of right now, a few studies have contrasted the physical-chemical properties of generic, name-brand, and over-the-counter medications.

One of the most widely used guanine analog antiviral medications is acyclovir (ACV). When phosphorylated in infected cells, it takes on its active form and stops the virus from growing [6, 7]. ACV is utilized to treat and prevent

TABLE 1: Additive of ACV ointment each formulation.

Brand name	Lot number	Serial number	Additive
Zovirax® Ointment 5%	3E7F	ACV-A	Macrogol 300, macrogol 1500
Acyclovir Ointment 5% “TEVA”	CAO11	ACV-B	Macrogol 300, macrogol 400, macrogol 4000
Acyclovir Ointment 5% “TOWA”	A125	ACV-C	Macrogol 400, macrogol 4000, pH adjuster
Activir®	UW3M	ACV-D	Macrogol
Hifuru AC	Y503	ACV-E	Macrogol

infections caused by herpes simplex virus I (cold sores) and herpes simplex virus II (genital herpes). ACV is used as a lotion, ointment, and internal medication. Additionally, both brand-name and generic medications are available for these ACV formulations. There have been prior reports of variations in the viscosity and viscoelasticity of generic and brand-name ACV creams [8]. OTC medications have recently been replaced with ACV ointments, which call for pharmacist supervision.

These ACV creams have previously reported on the viscosity and incompatibility of both generic and original medications [8]. However, the physical characteristics of both prescription and over-the-counter medications (both original and generic) were assessed in this investigation using ACV ointment. Conducting the evaluation using a friction meter is thought to help inform patients and healthcare professionals by predicting an indicator of usability in clinical settings. The physicochemical characteristics of ACV formulations, including brand-name Zovirax® Ointment 5%, generic Acyclovir Ointment 5% "TEVA," generic Aciclovir Ointment 5% "TOWA," and switch OTC medications Activir® and Hifuru AC, were investigated in this study. Macrogol is the main ingredient found in brand-name,

generic, and over-the-counter ACV ointments. According to reports, polyethylene glycol's viscosity, a macrogol,Tokyo Kasei Co., Ltd. was the supplier of ACV crystal. Special commercial grade reagents were also used (Wako Pure Chemical Industries Co., Ltd.).

2.2. Techniques

2.2.1. Test of Content Uniformity. About 100 mg of each ointment were weighed for the assay, followed by the addition and dissolution of 12.5 mL of diluted sodium hydroxide solution and 37.5 mL of distilled water. Test solutions were then made by mixing 7.5 mL of each ointment solution with 0.1 mol/L hydrochloric acid solution to create 100 mL. After weighing about 10 milligrams of ACV, 10 mL of diluted sodium hydroxide solution was added. The ACV solution was then mixed with 7.5 mL of diluted sodium hydroxide solution and 50 mL of distilled water. A standard solution was made by adding 0.1 mol/L of hydrochloric acid solution to 100 mL. A UV-vis recording spectrophotometer (Shimadzu: UV-2500PC) was used for the measurements. A control of 0.1 mol/L hydrochloric acid was used to measure the absorbance of the test and standard solutions at a wavelength of 255 nm.

The following formula was used to determine how much of each ACV ointment was needed:

changes according to the molecular weight average and that $\frac{AT}{1}$

differences in the feelings associated with the use of the preparation vary when polyethylene glycol is used as an additive [9]. Therefore, differences in the average molecular weight of macrogol were assessed, and the viscosity and viscoelasticity of each ointment were evaluated. Additionally, the skin friction of each ointment was measured, and the feeling of use on the skin was evaluated. Furthermore, to investigate the molecular behavior of the additive in each formulation, the near-infrared (NIR) absorption spectrum was measured. It would be considered to become an item in visualization information of each ointment difference, so mapping by main analysis statistical analysis was evaluated.

2. Materials and Methods

2.1. Materials. Commercial formulations of ACV ointments were purchased. The brand-name ointment was Zovirax® Ointment 5% (GlaxoSmithKline Co., Ltd.); generic ointments were Acyclovir Ointment 5% "TEVA" (Teva Takeda Pharma Ltd.) and Acyclovir Ointment 5% "TOWA" (Towa Phar- maceutical Co., Ltd.); and OTC ointments were Activir® (GlaxoSmithKline Consumer Healthcare Japan Co., Ltd.) and Hifuru AC (Bankyo Pharmaceutical Co., Ltd.). The properties and additives of each formulation are shown in Table 1.Amount of ACV (mg) = WS * $_{AS}$ * 2 (1)

where WS is weighed amount of ACV standard product converted into dehydrate (mg), AT is absorbance of test solution, and AS is absorbance of standard solution.

2.2.1. Measurement of Water Content. Water content was measured using a Karl-Fisher moisture content meter (Kyoto Electronics Manufacturing Co., Ltd.: MKV-710M). KEM AQUA TR-3 (Kyoto Electronics Manufacturing Co., Ltd.) was used as the titrant and KEM AQUA FAT (Kyoto Electronics Manufacturing Co., Ltd.) served as the dehydrated solvent. The water content in 0.03 g of each sample was measured three times at 25◦C.

2.2.2. Measurement of Flattening. Spreadability was mea- sured using a spread meter (Rigo) with a measuring temper- ature of 25◦C. Spread diameter was measured after 5, 10, 60, 120, 180, 240, 300, 360, 600, and 900 s.

The yield value was calculated from the following formula using the spread diameter after 180 s:

$$F = 47040 * G * \frac{V}{\pi^2} * D^5 \quad (2$$

TABLE 2: Content uniformity of ACV ointments.

Formulation	Uniformity (mean ± SD)
ACV-A	102.1 ± 2.0
ACV-B	100.8 ± 1.8
ACV-C	100.0 ± 1.4
ACV-D	103.1 ± 0.3
ACV-E	101.8 ± 0.8

Nonsignificant (n=3).

where G is the weight of the glass plate (115.5g), V is the sample size (cm3), D is the diameter (mm) when sample spreading stopped, and F is the yield value (dyne/cm2). 2.2.3. Viscoelasticity and viscosity. The type-E rotational viscometer (Toki Sangyo: TVE-20H) was used to test dynamic viscosity. The viscometer with a 3×× R9.7 cone rotor was used to measure the dynamic viscosity of 0.02 mL of each ointment for 553 s at 25°C. The shear rates used for the measurements were

0.01 s−1 (0.01 s−1: 60 s, the other shear rate: 30 s) and 0.01 s−1 (0.08 0.08 -0.01). For 276 seconds, the viscosity was measured at a shear rate of 0.08 s−1. Before the shear rate changed, viscoelasticity evaluated the stress and recovery at a shear rate of 1s. Under identical circumstances, the viscoelasticity of every ointment was assessed three times.

2.2.4. Spectroscopy of Near-Infrared Absorption. A Fourier-transform near-infrared analyzer (Buchi NIRFlex N-500) was used to record NIR absorption spectra. At a wavelength of 1000–2500 nm and a wavelength number of 10,000–4000 cm−1, spectroscopy was conducted. Spectra were taken for 8 seconds at 25∘C. NIR absorption spectra were taken at 1-nm intervals while each ointment was in a sample cup.

2.2.5. Evaluation of Skin Friction. The Frictiometer (Courage + Khazaka Electronic GmbH: FR 700) was used to measure the amount of skin friction that each medicament created. After applying a 0.1 g sample of each ointment on artificial skin at 25°C, skin friction was evaluated by agitating the skin for 20 seconds at 25 rpm.

2.2.6. Analysis of Statistics. Tukey's test was used for statistical analysis, and a difference is deemed significant if the p-value is less than 0.05.

3. Findings and Conversation

3.1. Test of Content Uniformity. To evaluate the equivalency of ACV content in each ointment, a uniformity of content test was performed (Table 2). ACV was 102.1 ± 2.0, 100.8 ± 1.8, 100.0 ± 1.4, 103.1 ± 0.310, and 101.8 ± 0.8% in ACV-A, ACV-B, ACV-C, ACV-D, and ACV-E. The uniformity of content in the five ointments did not differ significantly, according to Tukey's test. As a result, the ACV contents in ACV-A, ACV-B, ACV-C, ACV-D, and ACV-E were deemed consistent.

3.2. Moisture Content Measurement. Each formulation's moisture content was ascertained. The findings showed

TABLE 3: Spreadability of ACV ointments at 25∘C.

Formulation	Spreadability (mean ± SD)
ACV-A	22.9 ± 0.1
ACV-B	29.8 ± 0.2
ACV-C	26.5 ± 0.2
ACV-D	23.1 ± 0.3
ACV-E	23.8 ± 0.3

Value of the spreadability after 180 seconds (n=3).

The moisture content of ACV-A was 1.36 ± 0.27%, that of ACV-B was 3.22 ± 0.75%, that of ACV-C was 3.52 ± 0.43%, that of ACV-D was 1.29 ± 0.19%, and that of ACV-E was 4.56 ± 0.94%. This suggested that each formulation had a different moisture content.

2.2. Flattening measurement. employing a spread meter to measure extensibility and hardness—indices of spreadability and yield value—it is possible to gauge the sensation that comes with employing a semisolid preparation [10]. As a result, a spread meter was used to determine each ointment preparation's spreadability and yield value, and its physical characteristics were assessed (Table 3 and Figures 1 and 2). When the spreading of each ointment preparation was stabilized, the diameters were compared at 180 seconds to assess the spreadability. For ACV-A, ACV-B, ACV-C, D, and E, the diameter of the ointment spread in 180 seconds was 22.9 mm, 29.8 mm, 26.5 mm, 23.1 mm, and 23.8 mm, respectively. This revealed that, in comparison to the other ointments, the distribution of ACV-B covered a larger circumference. For ACV-A, ACV-D, and ACV-E, a comparable spread of almost 23 mm in diameter was discovered. Next, the ACV-A, ACV-B, ACV-C, ACV-D, and ACV-E yield values

which are hardness indices, were computed. ACV-A had a yield value of 4416.7 dyne/cm2, ACV-B had 1175.7 dyne/cm2, ACV-C had 2114.9 dyne/cm2, ACV-D had 4234.5 dyne/cm2, and ACV-E had 3620.7 dyne/cm2. ACV ointments are soft and extensible preparations in the order of ACV-B > ACV-C > ACV-E > ACV-D > ACV-A, according to the spreadability and yield value. Additionally, ACV-A and ACV-D showed hardness and extensibility in comparison to other ointments, and their spread diameters were comparable. The ingredients in the mixture are what give the ointment its extensibility [11]. Thus, each ointment's molecular weight and macrogol content—an additive—were impacted by variations in spreadability and yield value.

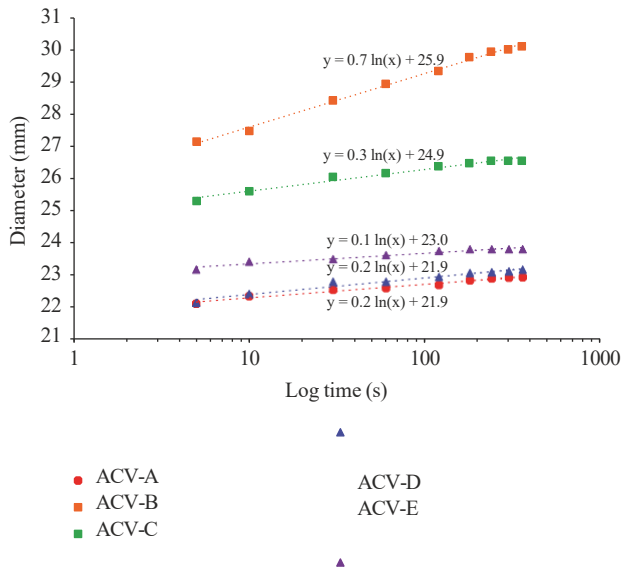


FIGURE 1: Average diameter of ACV ointments in Logarithm time.

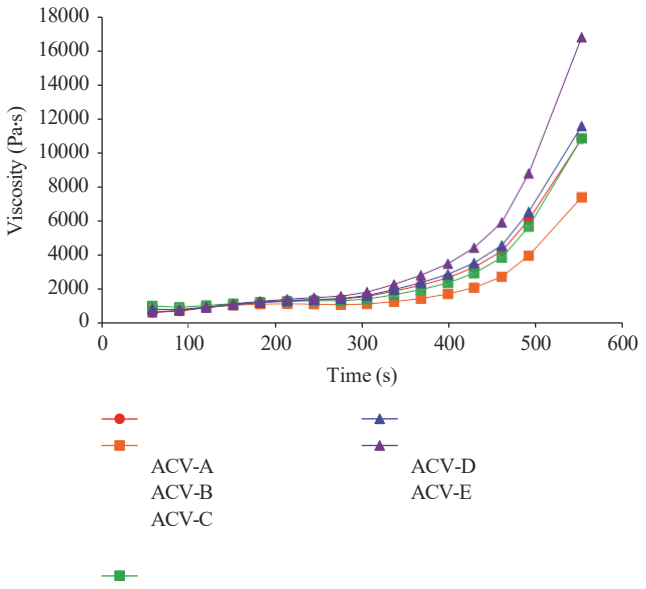
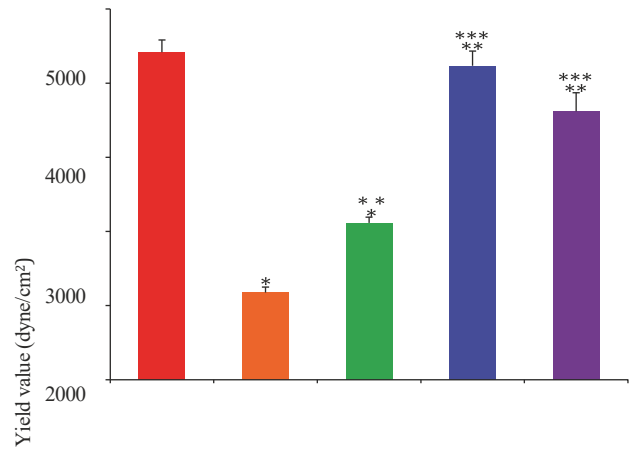
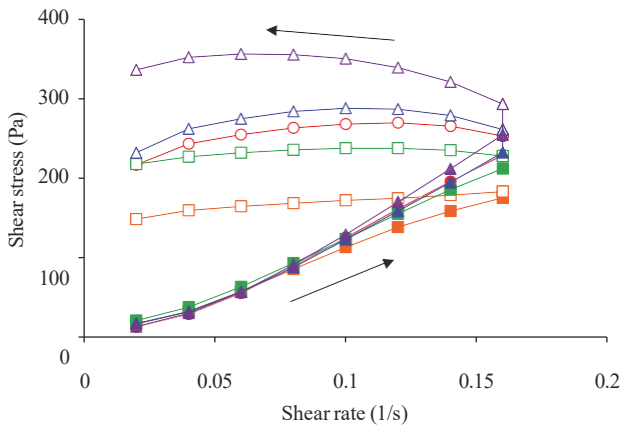


FIGURE 3: Viscosity curves of ACV ointments at 25°C.





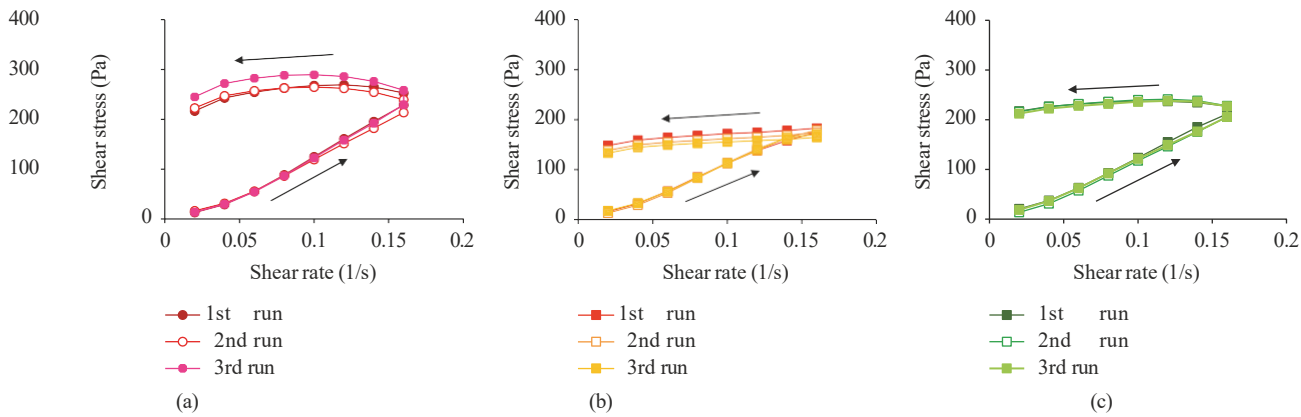
Yield value of ACV ointments at 25°C. Value of the spreadability after 180 seconds (mean ± SD, n=3). Tukey's test was given for official approval ($p<0.05$). ∗ indicates that significant differences were seen between ACV-A and ACV-B and between ACV-A and ACV-C ($p<0.05$ for each). ∗∗ indicates that significant differences were seen between ACV-B and ACV-C, between ACV- B and ACV-D, and between ACV-B and ACV-E ($p<0.05$ for each).

∗∗∗ indicates that significant differences were seen between ACV-C and ACV-D and between ACV-C and ACV-E ($p<0.05$ for each).

when subjected to shear stress. Conversely, the viscosity of ACV-E changed markedly over time compared with that of the other ointments. In addition, the viscosity of ACV- A, ACV-C, and ACV-D similarly increased with time. The differing changes in viscosity over time between ointments did not confirm the results obtained for moisture content and spreadability. As such, the varying changes in viscosity with time may have been due to differences in the molecular weight and content of the additive macrogol.FIGURE 4: Shear stress versus shear speed curves of ACV ointments.

The viscosity of each ointment preparation differed; therefore, the viscoelasticity of each ointment preparation was evaluated (Figure 4). The shear stress of ACV-B was low, while that of ACV-E was high compared with the other oint- ments. In addition, the shear stresses of ACV-A, ACV-C, and ACV-D were similar. These results indicate that ACV-B has properties of softness compared with the other formulations. Conversely, ACV-E has properties of strength compared with the other formulations. This was correlated with viscosity.

The rheogram observed with an increase in shear rate differed from that observed with a decrease in shear rate, and a hysteresis loop was observed for all ointment formulations. The presence of a hysteresis loop indicates that time is needed to recover the internal structure, which changed when the shear rate increased [12]. In addition, it is possible to evaluate the thixotropy, that is, the strength of the internal structure by the difference in the area of the hysteresis loop of flow curves



when the shear rate is up and down. The area of the hysteresis loop of ACV-B was small, and the area of the hysteresis loop of ACV-E was large compared with that of the other ointment preparations. From the results of the viscosity measurement, the stickiness was confirmed by adding the shear stress. Thus, from the results of viscosity and viscoelasticity, ACV- B was inferred to undergo less change in its internal

structure when subjected shear stress and to have properties of softness compared with the other ointments. Conversely, the internal structure of ACV-E was easily changed by shear stress, with a harder formulation compared with the other ointments.

Next, repeated measurements were performed to evaluate changes in the robustness, viscosity, and viscoelasticity of each ointment (Figure 5). When ACV-E was subjected to repeated shear stress, the shear stress decreased in the third run compared with the first and second runs. Thus, the internal structure of ACV-E may be susceptible to disruption when ACV-E is subjected to repeated shear stress. In addition, the shear stress of ACV-B and ACV-C underwent minimal change even under repeated shear stress. Thus, ACV-B and ACV-C were considered to possess viscoelasticity, and the internal structure of ACV-B and ACV-C could be main- tained, even under shear stress. Additionally, the shear stress of ACV-A and ACV-D increased in the third run compared to that in the first and second runs. Thus, when ACV-A and ACV-D were subjected to repeated shear stress, there was less disruption to their internal structures.

The results obtained for viscosity and viscoelasticity differed from those obtained for spreadability and yield value. This suggests that there are differences in the extensibility and change in the internal structure of each ointment. The viscosity and viscoelasticity of cream preparations have been reported to vary depending on the proportion of oil contained in cream [13]. Therefore, in this study, differences in viscosity and viscoelasticity among the ointment prepa- rations were due to differences in moisture content and the molecular weight and content of macrogol. In addition, from the results obtained thus far, ACV-A and ACV-D appear to have similar properties. Thus, macrogol, which is contained by ACV-A and ACV-D as an additive, accounted for their similar molecular weight and content.

Near-Infrared Absorption Spectroscopy. NIR absorption spectra were recorded to verify differences in the water or oil content of each formulation (Figure 6). The absorption spectrum of the olefin group (-CH_2) in the oleaginous base was observed at 4300 and 5800 cm^{-1}, and that of the hydroxyl group (-OH) caused by moisture was observed around 5200 cm^{-1}. The current study evaluated the oil and water content of each formulation focusing on these spectra [14, 15]. The sec- ond derivative of the NIR absorption spectrum revealed that ACV-B and ACV-C possessed a wider absorption spectrum than the other ointments due to the olefin group (Figure 6(a)). Moreover, ACV-E possessed a larger spectrum than the other

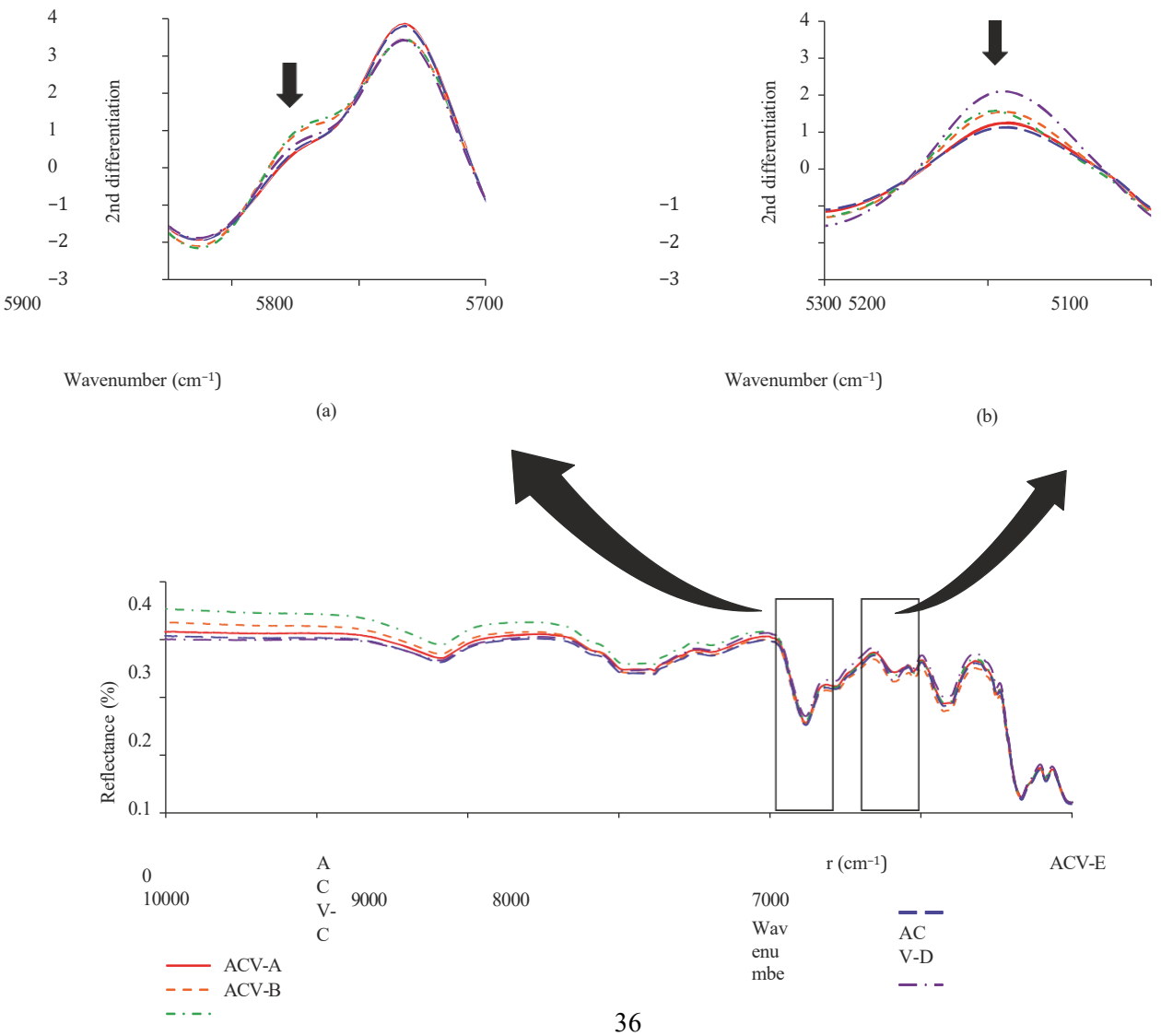
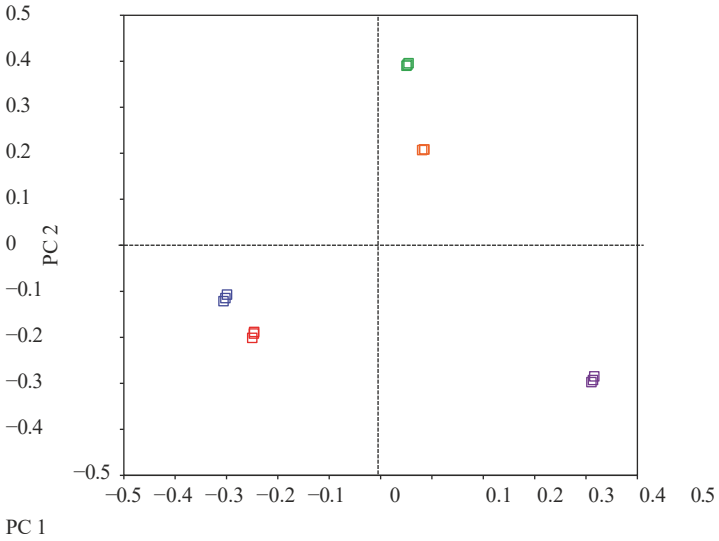


FIGURE 6: Near-infrared absorption spectra of ACV ointments, observed to 4000-10000 cm^{-1}. (a) 2nd differential near-infrared absorption spectra of ACV ointments, observed to 5700-5950 cm^{-1}. (b) 2nd differential near-infrared absorption spectra of ACV ointments, observed to 5100-5300 cm^{-1}.

ointments due to the hydroxyl group (Figure 6(b)). From these results, differences in oleaginous base and moisture content of each formulation were clarified.

To evaluate differences in the principal component of

each formulation, a principal component analysis was per- formed (Figure 7) [16]. In principal component 1 (PC1), ACV- A and ACV-D were similar, ACV-B and ACV-C were similar, and ACV-E differed from other ointments. In principal component 2 (PC2), ACV-A and ACV-D were similar, ACV-B and ACV-C were similar, and ACV-E differed from other ointments. Moisture content analysis and NIR absorption spectroscopy suggested that PC1 reflected differences in the water content of each formulation. PC2 differed between the five formulations. PC2 was considered to reflect differences in the molecular weight and the content of oleaginous bases and macrogol in ACV ointments. These results indicate that ointment spreadability is due to the moisture content of each formulation and the molecular weight and content of macrogol contained in each ointment. In addition, the viscosity and viscoelasticity of ointments were due to the molecular weight and content of macrogol contained in each ointment. Generally, macrogol is known to have different properties depending on the molecular weight of macrogol. For example, macrogol 400 is liquid and macrogol 4000 is solid at normal temperature, and the viscosity of macro- gol 400 is lower compared with the viscosity of macrogol 4000. Therefore, the results of spreadability, viscosity, and viscoelasticity are considered due to the difference of the molecular weight of macrogol and each macrogol content of each ointment. Comparing the additives contained in each ointment, ACV-B and ACV-C contain macrogol 4000. However, these results indicated that ACV-B and ACV-C were soft and extensible preparations compared to other oint- ments. Therefore, the properties of ACV-B and ACV-C were considered due to the difference of each macrogol content. In addition, the difference of the formulation process of each ointment was also considered to contribute to the properties of the ointment preparation. Furthermore, the molecular

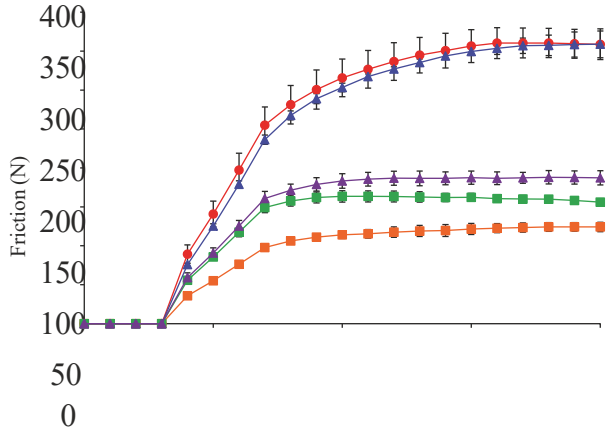


Skin Friction Measurement. The Frictiometer was used to measure friction in order to evaluate the feeling of the creams when applied to the skin (Figure 8). This was also used to evaluate the feeling of cosmetics on the skin [17]. After 15 s, ACV-A had a friction measurement of 356.5 N, ACV-B had 121.6 N, ACV-C had 162.4 N, ACV-D had 349.7 N, and ACV-E had 187.5 N. The magnitude of the friction force followed the same pattern as the yield value calculated with a spread meter. The force of friction was inversely correlated with the spreadability and slipperiness of a semisolid preparation and was correlated with the stickiness of the preparation. Thus, ACV-B was inferred to be not sticky and to spread easily when applied to human skin compared with the other ointments.

3. Conclusion

A uniformity of content test revealed that ACV-A, ACV- B, ACV-C, ACV-D, and ACV-E possess equivalent ACV contents. Evaluation of the properties of each ointment revealed the physicochemical properties of ACV-A, ACV-B, ACV-C, ACV-D, and ACV-E. A skin friction test revealed

FIGURE 7: Principal component analysis of ACV ointments.



0 5 10 15 20me (s)differences in the properties of ACV-A, ACV-B, ACV-C, ACV-D, and ACV-E. This study investigated the properties of different ACV formulations in a model scenario involving a brand-name ointment, a generic ointment, and a switch OTC ointment. In the future, pharmacists will need to investigate the properties of OTC formulations. This will help maintain the health of the community and encourage appropriate self- medication.

Data Availability

The data described in this article are not quoted from other studies and are new data obtained by this research. No data were used to support this study.FIGURE 8: Skin friction of ACV ointments, respectively (n=5).

weight of macrogol in ACV-D has not been reported. However, the moisture content, spreadability, viscosity, and viscoelasticity of ACV-D were similar to those of ACV-A; therefore, the molecular weight of macrogol contained in ACV-D was presumed to be 300 and 1500, which was the molecular weight of macrogol contained in ACV-A. The molecular weight of macrogol in ACV-E as an additive has not been reported. However, from the viscosity measurement and the second derivative of NIR absorption spectra, the molecular weight of macrogol with ACV-E was inferred to be lower than that with ACV-B and ACV-C. However, generally, the viscosity of high-molecular-weight macrogol is higher than the viscosity of low-molecular-weight macrogol. Therefore, the properties of ACV-E were considered due to the difference of each macrogol content and the production process of each ointment.Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Acknowledgments

The authors thank Dr. T. Tarumi of Japan Buchi Co., Ltd., for his helpful advice regarding NIR absorption measurements. They are grateful to Dr. Hiroaki Todo and Ms. Mika Futaki for measuring Frictiometer.

References

[1] N. J. Gauld, F. S. Kelly, N. Kurosawa, L. J. M. Bryant, L. M. Emmerton, and S. A. Buetow, “Widening consumer access to medicines through switching medicines to non-prescription: A six country comparison,” *PLoS ONE*, vol. 9, no. 9, Article ID 107726, 2014.

[2] N. Chowdhury, A. Haque, and F. Aysha, "A comparison between medical and nonmedical students in Chittagong City, Bangladesh: An investigation into self-medication of drugs for primary and adjunct therapy in psychiatric diseases," Indian Journal of Psychological Medicine, vol. 34, no. 4, pp. 313–317, 2012.

[3] "Medicine reclassification processes and regulations for proper use of over-the-counter self-care medicines in Japan," by K. Nomura, Y. Kitagawa, Y. Yuda, and H. Takano-Ohmuro, Risk Management and Healthcare Policy, vol. 9, pp. 173–183, 2016.

[4] "Regulation of generic drugs in Japan: the current situation and future prospects," by R. Kuribayashi, M. Matsuhama, and K. Mikami, The AAPS Journal, vol. 17, no. 5, pp. 1312–1316, 2015.

[5] "Characterization of prescription and over-the-counter formulations of vidarabine cream," World Journal of Pharmaceutical Sciences, vol. 5, no. 1, pp. 11–18, 2017, by Y. Inoue, R. Shiozawa, and D. Niiyama.

[6] R. Joseph and K. G. Kumar, "Electrochemical sensing of acyclovir at a gold electrode modified with 2-mercaptobenzothiazole-[5,10,15,20-tetrakis-(3-methoxy-4-hydroxyphenyl)porphy-rinato]copper(II),"

Analytical Sciences, vol. 27, no. 1, pp. 67–72, 2011.
[7] M. Suzuki, T. Okuda, and K. Shiraki, "Acyclovir and vidarabine exhibit synergistic antiviral activity against varicella-zoster virus and herpes simplex virus types 1 and 2," Antiviral Research, vol. 72, no. 2, pp. 157–161, 2006.
[8] "A comparison of the physicochemical properties and a sensory test of Acyclovir creams," International Journal of Pharmaceutics, vol. 436, no. 1-2, pp. 265–271, 2012, by Y. Inoue, K. Furuya, M. Matumoto, I. Murata, M. Kimura, and I. Kanamoto.
[9] "Density and viscosity of concentrated aqueous solutions of polyethylene glycol," Journal of Chemical & Engineering Data, vol. 39, no. 3, pp. 611–614, 1994; G. T. Pedro, F. Camacho, and B. Gabriel.
[10] "Comparation of the properties of brand-name and generic nadifloxacin creams," by Y. Inoue, M. Matsumoto, M. Kimura, T. Tanaka, and I. Kan-amoto Volume 47, Issue 11, pages 616–622, Medicina, 2011.
A study by S. Kitagawa, R. Yutani, R.-I. Kodani, and R. Teraoka titled "Differences in the rheological properties and mixing compatibility with heparinoid cream of brand name and generic steroidal ointments: The effects of their surfactants" was published in Results in Pharma Sciences in 2016.
[12] Y. Inoue, K. Suzuki, R. Maeda, A. Shimura, I. Murata, and I. Kanamoto, "Evaluation of formulation properties and skin penetration in the same additive-containing formulation," Results in Pharma Sciences, vol. 4, pp. 42–49, 2014.
[13] "Factors governing partial coalescence in oil-in-water emulsions," Advances in Colloid and Interface Science, vol. 153, no. 1-2, pp. 30–42, 2010, by E. Fredrick, P. Walstra, and K. Dewettinck.
[14] M. J. Maltesen, S. Bjerregaard, L. Hovgaard, S. Havelund, M. van de Weert, and H. Grohganz, "Multivariate analysis of phenol in freeze-dried and spray-dried insulin formulations by NIR and FTIR," AAPS PharmSciTech, vol. 12, no. 2, pp. 627–636, 2011.
[15] Archives of Pharmacal Research, vol. 28, no. 4, pp. 458–462, 2005; E.-J. Suh, Y.-A. Woo, and H.-J. Kim, "Determination of water content in skin by using an FT near infrared spectrometer." In the Journal of Pharmaceutical and Biomedical Analysis, volume 30, issue 3, pages 453–466, 2002, J. Luypaert, S. Heuerding, S. De Jong, and D. L. Massart evaluated direct orthogonal signal correction and other pre-processing techniques for the classification of clinical study lots of a dermatological cream.
[17] "Improvement of the methods for skin mechanical properties evaluation through correlation between different techniques and factor analysis," Skin Research and Technology, vol. 19, no. 4, pp. 405–416, 2013, P. Neto, M. Ferreira, F. Bahia, and P. Costa.