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The Effect of Storage Conditions on the Absorption Profile of 2% Lydocaine Hydrochloridum Injection by UV-Vis Spectrophotometry

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Abstract. Lidocaine HCl injection is a sterile product that is easily contaminated when opened. The temperature and humidity in the injection storage conditions also affect the quality of the drug that could be described from the UV-Vis spectrophotometric absorption profile. The aimed of this study is to find out how the effect of storage conditions on the absorption profile of 2% lydocaine HCl injection by UV-Vis spectrophotometry. The impact on the UV-Vis absorption spectral changed can described how molecular structure damage occur on the inappropriate storage condition of the drug. The study used 27 ampoules of 2% lidocaine HCl injection and was qualitatively analyzed using UV-Vis spectrophotometry. The study lasted for 14 days by first storing the injections in storage conditions at room temperature (25-27^{o}C), cold temperatures (5-10^{o}C), and exposed to Ultraviolet light (380 nm). Based on the results of laboratory tests, the most suitable storage condition used for storing lidocaine HCl injection was cold storage (5-10^{o}C) because there was no shift in the maximum wavelength as occurred during the 14th day of UV exposure storage.

Keywords: Absorption Profile, Lydocaine HCl, Storage, UV-Vis Spectrophotometry

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1. Introduction

The problem of pain is a problem that is very often found in the medical world. Pain can be said as a symptom that arises due to inflammation that occurs in the body. Pain stimuli send pain impulses into the spinal cord through the body's nerve cells (1). The international association for the study of pain (IASP) states that pain is a feeling of discomfort caused by a person's sensory and emotional connection or because of tissue damage. Pain can occur for several reasons including trauma, surgery, cancer, dysmenorrhea, arthritis, dental disease, etc. (2). After the operation, the patient will certainly have pain that starts to bother, so the medical staff will give anesthesia. Anesthesia is composed of Greek, namely an which means not, and ais thesis which

means feeling so that it can be said that anesthesia is a state of loss of sensation or feeling (1). Anesthesia is divided into two, namely local and systemic. Local anesthetics play a role in inhibiting sensory nerve conduction when used in certain places with the appropriate dose. Local anesthetics have a mechanism of action by blocking pain impulses to the central nervous system (CNS) so that pain, itching, heat or cold can be reduced (3).

Lydocaine injection is an example of an amide class of local anesthetic that has a fast onset of action with high potency and is frequently used. One of the studies conducted at the Temanggung District Hospital for the period January-June 2017 stated that the most widely used drug combination for the treatment of osteomyelitis pain was lidocaine injection combined with meloxicam, flamicort, ranitidine at 8.6% (4). Apart from being in the form of injection, lidocaine is also found in other topical dosage forms such as aerosols, ointments, and topical solutions (3). Lidocaine has a much better safety profile than other local anesthetics and has a low level of tissue toxicity, therefore it is preferred by practitioners as a local anesthetic (1). Research conducted by Mohammadi et al., 2016 showed results that patients induced by propofol with lidocaine premedication had a prevalence of no pain of 95% and mild pain of 4% (5). Lidocaine HCl injection is also widely used by dentists with a usage rate of 41.93% as a local anesthetic in tooth extraction because lidocaine HCl is able to anesthetize the mucosa when administered locally. In dentistry practice, adrenaline is often added as a vasoconstrictor from lidocaine HCl so that the anesthetic effect appears more quickly and lasts longer (1).

Maria Martina in her research in August 2013 revealed that there was an incidence of anaphylactic shock due to the use of local anesthetics, namely lidocaine, of less than 1%. However, even though the percentage rate is not high, preparatory measures for the possibility of an allergic reaction or anaphylactic shock in each patient must still be carried out. Allergic reactions that occur due to the use of local anesthetics such as lidocaine are rare cases, but do not rule out allergies to preservative substances (6).

Inappropriate drug storage is also a factor in decreasing the quality of drugs and causing losses to hospitals and patients. Improper storage can make the drug spoil more quickly before entering its expiration date so that the drug cannot be used (7). According to Akbar et al., in 2016, inappropriate drug storage will lead to the drug not being maintained, which will lead to irresponsible drug abuse, drug availability is not maintained, and it is difficult to monitor drug quality. Errors in storing drugs at the health centre can cause the drug to be damaged resulting in a decrease in drug levels/potency so that when consumed by patients it becomes ineffective in therapy (8).

Qualitative analysis of lidocaine HCl injection can be carried out using high performance liquid chromatography (HPLC) and visible spectrophotometry (3). Derivative spectrophotometry methods can be used for quantitative analysis of substances in mixtures where the spectra may be hidden in a form of large overlapping spectra regardless of the process of separating the substances first. The concept of the derivative was first introduced in 1950, where it was seen to provide many advantages. The main application of visible light ultraviolet derivative spectroscopy is for the qualitative identification and analysis of samples. Derivative spectroscopy methods are very suitable for the analysis of absorption bands that overlap or are too sloping (9). Evaluation of UV-Vis spectrophotometric absorption profile based on storage conditions has never been done. Therefore, researchers wanted to apply UV-Vis spectrophotometry to compare the absorption profile of lidocaine HCl in 2% lidocaine HCl injection (20 mg/mL) based on storage conditions.

2. Materials and Method

2.1. Materials

The materials used were 2% lidocaine HCl injection with a generic lidocaine HCl concentration of 20 mg/ml (@2mL) in 27 ampoules and Water For Injection. While the tools used were glassware in the form of a 25 mL measuring flask, 1000 IU micropipette, refrigerator, Grow Light LED 50w 220v, hygrometer, cold thermometer, UV-Vis Shimadzu UV-1800 spectrophotometer, and spina software version 3.0.

2.2. Method

This study used 27 ampoules of 2% lidocaine HCl injection obtained from PT. "X" with the same batch number. The study was started by treating three storage conditions to samples of 2% lidocaine HCl injection for 14 days of storage. Samples were prepared at a concentration of 300 ppm and analyzed qualitatively using UV-Vis spectrophotometry on days zero (0 hour), first (24 hour), second (48 hour), third (72 hour), fifth (120 hour), seventh (168 hour), ninth (216 hour), eleventh (264 hour), and fourteenth (336 hour), adjusting laboratory operating hours. Qualitative analysis was carried out with Spina software version 3.0 using absorbance values at a wavelength of 200 to 300 nanometers obtained by UV-Vis spectrophotometry. Evaluation of the absorption profile of 2% lidocaine HCl injection was carried out at the maximum UV-Vis wavelength profile obtained from conventional spectral data according to the time span of each absorption. The evaluation includes the number of spectral peaks shown, the differences in the resulting spectral patterns, the shift in the wavelength that appears in each sample using the 2nd derivative on Spina software version 3.0. Figure 1 describes schematic research method.

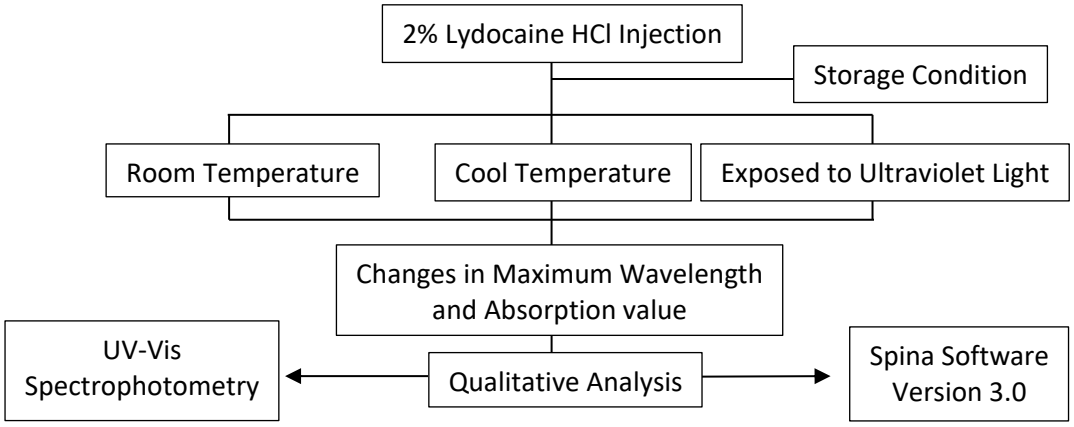

Figure 1. Research Method

3. Results and Discussion

Evaluation of the UV-Vis spectrophotometric maximum wavelength profile was carried out using the help of Spina software version 3.0 which was operated via a laptop. The maximum wavelength profile used in this evaluation is the wavelength profile when measuring absorbance values for assays starting from day 0 to day 14 with conventional spectral absorbance data at a wavelength of 200-300 nm. O'Haver (1979) stated that derivative spectroscopy is a spectrum measurement derived from the average change in absorbance with wavelength (9). Data on the absorbance values of replicates 1, 2, and 3 which are located at 200-300 nm in each storage condition and storage time are then averaged. After the data is averaged, it is then processed using Spina software version 3.0 by first changing the xlxs format be csv. Conventional Spectra data that already has a csv file format are then processed with spina 3.0 software and the 2nd derivative is determined.

The second derivative or often called the 2nd derivative is one of the second derivative analysis methods from the maximum wavelength of conventional spectra. Conventional spectral data is shown with red spectra lines, while the 2nd derivative is shown with green spectra lines. Display of Conventional Spectra data and 2nd derivative can be seen in Figure 2.

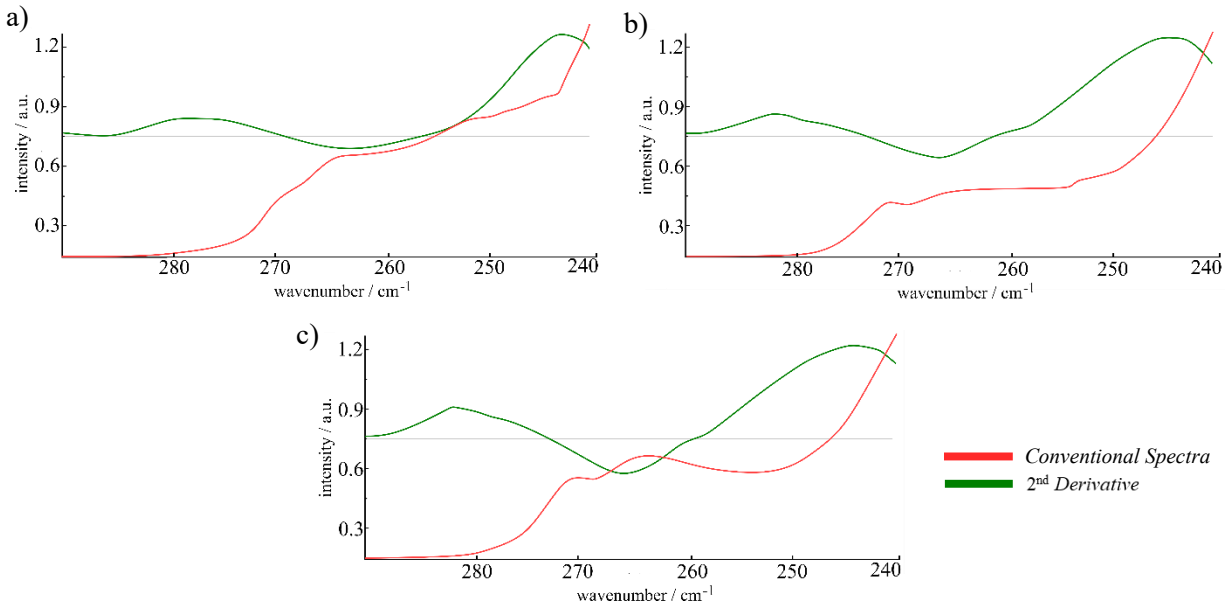

Figure 2. Conventional VS 2nd Derivative Spectra at storage conditions a) Room Temperature (25 – 27°C), b) Cold Temperature (5,5 – 9,5°C), c) UV Exposure (380 nm)

Figure 2a shows the spectra between the conventional spectra and the 2nd derivative at room temperature (AC) storage conditions. Figure 2b shows the spectra between the conventional spectra and the 2nd derivative under cold storage conditions. Figure 2c shows the spectra between the conventional spectra and the 2nd derivative under UV exposure. From the three spectral images it can be seen that the UV exposure storage conditions have a very strong peak 2nd derivative when compared to the cold temperature and room temperature (AC) storage conditions.

After obtaining the spectral profile of the second derivative, characterization is then carried out to determine the maximum wavelength in the second derivative spectra. Dismoothing data using the principle of the Zalvitzki Golay equation to remove background noise which often appears as false peaks and interferes when reading the spectral profile. Sometimes the peak position of the second derivative spectra will shift slightly due to the influence of the smoothing process being carried out. Then an analysis is carried out using the second derivative method where this method helps to ensure that the peaks produced are the true peaks. Sometimes there is only one visible peak in the conventional spectra but it can be seen that there are two overlapping peaks in the second derivative spectra as seen in the maximum wavelength table of the compound lidocaine HCl (9). Meanwhile, the maximum wavelength data in the conventional spectra can be seen in Table 1.

Table 1. Maximum Wavelength Data on Conventional UV-Vis Spectrophotometry Spectra

Storage Time (Days)	Maximum Wavelength (nm)		
	Room Temperature (25-27°C)	Cool Temperature (5,5-9,5°C)	Exposed UV Light (380 nm)
0	262	262	262
1	262	262	262
2	263	263	262

3	262	263	262
5	263	262	262
7	262	262	262
9	262	262	262
11	262	262	262
14	262	262	262

In the conventional spectra table, the maximum wavelength value at one peak is between 262 nm and 263 nm. This is due to broadening and overlapping of spectral patterns or peaks which causes a shift in the maximum wavelength as a result of temperature changes in storage conditions. Changes in spectral patterns occur at each storage condition accompanied by changes in absorption values in the spectra. Whereas in the 2nd derivative two peaks were found with a maximum change in wavelength from 262 nm to 266 nm and 263 nm on storage conditions on the 14th day of first peak UV exposure. The change in the maximum wavelength of the second derivative only occurs on the last day of UV exposure. This shows that the injection of 2% lidocaine HCl was not able to survive under UV light exposure until the 14th day. The change on the spectral behaviour reflects in the level of molecular change (10). Meanwhile, the maximum wavelength data in the 2nd derivative can be seen in Table 2.

Table 2. Maximum Wavelength Data on 2nd Derivative Software Spina

Storage Time (Days)	**Maximum Wavelength (nm)**					
	Room Temperature (25-27°C)		**Cool Temperature (5,5-9,5°C)**		**Exposed UV Light (380 nm)**	
	Peak		**Peak**		**Peak**	
	1	**2**	**1**	**2**	**1**	**2**
0	266	262	266	262	266	262
1	266	262	266	262	266	262
2	266	262	266	262	266	262
3	266	262	266	262	266	262
5	266	262	266	262	266	262
7	266	262	266	262	266	262
9	266	262	266	262	266	262
11	266	262	266	262	266	262
14	266	262	266	262	263	262

This is in accordance with the research by Putri et al (2014) that sometimes two peaks are found in the second derivative spectra even though in conventional spectra there is only one peak. In the 2nd derivative spectra, the maximum wavelength is produced at 266 nm because at that wavelength it gives a high peak intensity with a peak that is very clearly visible and always appears in every storage condition. The spectral profile of the conventional spectra and the second derivative can be seen in Figures 3 and 4.

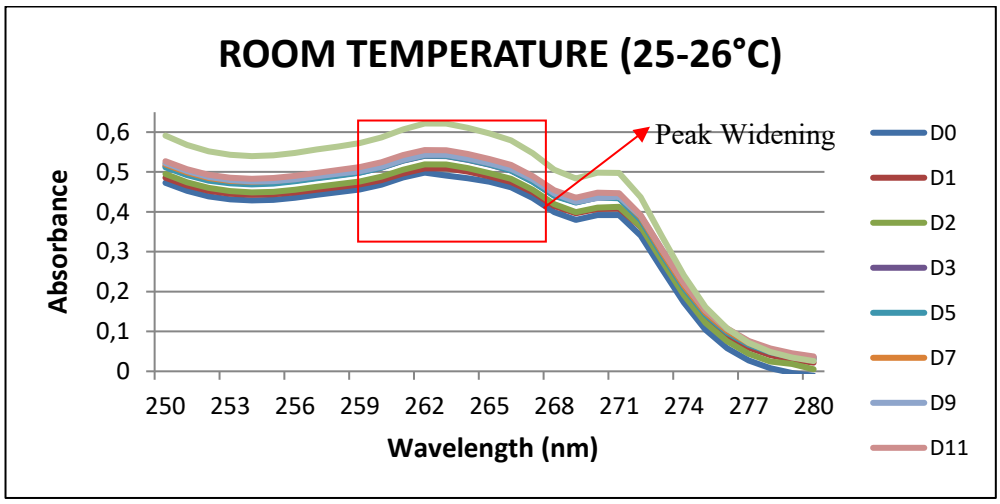

Figure 3. Wavelength profile of Room Temperature Conventional Spectra (D=Day)

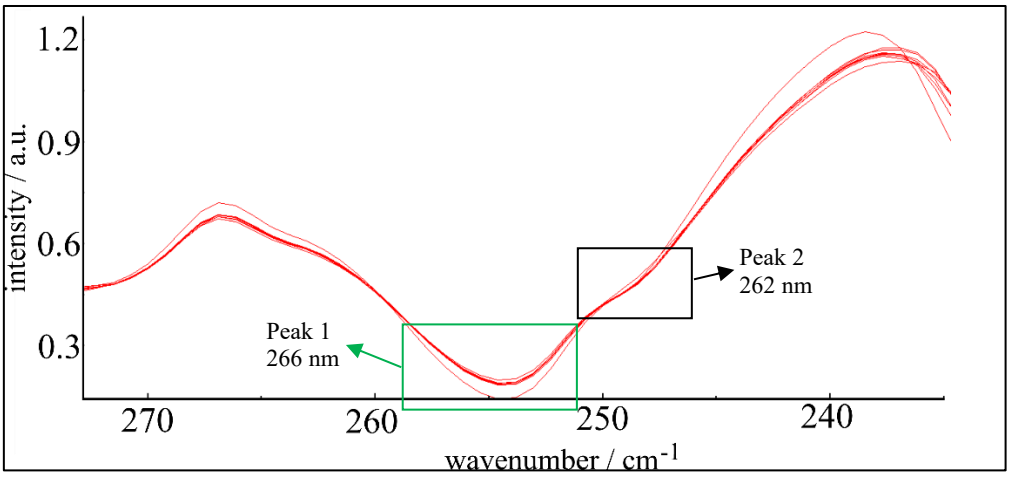

Figure 4. Wavelength profile of 2nd Room Temperature Derivative

In the 2nd derivative image, there is no shoulder peak at 272 nm which appears when an absorption scan is performed. But actually there are 2 peaks, namely 262 nm and 272 nm. At a maximum wavelength of 272 nm it has a weak peak intensity. This is proven in the 2nd derivative where the spectral pattern does not show any shoulder peaks and there are only 2 peaks with high intensity, namely at 266 nm and 262 nm, so that it can be said that the maximum wavelength of 272 nm is too weak to be used as a peak. A single peak at a wavelength of 262 nm when analyzed with the 2nd derivative will produce 2 peaks at a wavelength of 266 nm and 262 nm. A comparison graph of the maximum wavelength of the conventional spectra with the second derivative spectra at room temperature storage conditions can be seen in Figure 5.

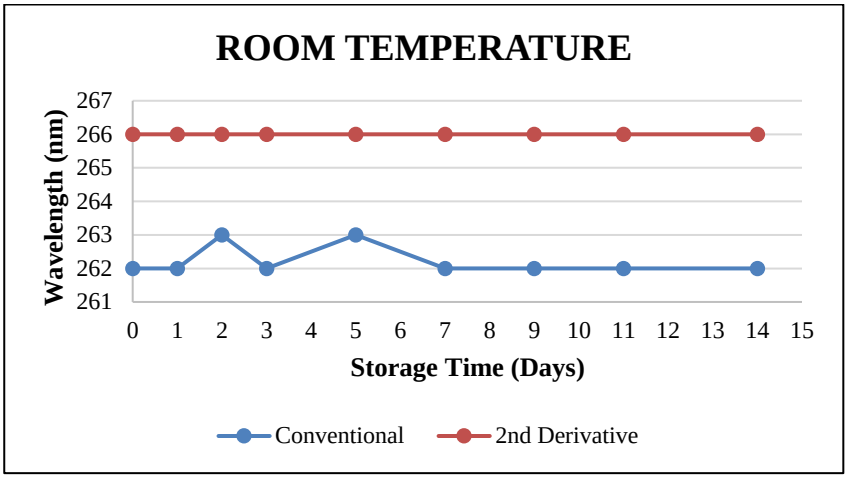

Figure 5. Graph of Maximum Lamda Comparison of Conventional Spectra VS 2nd Derivative Room Temperature Storage Conditions

From Figure 5, it can be seen that in the Conventional Spectra temperature storage conditions experienced a maximum wavelength shift from 262 nm to 263 nm on the 2nd and 5th day then shifted back to 262 nm. Meanwhile, the 2nd derivative does not experience a single wavelength shift so it can be said to be constant. The conventional and second-derivative spectral profiles and graphs for cold storage can be seen in Figures 6, 7 and 8.

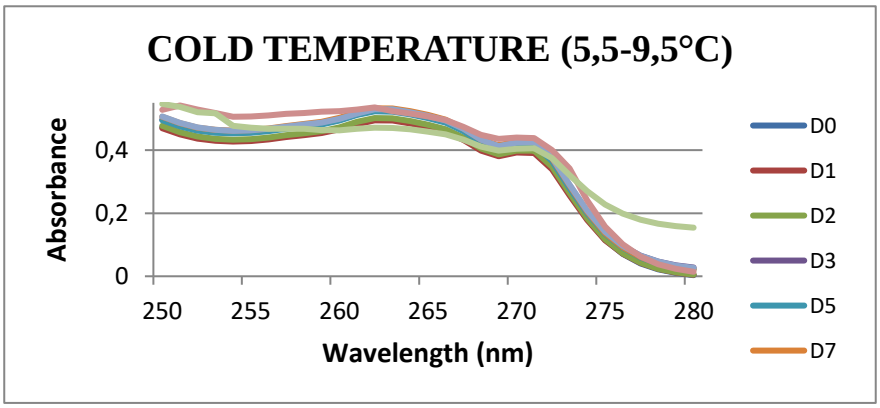

Figure 6. Wavelength profile Cold Temperature Conventional Spectra (D=Day)

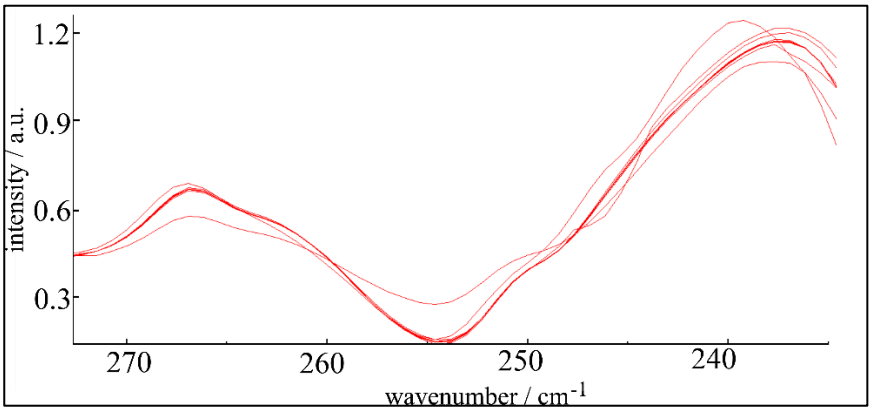

Figure 7. Wavelength profile of 2nd Cold Temperature Derivative

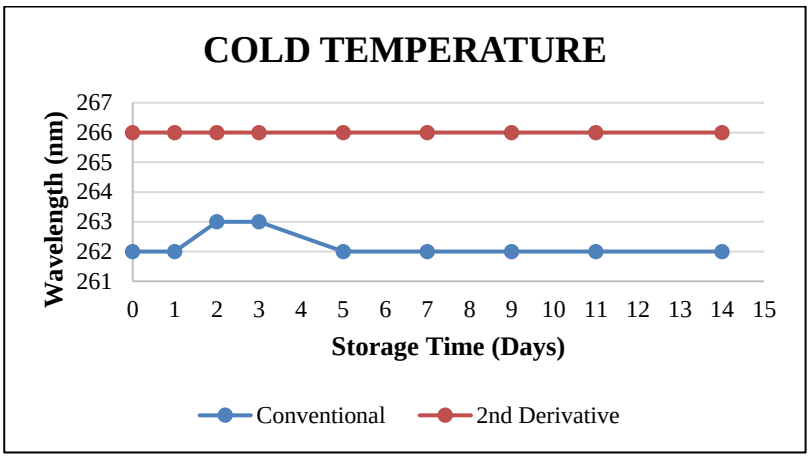

Figure 8. Graph of Maximum Lamda Comparison of Conventional Spectra VS 2nd Derivative Cold Storage Conditions

From Figure 8, it can be seen that in the Conventional Spectra under cold storage conditions, the maximum wavelength shifted from 262 nm to 263 nm on the 2nd and 3rd day and then shifted back to 262 nm. The graph shown is almost similar to the room temperature (AC) graph. Meanwhile, the 2nd derivative also does not experience a shift in either the first or second peak, which means even one wavelength, so it can be said to be constant at 266 nm as shown by a linear line on the graph of the 2nd derivative of cold temperatures. The spectral profiles of conventional spectra and second derivatives as well as graphs on UV exposure storage can be seen in Figures 9, 10 and 11.

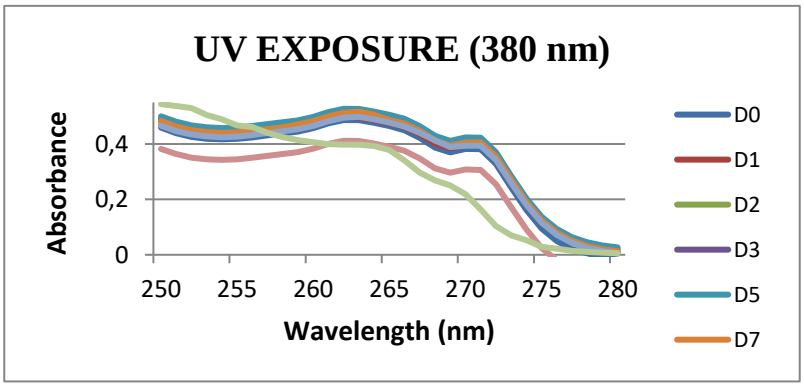

Figure 9. Wavelength profile Conventional UV Exposure Spectra (D=Day)

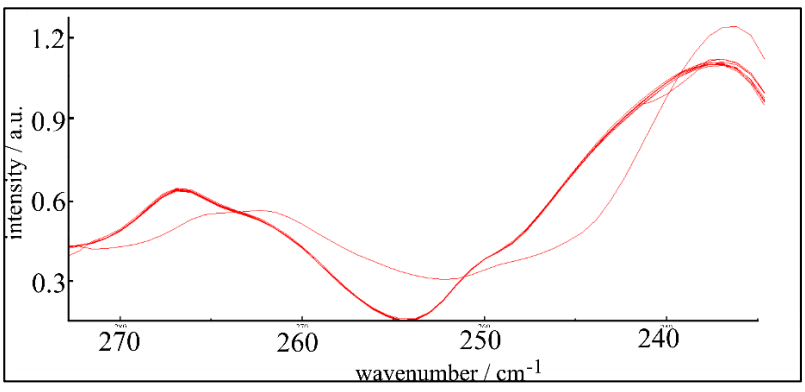

Figure 10. Wavelength profile 2nd Derivative UV Exposure Temperature

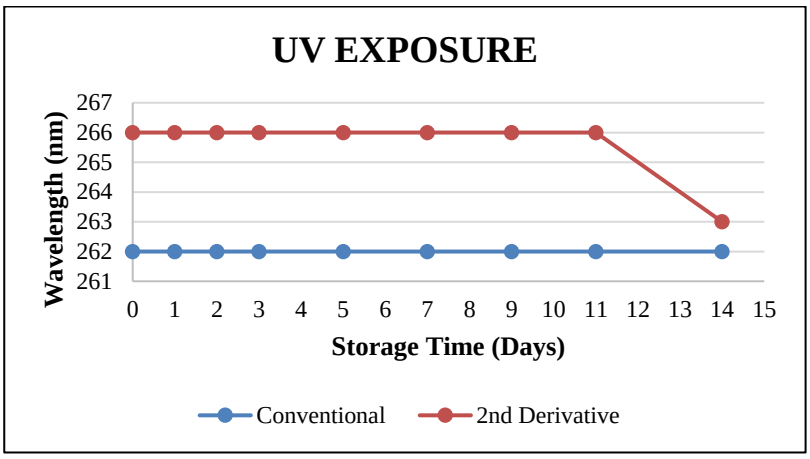

Figure 11. Graph of Maximum Lamda Comparison of Conventional Spectra VS 2nd Derivative UV Exposure Storage Conditions

In contrast to the previous conditions of room temperature (AC) and cold temperatures, the maximum wavelength profile in UV storage conditions experienced a 2nd derivative shift at the first peak. However, the Conventional Spectra does not experience the shift that occurs as in room temperature (AC) storage conditions and cold temperatures. The shift occurred on the 14th day, when the maximum wavelength of the 2nd derivative was shown at 266 nm and then shifted to 263 nm. With a shift in the maximum wavelength, it indicates a change in the spectral pattern, namely in the storage conditions of UV exposure.

4. Conclusion

Based on the laboratory research that has been done, it can be concluded that the UV-Vis spectrophotometric second derivative method can be used to analyze the compound lidocaine HCl in 2% lidocaine HCl injection preparations. Then there is a difference in the maximum wavelength profile in each storage condition indicated by a shift in the maximum wavelength in the Conventional Spectra from 262 nm to 266 nm in condition of storage at room temperature with air conditioning and cold temperature. The shift occurred again at 266 nm to 263 nm on UV exposure storage shown by the 2nd derivative. So that the most suitable storage conditions for storing 2% lidocaine HCl injection preparations are cold and room temperature storage conditions with temperatures of (5,5-9,5 ℃). and (25-27 ℃) respectively.

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