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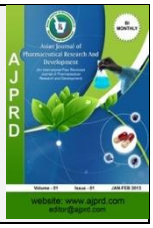

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Research Article

In Vitro Formulation and Evaluation of Preparations Cefixime Nanosuspension

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A B S T R A C T

Objective: To produce a nano-sized cefixime formulation and compare the cefixime formulation with the dissolution test of cefixime from nanosuspension.

Design: Nano-sized cefixime preparations were made with nanosuspension using ethanol and propylene glycol as a solvent and tween 80 as a surfactant. Then the nanosuspension and cefixime suspension were evaluated including organoleptic observations.

Interventions: The intervened variable were formulation an evaluation of cefixime nanosuspension

Main outcome measures: the main measurement in this study was dissolution of cefixime nanosuspension.

Results: The amount of soluble cefixime was measured by having a faster dissolution rate UV spectrophotometer at a wavelength of 285 nm. The average absorbance value of cefixime nanosuspension with propylene glycol solvent was 91.1192 ppm with a concentration of 1.05 nm, nanosuspension with ethanol solvent was 62.4998 ppm with a concentration of 0.72 nm

Conclusion: Nanosuspension with propylene glycol with a very fast dissolution rate. Cefixime can be formulated into nanosuspension preparations using ethanol or propylene glycol as solvent

Keywords: *Cefixime, nanosuspension, dissolution*

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INTRODUCTION

The solubility of the drug substance greatly affects whether or not the drug enters the circulatory system and produces a therapeutic effect of the drug. Drugs that are soluble in water have a more potent therapeutic effect. Meanwhile, the drug compounds that are not soluble in water show incomplete or erratic absorption or absorption. About 40% or more of new chemical entities are generated in the discovery of new drugs which have very poor water solubility[1].

This situation necessitates modification of the formula to improve the solubility of medicinal ingredients that have poor solubility in water. In general, many medicinal substances are easily soluble in organic solvents but have low solubility in water or are practically insoluble. Increasing the solubility and dissolution rate which is difficult to dissolve in water has been widely used, various techniques have been used including particle size reduction, cosolvent, pH adjustment, addition of surfactants, and preparation of solid dispersion preparations. One effective way to increase drug solubility and dissolution rate is to increase the surface area of the drug compound and change the particle size to be smaller [2,3].

Cefixime is the only oral third-generation cephalosporin with broad antimicrobial spectrum in Haemophilus influenzae, Moraxella catarrhalis, Neisseria gonorrheae, Escherichia coli and Klebsiella that is resistant to ampicillin, other oral cephalosporins, and trimethoprim-sulfamethoxazole. These characteristics of cefixime allow its use in urinary and respiratory tract infections[4]. However,

one of the main problems with this drug is its low water solubility leading to poor bioavailability (about 40-50%) after oral administration (classified as class II of BCS)[5]. Also, some evidence has shown that cefixime is absorbed limitedly in the gastrointestinal tract, stomach and upper intestine [6]. For this reason the rate of absorption and the degree of bioavailability are controlled by the rate of dissolution in the gastrointestinal fluid[7]. The most reported methods that have been used to increase the solubility and dissolution rate of cefixime are solid dispersion and the use of several hydrophilic compounds and polymers such as croscarmellose and -cyclodextrin in the formulation of solid dosage forms[8,9].

Nanotechnology is an excellent drug delivery system and has clear advantages in increasing the solubility and effectiveness of water-insoluble drugs. Nanosuspension is a type of submicron colloidal dispersion system and to stabilize the dispersion system, it is necessary to add an appropriate amount of surfactant. The surfactant used must have a strong affinity for drug molecules to strongly adsorb on the surface of drug particles and good affinity with water to avoid particle aggregation[10]. In accordance with the description of the literature study, the researchers are interested in conducting research on the manufacture of cefixime nanosuspension preparations with the precipitation method using a variety of ethanol and propylene glycol solvents.

MATERIALS AND METHODS

This research was conducted using an experimental method, cefixime nanosuspension preparations according to the nanoprecipitation method using aquades, ethanol, and propylene glycol and tween 80 as a surfactant. Evaluation of nanosuspension preparations was carried out through organoleptic observations. In vitro testing was carried out by dissolving cefixime nanosuspension using artificial gastric media using the paddle method.

Tools and Materials

The materials used in this study: Cefixime powder (PT Ifars farma) Aquades, Ethanol, Propylene glycol and Tween80.
The tools used in this study: Stirrer rod, Beaker glass, Dissolution tester, Erlenmeyer, measuring cup, Hotplate, Parchment paper, Magnetic stirrer, Analytical balance, Dropper pipette, UV-Vis Spectrophotometer, Stopwatch, and laboratory equipment that can be used.

Cefixime nanosuspension preparation

Dissolve 125 mg of cefixime into 2 ml of ethanol (for formula 2 ethanol is replaced with propylene glycol). Dissolve 2 ml of Tween 80 in 20 ml of distilled water. Added little by little and stirred using a magnetic stirrer at a temperature of 45℃ at a speed of 1300-1500 rpm for 1 hour until a nanosuspension is formed.

Evaluation of Cefixime nanosuspension

Evaluation of the preparations carried out included organoleptic (smell, color, and shape) and was carried out for 4 weeks with observations every 1 week.

Dissolution Test Preparation (In Vitro)

The dissolution test used an artificial gastric fluid dissolution medium without enzymes (pH1,2) stirring speed 100 rpm, medium temperature: 37 ± 0.5℃ using the paddle method. An aliquot of 1 ml was taken and the volume was kept at 900 ml at intervals of 1, 5,10, 20, 30, 40, 50, 60, 70, 80, 90 minutes. Samples were analyzed by spectrophotometer given a maximum wavelength of 285 nm to determine the concentration of cefixime.

Data Analysis

The research data were analyzed using the Statistical Product and Service Solution (SPSS) version 20 program, which used nonparametric analysis followed by the Kruskall-Wallis average difference test to find out which formula had the same or significantly different effect.

RESULT AND DISCUSSION

This research was carried out by making cefixime nanosuspension preparations by weighing 125 mg of cefixime then dissolved in 2 ml of ethanol (for formula 2 ethanol was replaced with propylene glycol) then dissolved 2 ml of tween 80 in 20 ml of distilled water, added little by little and stirred using a magnetic stirrer at a temperature of 45◦C at a speed of 1300-1500 rpm for 1 hour until nanosuspension is formed. The results of organoleptic observation of cefixime nanosuspension preparations for 4 weeks can be seen in table 1.

Table 1. Organoleptic observation data for 4 weeks storage.

Long storage (Week)	Organoleptic		
	Smell	Color	Shape
0	O	C	L
1	O	C	L
2	O	C	L
3	O	C	L
4	O	C	L

O: Odorless, P: Clear, L: Liquid

Determination of the maximum absorption wavelength of cefixime standard was made at a concentration of 10 ppm with 0.1 N HCL reagent added and aquadest, then measured using UV-Vis spectrophotometry so that a maximum wavelength of 285 nm was obtained, the results of the curve measuring the maximum absorption wavelength of cefixime.

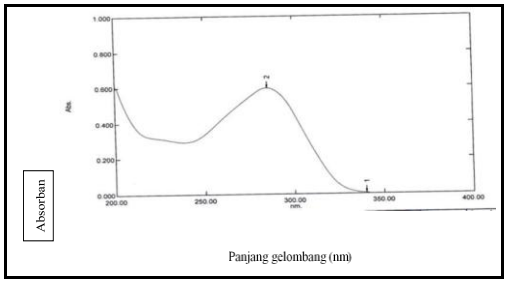

Figure 1: The maximum absorption wavelength curve of cefixime

The standard calibration curve of cefixime was measured at concentrations of 50, 75, 100, 125, 150 ppm at a wavelength of 285 nm. Cefixime absorbance values can be seen in Table 2 and the cefixime absorption curve.

Table 2: Cefixime absorbance value

Concentration	Absorbance
0	0.000
50	0.103
75	0.161
100	0.226
125	0.271
150	0.312

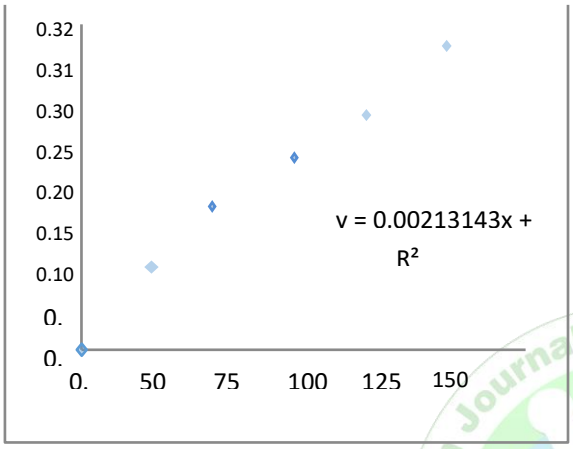

Figure 2. Cefixime absorption curve

Absorption curve is a curve that describes the relationship between absorbance and wavelength. This curve is made by plotting the absorbance value on the y-axis and concentration on the x-axis. Measurement of the cefixime calibration curve resulted in a regression equation y = 0.00213143x – 0.001214286 with a correlation coefficient of r2 = 0.998.

Table 3: Absorbance value of cefixime nanosuspension

Concentration	Absorbance	
	Ethanol	Propylene glycol
0	0.000	0.000
1	0.128	0.189
5	0.131	0.190
10	0.132	0.190
20	0.132	0.193
30	0.133	0.193
40	0.133	0.193
50	0.134	0.193
60	0.134	0.193
70	0.134	0.194
80	0.133	0.194
90	0.133	0.194

The results showed that the dissolution of cefixime with higher and faster yields was shown from nanosuspension preparations with propylene glycol solvent, where the amount of cefixime dissolved from highest to lowest was nanosuspension with ethanol solvent.

Measurement of levels total cefixime was measured based on the regression equation. Measure the absorbance of the resulting area at a wavelength of 285 nm with a UV Vis spectrophotometer. Cefixime levels were determined based on the cefixime linear regression equation[11].

Table 4: Total level of cefixime in the sample

Sample	Weight	Absorbance	Dilution	Levels
Ethanol	0,125	0,132	5,78	0,72
Propylene glycol	0,125	0,193	5,78	1,05

The table show that the levels of cefixime in nanosuspension (ethanol) are 0.72% and levels of cefixime in nanosuspension (propylene glycol) are 1.05%.

CONCLUSION

Based on the results of the research that has been done, it can be concluded that cefixime with the addition of distilled water, ethanol, propylene glycol and solvent tween 80 can be formulated into cefixime nanosuspension. There are results from the cefixime nanosuspension organoleptic test, namely the color: clear, Form: Liquid, Odor: odorless. The preparation that produces a faster dissolution rate than the results obtained is the cefixme nanosuspension preparation with propylene glycol as a solvent.

CONFLICT OF INTERESTS

All author have no to declare

REFERENCES

1. Wagh, K.S., Patil, S. K., Akarte, A. K., and Baviskar, D. T. International Journal of Pharmaceutical Sciences Review and Research, 2011; 8(2): 61- 65.
2. Kumar, S., & Singh, P. Various techniques for solubility enhancement: An overview. The Pharma Innovation, 2016; 5(1, Part A), 23.
3. Savjani KT, Gajjar AK, Savjani JS. Drug Solubility: Importance and Enhancement Techniques. ISRN Pharmaceutics Article ID195727, 2012, 1-10, doi:10.5402/2012/195727.
4. Williams J, Naber K, Bryskier A, Høby N, Gould I, Periti P, et al. Classification of oral cephalosporins. A matter for debate. Int J Antimicrob Agents 2001; 17:443-4450. doi:10.1016/s0924-8579(01)00309-0.
5. Ali T, Mohiuddin OA. In vitro interaction study of cefixime with diclofenac sodium, flurbiprofen, mefenamic acid and tiaprofenic acid. J Chem Pharm Res 2012; 4.
6. Rao NR, Ram P, Kulkarni U. Formulation and evaluation of gas powered system of cefixime tablets for controlled release using hydrophillic polymers. Int J Res Pharm Biomed Sci 2010; 1:82-91.
7. Ramirez E, Laosa O, Guerra P, Duque B, Mosquera B, Borobia AM, et al. Acceptability and characteristics of 124 human bioequivalence studies with active substances classified according to the biopharmaceutic classification system. Br J Clin Pharm 2010; 70:694-702. doi: 10.1111/j.1365-2125.2010.03757.x
8. Ramirez E, Laosa O, Guerra P, Duque B, Mosquera B, Borobia AM, et al. Acceptability and characteristics of 124 human bioequivalence studies with active substances classified according to the biopharmaceutic classification system. Br J Clin Pharm 2010; 70:694-702. doi: 10.1111/j.1365-2125.2010.03757.x
9. Mehta, P,. More, A., and Kulkarni, A. Effect of hydrophilic polymers on cefixime complexation with β-cyclodextrin. Int J Curr Pharm Res 2013; 5:66-70.
10. Li, N., Cai, H., Jiang, L., Hu, J., Bains, A., Hu, J., & Gu, Z. Enzyme-sensitive and amphiphilic PEGylated dendrimer-paclitaxel prodrug-based nanoparticles for enhanced stability and anticancer efficacy. ACS applied materials & interfaces, 2017; 9(8):6865-6877
11. Nayon, M. A. U., Nesa, J., Uddin, M. N., Amran, M. S., & Bushra U. Development and Validation of UV:Spectrometric Method for the Determination of Cefixime Trihydrate in Bulk and Pharmaceutical Formulation. Asian Journal of Biomedical and Pharmaceutical Sciences, 2013;3:(22), 15.
12.