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Determination of Isoniazid and Pyridoxine Hydrochloride Levels in Tablets with Ultraviolet Spectrophotometry by Successive Ratio Derivative

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ABSTRACT

Isoniazid and pyridoxine hydrochloride are a combination of anti-tuberculosis drugs that are often used as standard therapy. The advantage of this drug combination is to obtain treatment effectiveness and prevent the emergence of resistance. Examination of the quality of medicinal preparations, determination of the content of efficacious substances is an important part so that a reliable analytical method is needed as well as tools and operational costs that are relatively cheaper, easy to implement, but can provide results with good accuracy and precision. This study aims to determine the levels of isoniazid and pyridoxine hydrochloride in tablet preparations using successive ratio derivative ultraviolet spectrophotometry. isoniazid (10 g/mL) was then transformed into derivative 1 at 4. The results showed that the levels of isoniazid 101.4313% and pyridoxine hydrochloride 104.7125%. Based on the results of the research conducted, it can be concluded that the levels of isoniazid and pyridoxine hydrochloride meet the requirements for levels according to the Indonesian Pharmacopoeia Edition VI.

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1. INTRODUCTION

In general, Anti Tuberculosis Drugs (OAT) used are isoniazid, rifampin, ethambutol, pyrazinamide and streptomycin. This group of drugs is called the primary drug used as standard therapy. To obtain the effectiveness of treatment and prevent the emergence of resistance, it is necessary to avoid the use of monotherapy, by combining several types of drugs in sufficient quantities and in appropriate doses according to the treatment category. However, without quality assurance, the bioavailability of the drug will be reduced, the risk of toxicity or under-dose and over-dose can facilitate the development of drug resistance (1).

Determination of levels of efficacious substances in medicinal preparations is an important part in agencies that carry out drug levels determination such as the Food and Drug Supervisory Agency (BPOM) and the drug industry so that reliable analytical methods are needed as well as tools and operational costs that are relatively cheaper and easier to implement but can be implemented. gives good results and precision (2). The assay of the single form of isoniazid and pyridoxine hydrochloride tablets can be determined by the high performance liquid chromatography (HPLC) method (3). Isoniazid can be determined by ultraviolet spectrophotometry in aqueous solution at a wavelength of 266 nm and in 0.1N HCl at a wavelength of 265 nm. Pyridoxine hydrochloride can be determined by ultraviolet spectrophotometry in a solution of pH 7 at a wavelength of 254 nm and in 0.1N HCl at a wavelength of 291 nm (4).

Research that has been carried out by Solanki, et al (2015) in the development of two new spectrophotometric methods in determining the ternary mixture of formulation tablets used as antihypertensive therapy Olmesartan Medoxomil (OLM), Amlodipine Besilate (AMLO), and Hydrochlorthiazide (HCTZ) with methanol solvent using two the same method, namely the double divisor ratio spectra method (DDRSM) and successive ratio derivative (SRD), provides accurate, sensitive, simple, precise and reliable results. This method does not require a long preparation time, a large number of solvents, and can determine the compound drug mixture without prior separation (5).

Research conducted by Youssef S. H, et al (2018) in the analysis of paracetamol, pseudoephedrine and cetirizine in capsule preparations using spectrophotometric techniques, with double distilled water solvent using the SRD method, which gives accurate, selective and sensitive results. This method does not require a long preparation time, a large number of solvents, and can determine overlapping spectra at the same time without prior separation (6).

2. RESEARCH METHODE

This research was conducted at the USU Faculty of Pharmacy Research Laboratory in October-November 2021. The tools used in this research are complete ultraviolet-visible spectrophotometry (Shimadzu 1800) with a personal computer (PC) equipped with UV probe 2.42 software, MS Excel, sonicator (Branson), analytical balance (Sartorius), measuring flask (Pyrex). , measuring cup (Pyrex), beaker glass (Pyrex), maat pipette (kimax), mortar and pestle. The materials used in this study were tablets containing isoniazid 400 mg and pyridoxine hydrochloride 10 mg Pehadoxin Forte® (PT. Pharpros), isoniazid (BPFI), pyridoxine hydrochloride (BPFI), 0.1 N HCl and aquadest. The samples of this study were tablets containing isoniazid 400 mg and pyridoxine hydrochloride 10 mg Pehadoxin Forte® (PT. Pharpros) which were obtained from a pharmacy in Medan city. The data obtained is in the form of absorbance spectrum measurement results which are calculated with the help of UV Probe and Ms Excel software.

3. RESULT AND ANALYSIS

Absorption Spectrum

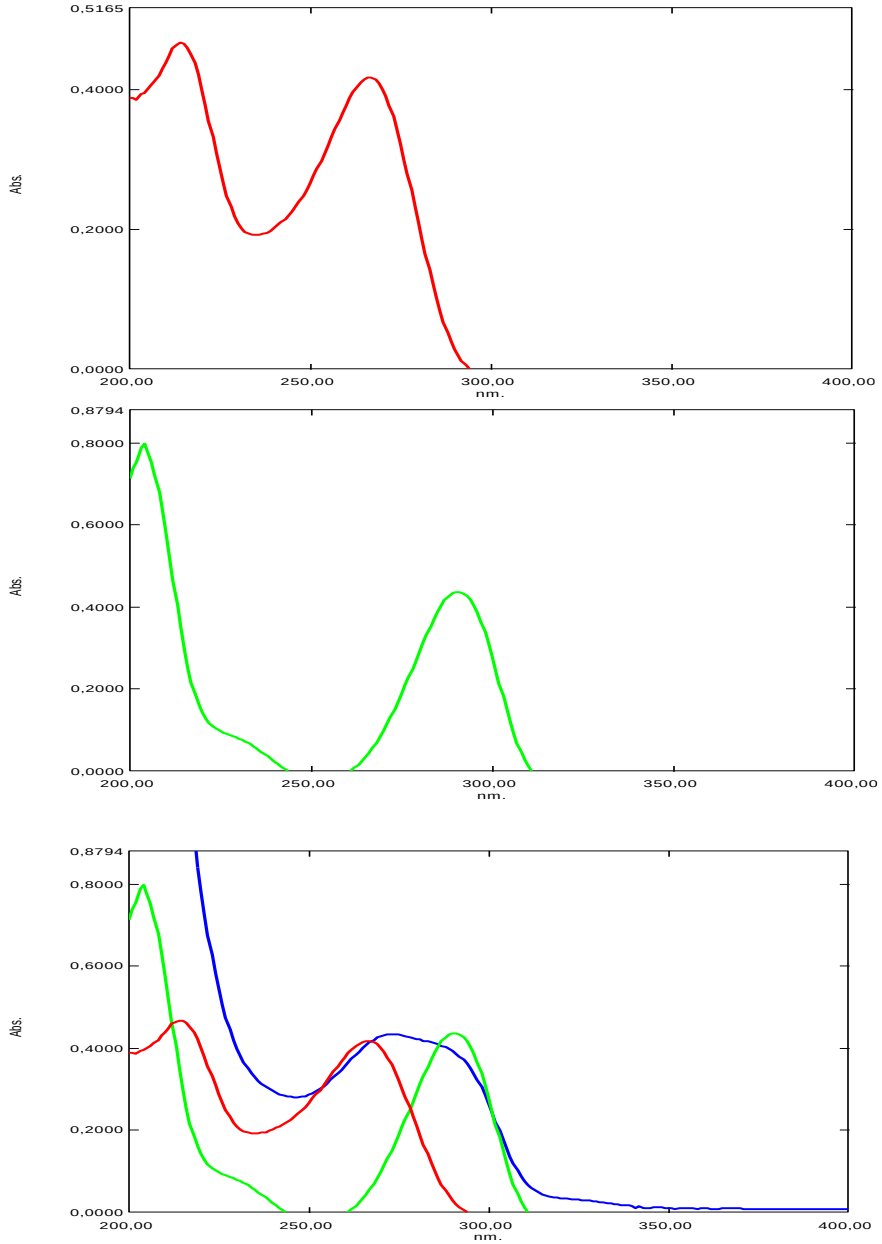

Image 1. Absorption spectrum (a) Isoniazid (b) Pyridoxine Hydrochloride, Maximum absorption spectrum (c) Isoniazid (d) Pyridoxine Hydrochloride(e) overlapping spectrum Isoniazid 10µg/mL Pyridoxine Hydrochloride 10 g/mL and standard mixture

Derivative Ratio Spectrum

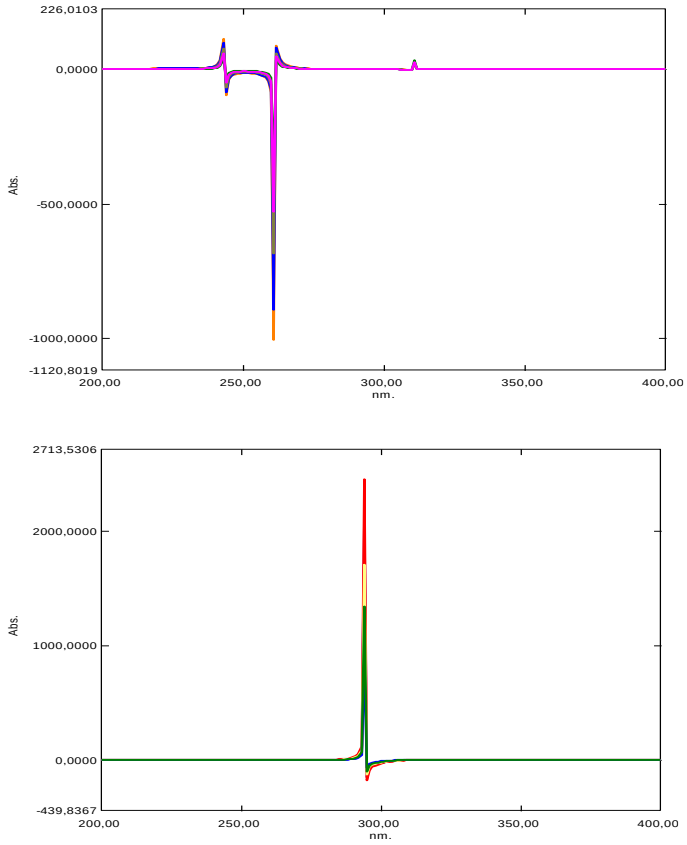

Image 2. Spectrum ratio derivatives (a) isoniazid (b) pyridoxine hydrochloride

This method begins with the selection of a divisor and analysis wavelength. The concentration of the divider used in this study is isoniazid 10 g/mL and pyridoxine hydrochloride 10 g/mL. After dividing all the spectra by their respective spectra, the ratio spectrum of isoniazid and pyridoxine hydrochloride is obtained. , then the spectrum is derived so that the derivative ratio spectrum is obtained to determine the analysis of isoniazid and pyridoxine hydrochloride (8).

Determination of Wavelength Analysis

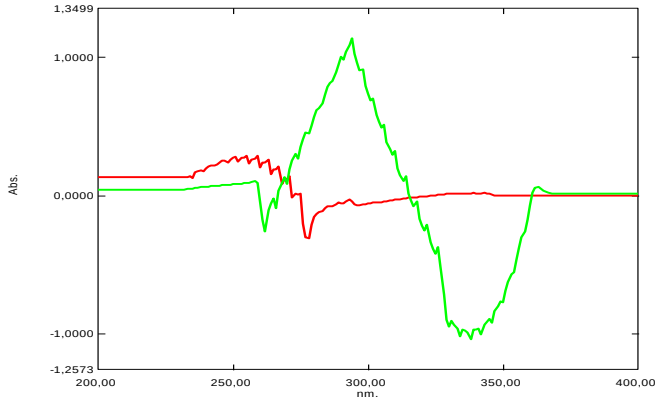

Figure3. Overlapping spectrum ratios of isoniazid and pyridoxine hydrochloride derivatives

In determining the wavelength of isoniazid, the zero-order spectrum of isoniazid is divided by the spectrum of pyridoxine hydrochloride (10 g/mL) to record the first ratio spectrum and then converted to derivative 1 at 4, then the stored spectrum is further divided by pyridoxine hydrochloride (10 g/mL) to record the second ratio spectrum and the result is transformed into derivative 1 at 4. Then the maximum or minimum wavelength is selected which gives the best correlation value, in which case the wavelength is 266.0 nm with a correlation coefficient value of 0.9966 given in the spectrum of derivative 1 at 4. In determining the wavelength of pyridoxine hydrochloride, the zero-order spectrum of pyridoxine hydrochloride is divided by the spectrum of isoniazid (10 g/mL) to record the first ratio spectrum and then converted to derivative 1 at 4, then the stored spectrum is divided again with isoniazid (10 g/mL) to record the second ratio spectra ua and the result is transformed into derivative 1 at 4. Then the maximum or minimum wavelength that gives the best correlation value is selected, in which case the wavelength is 279.0 nm with a correlation coefficient value of 0.9990 given to the derivative 1 spectrum at 4 (8)(11).

Method Validation

Accuracy, Precision (RSD), Linearity, Limit of Detection (LOD) and Limit of Quantity (LOQ)

Table 1. Accuracy, Precision (RSD), Linearity, Limit of Detection (LOD) and Limit of Quantity (LOQ)

No.	Parameter	Metode *successive ratio derivative*	
		Isoniazid	**Piridoksin Hidroklorida**
1	Akurasi (%)	98,7909	100,0205
2.	Presisi (RSD)(%)	0,3485	0,1013
3.	Linearitas (r)	0,9966	0,9990
4.	LOD (µg/mL)	1,0747	1,3687
5.	LOQ (µg/mL)	3,5833	4,5626

Table 1 shows that the successive ratio derivative method meets the validation requirements for the parameters of accuracy, precision, linearity as well as the limit of detection (LOD) and limit of quantification (LOQ). very good between concentration and absorbance. This indicates that as the concentration increases, the absorbance value also increases. The accuracy value obtained shows that this method meets the requirements for method validation (accuracy value requirements are 98%-102%)(7)(9)(12). Precision shows that the method gives results that are close to each other even though it has been tested in several replications. The precision parameter is reflected from the resulting RSD value, and from the results obtained the successive ratio derivative method meets the validation requirements (RSD <2 %) (7). The detection limit is the lowest analyte concentration in the sample that can still be detected, while the quantitation limit is defined as the lowest analyte concentration in the sample that can still meet the careful and thorough criteria (8)(10)(13).

Determination of the concentration of a mixture of isoniazid and pyridoxine hydrochloride in tablet preparations

Table 2. Levels of isoniazid and pyridoxine hydrochloride

Komponen	*Successive Ratio Derivative*		Klaim Dilabel (mg)	Persyaratan Farmakope Edisi VI 2020	
	%	Mg		%	mg
Isoniazid	101,4313	405	400	90-110	360-440

Piridoksin Hidroklorida	104,7125	10	10	95-115	9,5-11,5

Table 2 shows that the tablet preparations meet the requirements where the content of the substance is in the range of 90-110% for isoniazid and 95-115% for pyridoxine hydrochloride according to the Indonesian Pharmacopoeia edition VI (2020), this shows that the successive ratio derivative method can determine the levels in tablet preparations. with overlapping spectra without prior separation (5)(11).

4. CONCLUSION

Based on the research conducted, it can be concluded that the determination of the levels of isoniazid and pyridoxine hydrochloride in tablet preparations using the ultraviolet spectrophotometric method using successive ratio derivatives meets the requirements of the Indonesian Pharmacopoeia Edition VI..

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