



Study of Extraction Conditions of Indapamid Drug from Aqueous Environment

N.A. Abdullabekova¹, Z.U. Usmanalieva²

¹ Assistant, Tashkent Pharmaceutical Institute

² DSc, Associate Professor, Tashkent Pharmaceutical Institute

ARTICLE INFO	ABSTRACT
Published Online: 10 April 2023	There were studied moderate conditions for the extraction of indapamide from an aqueous medium (the influence of the pH–environment, the nature of the organic solvent, the effect of electrolytes and repeated extractions). It was determined that, when the pH of the solution medium was 4.01, when the number of extractions was increased five times using ethyl acetate as an extractant, 94.17% of indapamide was extracted under the influence of the electrolyte can be extracted.
Corresponding Author: N.A. Abdullabekova	
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INTRODUCTION

According to its chemical structure, the drug Indapamide belongs to the group of nonthiazide sulfonamide derivatives and retains the indole ring. In medicine, it is produced under the names Indap, Indapamid retard, Akripamid, Akripamid retard, Velpamid, Arifon retard and is widely used as a diuretic and antihypertensive agent. Cases of poisoning due to its wide use are reported in the literature. Taking into account the degree of toxicity of indapamide, it is important to make a correct diagnosis in order to provide emergency medical care to people in case of acute poisoning with it [1].

THE AIM OF THE WORK

In this regard, it was aimed to study the moderate conditions for the extraction of indapamide from aqueous media (effect of pH–media, nature of organic solvent, effect of electrolytes and repeated extraction). It is a pale yellow crystalline powder, a weak acid chemically different from thiazides, soluble in aqueous solutions of strong bases. Molecular weight is 365.84 g/mol.

EXPERIMENTAL PART

To study the effect of the nature of the organic solvent during the extraction process, benzene (Bp=80.1°C), ether (Bp=34.6°C), chloroform (Bp=61°C), hexane (Bp=69°C), solvents such as ethylacetate (Bp=77.1°C) were used. It is known that the pH index has a great influence on the process of extracting the tested substances from the aqueous medium. Therefore, there was studied the effect of pH on the extraction of indapamide from aqueous media. For this, using standard fixanals (state standard is 8.135–74 pN

standard), the parameters of the pH environment are 1.68; 3.56; 4.01; 6.86; 9.18; Buffer solutions of 12.45 were prepared. 9 ml of solutions with different pH values were taken in 100 ml tightly closed flasks, 1 ml of 100 mkg of indapamide storage solution was added to it, and 10 ml of organic solvents were added and shaken on a mechanical shaker for 5 minutes. The flasks were left for 5 min to separate the layers. After complete separation of the layer, the organic solvent layer was filtered using a separatory funnel through filter paper containing dehydrated sodium sulfate salt into porcelain bowls. The filter paper was washed with 3–5 ml of organic solvent and the teat was added to the main extract. The organic solvents from the extracts were evaporated to a dry residue under a stream of hot air. The dry residue was dissolved in 95% ethyl alcohol and made up to 10 ml. There was taken 1 ml and put into a measuring flask with a capacity of 25 ml, the volume was brought up to the mark with 95% ethyl alcohol and analyzed in a UV–spectrophotometer brand “Agilent Technologies” 8453E Spectroscopy System. The amount of indapamide in the aqueous medium was determined by the calibration plot of standard sample solutions of indapamide prepared in advance [2]. For this, the working standard sample solution of indapamide; 1; 2; 3; 4; 5; 6; 7; 8; 9; 10 mkg/ml solutions were prepared and analyzed in a spectrophotometer in a cuvette with a layer thickness of 10 mm at a wavelength of 243 nm. There was used 95% ethyl alcohol as a reference solution. Based on the data obtained as a result of the experiments, the relative and molar absorption index values of indapamide were calculated. The results of the performed analysis are presented in Table 1.

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Table 1. The results of determination relative and molar absorption of indapamide indicators (n=10)

Amount of substance, mkg/ml	Optical density (D)	Comparison absorbance index (E)	Molar absorbance index (ϵ)
1	0,103	103	3765
2	0,208	104	3801
3	0,309	103	3764
4	0,410	100	3655
5	0,518	104	3787
6	0,620	103	3776
7	0,728	104	3801
8	0,835	104	3801
9	0,940	104	3816
10	1,030	103	3765
Average		103	3774

According to the analysis results, it was determined that indapamide corresponds to the values of the average specific absorption index of 103 and the average molar absorption index of 3774 [3]. The process of studying the

effect of organic solvents and pH on the extraction process of indapamide from aqueous medium was carried out. The experimental results are presented in Table 2 and Figure 1.

Table 2. Results of the study of the effect of organic solvent and pH on the extraction of indapamide from aqueous medium (n=1)

pH indicator of the environment	Organic solvent									
	ethylacetate		ether		chloroform		benzene		hexane	
	mkg	%	mkg	%	mkg	%	mkg	%	mkg	%
1,68	28,10	28,10	7,72	7,72	6,01	6,01	4,65	4,65	1,12	1,12
3,56	34,99	34,99	15,30	15,30	12,02	12,02	10,9	10,9	5,25	5,25
4,01	61,86	61,86	49,56	49,56	24,23	24,23	18,7	18,7	10,6	10,6
6,86	40,24	40,24	35,31	35,31	14,25	14,25	13,4	13,40	5,61	5,61
9,18	31,02	31,02	24,20	24,20	10,2	10,22	8,11	8,11	3,53	3,53
12,45	29,60	29,60	7,72	7,72	5,56	5,56	4,90	4,90	1,65	1,65

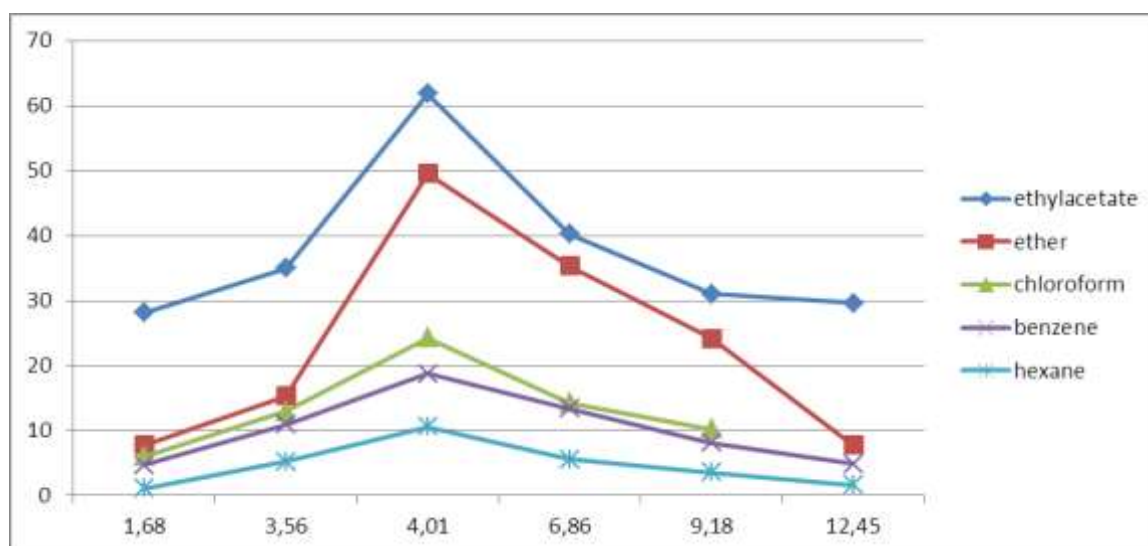


Figure 1. Study diagram of the effect of organic solvent and pH on the extraction of indapamide from aqueous media

According to the results of the analysis, it was possible to extract indapamide from the aqueous medium in

the amount of 61.86% after five re-extractions with ethylacetate under conditions of pH=4.01.

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It is known from the literature that the degree of extraction of most substances from the aqueous layer with the help of organic solvents depends on the participation of electrolytes in the extraction. In most cases, electrolytes help extract substances from the aquifer in greater quantities. In this case, under the influence of electrolytes, the solubility of the substance in water decreases, and they are also used to break up the formed emulsions or precipitate protein substances [4].

In the practice of forensic chemistry, ammonium sulfate, sodium chloride salts are widely used as electrolytes, and they also have the above-mentioned properties. Based on this, the effect of these electrolytes on the extraction process of indapamide from the aqueous layer was studied [5].

The study of the effect of electrolytes on the level of extraction was carried out as follows [6]. There were

prepared 5% and 25% saturated solutions of sodium chloride and ammonium sulfate. Then, 9 ml of pH=4.01 buffer solution and 2 ml of electrolyte and 100 mkg of indapamide were added to it in the separator funnel, and indapamide was extracted under the above conditions. At the same time, 1, 2, 3, 4, 5 extractions with ethyl acetate were carried out in order to study the influence of the extraction number on the complete transfer of the substance to the organic layer. The organic solvents from the extract were evaporated to a dry residue under a stream of hot air. The dry residue was dissolved in 95% ethyl alcohol, the volume was adjusted to 10 ml, and 1 ml was taken from it, put into a 25 ml volumetric flask, made up to the volume line with ethyl alcohol, and analyzed using a spectrophotometric method. The results of the experiment are presented in Table 3.

Table 3. Effect of electrolyte and extraction number on the extraction of indapamide (5)

Electrolyte	Extraction number and amount of indapamide extracted									
	once		twice		three times		four times		five times	
	mkg	%	mkg	%	mkg	%	mkg	%	mkg	%
Electrolyte not added	33,42	33,42	48,46	48,46	54,46	54,46	58,16	58,16	61,86	61,86
NaCl	37,43	37,43	54,31	54,31	71,11	71,11	78,27	78,27	84,05	84,05
(NH ₄) ₂ SO ₄	48,65	48,65	68,23	68,23	81,43	81,43	91,33	91,33	94,17	94,17

The extraction process of indapamide was significantly affected by ammonium sulfate electrolyte, while sodium chloride electrolyte was insignificant.

CONCLUSION

Factors affecting the extraction of indapamide from aqueous medium: the nature of organic substances, the pH of the solution, the number of extractions, and the effect of electrolytes were studied. In this case, when the pH value of the solution medium is brought to 4.01, when ethyl acetate is used as an extractant and the number of extractions without adding an electrolyte reaches 61.86%, under the influence of sodium chloride electrolyte, 84.05%, under the influence of ammonium sulfate electrolyte, the extraction of indapamide is 94.17%. it was found possible. In conclusion, in the extraction of indapamide from aqueous media, the ammonium sulfate electrolyte had a significant effect on the extraction process. The developed extraction conditions show that they can be used in the determination of indapamide from biological fluids.

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