Investigation and estimation of spectrophotometric values specific and molar absorbances for Losartan Potassium and Valsartan.

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Abstract.

The aim of current investigation was the investigation and estimation of spectrophotometric values specific ($A^{1\%}_{1cm}$) and molar (ε) absorbances for angiotensin receptor blockers Losartan Potassium and Valsartan.

The following experimental results were obtained: for solutions of referense standards Losartan Potassium (λmax = 208 nm) at $A > 0.2$ (3.10^{-7} g/ml ÷ $6.75.10^{-7}$ g/ml): $A^{1\%}_{1cm}$: 12113 ÷ 12778; ε: 558441 ÷ 589064; for Valsartan in 99.8 % ethanol at λmax = 252 nm for $A > 0.2$ (6.10^{-6} g/ml ÷ 1.10^{-5} g/ml): $A^{1\%}_{1cm}$: 774 ÷ 800; ε: 33730 ÷ 34840. For Valsartan in methanol at λmax = 250 nm for $A > 0.2$ ($3.5.10^{-6}$ g/ml ÷ 1.10^{-5} g/ml): $A^{1\%}_{1cm}$: 480 ÷ 628; ε: 20885 ÷ 27368. Specific ($A^{1\%}_{1cm}$) and molar (ε) absorbances for $A < 0.2$ were:

[C] g/ml	$A^{1\%}_{1cm}$	ε	
$3.5.10^{-8}$ ÷ 1.10^{-7}	13107 ÷ 16710	604252 ÷ 770348	Losartan Potassium
5.10^{-7} ÷ 2.10^{-6}	877 ÷ 880	38221 ÷ 38304	Valsartan (99.8 % ethanol)
$1.2.10^{-6}$ ÷ $2.5.10^{-6}$	574 ÷ 617	24997 ÷ 26875	Valsartan (methanol)

Key words: Losartan Potassium, Valsartan, spectrophotometry, specific, molar, absorbance.

Introduction.

Arterial hypertension is widespread disease [1]. Perseptive strategies and trends in hypertension treatment [1] are with new antihypertensive drugs [2]: angiotensin receptor blockers – sartans [3]. Losartan is applied for I and II stage of hypertension [4, 5]. Valsartan is approved for: I and II stage of hypertension [6, 7], metabolic syndrome [8], miocardial infarction [9], left ventricular systolic dysfunction [10], and diastolic dysfunction in heart failure [11].

Instrumental methods are applied for different analysis: phytochemical investigation of plants: TLC: leave extract of *Dendranthema indicum* (L Desmoul) [12]; stem bark extract of *Psorospermum senegalense* (Spach) [13]; GC assessment of organochlorine pesticides in cocoa beans [14]; spectrophotometry for Curcuminoid analogues [15], determination of cromium (VI) [16] and tantalum (V) (λ = 490 nm) [17] with hydroxythiophenol; assay for iron (III) with 5-(p-hydroxybenzylidene)-thiazolidone-2,4 at λ = 540 nm) [18] and cobalt (II) with 2-hydroxy-5-iodothiophenol at λ = 598 nm) [19]; quantification of fluoride using alizarin red S complex at λ = 624 nm) [20].

First derivative UV-spectrophotometry has been applied for determination of Losartan potassium tabl. [21, 22]; Losartan (λ = 271.6 nm) and Hydrochlorothiazide (λ = 335 nm) in combination [23].

For quantification of Valsartan in tabl. have been developed the following methods: UV-spectrophotometry at λ = 205.6 nm; second detivative spectrophotometry at λ = 221.6 nm and λ = 231.2 nm [24]. For simultaneous assay of Valsartan (λ = 264 nm) and Hydrochlorthiazide (λ = 270.5 nm) in tabl. UV-method have been described [25]. First detivative UV-spectrophotometry have been reported for quantification of: Valsartan Hydrochlorthiazide [26, 27]; Valsartan, Hydrochlorthiazide and Enalapril [28]; Valsartan (λ = 250 nm) and Amlodipine besilate (λ = 238 nm) [29]; Valsartan (λ = 250 nm) and Ramipril (λ = 218 nm) [30].

The aim of current investigation was the calculation and estimation of spectrophotometric values specific and molar absorbance for Losartan Potassium and Valsartan.

Materials.

I. Reference standards: Losartan Potassium (Sigma Aldrich, N: Y0001062); Valsartan (98 %) (Sigma Aldrich, N: SML 0142).

II. Reagents with analytical grade of puruty: 99.98 % ethanol (Sigma Aldrich, N: SZBD 0500 V UN 1170), methanol (99.9 %) (Sigma Aldrich, N: SZBD 063AV UN 1230), distilled water.

METHODS. UV-spectrophotometry.

I. Equipment – UV-VIS diode array spectrophotometer (Hullett Packard N: 8452 A).

II. Preparation of solutions of reference standard Losartan Potassium in distilled water.

An accurately weighed quantity of reference standard Losartan Potassium: 67.5 mg, 62.5 mg, 60 mg, 55 mg, 50 mg, 45 mg, 40 mg, 37 mg, 30 mg, 10 mg, 7 mg, 4 mg, 3,5 mg was dissolved in distilled water to 100.0 ml volumetric flasks. An aliquots part of 1.0 ml of all of the resulted preparations was diluted to 100.0 ml with the same solvent. From all of the obtained samples, aliquot parts of 1.0 ml was diluted with distilled water to 10.0 ml, to obtain solutions with concentrations of Losartan Potassium respectively: $6.75.10^{-7}$ g/ml; $6.25.10^{-7}$g/ml; 6.10^{-7}g/ml; $5.5.10^{-7}$g/ml; 5.10^{-7} g/ml; $4.5.10^{-7}$g/ml; 4.10^{-7}g/ml; $3.7.10^{-7}$g/ml; 3.10^{-7}g/ml; 1.10^{-7}g/ml; 7.10^{-8} g/ml; 4.10^{-8} g/ml; $3.5.10^{-8}$ g/ml which are analysed by UV- spectrophoto-metry, by measuring the absorbance at λ = 208 nm, using distilled water as blank solution.

III. Preparation of solutions of reference standard Valsartan in 99.98 % ethanol.

An accurately weighed quantities from reference standard Valsartan (10 mg, 20 mg, 60 mg, 120 mg, 140 mg, 160 mg, 200 mg) were dissolved in a volumetric flask of 200.0 ml in 99.98 % ethanol. From every solution an aliquot part of 1.0 ml separately was diluted with 99.98 % ethanol to 100.0 ml to obtain solutions with concentration of Valsartan respectively: 5.10^{-7} g/ml; 1.10^{-6} g/ml; 3.10^{-6} g/ml; 6.10^{-6} g/ml; 7.10^{-6} g/ml; 8.10^{-6} g/ml; 1.10^{-5} g/ml)

IV. Preparation of solutions of reference standard Valsartan in methanol.

An accurately weighed quantities from reference standard Valsartan (24 mg, 34 mg, 50 mg, 70 mg, 120 mg, 160 mg, 200 mg) were dissolved in a volumetric flask of 200.0 ml in methanol. From every solution an aliquot part of 1.0 ml separately was diluted with methanol to 100.0 ml to obtain solutions with concentration of Valsartan respectively: $1.2.10^{-6}$ g/ml; $1.7.10^{-6}$ g/ml; $2.5.10^{-6}$ g/ml; $3.5.10^{-6}$ g/ml; 6.10^{-6} g/ml; 8.10^{-6} g/ml; 1.10^{-5} g/ml.

All solutions in 99.98 % ethanol were analysed at λ = 252 nm against blank 99.98 % ethanol and the absorbance of solutions in methanol was measured at λ = 250 nm, using methanol as blank solution.

Results and discussion.

In our previous work [31], solutions of reference standard Telmisartan were prepared as follows: an accurately weighed quantity of reference standard Telmisartan: 125 mg, 100 mg, 90 mg, 80 mg, 50 mg, 40 mg, 30 mg, 10 mg, 5 mg, 2.5 mg was dissolved in 99.98 % ethanol in a volumetric flask of 100.0 ml. An aliquot part of 1.0 ml from all of the obtained samples was diluted with the same solvent to 100.0 ml. The resulting solutions had a concentration of Telmisartan respectively: $1.25.10^{-5}$ g/ml; 1.10^{-5} g/ml; 9.10^{-6} g/ml; 8.10^{-6} g/ml; 5.10^{-6} g/ml; 4.10^{-6} g/ml; 3.10^{-6}g/ml; 1.10^{-6} g/ml; 5.10^{-7}g/ml; $2.5.10^{-7}$g/ml. The absorbance of all solutions was measured at λ = 298 nm against compensation: 99.98 % ethanol.

The following results for specific ($A^{1\%}_{1cm}$) and molar (ε) absorbances were obtained:

1) A > 0.2: in 3.10^{-6} g/ml ÷ $1.25.10^{-5}$ g/ml: $A^{1\%}_{1cm}$: 725 ÷ 823; ε: 37347 ÷ 42335

2) A < 0.2: in $2.5.10^{-7}$ g/ml ÷ 1.10^{-6} g/ml: $A^{1\%}_{1cm}$: 1201 ÷ 1567; ε: 61816 ÷ 80651

In our previous investigations, UV-spectrophotometric methods for identification and determination of Losartan Potassium [32] and Valsartan [33] were validated for analytical parameters: selectivity, linearity, LOD, LOQ, accuracy and precision in accordancio woeu International Conference on Harmonization guidelines [34] and the validated UV-method was applied for Losartan Potassium in tablets [35].

I. Determination of specific ($A^{1\%}_{1cm}$) and molar (ε) absorbance of reference standards of Losartan Potassium in distilled water and Valsartan in 99.98 % ethanol and methanol.

The experimental results for the absorbances are used for the calculation of specific ($A^{1\%}_{1cm}$) and molar (ε) absorbance of reference standards of Losartan Potassium in distilled water at λmax = 208 nm. (Table 1.), Valsartan in 99.98 % ethanol at λ max = 252 nm (Table 2.) and Valsartan in methanol at λ max = 250 nm (Table 3.).

Table. 1. Specific ($A^{1\%}_{1cm}$) and molar (ε) absorbance of reference standards of Losartan Potassium ($3.5.10^{-8}$ g/ml ÷ $6.75.10^{-7}$ g/ml) in distilled water at λmax = 208 nm.

N:	C [g/ml]	C [g/100 ml]	A	($A^{1\%}_{1cm}$)	C [g/l]	C [mol/l]	ε
1.	$3.5.10^{-8}$	$3.5.10^{-6}$	0.04651	13289	$3.5.10^{-5}$	$7.5.10^{-8}$	612616
2.	4.10^{-8}	4.10^{-6}	0.05289	13223	4.10^{-5}	$8.6.10^{-8}$	609570
3	7.10^{-8}	7.10^{-6}	0.09175	13107	7.10^{-5}	$1.51.10^{-7}$	604252
4.	1.10^{-7}	1.10^{-5}	0.1671	16710	1.10^{-4}	$2.16.10^{-7}$	770348
5.	3.10^{-7}	3.10^{-5}	0.36386	12129	3.10^{-4}	$6.5.10^{-7}$	559144
6.	$3.5.10^{-7}$	$3.5.10^{-5}$	0.42397	12113	$3.5.10^{-4}$	$7.59.10^{-7}$	558441
7.	$3.7.10^{-7}$	$3.7.10^{-5}$	0.47047	12715	$3.7.10^{-4}$	$8.02.10^{-7}$	586192
8.	4.10^{-7}	4.10^{-5}	0.50270	12568	4.10^{-4}	$8.67.10^{-7}$	579374
9.	$4.3.10^{-7}$	$4.3.10^{-5}$	0.54944	12778	$4.3.10^{-4}$	$9.32.10^{-7}$	589064
10.	$4.5.10^{-7}$	$4.5.10^{-5}$	0.57045	12677	$4.5.10^{-4}$	$9.76.10^{-7}$	584407
11.	5.10^{-7}	5.10^{-5}	0.66003	13201	5.10^{-4}	$1.08.10^{-6}$	608560
12.	$5.5.10^{-7}$	$5.5.10^{-5}$	0.67903	12346	$5.5.10^{-4}$	$1.19.10^{-6}$	569163
13.	6.10^{-7}	6.10^{-5}	0.73882	12314	6.10^{-4}	$1.30.10^{-6}$	567672
14.	$6.25.10^{-7}$	$6.25.10^{-5}$	0.79494	12719	$6.25.10^{-4}$	$1.36.10^{-6}$	586360
15.	$6.75.10^{-7}$	$6.75.10^{-5}$	0.84961	12587	$6.75.10^{-4}$	$1.46.10^{-6}$	580265

Table 2. Specific ($A^{1\%}_{1cm}$) and molar (ε) absorbance of reference standards Valsartan (5.10^{-7} g/ml ÷ 1.10^{-5} g/ml) in 99.98 % ethanol at λ max = 252 nm.

N:	C [g/ml]	C [g/100 ml]	A	$A^{1\%}_{1cm}$	C [g/l]	C [mol/l]	ε
1.	5.10^{-7}	5.10^{-5}	0.04388	877	5.10^{-4}	$1.15.10^{-6}$	38221
2.	1.10^{-6}	1.10^{-4}	0.08795	880	1.10^{-3}	$2.30.10^{-6}$	38304
3	2.10^{-6}	2.10^{-4}	0.17590	880	2.10^{-3}	$4.59.10^{-6}$	38304
4	6.10^{-6}	6.10^{-4}	0.46730	779	6.10^{-3}	$1.38.10^{-5}$	33920
5.	7.10^{-6}	7.10^{-4}	0.54213	774	7.10^{-3}	$1.61.10^{-5}$	33730
6.	8.10^{-6}	8.10^{-4}	0.63997	800	8.10^{-3}	$1.84.10^{-5}$	34840
7.	1.10^{-5}	1.10^{-3}	0.79050	791	1.10^{-2}	$2.30.10^{-5}$	34428

Table 3. Specific ($A^{1\%}_{1cm}$) and molar (ε) absorbance of reference standards Valsartan ($1.2.10^{-6}$ g/ml ÷ 1.10^{-5} g/ml) in methanol at λ max = 250 nm.

N:	C [g/ml]	C [g/100 ml]	A	A 1% 1 cm	C [g/l]	C [mol/l]	ε
1.	$1.2.10^{-6}$	$1.2.10^{-4}$	0.07405	617	$1.2.10^{-3}$	$2.76.10^{-6}$	26875
2.	$1.7.10^{-6}$	$1.7.10^{-4}$	0.09866	580	$1.7.10^{-3}$	$3.9.10^{-6}$	25275
3.	$2.5.10^{-6}$	$2.5.10^{-4}$	0.14349	574	$2.5.10^{-3}$	$5.74.10^{-6}$	24997
4.	$3.5.10^{-6}$	$3.5.10^{-4}$	0.21994	628	$3.5.10^{-3}$	$8.04.10^{-6}$	27368
5.	6.10^{-6}	6.10^{-4}	0.35248	587	6.10^{-3}	$1.38.10^{-5}$	25585
6.	8.10^{-6}	8.10^{-4}	0.41620	520	8.10^{-3}	$1.84.10^{-5}$	22658
7.	1.10^{-5}	1.10^{-3}	0.47955	480	1.10^{-2}	$2.3.10^{-5}$	20885

The intervals for specific ($A^{1\%}_{1cm}$) and molar (ε) absorbance of reference standards Losartan Potassium and Valsartan are summarized on Table 4. (A > 0.2) and Table 5. (A < 0.2).

Table. 4 Intervals for specific ($A^{1\%}_{1cm}$) and molar (ε) absorbance for solutions of referense standards Losartan Potassium and Valsartan at A > 0.2.

N:	Сартан	C [g/ml]	C [g/100ml]	$A^{1\%}_{1cm}$	C [g/l]	C [mol/l]	ε
1.	Losartan Potassium (distilled water)	3.10^{-7} ÷ $6.75.10^{-7}$	3.10^{-5} ÷ $6.75.10^{-5}$	12113 ÷ 12778	3.10^{-4} ÷ $6.75.10^{-4}$	$6.5.10^{-7}$÷ $1.46.10^{-6}$	558441 ÷ 589064
2.	Valsartan 99.98% ethanol	6.10^{-6} ÷ 1.10^{-5}	6.10^{-4} ÷ 1.10^{-3}	774 ÷ 800	6.10^{-3} ÷ 1.10^{-2}	$1.38.10^{-6}$ ÷ $2.3.10^{-5}$	33730 ÷ 34840
3.	Valsartan methanol	$3.5.10^{-6}$ ÷ 1.10^{-5}	$3.5.10^{-4}$ ÷ 1.10^{-3}	480 ÷ 628	$3.5.10^{-3}$ ÷ 1.10^{-2}	$8.04.10^{-6}$ ÷ $2.30.10^{-5}$	20885 ÷ 27368

Table. 5. Intervals for specific ($A^{1\%}_{1cm}$) and molar (ε) absorbance for solutions of reference standards Losartan Potassium and Valsartan at A < 0.2.

N:	Сартан	C [g/ml]	C [g/100ml]	$A^{1\%}_{1cm}$	C [g/l]	C [mol/l]	ε
1.	Losartan Potassium (distilled water)	$3.5.10^{-8}$ ÷ 1.10^{-7}	$3.5.10^{-6}$ ÷ 1.10^{-5}	13107 ÷ 16710	$3.5.10^{-5}$ ÷ 1.10^{-4}	$7.5.10^{-8}$ ÷ $2.16.10^{-7}$	604252 ÷ 770348
2.	Valsartan 99.98% ethanol	5.10^{-7} ÷ 2.10^{-6}	5.10^{-5} ÷ 2.10^{-4}	877 ÷ 880	5.10^{-4} ÷ 2.10^{-3}	$1.15.10^{-6}$ ÷ $4.59.10^{-6}$	38221 ÷ 38304
3.	Valsartan methanol	$1.2.10^{-6}$ ÷ $2.5.10^{-6}$	$1.2.10^{-4}$ ÷ $2.5.10^{-4}$	574 ÷ 617	$1.2.10^{-3}$ ÷ $2.5.10^{-3}$	$2.76.10^{-6}$÷ $5.74.10^{-6}$	24997 ÷ 26875

Conclusion.

Specific ($A^{1\%}_{1cm}$) and molar (ε) absorbance for solutions of referense standards Losartan Potassium (λmax = 208 nm) and Valsartan (in 99.98 % ethanol at λmax = 252 nm and in methanol at λmax = 250 nm) for A > 0.2 and A < 0.2 in respective concentration intervals were determined. *For solutions of referense standards Losartan Potassium (λmax = 208 nm) at A > 0.2 (3.10^{-7}* g/ml *÷ $6.75.10^{-7}$* g/ml*), $A^{1\%}_{1cm}$: 12113 ÷ 12778; ε: 558441 ÷ 589064. For Valsartan in 99.98 % ethanol at λmax = 252 nm for A > 0.2 (6.10^{-6}* g/ml *÷1.10^{-5}* g/ml*), $A^{1\%}_{1cm}$: 774 ÷ 800; ε: 33730 ÷ 34840. For Valsartan in methanol at λmax = 250 nm for A > 0.2 ($3.5.10^{-6}$ g/ml ÷ 1.10^{-5} g/ml): $A^{1\%}_{1cm}$: 480 ÷ 628; ε: 20885 ÷ 27368. Specific ($A^{1\%}_{1cm}$) and molar (ε) absorbances for A < 0.2 were:*

[C] [g/ml]	$A^{1\%}_{1cm}$	ε	
$3.5.10^{-8} \div 1.10^{-7}$	13107 ÷ 16710	604252 ÷ 770348	Losartan Potassium
$5.10^{-7} \div 2.10^{-6}$	877 ÷ 880	38221 ÷38304	Valsartan (99.8 % ethanol)
$1.2.10^{-6} \div 2.5.10^{-6}$	574 ÷ 617	24997 ÷26875	Valsartan (methanol

Conflicts of interests.

All authors have none to declare.

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