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Spectrophotometric Determination of Zn(II) in Pharmaceuticals Using (Di Amino di Hydroxy Pyrimidine) as Complexing Agent

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Abstract – Heterocyclic compound diamino and dihydroxy-pyramidine was blended and proposed as chelating specialist for the assurance of follow measures of zinc. Zinc(II) frames the yellow mango colour complex with DADHP (Diaminodihydroxypyrimidine) in 1:3 stoichiometric proportion at pH-6 in acidic corrosive and sodium acetic acid derivation cushion within the sight of pyrideniumchloride as salting out specialist. The most extreme absorbance is seen at 480 nm. The Beer's law is obeyed in the range of 1-6 µg. The molar absorptivity (ε) and Sandell's sensitivity of the complex is 0.1484 x 104 L mol-1 cm-1 and 0.04545 µg cm-1 respectively. The method was successfully applied for the quantification of Zn (II) in pharmaceutical multi vitamin preparations in the presence of other trace elements. The statistical data evaluated reveals the sensitivity and accuracy of the method than the other methods reported.

Keywords: Zinc Determination, Direct and Derivative Spectrophotometry, DADHP

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INTRODUCTION

Zinc is the second most copious transition metal particle in the human body. It is a vital component for all creatures including individuals. Zinc is found in a few sustenances, for example, rice, oats, meat, liver, shellfish, cheeses nuts, in a few catalysts and DNA-restricting proteins. It assumes a noteworthy physiological job in individuals like mammalian proliferation, quality interpretation, insusceptible capacity, mind capacity and pathology. Zinc is a fundamental follow component to vegetation and fauna[1,2], that can cause side effects of deficiency [3,4]and can be dangerous when exposures surpass physiological needs[5,6]. It is a basic constituent of roughly 33% of all proteins[7]. Zinc will assume essential jobs in all replications, Gene articulation, energy transduction, cell flagging, arrangement of endo and exo skeletons and data transfer[8,9]. Checking of zinc in pharmaceuticals and other genuine examples is vital, normally the investigative strategies for the assurance of zinc are neutron initiation analysis (NAA), Atomic retention and outflow spectrophotometry, Inductively coupled plasma spectrophotometry (ICPMS) are the most broadly employed[10]. Be that as it may, in spite of the fact that these techniques are solid and touchy they experience the ill effects of the impediment of being fairly costly, tedious and not in every case promptly[11,12]. So as to accomplish precise, solid and touchy outcomes, spectrophotometric techniques which will in general be more affordable and work escalated are accessible choices, to those strategies requiring progressively advanced instruments. Further, the advancement of subsidiary spectrophotometry is exceptionally valuable methodology for deciding the centralization of parts in the blends with the covering spectra as it takes out a significant part of the interference[13-16]. Further, it was generally utilized in the analysis of pharmaceutical examples protein analysis, ecological example analysis[17].

The determination of trace amounts of Zinc(II) by ultra violet and visible spectrophotometry typically relies on four distinct characteristics[9] apart from the divalent cations. First when coordinated by ligand in any Geometry it has stereo chemical flexibility, second in terms of the hard-soft acid-base theory it has amphoteric property, third divalent zinc(II) has no redox activity[18]. Finally Zn^{2+} has chemical stability and it undergoes the complexation with selected sensitive chromophoric chelator[19]. Among the many reagents reported so far with heterocyclic rings[20-24] the present heterocyclic pyramidine (Scheme 1) has been shown to serve as an

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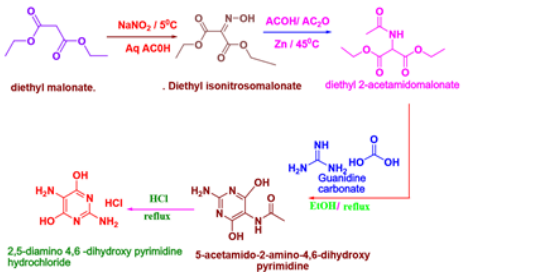
excellent chromophor for the quantification of zinc ions in

aqueous solution. The complexation is found to be quantitative in sodium acetate and acetic acid buffer in the presence of pyridinum chloride [pyridine+2 M HCl] as salting out agent.



Scheme1. Formation of 2,5-diamino-4,6-dihydroxypyrimidine

EXPERIMENTAL

2,5-Diamino-4,6-dihydroxypyrimidine was set up in three stages by the strategies detailed in the literature[25-26]. Diethylmalonote (47.4 mL) was blended with the blend of frosty acidic corrosive and water (1:1.5) and moved in to 500 mL round base jar fitted with mechanical stirrer and thermometer. The jar was cooled in an ice shower 0.65 g of $NaNO_2$ was included parts by keeping up the temperature around 5 ^{0}C with constant blending. After the expansion of all out $NaNO_2$ the ice shower was evacuated blending was proceeded for four hours. The response blend was separated with ether and dissipated to get diethyl-isonitrosomalonote.

Diethyl isonitrosomalonote blended with1:3 blend of acidic anhydride and frosty acidic corrosive in a three necked round base carafe fitted with mechanical stirrer, thermometer and dropping channel. 78.5 g of Zn dust was included little parts by keeping up the temperature at 40-50 ^{0}C pursued by discontinuous cooling. The response blend was sifted with suction, the filtrate and washings were vanished on the steam shower and after that cooled in an ice shower by fast mixing, diethyl acetamidomalonote isolates out as a white crystalline strong. The yield was 35-40 g, M.P was (95-97 ^{0}C).

Diethyl acetamidomalonote was blended with guanidinium carbonate and EtOH refluxed for 36 h, at that point the response blend was sifted by suction. The filtrate and the washings were dissipated and cooled in an ice shower to isolate out the 5-acetamido-2-amino-4,6-hydroxypyrimidine. This was refluxed with 100 mL of 1 M HCl for 1 h at that point cooled in an ice shower sifted pursued by washings with HCl and $CH3)_2CO$ then air dried at 40 ^{0}C to secure the 2,5-diamino-4,6-dihydroxypyrimidine (25 g). The structure was affirmed from Mass, IR, H^1 NMR Spectral examinations.

Preparation of solutions

Every one of the synthetic concoctions were of AnalaR grades from Fisher Scientific Qualigens India. Zn(II)- arrangement Stock standard Zn(II) arrangement was set up by dissolving 0.4397 g of Zn(II) sulfate hepta hydrate in twofold refined water containing 1000 µg/mL. The arrangement was institutionalized by complexometric titration utilizing EDTA27. The working standard solutions were set up by appropriate weakening of the stock arrangement. Support solutions.

Cushion solutions were set up by utilizing 0.1 M Acetic corrosive, 0.1 M sodium acetic acid derivation in the pH extend 2-8. Solutions of assorted particles.

Solutions of differing particles containing 1000 µg/mL were set up by dissolving required measures of salts of the comparing particles in twofold refined water. Ligand arrangement.

The reagent stock arrangement (0.1 M) was set up by dissolving 1.421 g of DADHP in ethylene glycol. This was weakened to the required focus utilizing ethylene glycol. Instruments.

Elico smaller scale processor based twofold bar UV-obvious spectrophotometer SL 210 furnished with 1 cm quartz cells were utilized for spectrophotometric estimations. The pH estimations are made with Elico computerized pH meter L.1 127 model.

General procedure to evaluate different parameters

Direct spectrophotometry

To evaluate the optimum conditions for the determination of Zn(II) an aliquots of solution containing microgram quantities of Zinc(II) were taken in a series of comparison tubes followed by the addition of 2 mL of pyridine and 1 mL of 2 M HCl, then the pH was adjusted to 6 using acetic acid and sodium acetate buffer. The solutions are equilibrated with 5 mL of DADHP (3 x 10^{-3} M) reagent solution and made up to 20 mL with double distilled water. The absorption of the ripen-mango-colour complex was measured at 480 nm against a similarly prepared reagent blank.

The composition of the complex was ensured by mole ratio, slope ratio and Job's continuous variation methods. The calibration plot was obtained in the range 1-6 µg. obeying the Beer's law.

Derivative spectrophotometry

For the above solutions the derivative spectras (1st, 2nd & 3rd order) were recorded with group size 9 and

degree of freedom 5 in the wavelength range 400-600 nm. The derivative peaks were measured by the peak zero method at respective wave length. The peak heights were plotted against the amount of zinc to obtain the calibration. The amount of zinc present in the pharmaceutical sample solutions were computed from the calibration plots, both in direct and derivative spectrophotometry. The calibration plots follow the straight line equation ChemSci Trans., 2013, Y=A+Bx where x is the concentration of solution, Y is the measured absorbance or peak height, A is the intercept and B is the slope. By substituting the experimental data in least square analysis, the equations were calculated as Y=-0.01143+0.0309x for zero order spectrophotometry $\partial A/\partial\lambda$=0.00396+0.00469x for first order derivative, $\partial^2 A/\partial\lambda^2$ = 0.00329+ 0.00247x for second order derivative and $\partial^3 A/\partial\lambda^3$ = 0.00362+0.00200x for the third order derivative spectrophotometry respctively.

RESULTS AND DISCUSSION

The yellow-mango-colour complex of [Zn(II) - DADHP] absorption spectra was examined in the wave length range 400-600 nm against the reagent blank. The complex shows the maximum absorption at 480 nm in acetic acid and sodium acetate buffer (Figure 1).

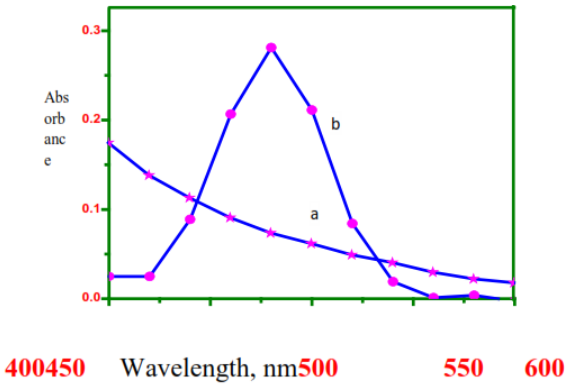


Figure 1: Absorption spectra of (a) DADHP *vs*. buffer blank (b) Zn(II)-DADHA complex *vs*. regent blank Zn(II) = 7.645x10^{-5} M (100 µg) DADHP = 7.62x10^{-5} M *Selection of pH*

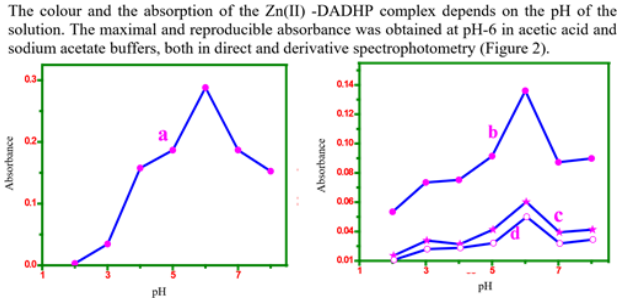


Figure 2. Influence of pH on the absorbance of Zn(II)-DADHP complex (a) Direct spectrophotometry (b) First derivative (c) Second derivative and (d) Third derivative spectrophotometry Zn(II) =7.645x10^{-5} (M (100 µg); DADHP =7.645x10^{-4} M

Effect of salting out agent

The complexation selectivity was investigated in different volumes of pyridine in the

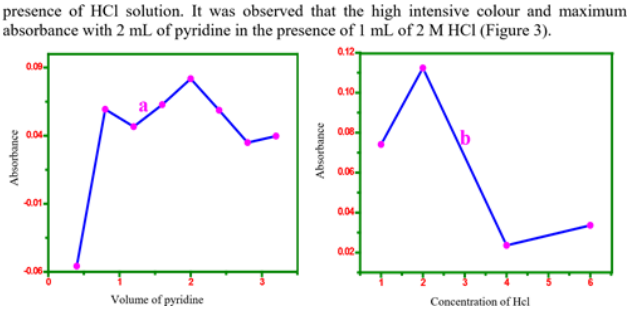


Figure 3. Effect of salting out agent on the absorbance of Zn(II)-DADHP complex (a) Effect of pyridine; (b) Effect of HClconcentrartionZn(II) =7.645x10^{-6} M (10 µg); DADHP = 7.645x10^{-4} M

Effect of reagent concentration

To achieve the complete complexation of Zn(II) and for the maximum colouration hundred folds excess of the reagent was necessary. The ripen-mango-colour formation between the Zn(II) and the reagent was instantaneous and the colour was stable for more than 48 h, (Figure 4).

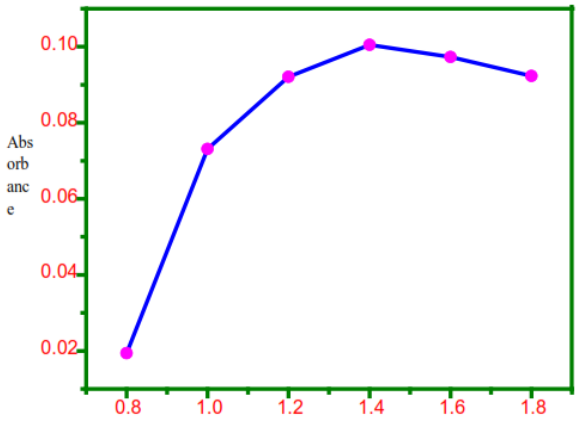


Figure 4: Effect of reagent on the absorbance of Zn(II)-DADHP complex Zn(II) =7.645x10^{-6} M

(10 µg); DADHP = 7.645x 10^{-4} M

ChemSci Trans., 2013,

Composition of the complex

Elating of experimental observations in mole ratio, Job's continuous variation method and slope ratio method confirms Zn(II) forms the 1:6 complex with the reagent and the

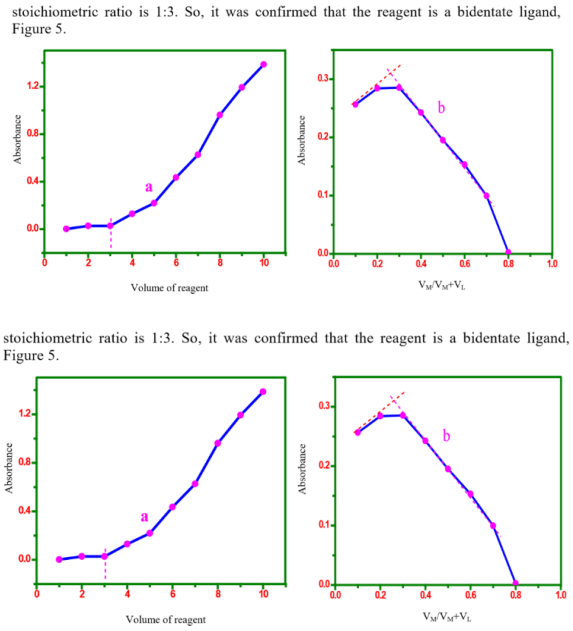
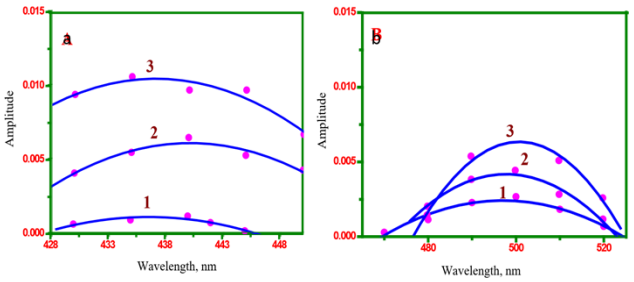


Figure 5. Evaluation of the composition of Zn(II)-DADHP complex; (a) Mole ratio method; Job's continuous variation method; (c) Slope ratio method; Zn(II) =3x10^{-3} M = DADHP

Performance for the calibration of proposed method

Calibration plots constructed in the range 1-6 µg obeying the Beer's law for both direct and derivative spectrophotometry, the molar absorptivity of the complex is 0.1484x10^{4} L.mole^{-1}.cm^{-1} and the Sandell's sensitivity of the method was 0.04545 µg cm^{-2}.In the derivative spectrophotometry it was clearly reflects the peak height is proportional to the amount of Zn(II) present in the solution (Figure 6). The standard deviation correlation co- efficient and other statistical parameters of the method were evaluated to ten replicate determinations (Table 1).



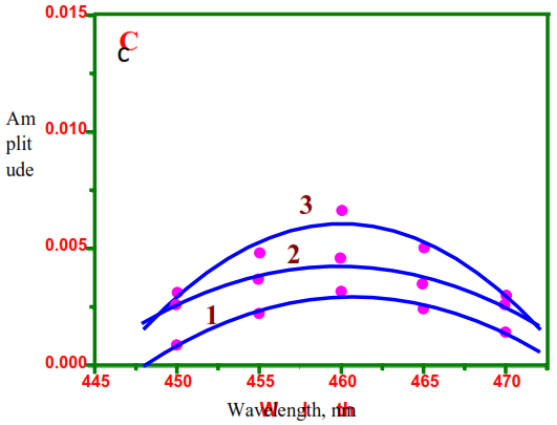


Figure 6. Derivative spectra of [Zn (II)-DADHP] system (a) First order; (b) Second order; Third order Zn(II) µg/mL (1) 0.2; (2) 0.4; (3) 0.6

Pharmaceutical samples

The pharmaceutical samples are prepared by an established procedure to destroy the organic matters present[29-31] based on the use of 0.01 M hydrochloric acid for repeated evaporation. Finally, the residue left over was shaken well with double distilled water, sonicated and filtered. The filtrate was diluted to 100 mL, 2 mL of aliquots of the solution was used for the quantification of zinc. The measured absorbance and amplitude values are compiled with calibration plots (Figure 7) and the results are summarized in Table 2.

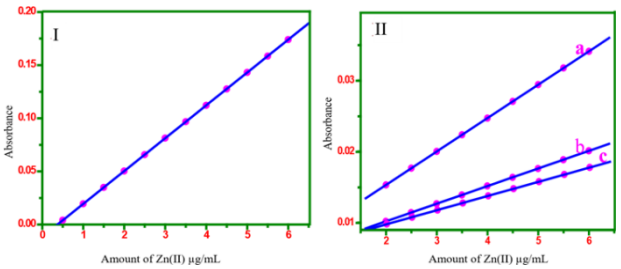


Figure 7. Calibration curve of Zn(II) obeying the Beer's law (0.5-6.0 µg/mL)

(I) Direct spectrophotometry;

(II) A- First; b- Second; c-Third derivative spectrophotometry

Table 2. Determination of zinc in pharmaceutical preparations

Pharmaceuticals	Form	Certified mg/tablet value	Found mg /tablet	Recovery%	RMSEP	REP%	RSD	Test t
ZINCOVIT	$ZnSO_4.H_2O$	22	23.10	105.001	0.1632	3.6546	0.5487	0.1123
1st derivative			18.467	83.940	0.1313	3.9901	0.7108	1.9595
2nd derivative			17.34	78.818	0.3656	3.7235	2.107	0.1902
3rd derivative			22.104	100.473	0.7066	3.6106	0.4777	0.2448
ZEVIT	$ZnSO_4.H_2O$	41.4	43.161	104.25	0.0574	1.3769	0.1330	0.8718
1st derivative			41.931	101.28	0.1580	1.3321	0.3768	0.5324
2nd derivative			43.199	104.34	0.3379	0.2578	0.7823	0.5000
3rd derivative			41.401	100.003	0.6230	0.0734	1.3213	0.2228
ANOFER	ZnO	25	27.028	108.111	0.0116	3.9035	0.0312	1.1709
1st derivative			24.363	97.456	0.2269	0.3121	0.9316	0.0195
2nd derivative			26.132	104.528	0.2276	0.0805	0.8709	1.5728
3rd derivative			19.854	79.460	0.1414	1.2811	7.1199	2.5591
ZINKĈ VIT	$ZnSO_4.H_2O$	22	22.632	102.87	0.11907	0.7312	0.5260	0.1779
1st derivative			17.9146	81.43	0.2488	0.7365	1.3888	0.2466
2nd derivative			14.6972	66.80	0.2593	0.6491	3.3204	0.2329
3rd derivative			13.6539	62.06	0.1359	0.0002	0.9955	0.2164
BECOZINC	$ZnSO_4.H_2O$	54.93	54.73	99.63	0.1426	0.6889	0.2605	0.6652
1st derivative			42.619	77.58	0.5704	5.9147	1.3465	0.0078
2nd derivative			52.076	94.80	0.3376	4.7426	0.6483	1.5960
3rd derivative			54.657	99.50	0.4944	1.1406	0.9045	2.6869
MULTIRICH	$ZnSO_4.H_2O$	31	30.37	97.97	0.2662	2.4333	0.8770	0.3825
1st derivative			32.55	105.00	0.5935	6.4662	1.2731	0.1097
2nd derivative			31.22	100.7	0.5092	7.7580	1.6359	0.0776
3rd derivative			26.43	85.25	0.7151	1.0382	2.7050	0.5081
ZINCOFER		55	54.386	98.87	0.3316	5.642	0.6096	1.1500
1st derivative			47.19	85.80	0.2306	0.1493	0.4883	0.4705
2nd derivative $ZnSO_4.H_2O$ 3rd derivative			28.43	51.59	0.3590	1.7599	1.2627	0.02113
			30.74	55.89	0.7148	1.2634	2.3248	0.2432
BECOSULES		41.4	41.61	100.52	0.0581	0.9657	0.1360	1.4526
			41.38	99.95	0.4788	1.0049	1.1570	0.0575
1st derivative			38.84	93.81	0.4982	1.6505	1.2860	0.3586
2nd derivative $ZnSO_4.H_2O$ 3rd derivative			21.69	52.39	1.0096	0.5968	2.6301	0.2156

Effect of diverse ions

The effect of various anions and cations on the determinations of Zn(II) (4 µg/mL) in the developed optimal conditions was examined and the tolerance limits were defined as the concentration of added solution causing less than ±2% relative error on the absorbance. The results are presented in the Table 3. The interference due to Cu^{2+}, Ni^{2+}, Cd^{2+}, Mn^{2+}, Fe^{2+} and Ag^{+} was eliminated using thiourea, citrate, ascorbic acid, fluoride as appropriate masking agent. But it was noticed that there was strong interference of EDTA in the determination of Zn(II).

Table 3. Tolerance limits of diverse ions in the determination of Zn(II) (4 µg/mL)

Ion	Tolerance limit, µg/mL	Ion	Tolerance limit, µg/mL
Na^{+}	2000	Sulphate	5000
NH_4^{+}	2000	Thiourea	3000
K^{+}	1500	Thiosulphate	3000
Mg^{2+}	1000	Nitrate	2000
Ca^{2+}	1000	Fluoride	2000
Ba^{2+}	1000**	Chloride	2000
Al^{3+}	1000	Ascorbic acid	1000
Cr^{2+}	1000	Iodide	1000
Co^{3+}	1000	Citrate	1000
Pb^{2+}	600	Meta phosphate	1000
Hg^{2+}	500	Phosphate	200
Bi^{2+}	500		
Ni^{2+}	100**		
Fe^{2+}	100**		
Mn^{2+}	100*		
Pd^{2+}	100***		
Ag^{+}	100**		
Cu^{2+}	100**		
Cd^{2+}	100***		

In most of the part of the cases the recuperations are under 100%, in first, second and third subsidiary spectrophotometric estimations. Just in few it is more prominent than 100%. Further, the third subordinate spectrophotometric technique was observed to be more delicate and precise than immediate, first and second subsidiary strategies, in which the recuperations are equivalent to 100% yet more prominent than half. The loss of the objective compounds could be brought about by a few variables. The most critical one is, the examples were estimated after absorption process with acids, in the interim the estimations of standard solutions of Zn(II) for setting up the alignment bends were done with no assimilation procedure. The principle favorable position of the proposed technique is adaptability of the framework, completely robotized and easy to collect and work. Tasteful recuperations were seen in the analysis of pharmaceutical arrangements, only in third subordinate technique the outcomes are great concurrence with the affirmed qualities.

Table.4. Comparison of Direct and Derivative Spectrophotometry

Pharmaceuticals	Direct	First derivative	Second derivative	Third derivative
ZINCOVIT	105.001	83.940	78.818	100.473
ZEVIT	104.25	101.28	104.34	100.003
ANOFER	108.111	97.456	104.528	79.460
ZINKĈ VIT	102.87	81.43	66.80	62.06
BECOZINC	99.63	77.58	94.80	99.50
MULTIRICH	97.97	105.00	100.7	85.25
ZINCOFER	98.87	85.80	51.59	55.89
BECOSULES	100.52	99.95	93.81	52.39

CONCLUSION

The results shown in the Table (4) indicates the recovery of Zn(II) from the pharmaceutical samples.

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