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Research Article

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SPECTROPHOTOMETRY METHOD FOR THE ANALYSIS OF ZOLMITRIPTAN IN FOMULATIONS

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ABSTRACT

The colorometric methods developed and validated for analysis of Zolmitriptan. The following reagents are used for analysis. i.e MBTH at 570 nm, TPoo at 490nm, Brucine at520 nm, A.Red.S at 420 nm, 2,4 bi pyrimidine at 590 nm, 1,10 Phenanthroline at 520 nm, FCF at420 nm, $K3FeCN_6$ at 780nm,PNA at 560 nm, 1,10 WFBBL at 600 nm.All methods are very accurate and results are within the limit. Our methods applicable to quantification of zolmitriptan in Bulk drugs and in formulations.

Key words: Zolmitriptan, accuracy, precision, linearity, colorimetry,

INTRODUCTION

Zolmitriptan is a selective serotonin receptor agonist of the 1B and 1Dsubtypes. It is a triptan, used in the acute treatment of migraine attacks with or without aura and cluster headaches. Zolmitriptan is a synthetic tryptamine derivative and appears as a white powder that is readily soluble in water. Zolmitriptan is used for the acute treatment of migraines with or without aura in adults. Zolmitriptan is not intended for the prophylactic therapy of migraine or for use in the management of hemiplegic or basilar migraine. Zolmitriptan is available as a swallowable tablet, an oral disintegrating tablet, and a nasal spray, in doses of 2.5 and 5 mg. People who get migraines from aspartame should not use the disintegrating tablet (Zomig ZMT), which contains aspartame.[2] Zolmitriptan should not be given to patients with ischemic heart disease (angina pectoris, history of myocardial infarction, or documented silent ischemia) or to patients who have symptoms or findings consistent with ischemic heart disease, coronary artery vasospasm, including Prinzmetal's angina, or other significant underlying cardiovascular disease.

Zolmitriptan may increase blood pressure, it should not be given to patients with uncontrolled hypertension, should not be used within 24 hours of treatment with another 5-HT1 agonist, or an ergotamine-containing or ergot-type medication like dihydroergotamine or methysergide, and should not be administered to patients with hemiplegic or basilar migraine.Concurrent administration of MAOI or use of zolmitriptan within 2 weeks of discontinuation of MAO-A inhibitor therapy is contraindicated.

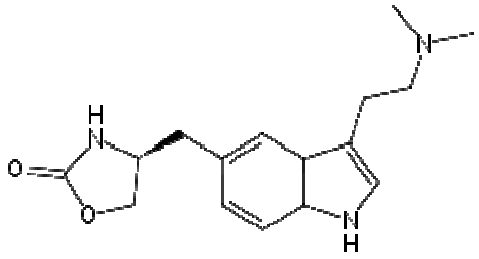


Figure-1: Structure of Zolmitriptan

MATERIALS AND METHODS

Spectro photometric Methods Development and validation:

Instrumentation:

Spectral and absorbance measurements are made with Genesys 10 UV split beam Spectrophotometer procured from Thermo Scientific Company marketed by Merck.

Standard and Sample solution of Zolmitriptan

10 mg of Frova (bulk dosage form), 10 mg of API was dissolved in 100 ml of was brought to 100 ml with methanol to give a concentration of 100 ppm.

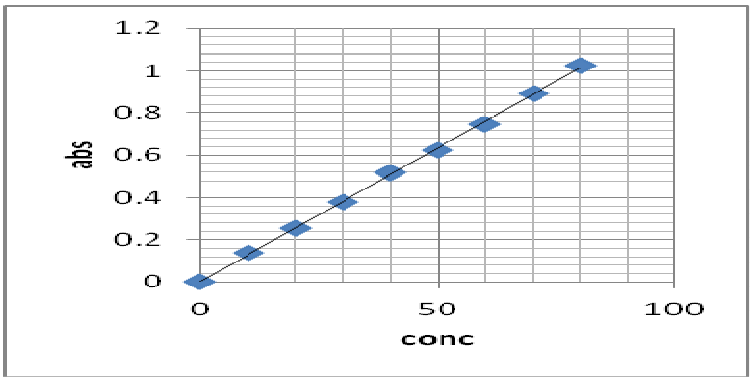
1. WFBBL Method:

WFB BL Solution: Prepared by dissolving Weigh accurately 200 mg of Wool Fast Blue and is dissolving in 100 mL of distilled water.

Buffer solution (pH 1.5): Prepared by mixing 289 mL of glycine solution (37.52 g glycine and 29.24 g of NaCl were dissolved in 500 mL distilled water) with 711 mL of 0.1 M HCl and the pH of solution was adjusted to 1.5.

Procedure: Into a series of 125 mL separating funnels containing aliquots of standard drug solution [0.5 –2.5 mL 20 µg/mL, 0.5 - 2.5 mL, 80 µg/mL, 6.0 Ml] of buffer solution [pH 1.5 (M_{1a}) or 0.1 M HCl] and 2.0 mL of dye solution WFB BL is added. The total volume of aqueous phase in each separating funnel was adjusted to 15mL with distilled water and 10 mL of $CHCl_3$ was added. The contents were shaken for 2 min. The two phases were allowed to separate and the absorbance of the separated organic layer was measured at 590 nm against a similar reagent blank after 10 min. The amount of drug was deduced from the calibration curve.

S.NO	CONCETRATION µg/ mL	ABSORBANCE
1	10	0.139
2	20	0.256
3	30	0.381
4	40	0.517
5	50	0.625
6	60	0.748
7	70	0.893
8	80	1.024



2. TPOOO Method:

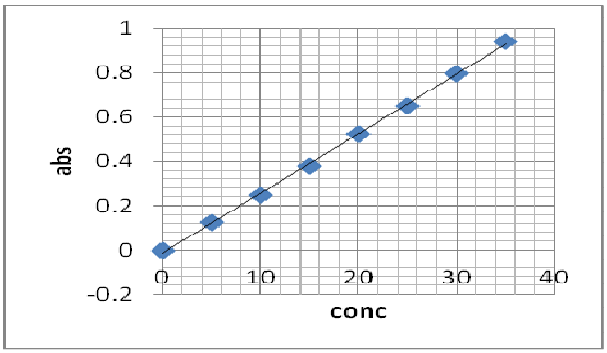
TP ooo solution: Weigh accurately 200 mg of tropaeolin ooo and is dissolved in 100 mL of distilled water.

HCl solution: dissolve 8.6 mL of concentrated hydrochloric acid in 1000 mL of distilled water and standardized.

Chloroform: AR grade chloroform was used.

Procedure: Into a series of 125 mL separating funnels containing aliquots of standard drug solution [0.5 –2.5 mL 20 µg/mL , 0.5 - 2.5 mL, 80 µg/mL], 6.0 mL of buffer solution [pH 1.5 or 0.1 M HCl (M_{1b})] and 2.0 mL of dye solution TPooo is added. The total volume of aqueous phase in each separating funnel was adjusted to 15mL with distilled water and 10 mL of $CHCl_3$ was added. The contents were shaken for 2 min. The two phases were allowed to separate and the absorbance of the separated organic layer were measured at 480 nm against a similar reagent blank after 10 min. The amount of drug was deduced from the calibration curve.

S.NO	CONCETRATION µg/ mL	ABSORBANCE
1	5	0.125
2	10	0.247
3	15	0.379
4	20	0.523
5	25	0.652
6	30	0.798
7	35	0.941



3. PNA Method:

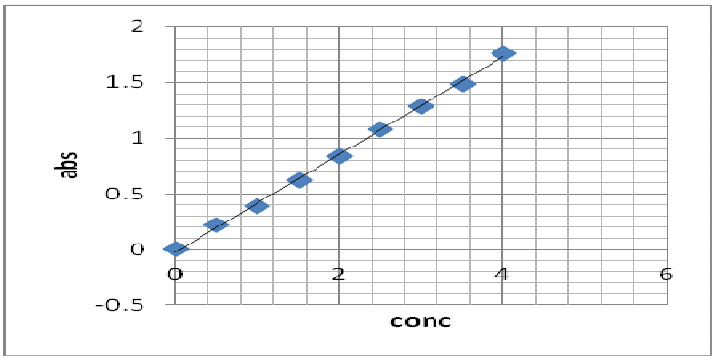
PNA solution: Dissolve 100 mg of PNA in 100 ml of 0.2 M HCl.

$NaNO_2$ solution: Dissolve 100 mg of $NaNO_2$ in 100 mL of distill water.

NaOH solution: Weigh accurately 4g of NaOH , dissolved in few ml of distill water and made up to the mark in a in 100 ml volumetric flask with distill water.

Procedure: Into a series of 10 ml graduated test tubes 1.0 ml of PNA solution and 1.0 ml of $NaNO_2$ solution were successively added and allowed to stand for 2 min. Later, aliquots of the standard drug delivered into the test tubes. Then 1.5 ml of NaOH solution was added and the volume in each tube was made up to 10 ml distill water. The absorbance was measured at 480 nm against a reagent blank.

S.NO	CONCETRATION µg/ mL	ABSORBANCE
1	0.5	0.217
2	1	0.386
3	1.5	0.623
4	2	0.836
5	2.5	1.081
6	3	1.287
7	3.5	1.486
8	4	1.762



4. Potassium ferricyanide Method:

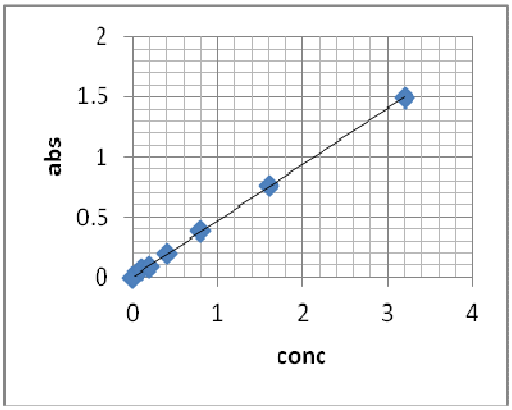
Potassium ferricyanide solution: Dissolve 100 mg of pot. Ferricyanide in 100 mL of Double distills water.

Fe(III) solution (Wilson Labs, 0.054 %, 3.32 X10-3 M) : Prepared by dissolving 54 mg of anhydrous ferric chloride in 100 mL of distill water.

HCl solution (1N) : solution is Prepared by diluting 86 ml of conc. HCl to 1000 mL with distill water and standardized.

Procedure: Into a series of 10ml of calibrated tubes, aliquots of standard drug were transferred and 1 mL of Fe(III) solution was added. The tubes were stopper immediately and shaken well for 5 min. Then 0.5 ml of pot. Ferricyanide solution was added into each tube and was closed with lids immediately. After 5 min, 1 mL of 1N HCl was added and the final volume was made upto 10 mL with distill water. The absorbance of the solution in each tube was measured immediately at 740 nm against a similar reagent blank.

S.NO	CONCETRATION µg/ mL	ABSORBANCE
1	0.1	0.217
2	0.2	0.386
3	0.4	0.623
4	0.8	0.836
5	1.6	1.081
6	3.2	1.287



5. MBTH Method:

MBTH solution: Solution is Prepared by dissolving 200 mg of MBTH in 100 mL of distill water.

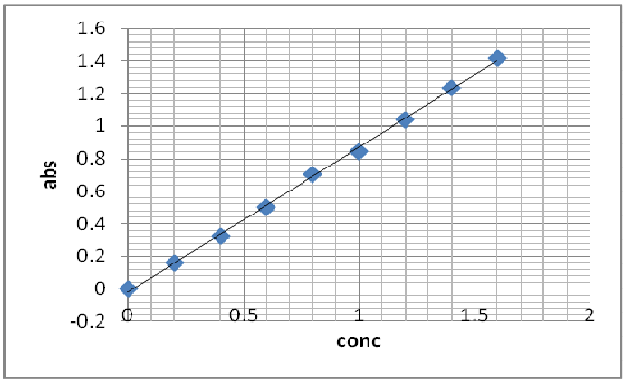
Fe(III) solution: Solution is Prepared by dissolving 250 mg o Fe(III) in 100 mL of distill water.

NaOH solution: Solution Prepared by dissolving 400 mg of NaOH to 100 mL of distill water and standardized.

Procedure: 1.0 mL of standard chloroformic BUD solution containing were transferred into a series of 25 ml calibrated tubes and gently evaporated on a boiling water-bath to dryness. Then 1 mL of water, 0.5 ml of 0.5% MBTH and 0.5 ml of 0.1 N NaOH were added to each tube. The contents were heated for 10 min in a water bath at 100 ^{0}C and cooled for 5 min in a water bath at 15 ^{0}C. Then 0.5 mL of 1N HCl

and 2 ml of Fe(III) solutions were added successively and kept side for 1 hr. The absorbance was measured at 620 nm against a reagent blank prepared in a similar way.

S.NO	CONCETRATION µg/ mL	ABSORBANCE
1	0.2	0.157
2	0.4	0.325
3	0.6	0.499
4	0.8	0.702
5	1.0	0.846
6	1.2	1.036
7	1.4	1.235
8	1.6	1.42



6. Brucine Method:

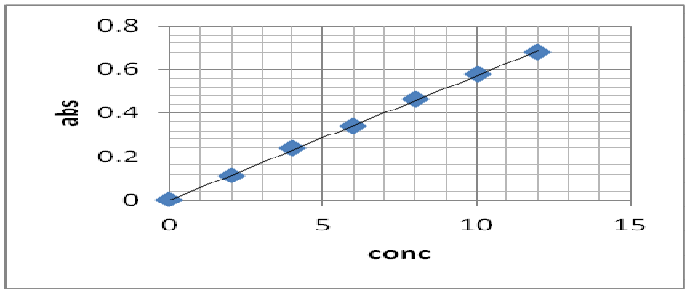
Brucine 0.2%: Weigh accurately 200 mg of Brucine and is dissolved in 100 ml distill water.

$NaIO_4$: Analytical grade is used.

H_2SO_4 (2.3M) :Dissolve 6.38 ml of 18 M H_2SO_4 in 100 ml distill water.

Procedure: Into a series of 10ml of calibrated tubes, aliquots of standard drug were transferred and add 3 mL of Brucine , 15 mL of $NaIO_4$, 2 mL of H_2SO_4 is added and total volume made upto 10 ml with distill water then heat for 15 mts. Cool, Readjust volume to 10 ml, measure absorbance at 510 – 520 nm, Stable for 40 mts.

S.NO	CONCETRATION µg/ mL	ABSORBANCE
1	2	0.157
2	4	0.325
3	6	0.499
4	8	0.702
5	10	0.846
6	12	1.036

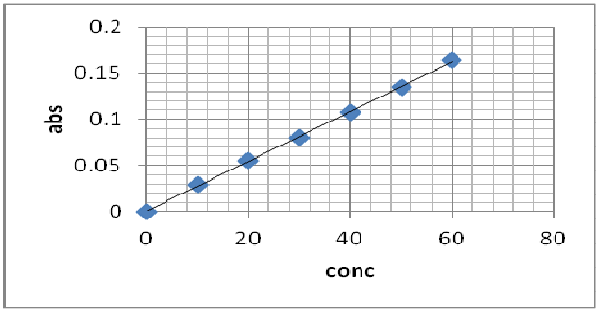


7. F.C.F METHOD

F.C. reagent (2N) supplied by S.d. Fine chem. India, Ltd., was used by diluting 50 mL to 100 mL with distilled water. Sodium hydroxide solution (4%) was prepared by dissolving 4g of sodium hydroxide in 100 mL of distilled water. 300 µg/mL Stock reference solution was freshly prepared from pure sample of Zolmitriptan by dissolving 0.03 g in 100 mL of distilled water. General procedure In to 10 mL measuring flasks, different aliquots of working standard solution were transferred to provide final concentration range 30.0 – 150.0 µg mL-1. To each flask, 1.5 mL of sodium hydroxide and 1.5mL of F-C

were successively added and kept a side for 5 min. The solutions were made up to volume with distilled water. The absorbance of each solution was measured at 760 nm against the reagent blank. The calibration graph was then prepared by plotting the absorbance versus concentration of the drug. The concentration of the unknown was read from the calibration graph or computed from the regression equation.

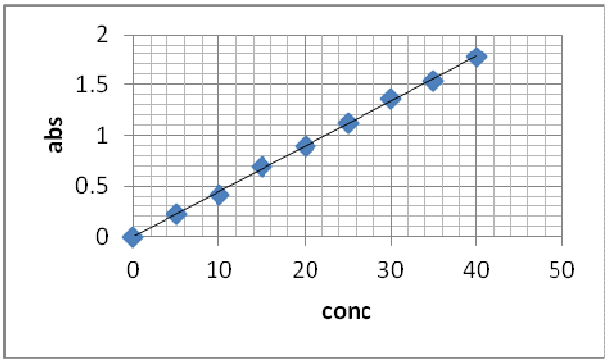
S.NO	CONCETRATION µg/ mL	ABSORBANCE
1	10	0.029
2	20	0.055
3	30	0.08
4	40	0.108
5	50	0.135
6	60	0.164



8. 1, 10 phenanthroline Method

To the working concentrated drug solution, 1 ml 1,10 Phenanthroline reagent added and diluted up to 50 ml. Absorbance measured at 520 nm wavelength. Fixed wavelength linearity, precision, recovery stability studies are carried out at this fixed wave length.

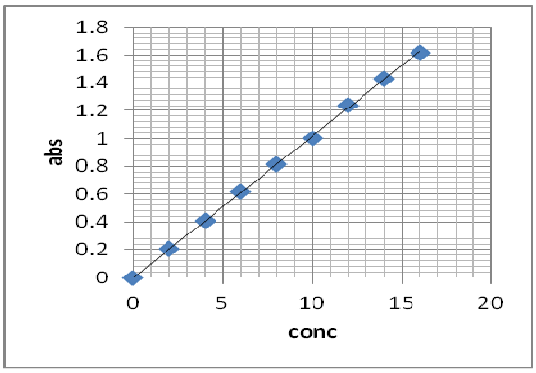
S.NO	CONCETRATION µg/ mL	ABSORBANCE
1	5	0.229
2	10	0.412
3	15	0.689
4	20	0.893
5	25	1.114
6	30	1.356
7	35	1.537
8	40	1.772



9. 2, 2 Bi pyrimidine

To the working concentrated drug solution, 2 ml 2, 2 Bi pyrimidine reagents added and diluted up to 25 ml. Absorbance measured at 590 nm wavelength. Fixed wavelength linearity, precision, recovery stability studies are carried out at this fixed wave length.

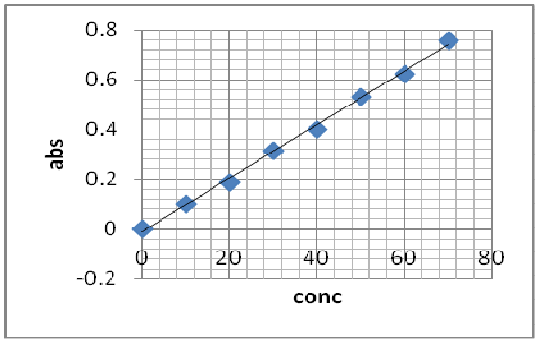
S.NO	CONCETRATION µg/ mL	ABSORBANCE
1	2	0.205
2	4	0.412
3	6	0.621
4	8	0.817
5	10	1.006
6	12	1.243
7	14	1.43
8	16	1.62



10. Alizarin Red S

To the working concentrated drug solution, 0.5 ml Alizarin Red .S reagents added and diluted up to 100 ml. Absorbance measured at 420 nm wavelength. Fixed wavelength linearity, precision, recovery stability studies are carried out at this fixed wave length.

S.NO	CONCETRATION µg/ mL	ABSORBANCE
1	10	0.0997
2	20	0.189
3	30	0.312
4	40	0.402
5	50	0.531
6	60	0.624
7	70	0.756



RESULTS AND DISCUSSION

Table 1: Spectrophotometric conditions

TEST	MBTH	FCF	$K_3Fe(CN)_6$	PNA	WFBBL
Linearity range	0.2-1.6 ppm	10-60 ppm	0.1-3.2ppm	0.5-4ppm	10-80 ppm
Precision R.S.D	0.763	1.801	0.763	0.262	0.22
Slope	0.0.4677	0.0027	0.4677	0.4371	0.01264
Intercept	0.0.00519	0.000464	0.00519	-00.2122	0.0034
Correlation coefficient	0.9998	0.9998	0.9998	0.9993	0.9997
Stability period	160 min	135 min	160 min	135 min	160 min
Accuracy	99.4%	99.3%	99.4%	98.7%	99.8%
Wave length	570 nm	420 nm	780 nm	560 nm	600 nm

Table.2 Spectrophotometric conditions

TEST	Brucine,	A.Red.S,	2,2 bi pyrimidine	1,10Phenanthroline	TPOOO
Linearity	2-12 ppm	10-70 ppm	2-16	5-40 ppm	5-35ppm
Precision R.S.D	0.79	0.46	0.24	1.5	0.35
Slope	0.057268	-0.010749	0.1014	0.0444	0.026931
Intercept	0.001821	-0.01202	0.005857	0.00125	-0.01317
Correlation coefficient	0.9997	0.999	0.9997	0.9993	0.99959
Stability period	145 min	180 min	160min	175 min	140 min
Accuracy	98.4 %	99.5%	99.2%	98.9%	99.8%
Wave length	520 nm	420 nm	590 nm	520 nm	490 nm

From above results, ARS method is user free because of wide linearity range i.e 10-70 ppm, and ARS method is also very stable up 180 min and 99.5 % accurate. According linearity range MBTH method is sensitive i.e. 0.2 ppm. Reaming all methods are accurate within the range 98.3%-99.5%, all methods are stable more than 120 min.

CONCLUSION

These colorimetric methods are more accurate and stable. Every method has applicable for rapid analysis of zolmitriptan in bulk and Formulations.

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