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Analytical method development and validation of L-Carnitine L-Tartarate in Pharmaceutical Dosage forms (Multivitamin tablets) using non aqueous titration

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ABSTRACT

The Non aqueous titration method was developed for quantitave analysis of L- Carnitine L-Tartarate in multivitamin tablets. The Non aqueous titration method was carried out using 0.1 N Perchloric acids. The present analytical method was validated according to ICH guidelines (ICH,Q2(R1)). The calibration curve was found to linear with correlation coefficient (r^2=0.99995), Bias (-0.35) in the range of 50 to 150 % of standard solution. The precision and recovery were determined and all the parameter value found within acceptance limit. The value for both method and intermediate precision were found to 0.57 % and recovery found to 99.11 to 99.59 %. The validation parameter study was method precision, intermediate precision, Linearity and recovery. This is a convenient, precise and rapid accurate method for the estimation of L-Carnitine L-Tartarate in Bulk and Pharmaceutical dosage forms (Multivitamin Tablets).

Keywords: AIDS, Linearity, Correlation coefficient, Bias, Precision and Recovery

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INTRODUCTION

In the literature survey it is observed that there are few analytical methods reported for the estimitation of L-Carnitine L- Tartarate in pharmaceutical tablet formulation. L-Carnitine is an essential drug commercially available as in tartaric acid form and chemically described as Bis [(2R)-3-carboxy-2-hydroxy-N,N,N-trimethyl-1-propanaminium] (2R,3R)-2,3-dihydroxysuccinate . L-Carnitine L-Tartarate is a white crystalline powder with a Molecular weight 472.49 ,Molecular formula $C_{18}H_{36}N_2O_{12}$ and highly soluble in Water.L-Carnitine an amino acids that is naturally produce in the body which is important for Heart,Brain function and Muscle movement.Due to too low of L-Carnitine disease may be Chest Pain,High Chlosterol,Brain development disorder,Diabetes and AIDS etc.The biologically active form of L-carnitine is a carrier molecule that transports activated long chain fatty acids from the cytosol to mitochondria where fatty acids are oxidized resulting in ATP production.The typical dose of L-Carnitine is in between 1 to 3 grams per day.This testing method is suitable when L-Carnitine L-Tartarate is in combination with Mecobalamin and folic Acid in tablets dosase form.Literature survey reveals that Non-aqueous titration methods used for quantitative estimation of L-Carnitine L-Tartarate is very Simple, accurate and low costing analysis.In the proposed methods optimization and validation are reported.

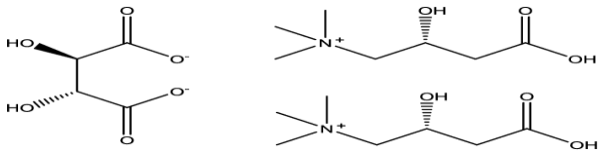

Fig. -1: Chemical structure of L-Carnitine L-Tartarate

MATERIAL AND METHODS

Reagents and Chemical: Reference standard of L-Carnitine L-Tartarate were used for spiking in recovery study. Glacial Acetic Acid, Crystal Violet Indicator and 0.1M Perchloric acid of A.R grade were used. The combined tablet formulation purchased from local market.

Quantitative determination of L-Carnitine L-Tartarate: Crush 10 tablets and weigh crush powder equivalent to 750 mg of L-Carnitine-L-tartrate of label claim mentioned on carton or strip of tablets into 250 ml volumetric flask,dissolve it into 60 ml of glacial acetic acid, add 2-3 drops of crystal violet indicator and titrate with 0.1M Perchloric Acid to green end point. Blank determination was performed out for necessary correction.

1ml of 0.1 M Perchloric Acid consumed is equivalent to 0.047249 g of L-Carnitine L- Tartarate.

Calculation

L-Carnitine L- Tartarate (mg/tab) (A) =

$$\frac{N \times V1 - V2 \times 0.047249 \times AW \times 1000}{0.1 \times W \times 2}$$

$$L - \text{Carnitine (mg/tab)} = \frac{A \times 32.24}{47.249}$$

Where,

N = Normality of Perchloric acid
V1 = Consumed volume due to sample
V2 = Consumed volume due to Blank
W = weight of the Sample in mg
AW = Average Weight of tablets
47.249 = Factor due to L-Carnitine L- Tartarate
32.24 = Factor due to L-Carnitine

VALIDATION PARAMETER:

Precision: The Method precision and Intermediate precision were studies by six different preperation of Test sample and its acceptance crieteria for % RSD of result should not more than 2.0%.The % RSD was determined by using the following equation.

$$\% \text{ RSD} = \frac{SD \times 100}{X}$$

Where, SD = Standard deviation X = Airthmatic Mean

Linearity : The Linearity was obtained using five different concentration of L-Carnitine L-tartarate standard solution 50%,80%,100%,120% and 150% .The consumed volume of each standard solution and standard weight were recorded. The Value for correlation coefficient,Slope, Intercept and Bias was calculated.

Accuracy : To perform accuracy ,recovery studies was carried out by adding standard weight to sample solution (Previously neutralized Sample solution) by three different concentration 50%,100% ,150% and each triplicate preperation. The Percentage recovery is calculated by the following equation.

$$\text{Percentage recovery} = \frac{\text{Titre Value} \times 100}{\text{True Titre Value}}$$

RESULT AND DISCUSSION

After obtaining data evaluating their statistical parameters which include Linearity,precision and Accuracy .The % RSD of result found for Method precision is 0.570 % and for Intermediate precision **(**Ruggedness) is also 0.570 % , which represents good precision of testing method. The results are listed in Table 1 , Table 2 and Table 5**.**

Table 1: Method Precision

Sr.No	Weight Taken	Normality	Burette Reading	Results(in %)
01	752.35	0.0996	24.2	98.98
02	751.16	0.0996	24.1	98.73
03	753.68	0.0996	24.3	99.21
04	748.95	0.0996	24.1	99.02
05	749.25	0.0996	24.4	100.21
06	755.35	0.0996	24.5	99.81
		Mean		99.33
		Standard Deviation		0.566
		RSD (Limit:Not more than 2.0%)		0.570

Table 2: Ruggedness (Intermediate Precision)

Sr.No	Weight Taken	Normality	Burette Reading	Results (in %)
01	751.69	0.0996	24.3	99.48
02	748.95	0.0996	24.2	99.43
03	755.69	0.0996	24.1	98.14
04	749.68	0.0996	24.3	99.74
05	748.36	0.0996	24.1	99.10
06	749.65	0.0996	24.2	99.34
		Mean		99.20
		Standard Deviation		0.563
		RSD (Limit:Not more than 2.0%)		0.570

LINEARITY : The Value for Correlation coefficient (0.99995) and Bias (-0.35) are found good closeness to Acceptance limit mentioned in Table 3.

Table 3 : Linearity Related Acceptance Value

Sr.No	Concentration	Burette Reading(Consumed Volume)
01	250.32 mg (50%)	12.1
02	402.15 mg (80%)	19.2
03	501.25 mg (100%)	24.1
04	601.3 mg (120%)	28.9
05	750.32 mg (150%)	36.2
Regression Values	Correlation(Limit :Not less than 0.9999)	0.99995
	Slope	0.05
	Intercept	-0.09
	Bias (Limit: ±3)	-0.35

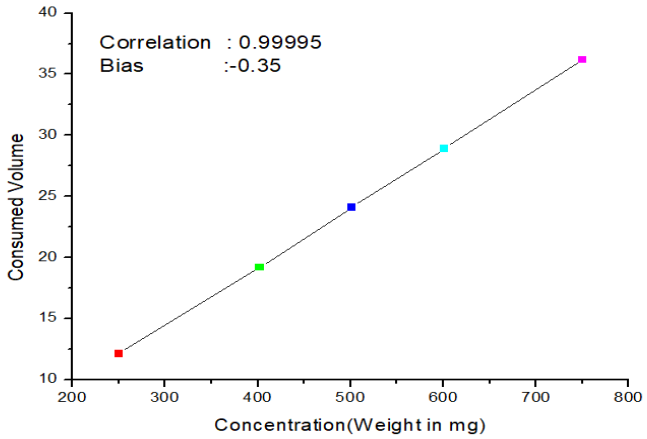

Figure 2 : Linearity Curve Between Concentration and Consumed Volume

ACCURACY : Accuracy was determined by three different concentration (50%,100% and 150%) and each triplicate preperation.The percentage recovery was found from 99.11% to 99.59 % listed in Table 4,which confirms the Accuracy of proposed method.

Table 4: Recovery and Accuracy

Spike	Weight Taken	%Assay	Results (in %)
50% -01	375.56	99.14	Mean : 99.17 % RSD : 0.64 %
50% -02	376.15	99.81	
50% -03	374.69	98.55	
100% -01	751.26	99.53	Mean : 99.59 % RSD : 0.33 %
100% -02	751.29	99.94	
100% -03	746.85	99.3	
150% -01	1125.68	98.96	Mean : 99.11 % RSD : 0.14 %
150% -02	1126.58	99.15	
150% -03	1128.95	99.22	
		RSD Limit:Not more than 2.0%	

Table - 5: Summary of all Results

Validation parameter	Results
Linearity	
(a) Correlation Coefficient	0.99995
(b) Bias	-0.35
Precision	
(a) Method Precision	0.57%
(b) Intermediate Precision	0.57%
Accuracy	
(a) 50 %	99.17 %
(b) 100%	99.59%
(c) 150%	99.11%

Roghaieh Khoshkam and Minoo Afshar develop RP HPLC method for determination of L-Carnitine L- Tartarate which is high cost analysis in comparison to Titration method. However the reported Non aqueous titration method of L-Carnitine L- Tartarate is low cost analysis completed in short duration.This methods can be used for routine analysis of L-Carnitine L- Tartarate in multivitamin tablet.

CONCLUSION

The proposed non-aqueous titration method was found to precise, accurate, rugged, Linearise and results are accordance with ICH Guidelines. Hence this method can easily and conveniently adopt for routine analysis of L-Carnitine L- Tartarate in pharmaceutical dosage forms.

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