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A COMMON TECHNIQUE WAS APPLIED FOR CARDIOVASCULAR DRUGS RECOVERIES IN SAME MOBILE PHASE IN DIFFERENT TYPES COLUMNS BY UPLC METHOD

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ABSTRACT- A rapid and stability-indicating ultra-performance liquid chromatography method was developed for quantification of Nebivolol, Valsartan, Ezetimibe, Atorvastatin, Canagliflozin to get some more advantages over other methods already developed in different methods we can single method. The method was developed according to ICH and to develop the calibration curve for all drugs using this method. In this method a simple isocratic conditions of mobile phase comprising 0.1% TFA and methanol in a ratio of 30:70, v/v at a flow rate of 0.5 mL/minute over kinetex C18, 100 × 4.6 mm, 2.6µm column at room temperature was maintained. The method showed excellent linear response with correlation coefficient (R^2) values of 0.999 for Nebivolol, Valsartan, Ezetimibe, Atorvastatin, Canagliflozin which was within the limit of correlation coefficient ($R^2 \geq 0.995$).

Keywords: UPLC, Nebivolol, Valsartan, Ezetimibe, Atorvastatin, Canagliflozin.

Introduction

Valsartan, sold under the brand name Diovan among others, is a medication used to treat high blood pressure[1], heart failure, and diabetic kidney disease.[2] It is a reasonable initial treatment for high blood pressure. It is taken by mouth. Versions are available as the combination valsartan/hydrochlorothiazide, valsartan/amlodipine, valsartan/amlodipine/hydrochlorothiazide, or valsartan/sacubitril.[3]

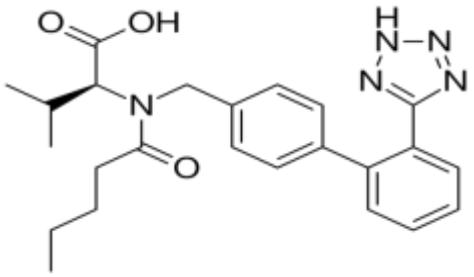

Fig 1: Chemical structure of Valsartan

Atorvastatin, sold under the brand name Lipitor among others, is a statin medication used to prevent cardiovascular disease in those at high risk and to treat abnormal lipid levels. For the prevention of cardiovascular disease[4], statins are a first-line treatment[5].It is taken by mouth.

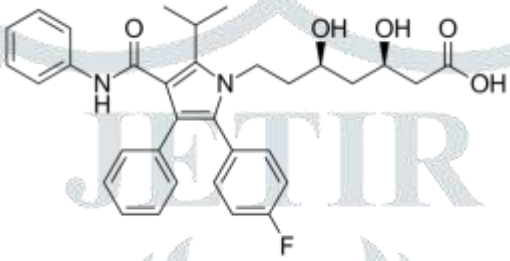

Fig 2: Chemical structure of Atorvastatin

Canagliflozin, sold under the brand name Invokana among others, is a medication used to treat type 2 diabetes. It is a third-line medication [6] to be tried after metformin, a first-line medication for type 2 diabetes.It is used together with exercise and diet. It is not recommended in type 1 diabetes[7].

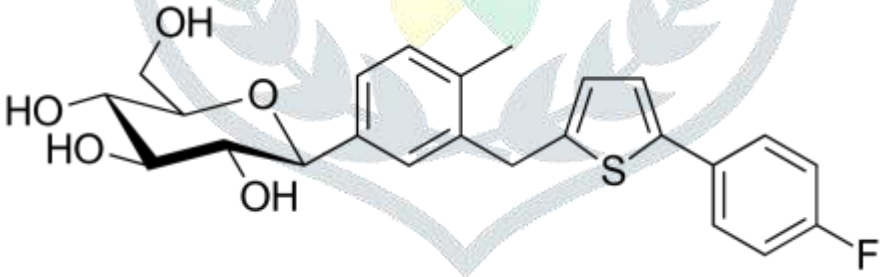

Fig 3: Chemical structure of Canagliflozin

Ezetimibe is a medication used to treat high blood cholesterol and certain other lipid abnormalities.Generally it is used together with dietary changes and a statin. Alone, it is less preferred than a statin[8].It is taken orally.

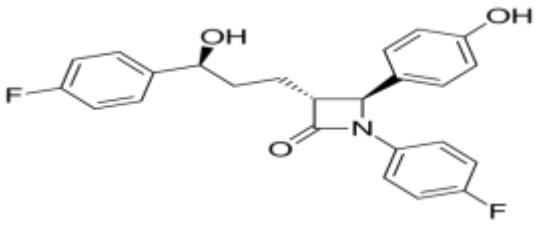

Fig 4: Chemical structure of Ezetimibe

Nebivolol is a beta blocker used to treat high blood pressure [9] and heart failure. As with other β-blockers, it is generally a less preferred treatment for high blood pressure. It may be used by itself or with other blood pressure medication. It is taken by mouth.

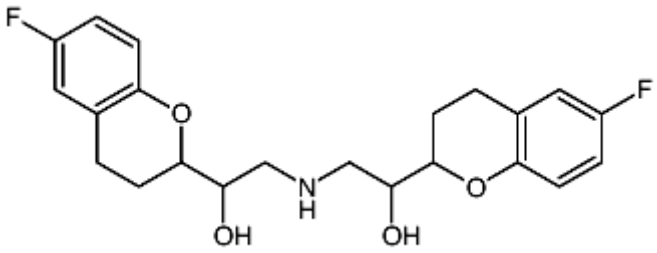

Fig 5: Chemical structure of Nebivolol

MATERIALS AND METHOD

Nebivolol, Valsartan, Ezetimibe, Atorvastatin, Canagliflozingift sample was provided by glenmark pharmaceuticals, mumbai. Water, acetonitrile, TFA , methanol UPLC grade from merck company, mumbai.

Selection of wavelength of detection

Nebivolol, Valsartan, Ezetimibe, Atorvastatin, Canagliflozinstandard solution of 100 ppm was scanned at 200-400 nm and UV Spectrum was recorded. By observing the spectrum of standard solution, λmax of 225 nm was taken for trails to develop the proposed method.

Instrumentation and Chromatographic Conditions

Ultra performance liquid chromatography Agilent 1200 series equipped with PDA detector and kinetex C18(100 mm × 4.6 mm, 2.6µm) containing 5 µm particle size column was used. Mobile phase comprising of 0.1% TFA :methanol in a ratio 30:70 % v/v at a flow rate of 0.5 ml/min and the effluent was detected at 225nm. The Column temperature was maintained at ambient and the volume of injection is 5µL.

Preparation ofMobile phase- A

0.1% TFA was prepared by transferred 1ml of tri flouoro acetic acid in 1000 mL of uplc grade water. solution was filtered through 0.45 µ Millipore Nylon filter.

Preparationof Mobile phase - B

Methanol

Preparationof Mobile phase A+B:

Take mobile phase a and b in the ratio of 30:70 v/v.

Diluent : Water and methanol in the ratio of 30:70 v/v

Preparation of solutions

Standard stock solution: Weigh each 5 mg of Nebivolol, Valsartan, Ezetimibe, Atorvastatin, Canagliflozinwas accurately weighed and transferred into 10 ml volumetric flaskadd 7 ml diluent sonicate for 30 minutes to dissolve the contents completely then make up to the mark with diluent.

Working Standard solution: 1mL of standard stock solution was pipetted into 10 mL volumetric flask and diluted up to the mark with diluent 2 and filtered through 0.45µ Millipore Nylon filter to obtained concentration of 10 µg/ml.

Method development:

Standard solution:

Nebivolol, Valsartan, Ezetimibe, Atorvastatin, Canagliflozin is weighed 5mg of each and taken in 10ml volumetric flask and make up to the mark with the suitable solvents (water,methanol). Pipette out 1ml analyte solution of each volumetric flask is taken in another 10ml volumetric flask and make up to the mark with suitable solvents (water, methanol).

Linearity 20%:

0.2 ml of stock solution is taken in to the 10ml volumetric flask and make up to the mark with methanol.

Linearity 40%:

0.4 ml of stock solution is taken in to the 10ml volumetric flask and make up to the mark with methanol.

Linearity 60%:

0.6 ml of stock solution is taken in to the 10ml volumetric flask and make up to the mark with methanol.

Linearity 80%:

0.8 ml of stock solution is taken in to the 10ml volumetric flask and make up to the mark with methanol.

Linearity 100%:

1 ml of stock solution is taken in to the 10ml volumetric flask and make up to the mark with methanol.

Linearity 120%:

1.2 ml of stock solution is taken in to the 10ml volumetric flask and make up to the mark with methanol.

Linearity 140%:

1.4 ml of stock solution is taken in to the 10ml volumetric flask and make up to the mark with methanol.

Linearity and range

Linearity of an analytical method is its ability to obtain results directly proportional to the concentration of the analyte in the sample within a definite range. The six series of standard solutions were selected for assessing linearity range. The calibration curve was plotted using peak area versus concentration of the standard solution and the regression equations were calculated. The least squares method was used to calculate the slope, intercept and correlation coefficient.

Results and Discussion

System suitability

The UPLC system was stabilized for 60min to get a stable baseline. Six replicate injections of the standard solution assessed to check the system suitability. The number of theoretical plate count and Tailing factor all the parameters were found to be within limit.

Table 1: System Suitability Results

Drug Name	USP Platecount	USP Resolution	USP Tailing
Valsartan	45896		0.89
Atorvastatin	9852	3.68	1.02
Ezetimibe	144789	4.12	1.63
Canagliflozin	26593	3.54	1.01
Nebivolol	69938	5.69	0.63

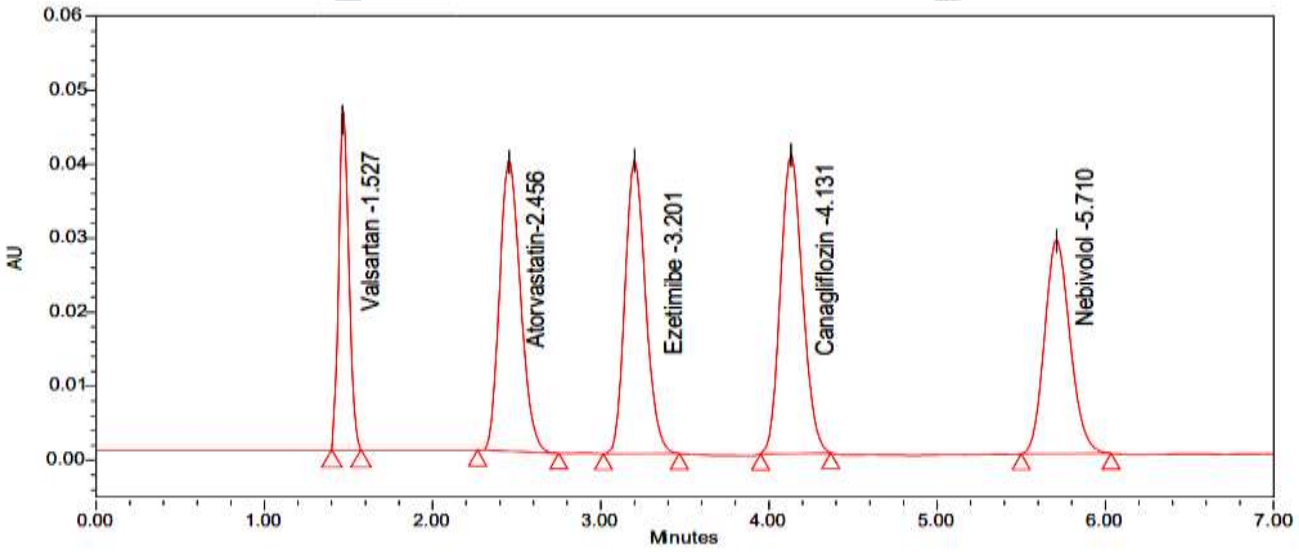

Fig 6: Chromatogram for Standard

Linearity

Linearity of the method was evaluated by preparing a standard solution . Sequential dilutions were performed to the given solutions at 20, 40, 60, 80, 100, 120 and 140% of the target concentrations. These were injected and the peak areas are used to plot calibration curves against the concentration. The correlation coefficient values of these analytes were 0.999. The results were shown in table

Table 2: Linearity results for Valsartan

S.No.	Linearity	Conc. of Valsartan	Area Counts of Valsartan
1	20%	10	146581
2	40%	20	322669
3	60%	30	526341
4	80%	40	711593
5	100%	50	895033
6	120%	60	1090570
7	140%	70	1266743

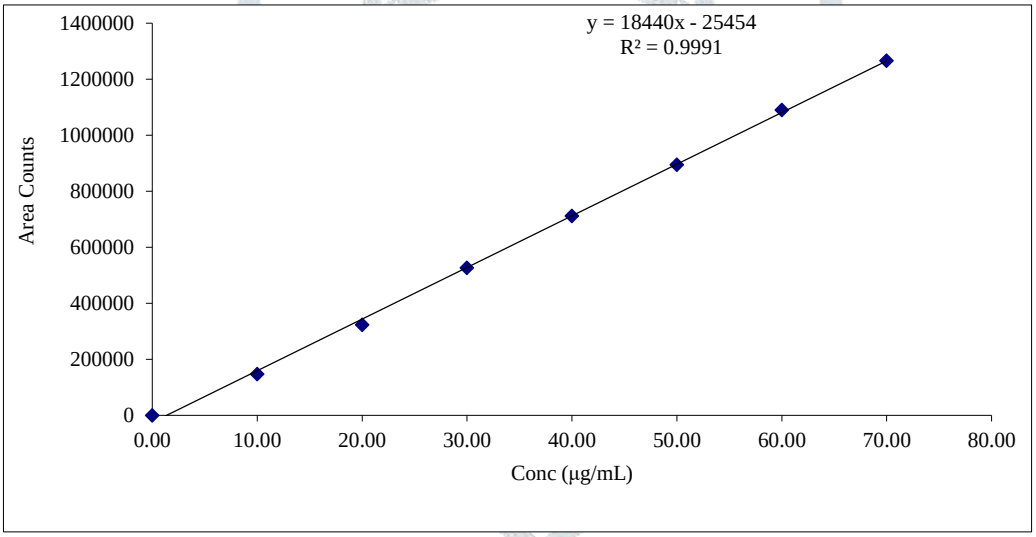

Fig 7: Linearity plot for Valsartan

Table 3: Linearity results for Atorvastatin

S.No.	Linearity	Conc. of Atorvastatin	Area Counts of Atorvastatin
1	20%	10	459865
2	40%	20	965716
3	60%	30	1425581
4	80%	40	1931433

5	100%	50	2391298
6	120%	60	2851163
7	140%	70	3311028

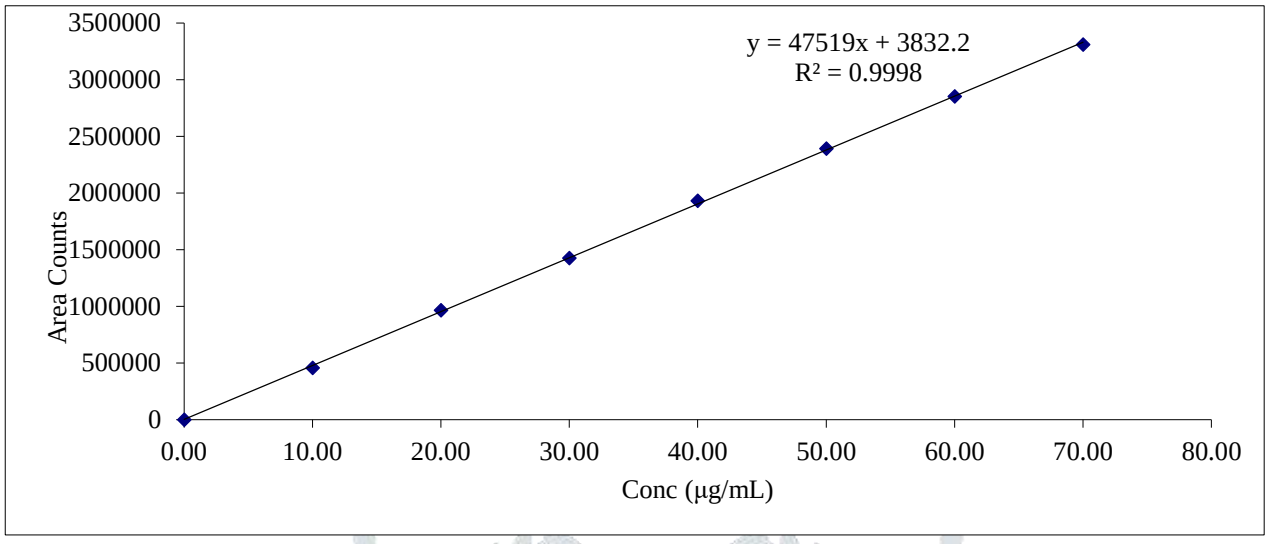

Fig 8: Linearity plot for Atorvastatin

Table 4: Linearity results for Ezetimibe

S.No.	Linearity	Conc. of Ezetimibe	Area Counts of Ezetimibe
1	20%	10	512469
2	40%	20	1076184.9
3	60%	30	1588653.9
4	80%	40	2152370
5	100%	50	2664839
6	120%	60	3177308
7	140%	70	3689777

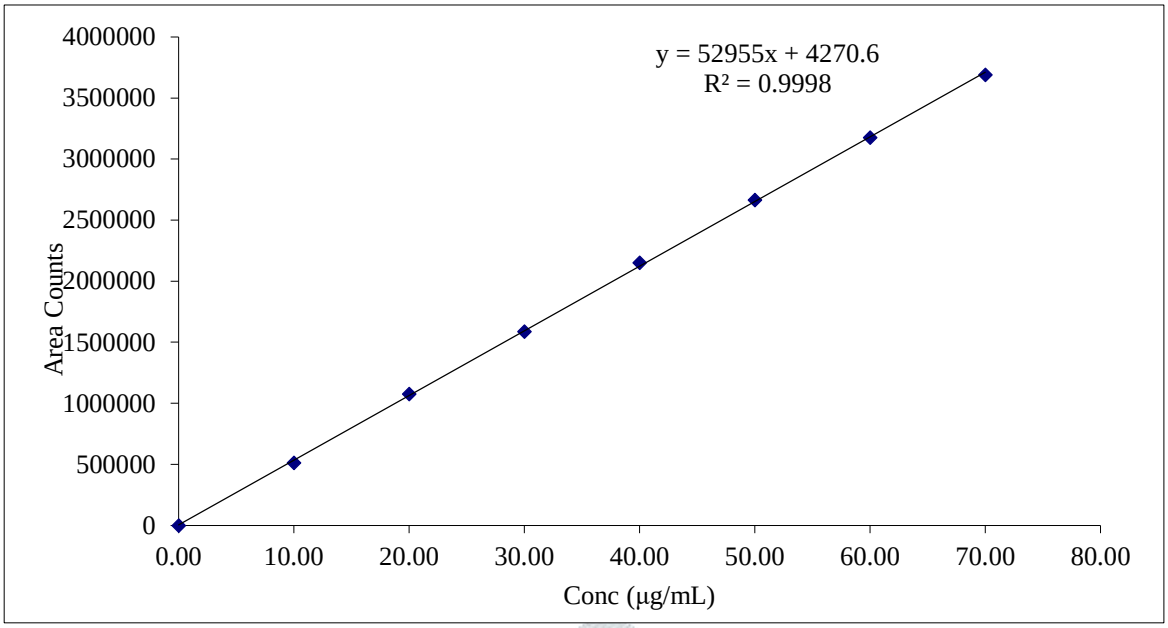

Fig 9: Linearity plot for Ezetimibe

Table 5: Linearity results for Canagliflozin

S.No.	Linearity	Conc. of Canagliflozin	Area Counts of Canagliflozin
1	20%	10	289456
2	40%	20	607858
3	60%	30	897314
4	80%	40	1215716
5	100%	50	1505171
6	120%	60	1794627
7	140%	70	2084083

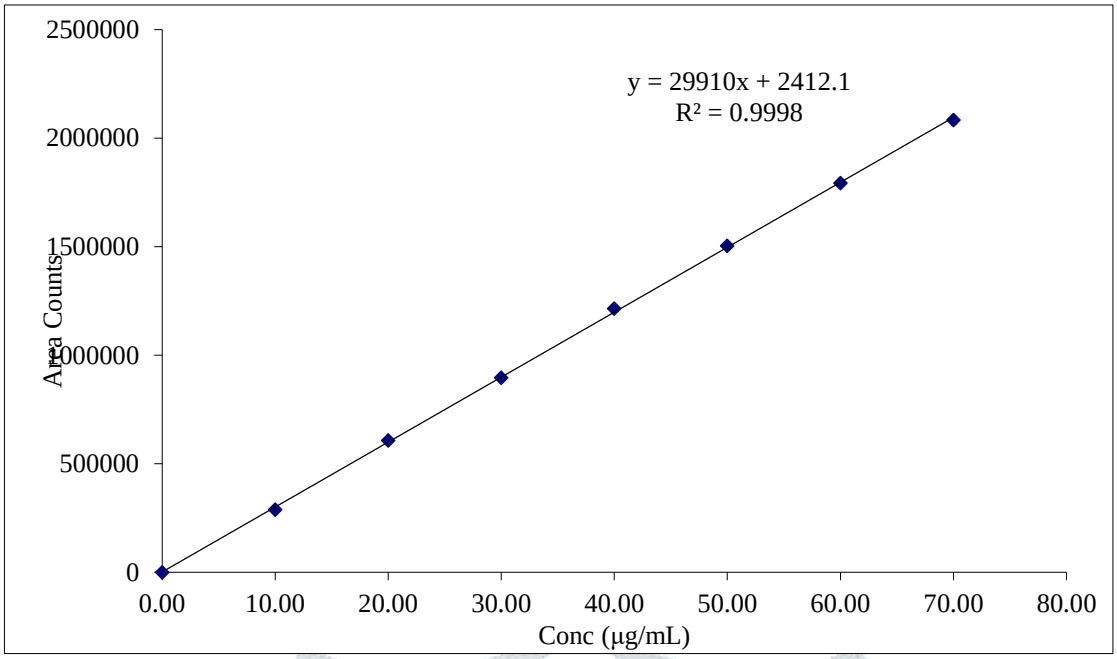

Fig 10: Linearity plot for Canagliflozin

Table 6: Linearity results for Nebivolol

S.No.	Linearity	Conc. of Nebivolol	Area Counts of Nebivolol
1	20%	10	3145982
2	40%	20	6606562
3	60%	30	9752544
4	80%	40	13213124
5	100%	50	16359106
6	120%	60	19505088
7	140%	70	22651070

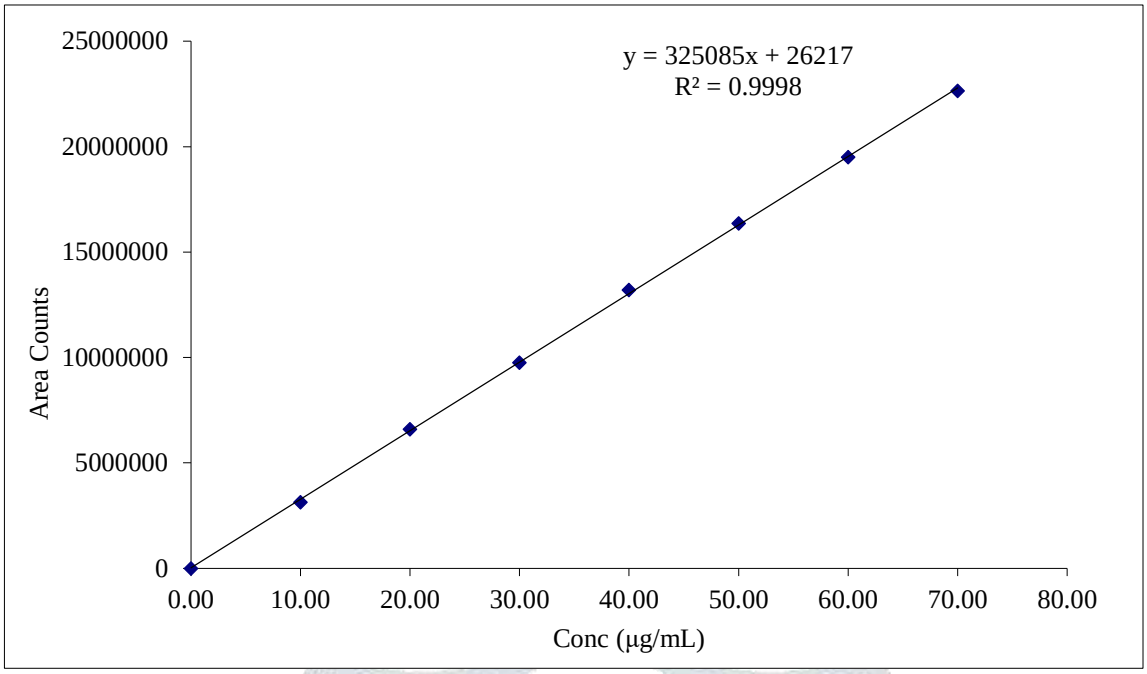

Fig 11: Linearity plot for Nebivolol

Conclusion:

The study showed that the proposed single UPLC method can be used for the assessment of drug purity, stability, solubility and lipid-formulation release profile with no interference of excipients or related substances of active pharmaceutical ingredient for Nebivolol, Valsartan, Ezetimibe, Atorvastatin, Canagliflozin drugs.

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