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ESTIMATION OF FOUR DIFFERENT ONCOLOGY DRUGS USING ADVANCED LIQUID CHROMATOGRAPHY TECHNIQUE (UPLC)

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ABSTRACT : A rapid and stability-indicating ultra-performance liquid chromatography method was developed for quantification of Avelumab,, Trifluridine, Daunorubicin, Axitinib 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 water and Acetonitrile in a ratio of 20:80, v/v at a flow rate of 0.5 mL/minute over waters x bridge C18, 50 × 4.6 mm, 3.5µm column at room temperature was maintained. The method showed excellent linear response with correlation coefficient (R^2) values of 0.999 for Avelumab,, Trifluridine, Daunorubicin, Axitinib which was within the limit of correlation coefficient.

Keywords: UPLC, Avelumab, Trifluridine, Daunorubicin, Axitinib.

INTRODUCTION

Avelumab, sold under the brand name Bavencio, is a fully human monoclonal antibody [1] medication for the treatment of Merkel cell carcinoma [2], urothelial carcinoma [3], and renal cell carcinoma [4]. Common side effects include fatigue, musculoskeletal pain, diarrhea, nausea, infusion-related reactions, rash, decreased appetite and swelling of the limbs (peripheral edema) [5]. Avelumab targets the protein programmed death-ligand 1 (PD-L1).

Trifluridine (also called trifluorothymidine; abbreviation TFT or FTD) is an anti-herpes virus antiviral drug, used primarily on the eye. It is also a component of the anti-cancer drug trifluridine/tipiracil [6], which is taken by mouth. Common side effects of trifluridine eye drops include transient burning, stinging, local irritation,

and edema of the eyelids. Adverse effects of the anti-cancer formulation have only been evaluated for the combination trifluridine/tipiracil, not for the individual components.

Daunorubicin, also known as daunomycin, is a chemotherapy medication used to treat cancer. Specifically it is used for acute myeloid leukemia [7] (AML), acute lymphoblastic leukemia [8] (ALL), chronic myelogenous leukemia [9] (CML), and Kaposi's sarcoma. It is used by injection into a vein. A liposomal formulation known as liposomal daunorubicin also exists. Common side effects include hair loss, vomiting, bone marrow suppression, and inflammation of the inside of the mouth. Other severe side effects include heart disease and tissue death at the site of injection. Use in pregnancy may harm the baby. Daunorubicin is in the anthracycline family of medication. It works in part by blocking the function of topoisomerase II [10].

Axitinib, sold under the brand name Inlyta, is a small molecule tyrosine kinase inhibitor [11, 12] developed by Pfizer. It has been shown to significantly inhibit growth of breast cancer in animal (xenograft) models and has shown partial responses in clinical trials with renal cell carcinoma (RCC) and several other tumor types.

MATERIALS AND METHOD

Avelumab, Trifluridine, Daunorubicin, Axitinib standards were provided by Glenmark Pharmaceuticals, Mumbai. Water, Acetonitrile HPLC grade from Merck company, Mumbai.

Selection of wavelength of detection

Avelumab, Trifluridine, Daunorubicin, Axitinib standard solution of 100 ppm was scanned at 200-400 nm and UV Spectrum was recorded. By observing the spectrum of standard solution, λ_{max} 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 water x bridge C18 (50 mm × 4.6 mm, 3.5µm) containing 3.5 µm particle size column was used. Mobile phase comprising of water and acetonitrile in a ratio 20:80 % 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.

Mobile phase- A

HPLC grade water

Mobile phase - B

Acetonitrile

Preparation of Mobile phase:

Take mobile phase A and B in the ratio of 20:80 v/v.

Diluent: Water and acetonitrile in the ratio of 20:80 v/v

Preparation of solutions

Standard stock solution: Weigh each 5 mg of Avelumab, Trifluridine, Daunorubicin, Axitinib accurately weighed and transferred into 10 ml volumetric flask add 7 ml diluent sonicate for 30 minutes to dissolve the contents completely then make up to the mark with diluent.

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

Preparation of Linearity stock solution:

Avelumab, Trifluridine, Daunorubicin, Axitinib is weighed 5mg of each and taken in 10ml volumetric flask and make up to the mark with diluents. Pipette out 1ml analyte solution of each volumetric flask is taken in another 10ml volumetric flask and make up to the mark with diluent.

Linearity 25%:

0.25 ml of stock solution is taken in to the 10ml volumetric flask and make up to the mark with HPLC grade water.

Linearity 50%:

0.5 ml of stock solution is taken in to the 10ml volumetric flask and make up to the mark with HPLC grade water.

Linearity 75%:

0.75 ml of stock solution is taken in to the 10ml volumetric flask and make up to the mark with HPLC grade water.

Linearity 100%:

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

Linearity 125%:

1.25 ml of stock solution is taken in to the 10ml volumetric flask and make up to the mark with HPLC grade water.

Linearity 150%:

1.5 ml of stock solution is taken in to the 10ml volumetric flask and make up to the mark with HPLC grade water.

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 Plate count	USP Resolution	USP Tailing
Trifluridine	4751		1.10
Axitinib	8784	5.29	0.88
Daunorubicin	14623	4.36	0.59
Avelumab	8870	5.45	1.08

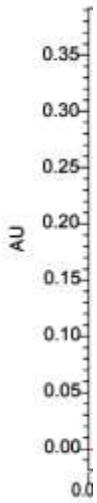

Fig 1: Chromatogram for Standard

Linearity

Linearity of the method was evaluated by preparing a standard solution. Sequential dilutions were performed to the given solutions at 25, 50, 75, 100, 125 and 150% 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 2.

Table 2: Linearity results for Trifluridine

S.No.	Linearity	Conc. of Trifluridine	Area Counts of Trifluridine
1	25%	12.5	459822
2	50%	25	935456
3	75%	37.5	1348591
4	100%	50	1846362
5	125%	62.5	2301446
6	150%	75	2756479

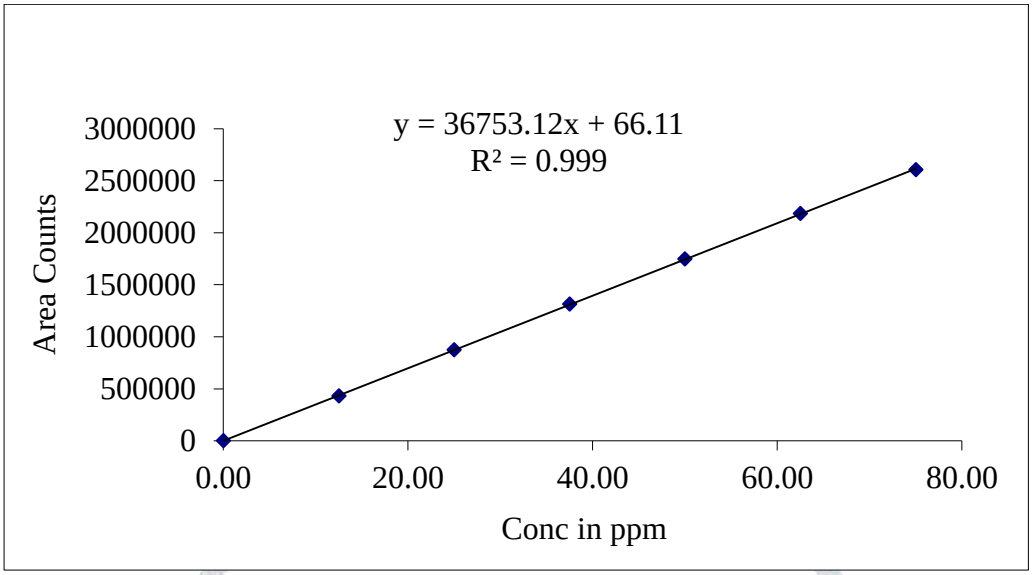

Fig 2: Linearity plot for Trifluridine

Table 3: Linearity results for Axitinib

S.No.	Linearity	Conc. of Axitinib	Area Counts of Axitinib
1	25%	12.5	25112
2	50%	25	52647
3	75%	37.5	78551
4	100%	50	104636
5	125%	62.5	130545
6	150%	75	151489

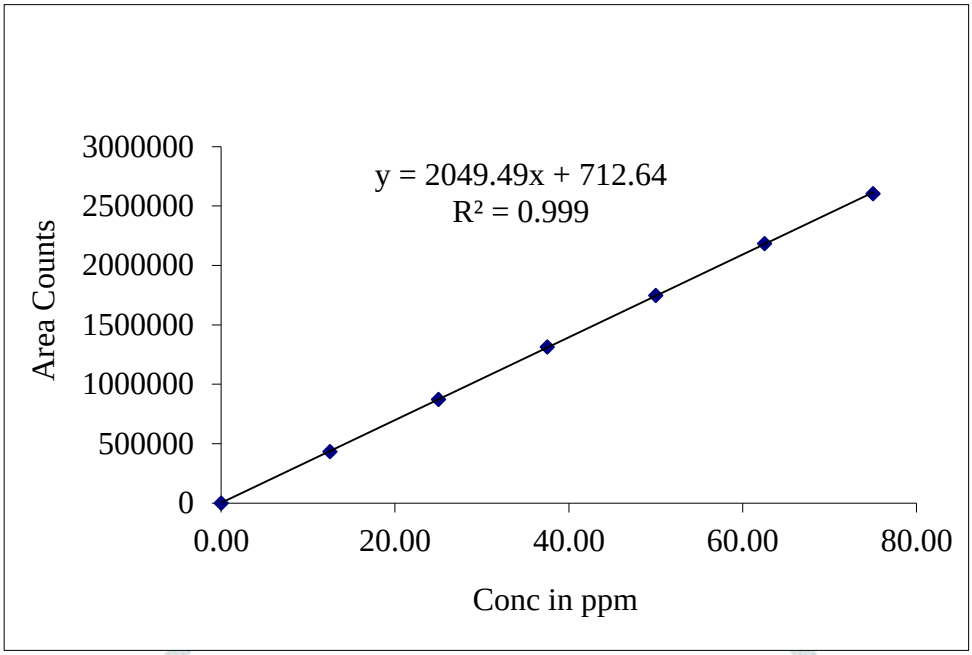

Fig 3: Linearity plot for Axitinib

Table 4: Linearity results for Daunorubicin

S.No.	Linearity	Conc. of Daunorubicin	Area Counts of Daunorubicin
1	25%	12.5	810234
2	50%	25	1627459
3	75%	37.5	2487563
4	100%	50	3254598
5	125%	62.5	4068982
6	150%	75	4887967

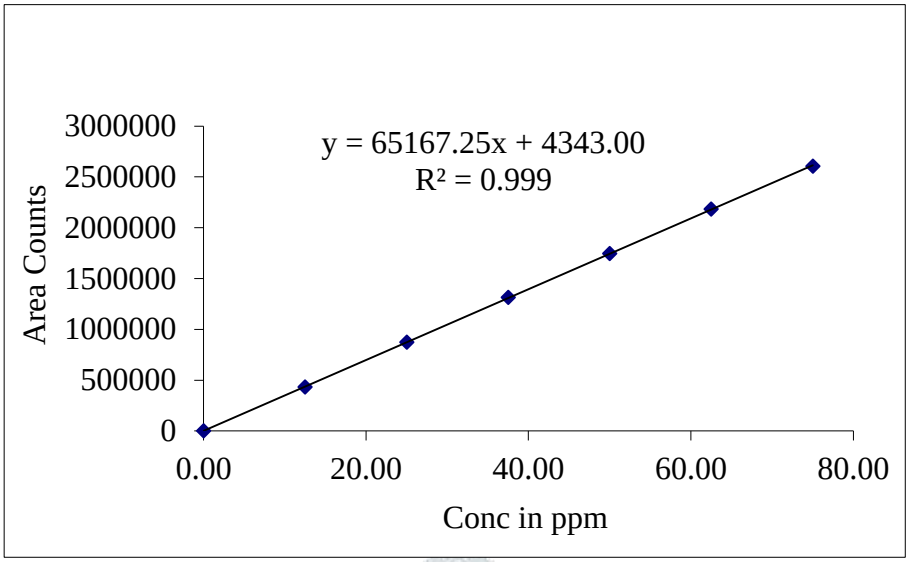

Fig 4 Linearity plot for Daunorubicin

Table 5: Linearity results for Avelumab

S.No.	Linearity	Conc. of Avelumab	Area Counts of Avelumab
1	25%	12.5	432658
2	50%	25	872659
3	75%	37.5	1314453
4	100%	50	1745982
5	125%	62.5	2183698
6	150%	75	2604593

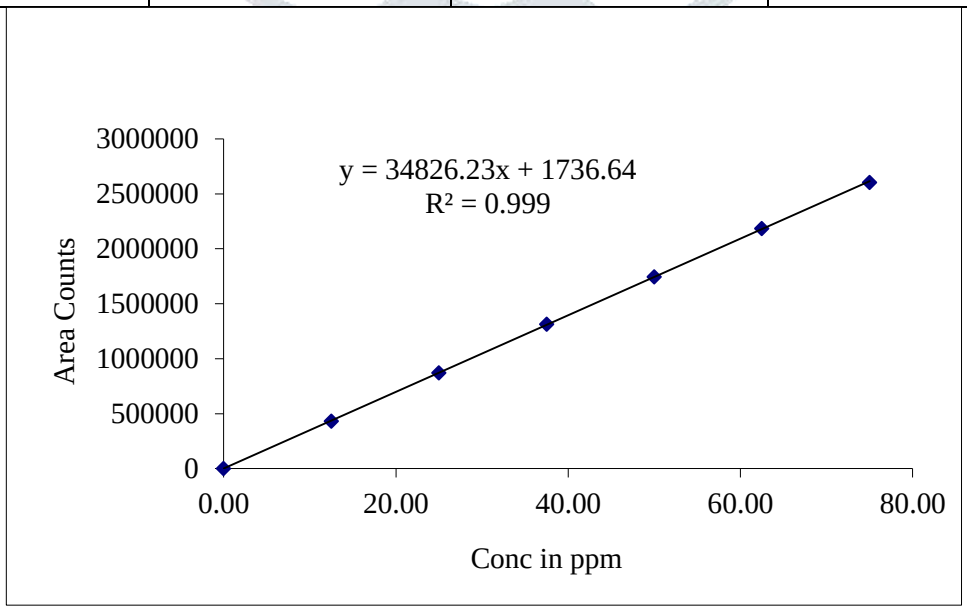

Fig 5: Linearity plot for Avelumab

CONCLUSION:

This 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 ingredients for Trifluridine, Axitinib, Daunorubicin and Avelumab drugs.

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