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Method for anticancer drugs in their pharmaceutic dosage form

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Abstract

The antiviral medications in pharmaceutical dose forms were identified by the anticancer drugs were calculated using RP-HPLC, while their separated forms were evaluated using UPLC. Since the placebo peak did not interact with the medication peaks, all of the approaches were determined to be selective. Since the percentages of recovery and RSD were within the specified ranges, it was determined that the procedures were accurate and exact as well. At concentrations within their respective limits, all of the approaches exhibited Beer's law compliance ($r=0.999$). The approach was deemed robust since the % RSD remained within the specified parameters. We tested the method's resilience by changing the mobile phase's organic phase composition, flow rate, and column oven temperature. We discovered that it worked well. The pharmaceuticals remained stable throughout a wide range of circumstances, including from heat to acidic to basic to oxidative to neutral to photolytic to photolytic of all approaches. According to the results, both the peak purity angle and the net deterioration were below the peak purity criterion.

Keywords: Pharmaceutic, Dosage, Form, Mobile and Medication

Introduction

Herpes is a family of viruses that includes infectious mononucleosis, genital herpes, chickenpox, and retinitis. The viral particle uncoils and connects to the cell membrane. Then, it moves to the nucleus to have its DNA translated into viral mRNA, which the virus uses to make its proteins. The DNA replication process is disrupted by herpesvirus-effective drugs. The nucleoside analogs inhibit viral DNA polymerase, an essential enzyme in DNA synthesis, by acting similarly to the regular nucleoside. Before any nucleoside analog may exert antiviral action, a phosphate group must be added to it. Some of the drugs target only cells with viral particles because they are triggered by viral enzymes. Less specificity is associated with some drugs since they are triggered by cellular enzymes. One example of a non-nucleoside inhibitor of herpesvirus replication is foscarnet. It works by blocking the viral DNA polymerase, which in turn prevents the virus from replicating.

Developing analytical techniques, identifying and

characterizing impurities, and validating methods are crucial steps in the pharmaceutical industry's research, development, and production processes. The number of new medications that are launched to the market is growing annually. Medications in this category can be entirely novel compounds or existing ones with slight structural changes. Evidence of side effects suggests that these medications should be used more widely. Upon their release, these novel medications may be included in official pharmacopeias as a more suitable substitute. Even if the number quantity of narcotics and related items sold is rising every year, we are unable to detect these medicines and impurities because of the lag time, analytical processes, and standards that may not be accessible in the relevant pharmacopeia. Medications and pharmaceutical byproducts might be brand new or modified versions of existing drugs with minor structural changes. This occurs as a result of the drug ingredients and drug products being used more often and extensively, as well as potential uncertainties, rival drug companies releasing superior medications, and allegations

of hazardous impurities.

The pharmacopoeias may not have analytical methods or standards for these medications or related chemicals at this time. When two or more medications' therapeutic properties are combined in a single product, the result is a combination product that offers patients access to more than one treatment. Innovation in analytical methodologies is crucial in these types of situations. Pharmaceutical chemistry encompasses the study of medicinal substances, including their structure, chemical nature, synthesis, composition, biochemical actions, effects on living organisms, physical and chemical properties, quality control methods, and storage conditions. In terms of pharmaceuticals, India is unrivaled. India is capitalizing on the high demand for these drugs in developed nations like the US, Australia, and the UK by advertising them there. Many industrialized nations are now receiving our formulations for export, but they are imposing their regulatory standards on us before we can sell our goods in their markets.

Literature Review

Shayne Cox Gad (2017) ^[1] New medicine development During lead optimisation, a solid preclinical candidate is often sought for. Optimal potency, pharmacokinetics (PK) and pharmacodynamics (PD), and toxicity are all carefully considered and optimised at this stage. Lead had to reach large doses in order to investigate a tolerable toxicological profile. Hence, the preformulation should be acknowledged as a crucial component of lead selection. An essential aspect of the pharmacokinetic profile is the biotransformation of some compounds in the liver after oral ingestion. In most cases, the proportion of the dosage that reaches the systemic circulation after oral delivery is used to determine bioavailability. Pharmaceutical safety evaluation takes an unexpected turn when compared to the majority of industrial toxicology when it comes to formulations used to deliver prospective medications in development. The tests that are required to guarantee human safety for the anticipated period of exposure are carried out using a tiered approach.

Milind Baburao Ubale *et al.* (2012) ^[2] A novel HPLC technique for the quantitative detection of Acyclovir in bulk pharmaceuticals was developed and validated using isocratic reversed phase stability indicators. The drug and its degradation products were separated using an isocratic reversed-phase HPLC method. A Water Nova Pack C18 column measuring 250 x 4.6 mm and a mobile phase consisting of 1.0 gm sodium dihydrogen phosphate and 1.0 gm 1-octane sulphuric acid salt in 1000 ml of water filter were mixed. Make a uniform mixture of 50:20:30 v/v/v of acetonitrile, methanol, and buffer. A wavelength of 264 nm was used for the detection. In order to evaluate the created approach, we looked at its linearity, accuracy (recovery), precision, system appropriateness, selectivity γ , and robustness. These factors show that the method is stable and reliable.

Sanjay Sawant *et al.* (2014) ^[3] This research set out to use data from forced degradation experiments to report on the stability of valganciclovir, a new antiviral medication. In compliance with the ICH recommendation Q1A (R2), valganciclovir was put through a series of controlled experiments that included hydrolytic (acidic, alkaline, and

neutral), oxidative, photolytic, and thermal stress. While the medicine remained stable under all other stress conditions, it only exhibited lability when exposed to acidic or photoacidic environments. A Hypersil Gold C-18 column (4.6 × 250 mm, 5 μm) was used to resolve the drug and degradation products. The solvents used were acetonitrile (A) and potassium dihydrogen ortho phosphate buffer (pH 5.0; 0.01M) in a 5:95 (v/v) ratio, with a flow rate of 0.6 ml/min and a detection wavelength of 252 nm. Using LC-MS/MS, we were able to identify the primary acidic stress degradation product and suggest a route for its fragmentation. Following ICH guidelines, the LC-DAD technique was validated. Commercially available data was analysed using the approach, which fulfilled all requirements available tablets.

Ankit Dinesh Doshi *et al.* (2024) ^[7] Many sensitive, fast, and straightforward analytical methods have been developed and validated for the aim of quantifying sofosbuvir. These methods include RP-HPLC and UV-visible spectrophotometry. From selecting the solvent, buffer, and wavelength to using the right parameters and making standard solutions, this research covers it all in terms of stability. Experiments revealed that the optimal mobile phase for analysis was a 30:70 ratio of 0.01 M KH₂PO₄ to acetonitrile pH 3.0 (which included ortho phosphoric acid). At 264 nm, the absorbance was likewise at its peak. After that, we checked the best analytical development approach against the ICH guidelines for precision, accuracy, and ruggedness, and we got excellent results across the board. The findings demonstrated a linearity between 5 and 25 μg mL, a precision percentage ranging from 0.7477 to 0.8299 from one day to the next, and a recovery percentage of 0.208% at 100% accuracy. It has been determined that the method used for developing and validating the analyses is extremely reliable, economical, and repeatable. The pharmaceutical industry's quality control section may benefit from this.

A. Ahamed *et al.* (2012) ^[5] A unique quick, sensitive and repeatable mass compatible, In order to quantitatively identify etravirine in active pharmaceutical components and dosage forms, an ultra-performance liquid chromatographic technology was developed. Medication for the treatment of human immunodeficiency virus (HIV) infections is now available. etravirine. It is an NNRTI, or non-nucleoside reverse transcriptase inhibitor, which is a class of medications used to combat HIV. This approach may be used to measure etravirine drug assays and related substances. A gradient elution was accomplished within 7.0 minutes using a YMC's UltraHT Pro C18 50 × 3.0 mm, 2.0μm column to chromatographically separate the medication from any potential contaminants and degradation products. An acetonitrile and formic acid (0.1%) in water solution made up the solvent system. At 40°C for the column temperature and 0.8 mL/min for the flow rate, detection was performed at 310 and 250 nm. The already-established UPLC method was subjected to further testing, which comprised hydrolytic, oxidative, photolytic, and thermal stress stages. Criteria for evaluating the method's performance included its linearity, accuracy, precision, robustness, and limit of quantification, among others, in line with the current ICH standards.

Method development and validation of antiviral drugs developing and validating anti-viral components Abacavir, Lamivudine and Dolutegravir

- a. Reagents & Chemicals:** In this study, abacavir, Lamivudine, and Dolutegravir were tested using their respective working standards, which had a purity of 99.8% on a dry basis. Water that has been purified using the Millipore technology. Merck supplied ACN. The analysis strictly adhered to AR grade chemicals for all other substances, including potassium dihydrogen phosphate, sodium hydroxide, hydrogen peroxide, hydrochloric acid, and ortho-phosphoric acid.
- b. Instrumental and Analytical conditions:** A software-enabled autosampler and PDA detection unit were used in the experiment conducted with the waters model 2998. This experiment used a BDS column with dimensions of 250 mm x 4.6 mm and a 5 μ gradient. At 240 nm, UV detection was carried out. Ten microliters of the sample was injected. At a flow rate of 1 ml/min, an isocratic mobile phase was prepared using acetonitrile and buffer (0.01N) at a 45:55 (v/v) ratio. The column's temperature was kept at 30 °C.
- c. Buffer Preparation: (0.01N Potassium dihydrogen phosphate):** Break down sodium dihydrogen phosphate, 1.36 grams, in 1000 milliliters of water
- d. Preparation of mobile phase:** Combine 45 parts buffer and 55 parts ACN.
- e. Preparation of Diluent:** In a volume-for-volume (v/v) ratio of 50:50, combine the water and CAN.
- f. Standard Preparation:** (Abacavir 120 μ g/ml, Lamivudine 60 μ g/ml, and Dolutegravir 10 μ g/ml)! The following standard medications were dissolved in 10 milliliters of diluent: 120 milligrams of Abacavir, 60 milligrams of Lamivudine, and 10 milligrams of Dolutegravir. Using a 10 milliliter diluent, diluted 1 milliliter of solid stock solution
- g. Sample Preparation:** Twenty Trimet pills, each containing 120 milligrams, were used to determine the average weight. We dissolved 10 milliliters of abacavir in water. Use an HPLC filter to filter it. Dilute 1 milliliter with 10 milliliters of diluent.

Wavelength Detection

The spectra showed that its wavelength of 240 nm is ideal.

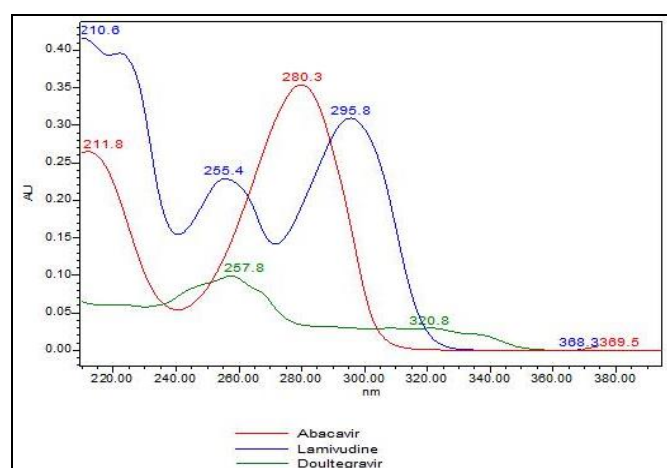


Fig 1: Overlain UV Spectrum for Abacavir, Lamivudine & Dolutegravir

HPLC Method development trails

A) I Trial

Column: BDS (250mm x 4.6 mm, 5 μ)
 Mobile section: H2O: Methanol (fifty: fifty)
 Diluent: H2O: ACN (50:50)
 Mode: Isocratic
 Rate of flow: 1mL/minute
 Temperature in column: 30°C
 Volume of injection: 10 μ L
 Detection Wave Length: 240nm
 Plate Count of USP: 6294(Abacavir), 10944 (Lamivudine)
 USP Tailing: 1.3 (Abacavir), 1.2 (Lamivudine)
 USP Resolution: 13.0

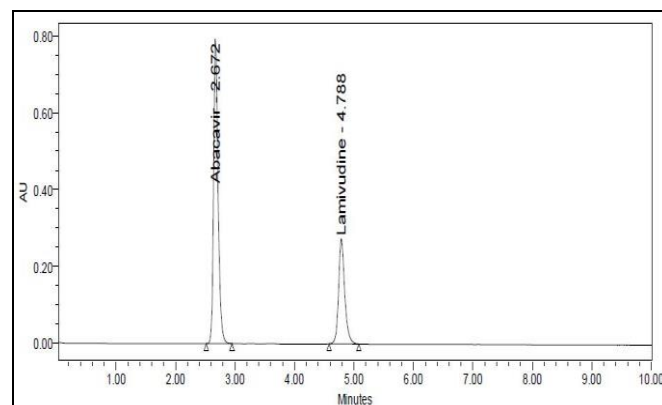


Fig 2: HPLC trail 1 chromatogram of Abacavir, Lamivudine and Dolutegravir

Observation: Only two peaks were eluted, so proceeded to next trail.

B) II Trial

Column: BDS (250mm x 4.6 mm, 5 μ)
 Mobile phase: H2O: ACN (fifty: fifty)
 Diluent: H2O: ACN (fifty: fifty)
 Mode: Isocratic
 Flow Rate: 1.0mL/min
 Column Temperature: 30 °C
 Injection Volume: 10 μ L
 Wave Length: 240nm
 Plate Count of USP: 5314 (Abacavir), 13735 (Lamivudine)
 USP Tailing: 1.2 (Abacavir), 1.2 (Lamivudine)
 USP Resolution: 11.4

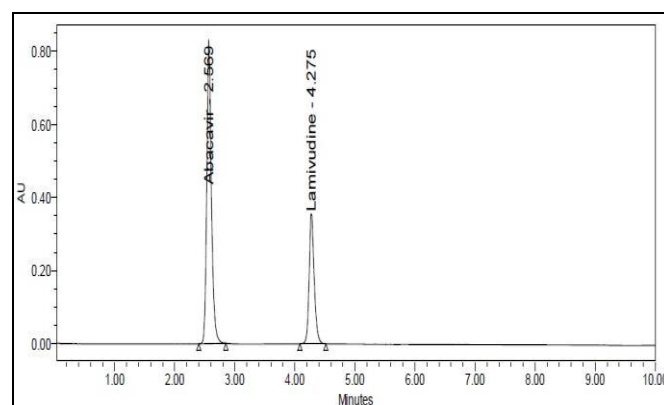


Fig 3: HPLC trail 2 chromatogram of Abacavir, Lamivudine and Dolutegravir

Observation: Only two peaks were eluted, so proceeded to next trail

C) III Trial

Column: BDS (250mm x 4.6 mm, 5 μ)
 Mobile phase: Perchloric acid (0.01N): Acetonitrile (50:50)
 Diluent: Water: Acetonitrile (50:50)
 Mode: Isocratic
 Flow Rate: 1.0mL/min
 Column Temperature: 30 $^{\circ}$ C
 Injection Volume: 10 μ L
 Wave Length: 240nm
 Plate Count of USP: 6816 (Abacavir), 7489 (Lamivudine) & 10137 (Dolutegravir)
 USP Tailing: 1.5 (Abacavir), 1.1 (Lamivudine) & 1.2 (Dolutegravir)
 USP Resolution: 6.9 & 2.1

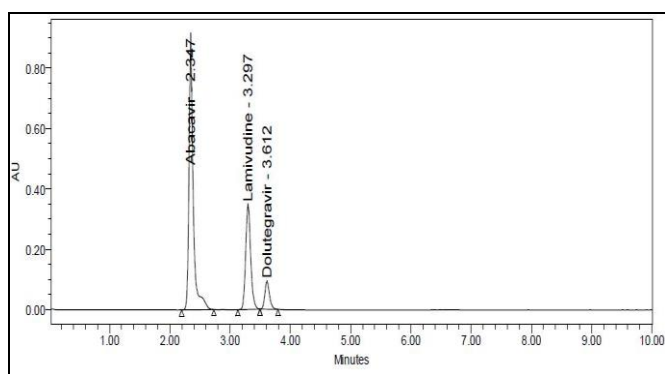


Fig 4: HPLC trail 3 chromatograms of Abacavir, Lamivudine and Dolutegravir

System Suitability

Table 1: System suitability results of Abacavir, Lamivudine and Dolutegravir

S. No.	System Suitability Parameter	Observed value			Acceptance criteria
		Abacavir	Lamivudine	Dolutegravir	
1	% RSD	0.4	0.6	0.6	< 2
2	USP factor for tailing	1.17	1.20	1.12	< 2
3	Plate Count of USP	6066	8154	9106	NLT 2000
4	USP Resolution		6.8	3.9	NLT 2

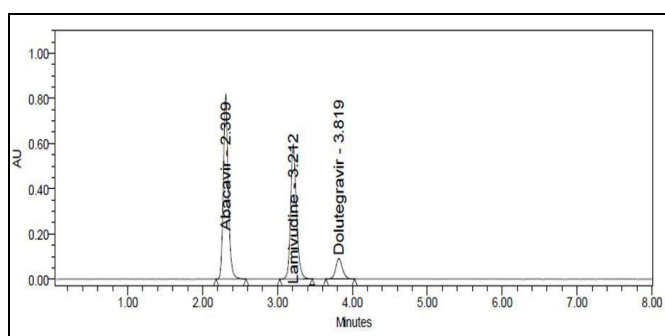


Fig 5: Chromatographic image for Abacavir, Lamivudine and Dolutegravir standard solution

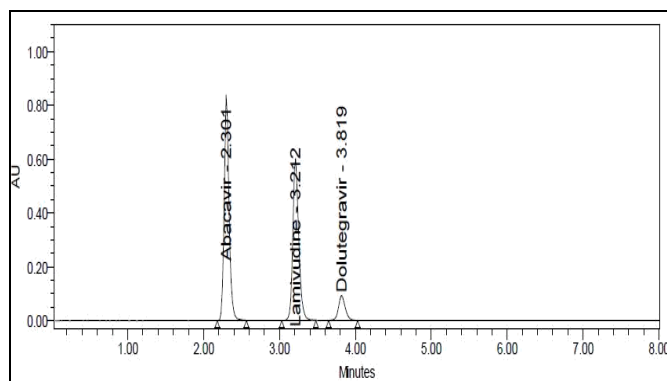


Fig 6: Chromatographic image for Abacavir, Lamivudine and Dolutegravir sample solution

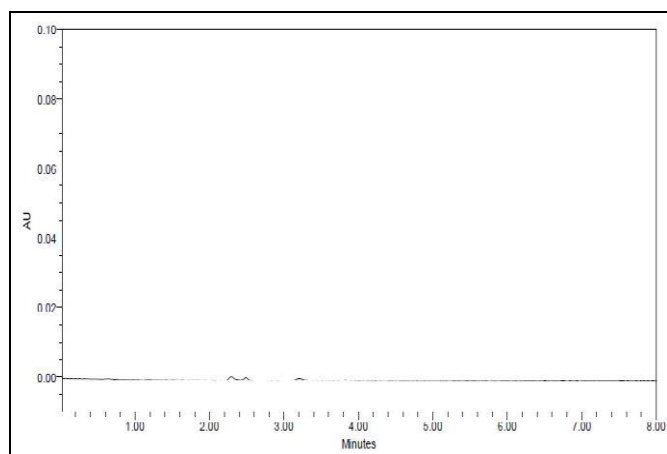


Fig 7: Chromatographic image for blank solution

Specificity

Table 2: Specificity results for Abacavir, Lamivudine and Dolutegravir

Chromatogram	Peak found
1	No
2	No

Criteria for acceptance: At the recommended time of administration (RT) of Abacavir, Lamivudine, and Dolutegravir, the chromatogram should not exhibit any interference for placebo.

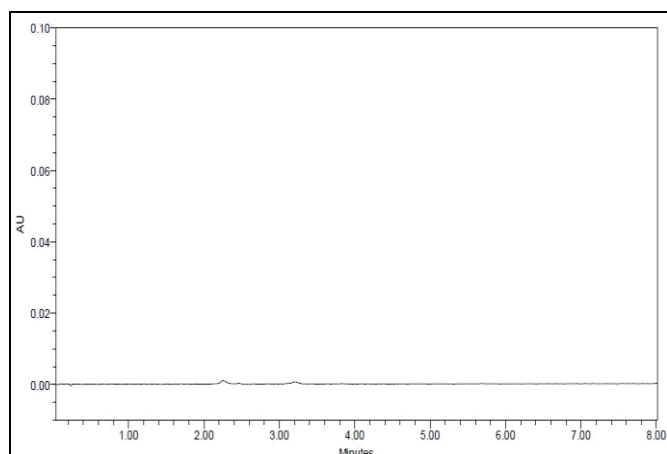


Fig 8: Chromatographic image for Placebo solution

Precision

Table 3: Precision results for Abacavir, Lamivudine and Dolutegravir

Sample Name	Abacavir		Lamivudine		Dolutegravir	
	Sample Area	% Assay	Sample Area	% Assay	Sample Area	% Assay
Sample-1	3682017	98.97	3204896	98.14	571787	99.35
Sample-2	3682702	98.99	3236396	99.11	571945	99.37
Sample-3	3694424	99.30	3220171	98.61	574560	99.83
Sample-4	3694921	99.32	3250930	99.55	570962	99.20
Sample-5	3692313	99.25	3234933	99.06	572820	99.53
Sample-6	3686065	99.08	3214271	98.43	574206	99.77
Average	3688740	99.15	3226933	98.82	572713	99.51
%RSD	0.2	0.2	0.5	0.5	0.2	0.2

Acceptance Criteria: Abacavir, Lamivudine, and Dolutegravir assay results from any of the six sample preparations must have a relative standard deviation (RSD) of no more than 2.0%. It is important that the individual % Assay for Abacavir, Lamivudine, and Dolutegravir be between 98.0% and 102.0%.

Conclusion

Emtricitabine, Efavirenz, and Tenofovir were all measured in pharmaceutical and bulk drug dosage form using an RP-HPLC method that indicates stability. According to the protocol forth by the ICH, the approach underwent validation. The approach was determined to be dependable, strong, exact, steady, precise, and robust. It was determined from the degradation experiments that the medications remained stable under stress. We apply the suggested approach to estimate emtricitabine, efavirenz, and tenofovir in tablet formulations for both routine and quality control analyses.

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