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Review

A Review on RP HPLC Estimation Techniques for Epirubicin and Docetaxel in Bulk and Dosage Forms

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Abstract

Epirubicin(10-(4-amino-5-hydroxy-6-methyl-oxan-2-yl)oxy-6,8,11-trihydroxy-8-(2hydroxyacetyl)-1-methoxy-9,10-dihydro-7H-tetracene-5,12-dione) is an anthracycline anticancer agent used to treat node-positive breast cancer, ovarian cancer, gastric cancer, lung cancer, and lymphomas (Neil,2006). Streptomyces peucetius strains produce epirubicin through chemical transformation. It interferes with DNA and RNA production by creating a compound and intercalating into nucleotide base pairs. It is preferred over doxorubicin due to its lower toxicity at equimolar dose. This may be due to the opposite chirality caused by the hydroxyl group at the 4' carbon of the sugar moiety, resulting in faster elimination and less toxicity. Docetaxel is a toxoid medication with anti-cancer effects. The semi-synthetic procedure begins with a precursor derived from regenerated yew needles. Docetaxel is available in two forms: anhydrous and trihydrate. Aventis Pharmaceuticals developed Docetaxel, popularly known as Taxotere, to treat a specific kind of cancer. The medication is currently authorised in 90 nations for treating advanced lung cancer and 70 countries for treating advanced non-small cell lung cancer.

Keywords: Epirubicin, Docetaxel, RP HPLC, Anti-cancer Drugs.

INTRODUCTION

The anthracycline anticancer drug epirubicin (10-(4-amino-5-hydroxy-6-methyl-oxan-2-yl)oxy-6,8,11-trihydroxy-8-(2hydroxy acetyl)- 1-methoxy-9,10-dihydro-7H-tetracene-5,12-dione) is used to treat lymphomas, ovarian cancer, gastric cancer, lung cancer, and node-positive breast cancer.

A material generated by specific Streptomyces peucetius strains is chemically transformed to yield epirubicin. It inhibits the production of DNA and RNA by intercalating into nucleotide base pairs to form a complex with DNA. It is preferred over doxorubicin because it is less toxic at equimolar doses. This could be because the hydroxyl group at the sugar moiety's 4' carbon has a different spatial orientation, resulting in opposite chirality that speeds up elimination and lowers toxicity.Epirubicin intercalates into DNA, blocking

topoisomerase II and so halting DNA replication and transcription. It also produces free radicals, which lead to cellular damage and apoptosis.[1]

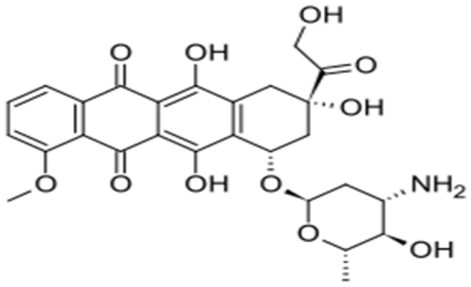

Fig 1: Structure of Epirubicin

Docetaxel is a toxoid drug with anti-cancer properties. The semi-synthetic technique starts with a precursor made from regenerated yew needles. Docetaxel comes in two forms: anhydrous and trihydrate.Aventis Pharmaceuticals developed Docetaxel, popularly known as Taxotere, to treat a specific kind of cancer. The medication is currently authorised in 90 nations for treating advanced lung cancer and 70 countries for treating advanced non-small cell lung cancer. Before release, all pharmaceuticals must undergo stability testing using an assay method that follows current good manufacturing practices. Developing a simple, accurate, and precise HPLC method for determining Docetaxel is worthwhile.Docetaxel stabilizes microtubules by binding to tubulin and blocking disintegration, which prevents mitosis and induces death.[2]

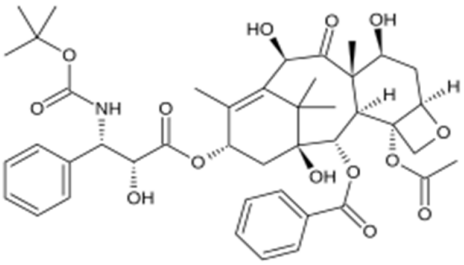

Fig 2: Structure of Docetaxel

LITERATURE REVIEW

Shreeshail Tumbagi et al., Development and Validation of a Novel HPLC Method for the Determination of Docetaxel in Pharmaceutical Dosage Form (2023)

To create a rapid, exact, linear, focused, and accurate RP-HPLC method for determining active content while also validating the Docetaxel assay in bulk medication and pharmaceutical dosage form goods. The developed approach was validated according to the ICH Guidelines Q2 (R1). The chromatographic condition was attained using a 15 cm x 4.6 mm C18(5µm) column with a flow rate of 1.5 mL/min and an isocratic mobile phase generated using Acetonitrile and Water at 45% and 55%, respectively.

The presented method has been validated in terms of specificity, interference study, solution stability, linearity, and rangeThe determination ranged from 100 to 300 PPM. The correlation coefficient was calculated to be 1.0. The established approach is easy, accurate, and exact for estimating Docetaxel in bulk medicine and pharmaceutical dosage forms. It can be utilized in any pharmaceutical company as part of an in-process clearance check.[3]

Mohammad Tariq et al.Developed and validated stability indicating HPLC method for the determination of epirubicin in bulk drug, marketed injection and polymeric nanoparticles(2018)

The current study aims to establish a simple, sensitive, robust, and dependable HPLC approach for routine quality monitoring of epirubicin (EPI) in bulk drugs, commercial injections, and polymeric nanoparticles. The separation was performed using a C18 column. Isocratic elution was carried out using mobile phase A: 0.16% o-phosphoric acid solution, B: acetonitrile and methanol combination (80:20, v/v) in the ratio of 60:40 (A: B), and the flow rate was kept at 1mL/min. The analyses were carried out at 233.5 nm with a PDA detector. Peak-area exhibited a strong linear correlation with drug concentration in the range of 1.0-100.0 µg/mL (r2, 0.999). The developed approach demonstrated sensitivity (limits of detection and quantification were ~8

ng/mL and ~25 ng/mL, respectively) and precision (RSD <1.0%)for repeatability and <2.0% for intermediate precision, within acceptable ranges of accuracy), accurate (recovery in varied dose forms, 94.65-100.26%, within acceptable range, 80–120%), specific, and robust (% RSD <2, for system suitability characteristics). Stress-induced degradation experiments showed that the approach is suitable for use with degradants. The developed method has been effectively used to the determination of entrapment efficiency, drug loading, in vitro release profile, in vitro permeation investigations, and polymeric nanoparticle stability assessment.[4]

Md.ZahidHossain, Analytical method and validation of pharmaceutical products using HPLC (2015).

A Reproducible and simple method was developed for Docetaxel using RP-HPLC.The separation was accomplished using a C18 column at varied temperatures for different techniques, with different buffers, acetonitrile, methanol, and water employed as mobile phases at varying flow rates. The detection was carried out using a PDA (Photodiode array detection) detector; photo diode array UV-Visible detectors were utilized at various wavelengths. The limits of detection (LOD) and quantitation (LOQ) varied from 0.011 µg/mL to 1.16 µg/mL and 0.047 µg/mL to 1.413 µg/mL, respectively. The linearity attained is almost 0.999, and the recovery computed was within the range of 98% to 102% of the Specified limits.[5]

Jan Gerard Maraing, et al., Determination of Epirubicin and its Metabolite Epirubicinol in Saliva and Plasma by HPLC (2003).

We offer a high-performance liquid chromatography (HPLC) approach for the detection of epirubicin and its metabolite epirubicinol in saliva and plasma. Saliva and plasma samples were prepared by extracting analytes with a chloroform:2-propanol combination (6:1, vol/vol) and evaporating the organic phase to dryness under vacuum at about 45°C. The anthracyclines were analysed using reversed-phase isocratic elution on a Chromsep stainless steel HPLC column (150 × 4.6 mm I.D.) packed with Nucleosil 100 S C18 material with a particle size of 5 µm. The detection was done using spectrofluorimetric with excitation and emission wavelengths of 474 and 551 nm, respectively. The anthracyclines eluted within 10 minutes of injection, and the approach seemed to be specific.The method has a linear concentration range of 5 to 1000 µg/L for epirubicin and 2 to 400 µg/L for epirubicinol (r > 0.99) in saliva and plasma. Epirubicin, epirubicinol, and the internal standard doxorubicin were recovered from saliva and plasma at rates of 88.9 and 69.0%, 87.6 and 77.3%, and 80 and 67.9%, respectively. The lower limit of quantification for epirubicin and epirubicinol was 5 µg/L and 2 µg/L, respectively. The approach was precise and accurate, with coefficients of variation less than 10% both within and between days. Overall, the results show that our approach is acceptable for bioanalysis of epirubicin and epirubicinol in saliva and plasma.[6]

MoloudKazemi, et al., Development of a RP-HPLC method for analysis of docetaxel in tumor-bearing mice plasma and tissues following injection of docetaxel-loaded pH responsive targeting polymeric micelles (2020).

To detect docetaxel (DTX) in the plasma and homogenate tissues of tumour-bearing mice, a straightforward, quick, and sensitive reversed-phase high-performance liquid chromatography (RP-HPLC) approach based on liquid-liquid extraction was created and verified. Researchers created and verified a straightforward, quick, and sensitive reversed-phase high-performance liquid chromatography (RP-HPLC) approach based on liquid-liquid extraction to detect docetaxel (DTX) in the plasma and homogenate tissues of tumour-bearing mice.With a satisfactory level of precision and accuracy, calibration curves were linear in the concentration range of 0.1–10 µg/mL of DTX in plasma and 0.25–50 µg/mL in tissue homogenates. The average drug recovery from plasma extraction was 94.6 ± 1.44%, but tissue homogenates had recoveries varying from 73.5 ± 3.2 to 85.3 ± 2.8%, contingent on the tissue type. Following three freeze-thaw cycles and two months of storage at -70 ± 15°C, DTX remained stable in biological samples with no signs of deterioration. Following the intravenous administration of a 7.5 mg equivalent DTX/kg dose of DTX-loaded folic acid-polyethylene glycol-heparin-tocopherol (FA-PEG-HEP-CA-TOC) micelle formulation to female Balb/c mice, the proposed HPLC method was used to quantify DTX in the mouse plasma and tissues.[7]

D. Suchitra, et al., Rp-Hplc Method Development and Validation tor the Estimation of Docetaxel an Pharmaceutical Dosage Forms (2023).

For the analysis of docetaxel, a chemotherapy drug used to treat many cancer types, a straightforward, precise, stable, and selective RP-HPLC method has been created and approved. Using methanol, acetonitrile, and water (40:40:20 v/v) as the mobile phase at a flow rate of 0.9 mL/min, the chromatographic separation was accomplished using an Agilent ZORBAX Eclipse Plus C18 column. Docetaxel showed a strong peak at a retention duration of 7.12 minutes after detection at 237 nm. Using the formula y = 6816x + 67048, the calibration curve demonstrated a solid linear connection between response and concentration. The regression coefficient was 0.999 for the concentration range of 20–120 µg/mL. The corresponding limits of quantitation (LOQ) and detection (LOD) were 0.15 µg/mL and 0.04 µg/mL.In compliance with ICH criteria, the method's

accuracy, precision, repeatability, specificity, robustness, and detection and quantification limits were all validated. The deteriorated products were effectively isolated from the stress degradation conditions using this approach. The method's broad linearity range, accuracy, and straightforward mobile phase suggest that it can be used for routine, very precise docetaxel quantification.[8]

Linga Reddy Mallampati R, et al., Development and Validation of RP-Hplc Method for the Quantitative Determination of Organic Impurities of Docetaxel in Parenteral Formulation of Docetaxel using UV Detector (2024).

The goal is to create a new reverse-phase high-performance liquid chromatography (RP-HPLC) technique that is quick, easy, accurate, precise, and repeatable for the quantitative assessment of organic contaminants in docetaxel (DTX) parenteral formulation using high-performance liquid chromatography (HPLC). A reversed-phase C18 column with a particle size of 3 µm and a dimension of 4.6×150 mm was subjected to final chromatographic conditions, using acetonitrile as mobile phase B and water as mobile phase A. With gradient elution and ultraviolet (UV) detection at 232 nm, the flow rate is 1.2 mL/min. The diluent is acetonitrile, water, and glacial acetic acid in the ratio 100:100:0.1 (v/v/v).It was confirmed that the analytical test method for the quantitative determination of organic impurities of DTX in parenteral formulation of DTX using HPLC with a UV detector was linear over the tested concentration range for all impurities (10-deacetylbaccatin: 0.032–0.466 µg/mL; DTX: 0.015–0.151 µg/mL; 6-oxodocetaxel: 0.023–2.080 µg/mL; 4-epidocetaxel: 0.022–1.380 µg/mL; 4-epi-6-oxodocetaxel: 0.021–0.673 µg/mL). The plotted calibration charts had a regression coefficient of R^2>0.999 and were linear. Results that were method-specific were judged to meet the requirements for acceptance. In relation to test concentration, limits of detection and quantification were set for the active substances and their contaminants.[9]

PrachiBalaramKharkar, et al., A Rapid and Sensitive Bio Analytical RP-HPLC Method for Detection of Docetaxel: Development and Validation(2017).

Using ketoconazole (KCZ) as an internal standard in biological fluids, a quick and accurate high-performance liquid chromatographic (HPLC) technique for docetaxel anhydrous (DTX) has been created and verified. Techniques: Acetonitrile was used in a liquid-liquid extraction procedure to remove the analyte from human plasma. A mobile phase consisting of 0.2% triethylamine (pH 6.4 with orthophosphoric acid) (45%) and acetonitrile (55%), with isocratic elution, was used to perform the analysis on a Licrosphere IV, C8 column (LC–GC Chromatography Solutions Pvt. Ltd., Mumbai, India) measuring 4.6 x 250 mm. The absorbance wavelength was 230 nm, and the flow rate was 1.5 ml/min.It was discovered that the devised approach had correlation coefficients of roughly 0.999 and was linear over the 100–2500 ng/mL range. Docetaxel's limit of quantification was determined to be 100 ng/mL. 50 ng/mL was determined to be the limit of detection. It was found that the accuracy ranged from 99 to 105% and the intra- and inter-day precision was less than 5%. For docetaxel, the total recovery was between 89.0% and 91.0%. The analysis took only 10.0 minutes in total. The technique was effectively used to determine the pharmacokinetic characteristics of a commercial formulation by measuring the amount of DTX in rat plasma.[10]

CONCLUSION

The comprehensive literature review highlighted a limited number of methods available for the simultaneous estimation of Epirubicin andDocetaxel, particularly using RP-HPLC techniques. There is a need to develop a simple, sensitive, and economical method, validated per ICH guidelines, to address gaps and ensure accuracy, precision, and robustness for routine quality control.

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