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Ensuring Tigecycline Drug Quality: An In-depth Exploration of Assay and Related Substances

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Abstract
To study assay and related substance of Tigecycline in pharmaceutical dosage form. Studying of assay and related impurity substances in Tigecycline. The results of the assay and related substances should be reported in the appropriate units of measurement, along with the method used, validation data, and any relevant calculations. The results should be compared against the acceptance criteria specified in the applicable pharmacopoeial monograph or in-house specification. Based on the results obtained, a conclusion can be drawn regarding the quality of the Tigecycline in the dosage form. If the results meet the acceptance criteria, the dosage form can be considered to be of acceptable quality. If not, corrective actions should be taken to improve the quality of the product.

Keywords: Assay, Tigecycline, Pharmaceutical Dosage Form, Pharmacopoeia

Introduction

A pharmaceutical drug, also referred to as a medicine or medication, officially called medicinal product, can be loosely defined as any chemical substance formulated or compounded as single active ingredient or in combination of other pharmacologically active substance, it may be in a separate but packed in a single unit pack as combination product intended for internal, or external or for use in the medical diagnosis, cure, treatment, or prevention of disease.

Medications are Classified in Various Ways:

One of the key divisions is between traditional small molecule drugs, usually derived from chemical synthesis, and biologic medical products, which include recombinant proteins, vaccines, blood products used therapeutically (such as IVIG), gene therapy, and cell therapy (for instance, stem cell therapies).

Pharmaceuticals are classified in various other groups besides their origin on the basis of pharmacological properties like mode of action and their pharmacological action or activity, route of administration, biological system affected, or therapeutic effects. An elaborate and widely used classification system is the Anatomical Therapeutic chemical Classification System (ATC system). The World Health organization keeps a list of essential medicines.

Dosage form (also called unit doses) are pharmaceutical products in the form in which they are marketed for use, typically involving a mixture of active drug components and nondrug components (recipients), along with other non- reusable material that may not be considered either ingredient or packaging (such as a capsule shell, for example).

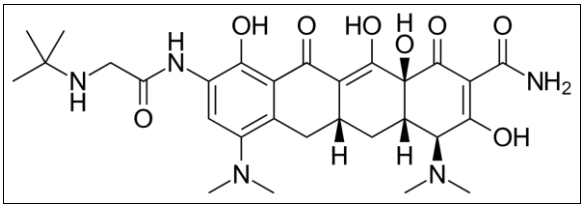
The term unit dose can also sometimes encompass non- reusable packaging as well (especially when each drug product is individually packaged), the FDA distinguishes that by unit-dose "packaging" or "dispensing". Depending on the context, multiple unit doses can refer to distinct drug products packaged together, or to a single drug product containing multiple drugs and/ or doses. The term dosage form can also sometimes refer only to the chemical formulation of a drug product's constituent drug substance(s) and any blends involved, without considering matters beyond that (like how it's ultimately configured as a consumable product such as a capsule, patch, etc.

Tigecycline, sold under the brand name Tygacil, is a tetracycline antibiotic medication for a number of bacterial infections. It is a glycylcycline administered intravenously.It was developed in response to the growing rate of antibiotic resistant bacteria such as Staphylococcus aureus, Acinetobacter baumannii, and E. coli as a tetracycline derivative antibiotic, its structural modifications has expanded its therapeutic activity to include Gram-positive and Gram-negative organisms, including those of multi-drug resistance. Tigecycline is chemically (4S, 4aS, 5aR, 12aR)-9-[[2-(tert- butylamino)acetyl]amino]-4,7-bis(dimethylamino)-1,10,11,12a-tetrahydroxy- 3,12-dioxo-4a,5,5a,6-tetrahydro-4H-tetracene-2- carboxamide.

It was given a U.S. Food and Drug Administration (FDA) fast-track approval and was approved on 17 June 2005. It was

approved for medical use in the European Union in April 2006. It was removed from the World Health Organization's List of Essential Medicines in 2019. The World Health Organization classifies Tigecycline as critically important for human medicine.

Tigecycline is used to treat different kinds of bacterial infections, including complicated skin and structure infections, complicated intra-abdominal infections and community-acquired bacterial pneumonia. Tigecycline does not require dose adjustment for people with mild to moderate liver problems. Tigecycline is metabolized through glucuronidation into glucuronide conjugates and N-acetyl-9-aminominocycline metabolite.



Tigecycline

Assay Determination of Tigecylene by Using HPLC:

An assay is an investigative procedure for qualitatively assessing or quantitatively measuring the presence or amount or the functional activity of a target entity (the analyte) which can be a drug or biological substance or organic sample.

Materials and Methods

Chemicals and reagents: Tigecycline is buying from online source. Acetonitrile, dibasic potassium phosphate, EDTA, KOH (all reagents and chemical used in this study were of analytical grade).

Instrument and Chromatographic Conditions: The Thermo scientific waters empower 2695 HPLC system with UV detector Chromatographic separation was executed on synchronies C18 (150mm×4.6mm) 5µm or equivalent. Mobile phase mixture of 860 volume of buffer preparation and 140 volumes of Acetonitrile used in a Gradient mode. The mobile phase was initially filtered through 0.45 µ nylon filter and sonicated for 15 min before use. The flow rate was maintained at 1ml/min and the injection volume was 20µL. The UV detection was performed at 248 nm and the separation was achieved at 30ºC.

System suitability solution:

Dilute 5.0mL of the system suitability stock solution 50mL with water and mix.

Standard solution preparation:

Weigh accurately about 20.0mg of Tigecycline standard or reference material and transfer it into 200mL volumetric flask.

Add 170mL of diluent and sonicate to dissolve, mix and make up the volume with diluent and mix.

Test solution preparation:

Weigh accurately about 20.0mg of substance and transfer it into 200mL volumetric flask.

Add 170mL of diluent and sonicate to dissolve, mix and make up the volume with diluents and mix.

Procedure

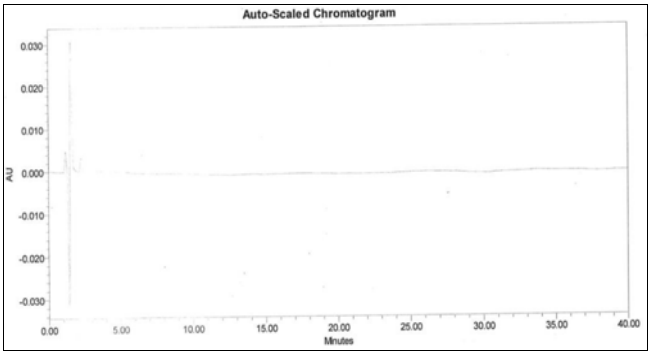


Fig 1: Trial 1 of Tigecycline

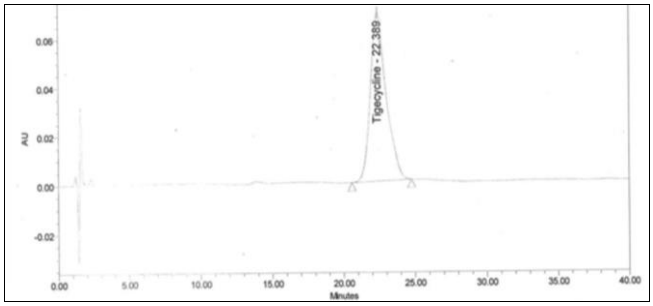


Fig 2: Trial 2 of Tigecyclin

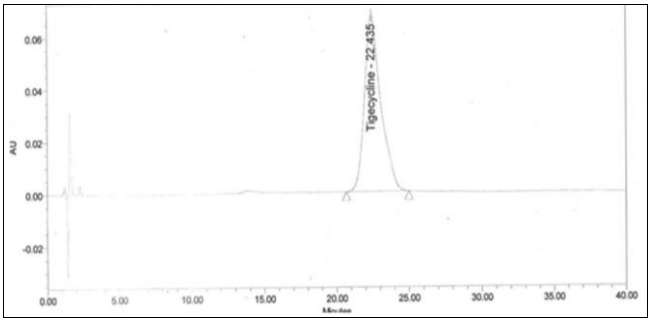


Fig 3: Trial 3 of Tigecycline

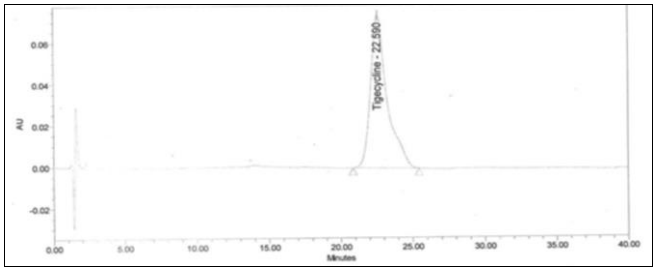


Fig 4: Method Optimized of Tigecycline

Calculation of Assay in Tigecycline

$$\text{\% Assay on anhydrous basis} = \frac{AT}{AS} \times \frac{WS}{200} \times \frac{200}{WT} \times \frac{P}{100 - \%\,Water\ Content} \times 100$$

$$= \frac{5956923}{5306303} \times \frac{20}{200} \times \frac{200}{20} \times \frac{97.2}{99.47} \times 100$$

$$= 1.122613 \times 0.1 \times 10 \times 0.977 \times 100$$

= 109.70 (Limit: 90% to 110%)

Where:

A_T = Mean peak area of Tigecycline peak obtained with test solution preparation

A_S = Mean peak area of Tigecycline peak obtained with standard solution preparation

W_T = Weight of sample in mg

W_S = Weight of Tigecycline standard or reference material in mg

P = Potency

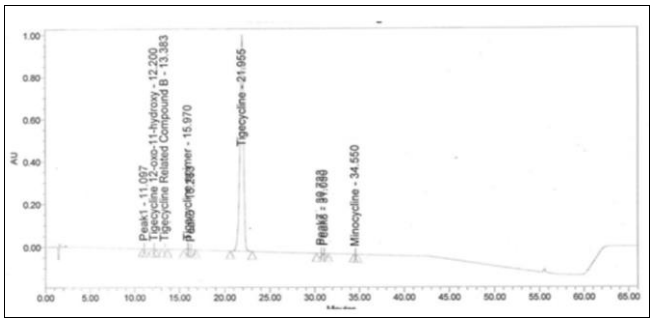


Fig 5: Related Substance of Tigecycline drug

Calculation

$$\textbf{\% of Each Impurity} = \frac{RU}{RS} \times \frac{WS}{50} \times \frac{1}{50} \times \frac{20}{WT} \times \frac{P}{100} \times \mathbf{100}$$

Where:

R_U = Area of each impurity in test solution chromatography

R_S = Average area of Tigecycline peak in replicate injection of standard solution

W_S = Weight of Tigecycline standard from standard solution

W_T = Weight of test solution

$$\textbf{\%Impurity of Peak 1} = \frac{4234}{236951} \times \frac{12.52}{50} \times \frac{1}{50} \times \frac{25}{12.5} \times \frac{97.2}{100} \times 100$$

$= 0.036012 \times 0.2504 \times 0.02 \times 2 \times 0.972 \times 10$

= 0.0351

%Impurity of Tigecycline related compound – B

$$= \frac{12229}{236951} \times \frac{12.52}{50} \times \frac{1}{50} \times \frac{25}{12.5} \times \frac{97.2}{100} \times 100$$

$= 0.05161 \times 0.2504 \times 0.02 \times 2 \times 0.972 \times 10$

$= 0.0502$

$$\textbf{\%Impurity of Tigecycline epimer} = \frac{147995}{236951} \times \frac{12.52}{50} \times \frac{1}{50} \times \frac{25}{12.5} \times \frac{97.2}{100} \times 100$$

$= 0.624581 \times 0.2504 \times 0.02 \times 2 \times 0.972 \times 10$

$= 0.6081$

$$\textbf{\%Impurity of Peak 5} = \frac{21642}{236951} \times \frac{12.52}{50} \times \frac{1}{50} \times \frac{25}{12.5} \times \frac{97.2}{100} \times 100$$

$= 0.091335 \times 0.2504 \times 0.02 \times 2 \times 0.972 \times 10$

$= 0.0889$

$$\textbf{\%Impurity of Peak 7} = \frac{18202}{236951} \times \frac{12.52}{50} \times \frac{1}{50} \times \frac{25}{12.5} \times \frac{97.2}{100} \times 100$$

$= 0.020506 \times 0.2504 \times 0.02 \times 2 \times 0.972 \times 10$

= 0.0200

$$\textbf{\%Impurity of Minocycline} = \frac{1530}{236951} \times \frac{12.52}{50} \times \frac{1}{50} \times \frac{25}{12.5} \times \frac{97.2}{100} \times 100$$

$= 0.0064570 \times 0.2504 \times 0.02 \times 2 \times 0.972 \times 10$

= 0.0063

Results and Discussion

The results of the assay and related substances should be reported in the appropriate units of measurement, along with the method used, validation data, and any relevant calculations. The results should be compared against the acceptance criteria specified in the applicable pharmacopoeial monograph or in-house specification. Developed new and advanced skills. Developed leadership quality. Gain administrative functions and company culture. Explore options in QA & QC fields. Ability to communicate efficiently. Enthusiasm for self-improvement through continuous professional development. Become updated with all the latest challenges in technological world. Developed team work quality. In starting of the training, the owner helped us to get information about startups. We've learned how to run equipment smoothly without any failure. How to do calibration and validation of instruments. Industry is equipped with modern instruments so it is extremely useful for us to run them. This training helps us to build entrepreneurships and marketing strategies throughout world. Developed skills and responsibilities.

Based on the results obtained, a conclusion can be drawn regarding the quality of the Tigecycline in the dosage form. If the results meet the acceptance criteria, the dosage form can be considered to be of acceptable quality. If not, corrective actions should be taken to improve the quality of the product. This industrial training provided a valuable learning experience in the career exploration process and gave us unexpected benefit. Now we've evaluated the class room taught facts and ideas and applied them to the real-life situation. The basic laboratory requirement for validation and quality assurance of various pharmaceutical products, the variety of machine used in the large-scale industries of medicine etc. These and many other factors cause the enhance of our knowledge and have created a lifelong interest to learning through an exposure to new educational experience. The main aim of the pharmaceutical drugs is to serve the human to make them free from potential illness or prevention of the disease. For the medicine to serve its intended purpose they should be free from impurity or other interference which might harm humans. This is aimed at focusing the role of various analytical instruments in the assay of pharmaceuticals and giving a thorough survey of the instrumentation involved in pharmaceutical analysis. This also highlights the advancement of the analytical techniques beginning from the older titrimetric method and reaching the advanced hyphenated technique stages.

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