INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA):IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

**Review Article**

# Evaluation Parameters Of Tigecycline : Tetracycline Antibiotic

**Sakshi D. Surade*, Vikas S. Shinde**

*S.N.D College Of Pharmacy*

ARTICLE INFO

Received: 16 Dec 2023
Accepted: 20 Dec 2023
Published: 30 Jan 2024

Keywords:
Tigecycline,
Lyophillization

DOI:
10.5281/zenodo.10588903

## ABSTRACT

It is tetracycline antibiotic. Tigecycline is a new intravenous broad spectrum antibiotic with activity against many drug-resistant organisms. Tigecycline is the first drug in the glycycline class of antibiotic. It is derivative of minocycline .It is developed in respond to growing rate of antibiotic resistant bacteria such as Staphylococcus aureus, Acinetobacter baumannii, and E. coli. Tigecycline has a broad spectrum of activity, including activity against drug-resistant gram-positive organisms. The dose of Tigecycline 50mg intravenously every 12 hours after a 100 mg loading dose. Tigecycline has historically been administered intravenously because it exhibits generally poor bioavaibility when given orally. Tigecycline is currently manufactured as a lyophilized powder. Due to the propensity for tigecycline to degrade, these powders are prepared under low-oxygen and low-temperature conditions in order to minimize degradation. Such processing is expensive because it requires special equipment and handling. 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.

## INTRODUCTION

Tigecycline has a broad spectrum activity against gram positive and gram negative bacteria. Tigecycline is(4S,4aS,5A,12S)symmetrical.9[2(tertbutylamino)acetamido]4,7bis(dimethylamino)1,4,4a,5,5a,6,11,12aoctahydro 3,10,12,12atetrahydroxy-1,11-dioxo-2-naphthacenecarboxamide. The chemical formula of tigecycline is C29H39N5O8, and its molecular mass is 585.65 daltons. The chemical structure of tigecycline is shown in Figure 1. This powder is orange in colour. A 1% tigecycline aqueous solution has a pH between 7.7 and 8.2. Tigecycline melts between 170 and 172 degrees Celsius, forming a yellow liquid that disintegrates around 185 degrees Celsius. The reconstituted solution is yellow to orange in colour and is virtually devoid of impurities. Tigecycline is available in single dose 10ml vial which contains 50mg of tigecycline lyophilized powder. Lyophillization is a low temperature dehydration process that involves freezing the product and

***Corresponding Author:** Sakshi D. Surade
**Address**: *S.N.D College Of Pharmacy*
**Email** : sakshisurade03@gmail.com

**Relevant conflicts of interest/financial disclosures**: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

lowering the pressure,removing the ice by sublimation.In this process.This is the process in which water is removed from a product after it is frozen and placed under a vaccume,allowing the ice to change directly from solid to vapour without changing into the liquid state.The principle behind the lyophillization is sublimation. The lyophillization involves three main steps : 1) Freezing , 2) Primary drying, 3) Secondary drying .The material first frozen at very less temperature and when it get frozen then remaining water content is removed by applying vaccume pressure,nd then the product is dried and it remains as a cake. The "D" tetracycline ring's C9 carbon has a t-butylglycylamido side chain added to it, making tigecycline a chemically altered version of minocycline.94 Most efflux pumps and ribosome protection proteins, which reduce the activity of other tetracyclines, have no effect on tigecycline. In comparison to other tetracycline agents, tigecycline has a higher binding affinity to the ribosomal binding site (see Table 292.2) and a wider spectrum of activity. Bone discolouration in rat models has been seen, which suggests that tigecycline similarly to other tetracyclines generates calcium complexes in bone. Given its action against enteric gram-negative bacilli and anaerobes, including B. fragilis, tigecycline is licenced for use in treating difficult infections of the skin, skin structure, and complicated intra-abdominal infections in adults.

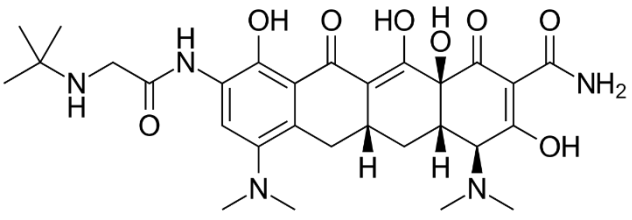


**Fig.no. 1 Tigecycline**

Tigecycline, a glycylcycline, prevents amino-acyl tRNA molecules from entering the ribosome's A site by attaching to the 30S ribosomal subunit in bacteria. This stops amino acid residues from being incorporated into peptide chains that are growing longer. The 9-position of minocycline bears a glycylamido moiety in tigecycline. The substitution pattern gives tigecycline specific microbiologic characteristics and is absent from any naturally occurring or semi-synthetic tetracycline. The two main tetracycline resistance mechanisms, ribosome protection and efflux, are unaffected by tigecycline. As a result, tigecycline has proven to be active both in vitro and in vivo against a variety of bacterial infections. No evidence of cross resistance between tigecycline and other antibiotics has been found. Beta-lactamases and other resistance mechanisms do not harm tigecycline.

**Introduction to Lyophillization:**

**What is Lyophillization** ?

Lyophillization is the process of removal of ice or other frozen solvents from a material through the process of sublimation and the removal of bound water molecules through the process of desorption. This process, called sublimation, transforms the ice directly into water vapor without first passing through the liquid state. The water vapor given off by the product in the sublimation phase condenses as ice on a collection trap, known as condenser.

**There are three key stages to the process: freezing, primary drying, and secondary drying**

The water in the sample is frozen during the first stage, called FREEZING, which enables it to separate from the other components in the combination. The sample(s) is then placed in the freeze-drying apparatus after this is completed. A standard freezer (-30°C), an ultralow temperature freezer (-80°C), or even liquid nitrogen (-196°C) can be used for this. It takes a few hours to finish this phase. Sublimation takes control during the PRIMARY DRYING step, which is the second. Solid water can turn into vapor by absorbing heat from the sample once it is placed in the lyophilizer at the proper temperature and vacuum. Here, the pressure is lower and the vapor is sent directly into the collecting chamber. The third stage, known as

SECONDARY DRYING, is the most important because it involves eliminating non-freezing water in order to lower the water content to acceptable levels. Vestigial water might affect the stability and quality of the final product.Freeze-drying has trouble with samples that contain volatile materials, like solvents other than water. These materials have an impact on the eutectic temperature, can increase the vapor pressure at the sample surface, and require less heat in order to sublimate. As a result, samples that contain volatile substances will melt in flasks that are left to room temperature. Additionally, general equipment and/or equipment parts may sustain damage.

**Pharmacokinetic and Pharmacodynamics properties Tigecycline:**

Tigecycline is administered intravenously for 30 to 60 minutes every 12 hours due to poor absorption from the intestines. The amount of tigecycline that was able to bind to plasma proteins in vitro at concentrations of 0.1, 1, and 15 ug/mL was reported as 71, 89, and 96, respectively. This demonstrated nonlinear plasma-protein-binding behavior because the amount of tigecycline that was unbound reduced as the overall concentration of tigecycline increased. Tigecycline has a broad distribution into different tissues, a substantial volume of distribution (7–10 L/kg), and a systemic clearance (from 0.2 to 0.3 L/h/kg) [10]. An initial dose of 100 mg, followed by 50 mg every 12 hours, is the suggested standard dosage regimen for tigecycline. Tigecycline should be taken for 5-14 and 7-14 days, respectively, depending on whether the condition being treated is cSSTI, cIAI, or CAP.

**Antibacterial Activity**

Alterations to the tetracycline structure resulted in an expansion of tigecycline's spectrum of an antibacterial activity against a wide spectrum of Gram-positive and Gram-negative pathogens. Currently, due to its effectiveness, tigecycline is the last-line treatment option against MDR bacterial pathogens, especially carbapenem-resistant Enterobacteriaceae . Tigecycline showed good activity against methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE), extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae, and penicillin-resistant Streptococ

## MATERIAL AND METHOD:

### MATERIAL:

Sequoia Research Products (Pangbourne, UK) provided the tigecycline powder. The seller of Oxyrase was Oxyrase, Inc. (Mansfield, OH). Thermo Fisher Scientific supplied the clone fetal calf serum (Rockford, IL). L-glutamine was obtained from Life Technologies (Burlington, ON, Canada), while stem cell factor (SCF) and interleukin 3 (IL-3) were obtained from R&D Systems (Burlington, ON, Canada). Mueller Hinton Broth was acquired from BD (Franklin Lakes, NJ), and the Ontario Cancer Institute Tissue Culture Media Facility (Toronto, ON, Canada) made Iscove's modified Dulbecco's media (IMDM) from powder (Cat # 12200, Invitrogen (Burlington, ON, Canada). Unless specified, all other reagents were acquired from Sigma.

### METHOD OF PREPARATION

1. Before starting bulk formulation stage, purge with filtered nitrogen the formulation & filling lines, product transfer line & the formulation, intermediate & holding tank
2. Add approx 95% (76L) of required amount of water for injection in the formulation tank f chill the water to 2°C -8°8 while sparging with filtered nitrogen, until the dissolved oxygen content is <0.5 mg/l (ppm).
3. Measure the dissolve oxygen content of the water. If the dissolved oxygen content is greater than 0.5mg/l, continue to sparge the water with filtered nitrogen until dissolved oxygen content is <0.5MG/L(PPM) and the temperature is 2°C-8°C.

4. Continue sparging and pressurize the holding tank with filtered nitrogen. Discontinue sparging of the water in the formulation tank prior to adding the drug substance and Continue with a filtered nitrogen blanket.
5. Add 1600 g of drug substance to the tank ensuring that the drug substance is not exposed to air by maintaining filtered nitrogen flow during the entire process.
6. Mix the bulk solution. The solution temperature must be 2°C-8°C.
7. Add water for injection to formulation tank until the final volume/wt. (80L) is reached and mix the solution.
8. Maintain a filtered nitrogen blanket in the formulation tank. Measure the dissolved oxygen content.
9. It is dissolved oxygen content of the solution is more than 0.5 mg/L, continue filtered nitrogen sparging until a stable dissolved oxygen content measure is obtained.

**Evaluation Parameters :**

**1. Description :**

Weigh approximate 1 vial of sample and transfer it in a cleaned and dry petri dish. Observed the appearance against white background.

2. **Identification:**

A. **By HPLC:**

Compare the retention time of the major peak of the Sample solution to that of the Standard solution, as obtained in the Assay.

B. **By UV:**

Procedure: Prepare sample and standard solution as per assay. Compare the UV spectrum of the major peak of the Sample solution to that of the Standard solution (Spectral range 200 nm to 400 nm).

C. **pH:**

Reconstitute the S vials as per directed on the label and determine the pH of the solution.

**3. Clarity and Colour of Solution:**

Transfer a suitable volume of the solution under examination. Into another matched test tube add the same volume of the freshly prepared opalescence standard. After 5 minutes, compare the contents of the test tubes against black background by viewing under diffused light down the vertical axis of the tubes.

**4. Assay (By HPLC):**

**Preparation of Sample Solution**:

Accurately weigh and transfer 10 mg of Sample to a 100 ml amber color volumetric flask, add 50 ml diluent, sonicate to dissolve, dilute to volume with diluent and mix.

**Preparation of Standard Solution:**

Accurately weigh and transfer 10 mg of USP Tigecycline RS to a 100 ml amber color volumetric flask, add 50 ml diluent, sonicate to dissolve, dilute to volume with diluent and mix.

**Preparation of Diluent:**

Weigh 4.35 gm of dibasic potassium phosphate and 0.5 gm of sodium bisulfite in 1000 ml water. Adjust with 1 N potassium hydroxide to a pH of 8.0.

**Preparation of Buffer:**

Weigh 4.35 gm of dibasic potassium phosphate and 0.93 gm of edetate disodium in 1000 ml water. Adjust with phosphoric acid to a pH of 6.2.

**5. Organic Impurities (By HPLC):**

**Preparation of Mobile Phase:**

**Mobile Phase A:**

Dissolve 4.35 g of dibasic potassium phosphate and 0.93 g of edetate disodium in 950 ml of water. Adjust with phosphoric acid to a pH of 6.4 ±0.05, and add 50 ml of acetonitrile.

**Mobile Phase B:**

Dissolve 4.35 g of dibasic potassium phosphate and 0.93 g of edetate disodium in 500 mL of water. Adjust with phosphoric acid to a pH of 6.4± 0.05, and add 500 mL of acetonitrile.

| Time (in min) | Mobile Phase A (%) | Mobile Phase B (%) |
|---|---|---|
| 0 | 85 | 15 |
| 40 | 57 | 43 |

| | | |
|---|---|---|
| 55 | 0 | 100 |
| 58 | 0 | 100 |
| 59 | 85 | 15 |
| 66 | 85 | 15 |

**Preparation of Diluent :**

Weigh 4.35 gm of dibasic potassium phosphate and 0.5 gm of sodium bisulfite in 1000 ml water. Adjust with 1 N potassium hydroxide to a pH of 8.0

**System Suitability Solution:**

Weigh 500 mg of USP Tigecycline RS and dilute to 100 ml with Diluent (Solution A). Then weigh 5 mg of USP Tigecycline Related Compound B RS and dilute to 100 ml with Diluent (Solution B). Pipette 10 ml of Solution A and 4.8 ml of Solution B in a volumetric flask. Mix the solution and dilute with Diluent to 100 ml.

**Sensitivity Solution .**

Weigh 5 mg of USP Tigecycline RS and dilute to 100 ml with diluent. Take 1 ml of the solution and dilute to 200 ml with diluent. (0.25 µg/ml).

**Standard Solution:**

Weigh 25 mg of USP Tigecycline RS and dilute to 100 ml with Diluent. Take 2 ml of the solution and dilute to 100 ml with Diluent.

**Sample Solution:**

Weigh 50 mg of Tigecycline from the combined contents of NLT 5 vials of Tigecycline for Injection and dilute it to 100 ml with Diluent.

**CHROMATOGRAPHIC CONDITIONS:**

Detector : UV detector
Column : 4.6-mm x 15-cm; 3-um packing (LI)
Column Temperature : 30°C
Autosampler Temperature : 10°C
Flow Rate : 1 ml/min
Wavelength : 248nm
Injection Volume : 25µl
Run Time :

| Sr . No | Order Of Injection | No Of Injections |
|---|---|---|
| 1 | Mobile Phase | 1 |
| 2 | Diluent | 1 |
| 3 | System Suitability Solution | 1 |
| 4 | Sensitivity Solution | 1 |
| 5 | Standard Solution | 6 |
| 6 | Sample Solution | 1 |
| 7 | BKT | 1 |

**Sequences :**

**Solubility Requirements :**

**Resolution :**

NLT 1.5 between tigecycline related compound B and the tigecycline epimer ,System suitability solution .

**Tailing Factor :**

0.7 - 1.5, Standard solution

**Relative standard deviation :**

NMT 5.0%, Standard solution

**Signal - to - noise ratio :**

NLT 10 , Sensitivity solution

**Calculations :**

Calculate the percentage of the labeled amount of tigecycline (C H N O) in the portion of Tigecycline for injection taken :

**Result = (ru/rs)X (Cs/Cu) X 100**

**% of individual unknown impurity = ru/rs X 25/100 X 2/100 X 100/50 X 100**

**% Of total unknown impurities = sum of all % impurity**

Where ,

ru = peak response of tigecycline from the sample solution

rs = peak response of tigecycline from the standard solution

Cu = concentration of USP Tigecycline RS in the Standard solution (mg/ml)

Cs = nominal concentration of tigecycline in the Sample solution (mg/ml)

**6. Bacterial Endotoxins :**

**Procedure :**

NMT 1.75 USP Endotoxin per mg.

**Procedure :**

Prepare the standard control series by using LRW (4 λ).

**Negative Product Control:**

Dispense 50 uL of sample MVD/2 or MVD/4 in duplicate of depyrogenated test tube and Add 50 uL LRW and label it as Test sample. Add 100 µl of lysate into Idispensed tube of sample dilution MVD/2 or MVD/4 in duplicate.

Product Positive Control: 50 µL of Standard dilution (Concentration 0.5 EU/mL. that is 42) + 50 HL of sample dilution tube MVD/2 in duplicate and label it as product positive control (PPC). Transfer 100 µL of Lysate in assay tube and label it as positive control (PC). Negative Control: 100 µL of LRW and label it as negatives control (NC).

**NOTE:** After addition of test sample, CSE, LRW in the depyrogenated labelled test tube add the 100 µL lysate in each test tube before start the incubation.

Swirl gently the tube and incubate at 37°C 1°C for 60+ 2 minutes in heating dry block.

After the incubation period, carefully remove the assay tubes for observation.

**Observation and Interpretation:**

- A positive reaction is characterized by the formation of a firm gel that remains when inverted through 180°, record such a result as positive (+). A negative result is characterized by the absence of such firm gel, record such a result as Negative (-).
- Interpretation: The article meets the requirements of the test if the concentration of Endotoxin is not more than that specified in the specifications.
- Add 100 µL of Lysate previously reconstituted with LRW in Assay tube, Sample, Negative control, PC and PPC tube in duplicate. Swirl gently and incubate at 37°C 1°C on heating dry block for 60+ 2 minutes.
- After completion of incubation period, check the integrity of gel in tube take each tube directly from the heating block and invert it approximately 180° in one smooth motion, if a firm gel form that remains in place upon inversion, record the result as positive and result is negative when firm gel is not formed.
- The test is invalid only if positive control tube do not show clot formation and the negative control tube show firm colt.
- When any new bottle of Lysate, CSE, and LRW is opened record the date of opening on the bottle itself and use it before its expiry period.

**7. Uniformity Of Dosage Units :**

Accurately weigh 10 containers individually, taking care to preserve the identity of each container. Remove the contents of each container by a suitable means. Accurately weigh the emptied container individually, and calculate for each container the net weight of its contents by subtracting the weight of the container from the respective gross weight. Calculate the drug substance content of each vial from the net weight of the individual vial content and the result of the Assay. Calculate the acceptance value.

**8. Particulate Matter:**

Procedure: Constitute the injection as directed on the label. Observe the solution for Particulate Matter.

**9. Sterility:**

**Preparation of test Solution:**

Transfer about 10.0 gm of sample, transfer into a conical flask containing 100 ml sterile water for injection, mix & dissolve.

**Media Preparation:**

Prepare 3 set of 4 test tubes with 100 ml Fluid Thioglycolate Medium (FTGM) and 3 set of 4 test tubes with 100 ml Soyabean Casein Digest Medium (SCDM). Preincubate both the media at 30°to 35°C for 24 hrs.

**Culture Required:**

Fluid thioglycolate medium is primarily intended for the culture of anaerobic bacteria i... Bacillus

subtilis, Pseudomonas aeruginosa. Staphylococcus aureus, Clostridium sporogenesis. Soyabean-cascin digest medium is suitable for the culture of both fungi and aerobic bacteria i.e., Aspergillus brasiliensis, Candida albicans.

**Procedure:**

- Take out sterile membrane filtration unit and place sterile membrane in the filtration flask by means of sterile forceps. Wet the membrane by adding 25 ml of 0.1% w/v sterile peptone and filter it off using Vacuum pump.Filter the test sample using vacuum pump filtration.Rinse the membrane with 3 x 100 ml of sterile 0.1 w/v peptone using vacuum pump.
- Dis-assemble the membrane filtration unit and aseptically cut the membrane filter into two halves by using sterile scissor.
- Transfer one half of the membrane filter into the test tube containing 100 ml SCDM and another half into test tube containing 100 ml FTGM by using sterile forceps
- Incubate the SCDM tubes at 20-25°C and FTGM tubes at 30-35°C for not less than 14 days.

**Positive & Negative Control:**

From set of FTGM and SCDM Media prepared test tube I tube is used as positive control which is inoculated after test sample inoculation. Whereas negative control is the uninoculated tube. Another test tube is used as open for observing air contamination during testing.

## REFERENCES


1. Wyeth Pharmaceutics . Tygacil (Tigecycline) for Injection [package insert] Philadelphia, PA: Wyeth Pharmaceuticals Inc.; 2005.
2. Garrison MW, Neumiller JJ, Setter SM. Tigecycline: an investigational glycylcycline antimicrobial with activity against resistant gram-positive organisms. Clin Ther. 2005;27(1):12–22.
3. Zhanel GG, Homenuik K, Nichol K, Noreddin A, Vercaigne L, Embil J, Gin A, Karlowsky JA, Hoban DJ. The glycylcyclines: a comparative review with the tetracyclines. Drugs. 2004;64(1):63–88.
4. Nathwani D. Tigecycline: clinical evidence and formulary positioning. Int J Antimicrob Agents. 2005;25(3):185–192
5. Bauer G, Berens C, Projan SJ, Hillen W. Comparison of tetracycline and tigecycline binding to ribosomes mapped by dimethylsulphate and drug-directed Fe2+ cleavage of 16S rRNA. J Antimicrob Chemother. 2004;53(4):592–599.
6. Muralidharan G, Micalizzi M, Speth J, Raible D, Troy S. Pharmacokinetics of tigecycline after single and multiple doses in healthy subjects. Antimicrob Agents Chemother. 2005;49(1):220–229.
7. Sun HK, Ong CT, Umer A, Harper D, Troy S, Nightingale CH, Nicolau DP. Pharmacokinetic profile of tigecycline in serum and skin blister fluid of healthy subjects after multiple intravenous administrations. Antimicrob Agents Chemother. 2005;49(4):1629–1632.
8. Muralidharan G, Fruncillo RJ, Micalizzi M, Raible DG, Troy SM. Effects of age and sex on single-dose pharmacokinetics of tigecycline in healthy subjects. Antimicrob Agents Chemother. 2005;49(4):1656–1659
9. Fritsche TR, Jones RN. Antimicrobial activity of tigecycline (GAR-936) tested against 3498 recent isolates of Staphylococcus aureus recovered from nosocomial and community-acquired infections. Int J Antimicrob Agents. 2004;24(6):567–571
10. Pachon-Ibanez ME, Jimenez-Mejias ME, Pichardo C, Llanos AC, Pachon J. Activity of tigecycline (GAR-936) against Acinetobacter baumannii strains, including those resistant to

imipenem. Antimicrob Agents Chemother. 2004;48(11):4479–4481

11. LaPlante KL, Rybak MJ. Clinical glycopeptide-intermediate staphylococci tested against arbekacin, daptomycin, and tigecycline. Diagn Microbiol Infect Dis. 2004;50(2):125–130.
12. Postier RG, Green SL, Klein SR, Ellis-Grosse EJ, Loh E, Tigecycline 200 Study Group Results of a multicenter, randomized, open-label efficacy and safety study of two doses of tigecycline for complicated skin and skin-structure infections in hospitalized patients. Clin Ther. 2004;26(5):704–714.
13. Solomkin JS, Mazuski JE, Baron EJ, Sawyer RG, Nathens AB, DiPiro JT, Buchman T, Dellinger EP, Jernigan J, Gorbach S, Chow AW, Bartlett J, Infectious Diseases Society of America Guidelines for the selection of anti-infective agents for complicated intra-abdominal infections. Clin Infect Dis. 2003;37(8):997–1005.
14. Babinchak T, Ellis-Grosse E, Dartois N, Rose GM, Loh E, Tigecycline 301 Study Group. Tigecycline 306 Study Group The efficacy and safety of tigecycline for the treatment of complicated intra-abdominal infections: analysis of pooled clinical trial data. Clin Infect Dis. 2005;41(Suppl 5):S354–366.
15. Stevens DL, Bisno AL, Chambers HF, Everett ED, Dellinger P, Goldstein EJ, Gorbach SL, Hirschmann JV, Kaplan EL, Montoya JG, Wade JC. Practice guidelines for the diagnosis and management of skin and soft-tissue infections. Clin Infect Dis. 2005;41(10):1373–1406.
16. Ellis-Grosse EJ, Babinchak T, Dartois N, Rose G, Loh E, Tigecycline 300 cSSSI Study Group. Tigecycline 305 cSSSI Study Group The efficacy and safety of tigecycline in the treatment of skin and skin-structure infections: results of 2 double-blind phase 3 comparison studies with vancomycinaztreonam. Clin Infect Dis. 2005;41(Suppl 5):S341–353.
17. Fluit AC, Florijn A, Verhoef J, Milatovic D. Presence of tetracycline resistance determinants and susceptibility to tigecycline and minocycline. Antimicrob Agents Chemother. 2005;49(4):1636–1638.
18. Ruzin A, Keeney D, Bradford PA. AcrAB efflux pump plays a role in decreased susceptibility to tigecycline in Morganella morganii. Antimicrob Agents Chemother. 2005;49(2):791–793.

HOW TO CITE: Sakshi D. Surade, Vikas S. Shinde, Evaluation Parameters Of Tigecycline : Tetracycline Antibiotic, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 1, 818-825. https://doi.org/10.5281/zenodo.10588903