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Hyperfine Nano-Structural investigations of Solid Phase Cefixime Antibiotic Drug

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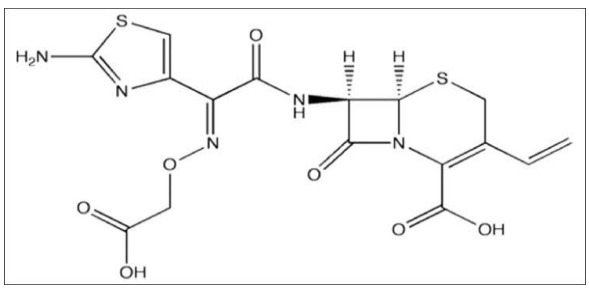
Abstract: It well known that cefixime, an antibiotic, is a third-generation cephalosporin like ceftriaxone and cefotaxime. Cefixime is highly stable in the presence of beta-lactamase enzymes. As a result, many organisms resistant to penicillins and some cephalosporins due to the presence of beta-lactamases, may be susceptible to cefixime. For these importance, we introduce hyperfine nano-structural features for cefixime via high resolution 3D-AFM-investigations to understand how this hetero-molecule is suitable structurally to their function as antibacterial antibiotic.
Keywords : 3D-AFM; XRD; Cefixime; Microstructure; Grain Size; Antibacterial.

I. Introduction

Cefixime is a synthetic fluoroquinolone antibiotic[1] and is chemically 7-{[2-(2-amino-1,3-thiazol-4-yl)-2 (carboxymethoxyimino)acetyl]amino}-3-ethenyl-8-oxo-5thia-1-azabicyclooct-2-ene-2-carbo xylic acid. It is prescribed for urinary tract infection, bronchitis, pneumonia,prostatitis, syphilis and infections of reproductive organs[2]. Literature survey revealed the estimation of Cefixime has been determined along with other drugs by UV[3-4], HPLC[5-9], flow injection analysis[10] and HPTLC[11].



Cefixime is (6*R*,7*R*)-7-{[2-(2-amino-1,3-thiazol-4-yl)-2-(carbomethoxyimino) acetyl] amino}-3-ethenyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.

Cefixime is a β-lactam third-generation antibiotic used in treatment of various infections caused by gram negative bacteria like Haemophilius influenzae, Moraxella catarrhalis, Escherichia coli, Klebsiella spp. Literature survey revealed HPTLC determination of Cefixime, Reversed phase HPLC determination of

Cefixime are the few methods available for it's estimation[13-15]. It is well known that cefixime is poorly soluble in water. Special techniques are required to solubilize poorly water-soluble drugs[16,17]. Several methods have been reported in the literature to enhance the aqueous solubilites of poorly watersoluble drugs[18]. Hydrotropic solubilization is one of them.

It is a phenomenon where addition of large amount of second solute results in an increase in aqueous solubility of another solute. Concentrated aqueous hydrotropic solutions of sodium benzoate, niacinamide, sodium citrate, sodium glycinate and urea have been observed to enhance aqueous solubility of insoluble and slightly soluble drugs. Hydrotropic solutions can be employed to replace organic solvents employed in analysis of poorly water-soluble drugs.

The primary objective of many investigations[19] were to employ the solubilising agent in the tablet formulation and in analytical stock solutions to a poorly water-soluble drug, Cefixime, from its dosage form, is well dissolved precluding the use of costlier organic solvent. Results of analysis by the proposed method compared with results obtained by United states Pharmacopoeial method[20-22]. The solubilising hydrotropic agent, sodium lauryl sulphate and commonly used tablet excipients did not interfere in spectrophotometric determination at λ max 288nm. Beer's law was obeyed in the concentration range of 5-30μg/ml. The results of analysis have been validated statistically[23].

II. Experimental

II.I. Sample Source :

A commercial structurally well confirmed sample of highly pure solid-phase Cefixime which is a β-lactam third-generation antibiotic used in treatment of various infections was supplied from EDWIC company of pharmaceutics (EGYPT) and applied as model for testing micro-structural features and surface topology of Cefixime which is a β-lactam third-generation antibiotic.

II.II.Nano-/Micro-Structural Investigations :

Scanning electron microscopy (SEM): measurements were carried out along ab-plane using a small amount of sample powder by using a computerized SEM camera with elemental analyzer unit Shimadzu (Japan). Atomic force microscopy (AFM): High-resolution Atomic Force microscopy (AFM) is used for testing morphological features and topological map (Veeco-di Innova Model-2009-AFM-USA).The applied mode was tapping non-contacting mode. For accurate mapping of the surface topology AFM-raw data were forwarded to the Origin-Lab version 6-USA program to visualize more accurate three dimension surface of the sample under investigation Cefixime which is a β-lactam third-generation antibiotic .

This process is new trend to get high resolution 3D-mapped surface for very small area ~ 0.1x0.1 μm^2.

II.III. FT-Infrared Spectroscopy :

The infrared spectra of the solid products obtained were recorded from KBr discs using a Shimadzu FT-IR Spectrophotometer in the range from 400 to 4000 cm^{-1}.

III. Results & Discussions

Cefixime which is a β-lactam third-generation antibiotic was examined and detected well structurally and spectrophotometrically by both of X-ray diffractionFig.1a and measuring infrared absorption spectrum in the whole range as shown in Fig.1b .The marked red cycles refer to different kind of functional group that present in the structure moiety of cefixime namely –COOH, NH2- ,-OH, -NH and C=O respectively as it clear in Fig.1b [3,4,5 and 6]. Fig.1a display x-ray diffraction pattern of poly crystalline cefixime phase and red circles refer to pure tri-clinic crystal phase of cefixime drug.

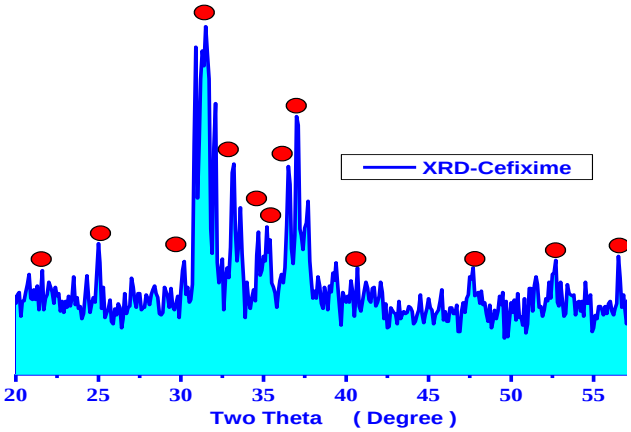


Fig.1a : XRD-profile for poly-crystalline Cefixime .

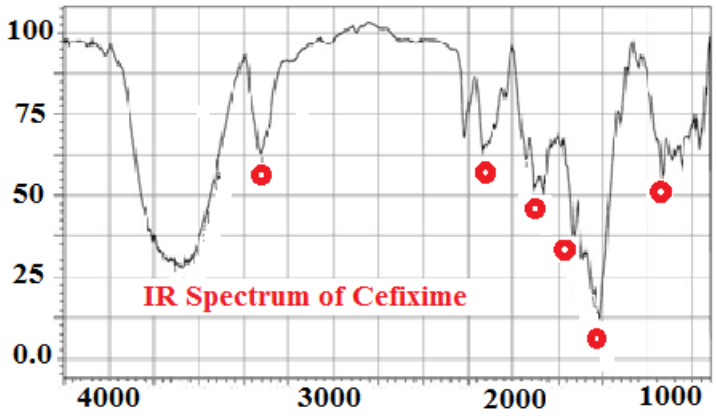


Fig.1b : FT-IR spectrum of Cefixime antibiotic drug powder .

As it clear in Fig.1b the broad band ~ lies in the region 3600-3750 cm-1 may be attributable to the overlapping and intercoupling of groups such as N=C and S=C with surrounding function groups (interference coupling groups effects).

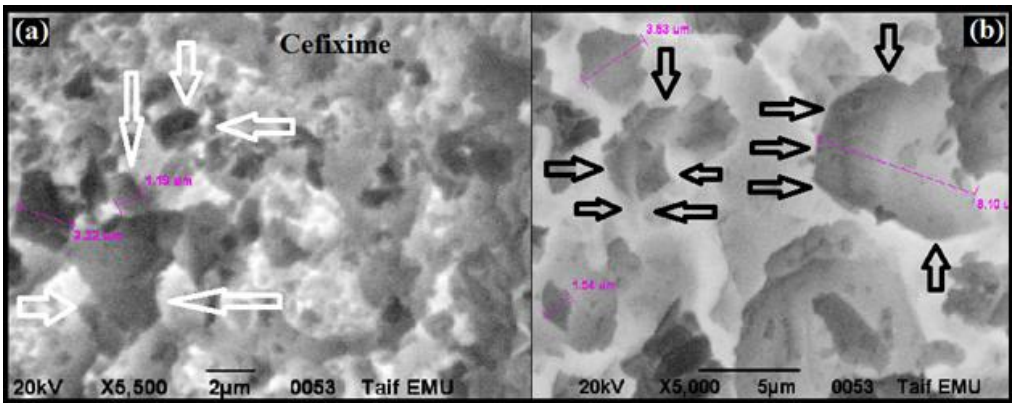


Fig.2a,b : SE-micrograph captured for cefixime with 2 and 5 µm magnification factors

Nano- and Micro-structural features of cefixime were investigated carefully via two different technique 1st scanning electron microscopy (SEM) Fig.2a,b and atomic force microscope (AFM) Fig.3A,B .

As antibacterial drug cefixime interfacial properties is important to evaluate its strength as reactive surface sensitive to bacteria .Fig.2a, b shows SE-micrograph captured for cefixime with 2 and 5 µm magnification factors with grain size averaged in between 0.25-2.5µm which confirm that the cefixime drug has wide range fractionation of particle and grains which are experimental condition dependent[12,13]. Black and white arrows in Fig.2a,b refer to variation of estimated grain size that confirm the experimental conditions play an important role and control in the synthesized grain size.

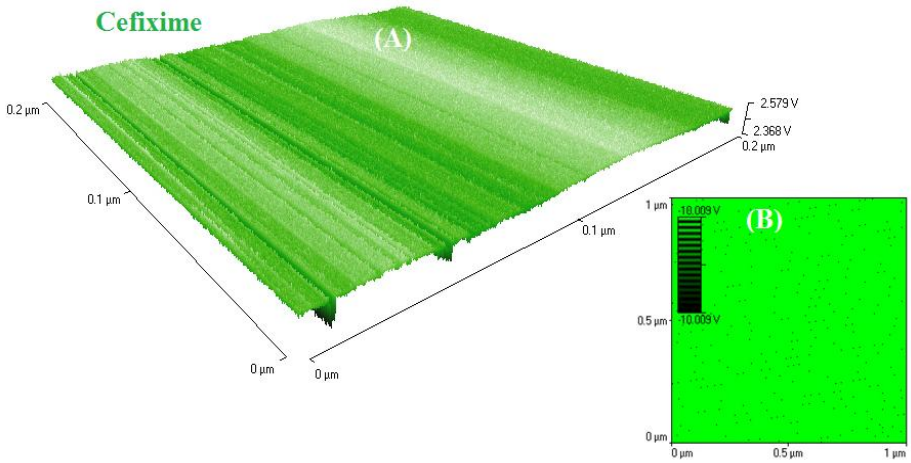


Fig.3A,B : 3D-AFM nano-graph and TM-deflection centers of Cefixime drug

Fig.3A: describes 3D-image of cefixime drug surface topology with 0.2x0.2µm scanned area applying non-contact tapping mode for sensitive samples .One can notify that the arrays are repeated regularly without violation on the whole scanned area 0.2x0.2µm only depth pattern which appeared at ~ 0.035 µm does not repeated in regular manner on the scanned area .

Fig.3B shows TM-deflection centers which can be benefit to understand conductivity behavior of cefixime drug or mapping charts of the surface topology. It is clear that back dots could be represent pinning centers of the material bulk and consequently reactivity of the surface is function and dependent on theses pinning centers numbers.

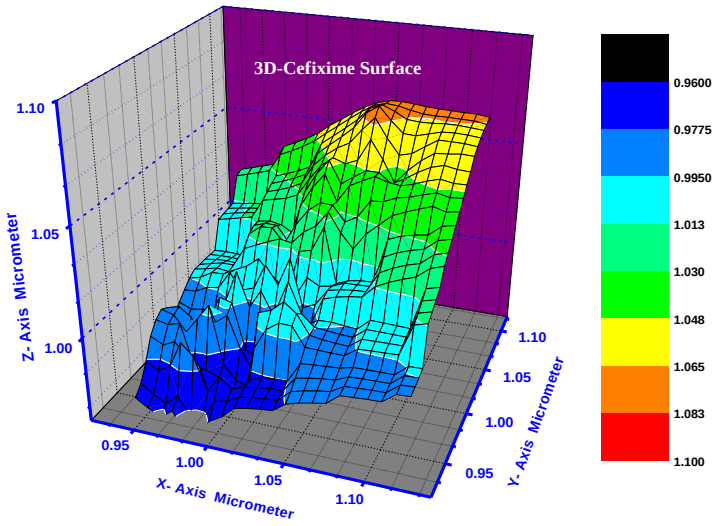


Fig.4: 3D-visuallized AFM-image for Cefixime Drug.

For accurate mapping of the surface topology AFM-raw data were forwarded to the Origin-Lab version 6-USA program to visualize more accurate three dimension surface of the sample under investigation Cefixime which is a β-lactam third-generation antibiotic see Fig.4.

As it clear in Fig.4 which represent very narrow 3D-scanned area with dimensional 0.2x0.2x0.2 μm .The accurate analysis of this figure one can conclude the following facts ; 1st the maximum heights gradient ranged in between (1.065–1.10μm) orange-red zones ,2nd the minimum depth gradient is ranged in between (0.96-0.995 μm) pale –dark blue zones .3rd higher than 50 % of the scanned area moderate in heights and ranged in between 0.99-1.048 μm.

Those represented by blue-green colors. These accurate investigations interpret why cefixime drug has huge unique surface area with different gradients on the surface topology in contrast with others drugs.

IV. Summary

In conclusion Cefixine antibiotic drug has specific nano-structured features with unique huge reactive surface topology qualify it to be one of the most strongest antibiotic families.

V. References

1. Maryadele J. O' Neil, The Merck Index: An Encyclopedia of chemicals, drugs and biologicals, 14th ed. New Jersey: Published by Merck Research Laboratories, Division of Merck and Co., Inc. White House Station. 2006; p. 1924.
2. Abdel Fattah M. El-Walily, Azza A. Gazy, Saied F. Belal and Essam F. Khamis,Quantitative determination of some thiazolecephalosporins through complexation with palladium(II) chloride.J Pharm Biomedical Anal. 2000;22(5-6): 385-392.
3. Cesme M, Tarinc D, Golcu A, Spectrophotometric Determination of Metoprolol Tartrate in Pharmaceutical Dosage Forms on Complex Formation with Cu(II). Pharmaceuticals,2011; 4**:** 964-975**.**
4. Agbaba D, Eric S, Karljikovic-Rajic K, Vladimirov S,Zivanov- Stakic D, Spectrophotometric Determination of Certain Cephalosporins Using Ferrihydroxamate Method. Spectroscopy Letters: An International Journal for Rapid Communication,1997; 30(2), 309-319.
5. Gameiro P, Rodrigus C, Baptista T, Sousa I, Castro B, Solution studies on binary and ternary complexes of copper(II) with some fluoroquinolones and 1,10-phenanthroline: Antimicrobial activity of ternary metalloantibiotics. International Journal of Pharmaceutics, 2007; 334(1): 129-136.
6. Juan R Anacona, Jesus Estacio, Synthesis and antibacterial activity of cefixime metal complexes. Transition Metal Chem, 2006; 31: 227-251.
7. Al-Momani F, Spectrophotometric determination of selected cephalosporins in drug formulations using flow injection analysis. J Pharm Biomedical Anal. 2001,25(5-6): 751-757.
8. Shankar DG, Sushma K, LAkshmi RV, Reddy MN, Murthy TK, RaoSrinivasa Y, Spectrophotometric determination of cefixime trihydrate.Asian J Chem, 2001; 13(4):1649-1651.
9. Shah Paresh B, Kilambi Pundarikakshudu, Spectrophotometric,Difference Spectroscopic, and High-Performance Liquid Chromatographic Methods for the Determination of Cefixime in Pharmaceutical Formulations. J of AOAC Int, 2006; 89(4): 987-994.
10. Kumar Rajnish. et al. Development of colorimetric method for the analysis of pharmaceutical formulation containing both Ofloxacin and Cefixime. Int J Pharmacy and Pharm Sci, 2011; 3 (2): 178-9.
11. El-Shaboury SR, Mohamed FA, SalehGA,Rageh AH, Kinetic spectrophotometric determination of certain cephalosporins using iodate/iodide mixture.*Natural Science*, 2010; 2(5): 432-442.
12. Rageh AH, El-Shaboury SR, Saleh GA, Mohamed FA,Spectophotometric method for determination of certain cephalosporins using 4-chloro-7-nitrobenzo-2-oxa-1,3-diazole (NBD-Cl).*Natural Science*, 2010; 2(8): 828-840.
13. Virupaxappa BS, Shivaprasad KH, Latha MS, A Simple Method For The Spectrophotometric determination of cefixime in pharmaceuticals. *Int J Chemical Eng Research*, 2010; 2(1), 23-28.

14. Kumar R, Singh P, Singh H, Development of colorimetric method for the analysis of pharmaceutical formulation containing both ofloxacin and cefixime. Int J Pharmacy and Pharm Sci,**3**(2), 178(2011).
15. Patel Satish A, Patel Natavarlal J, Development and validation of dual wavelength spectrophotometric method for simultaneous estimation of cefiximetrihydrate and ofloxacin in tablet dosage form. IRJP, 2011; 2(7):145-148.
16. Olajire A. Adegoke, Monsurat O. Quadri, Novel spectrophotometric determinations of some cephalosporins following azo dye formation with pdimethylaminobenzaldehyde. Arabian J Chem, 2012; 2,44-48.
17. Patil VP, Gaikwad AD, Kulkarni VS, Devdhe SJ, Kale SH, Spectrophotometric determination of cefixime in bulk drug using ninhydrin- a modified approach. Inventi Rapid: Pharm Ana & Qual Assur, 2012; In press.
18. Ramadan AA, Mandil H, Dhhan M, Spectrophotometric determination of cefixime in pure form and in Syrian pharmaceuticals through complexation with Cu(II) in acetatebuffer at pH7.8, Asian J Chem, 2013; 25(4)33-39.
19. Gandhi Santosh V. et al. A simple and sensitive RP-HPLC method for simultaneous estimation of Cefixime and Ofloxacin in combined tablet dosage form. Int J Pharmacy and Pharm Sci, 2011; 3: 46-8.
20. Shah J, Rasul Jan M, Inayatullah S Sh, Spectrofluorimetric Method for Determination and Validation of Cefixime in Pharmaceutical Preparations. J Fluoresc, 2011; 21: 579-585.
21. Patel Satish A, Patel Paresh U, Patel NatavarlalJ, Simultaneous spectrophotometric determination of cefixime trihydrate and ofloxacin in tablets. IRJP, 2011; 2(8):105-108.
22. Kapil S. Khandagle, Santosh V. Gandhi, Padmanbh B. Deshpande, Nilesh V.Gaikwad, A simple and sensitive RPHPLC method for simultaneous estimation of cefixime and ofloxacin in combined tablet dosage form. Int J Pharmacy and Pharm Sci,2011; 2(1): 46-48.
23. Ramadan AA, Bodakji A, Mahmoud I, TLC-Densitometric Determination of Vitamins B1, B6 and B12 in Pure and Pharmaceutical Formulations Using Treated Aleppo Bentonite.Asian J Chem, 2010; 22: 3281-3291.

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