Khaled M. Elsabawy & Waheed F.El-Hawary./ *International Journal of Phytopharmacology.* 5(4), 2014, 284-287.

e- ISSN 0975 – 9328
Print ISSN 2229 – 7472

International Journal of Phytopharmacology

Journal homepage: www.onlineijp.com

IJP

SPOTLIGHT ON NANO-STRUCTURAL FEATURES OF SOLID-PHASE MOXIFLOXACIN ANTIBIOTIC AN AFM-INVESTIGATIONS

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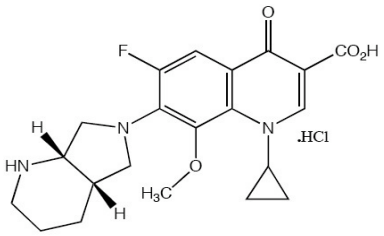
ABSTRACT

The present AFM-nano-structural investigations introduce informative precise data for the internal nano-properties of moxifloxacin solid /powder phase. Grain sizes of moxifloxacin solid molecules were estimated and found to be ranged in between 200-390 nm and line array repeated regularly each ~0.005 μm. These data enhance manufacturer of pharmaceutics to formulate new powder technologies. Many of micro-structural parameters such as TM-deflection centers, interspacing distances between arrays of solid phase and surface roughness were measured and discussed in details.

Key words: Antibacterial Drug; AFM; Nano-Features; Deflection centers; grain size.

INTRODUCTION

Moxifloxacin is advanced generation of fluoroquinolone antibiotic that exerts its effects by trapping a DNA drug enzyme complex and specifically inhibiting ATP-dependent enzymes topoisomerase II (DNA gyrase) and topoisomerase IV.



Structural Formula of Moxifloxacin Drug

Currently, moxifloxacin is being extensively used in the treatment of respiratory system diseases as broad spectrum of antimicrobial activity ((Ferrara AM, 2007; Miravitlles M, 2007; Dalhoff A *et al*., 1996; Rouse MS *et al*., 1996). The favorable pharmacokinetics of moxifloxacin, including a high mean apparent volume of distribution and a long terminal half life, supports a once-daily dosing regimen in the treatment of infectious disease (Stass H *et al*., 1998). It is revealed that moxifloxacin is primarily eliminated in the liver (Stass H and Kubitza D, 1999).

In recent years, a variety of methods on high-performance liquid chromatography (HPLC) for measuring moxifloxacin concentration in plasma have been reported. Fluorescence detector was applied in several methods for its advantage of sensitivity. However, some complex techniques such as gradient elution and on-column focusing (Stass H and Dalhoff A, 1997), pre-column derivatisation (Tatar Ulu S, 2007), or special column (Laban-Djurdjević A *et al*., 2006), were employed. Although a few methods applied HPLC with UV detector to determine moxifloxacin in plasma (Lemoine T *et al*., 2000; Srinivas N *et al*., 2008; Liang H *et al*., 2002; Xu YH, *et al*., 2010), automated extraction methods with a polymeric cartridge (Lemoine T *et al*., 2000), poor extraction recovery (Srinivas N *et al*., 2008), or complicated flow phase (Liang H *et al*., 2002) were involved. LC/ESI-MS/MS methods have also been reported (Vishwanathan K *et al*., 2002; Pranger AD *et al*., 2010), but these advanced techniques are not suitable for clinical routine. Furthermore simple complex formation

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was applied as analytical tool to estimate moxifloxacin as reported in (El-Hawary WF and Al-Gethami FK, 2003).

The major goal of present AFM-investigation is to focus on different nano- structural features of internal lattice structure of moxifloxacin that enhance pharmaceutics manufacturers to produce new advanced powder technologies .

EXPERIMENTAL

Source and Ultra-Crystallization of Moxifloxacin Drug (MOX)

Pure MOX was provided by Jamjoom Pharma, Jeddah, KSA. MOX tablets (Maxim) was produced by Jamjoom Pharma and purchased from local market. The equivalent weights of highly pure moxifloxacin as hydrochloride (MOX.HCl) powders (each of 0.6 gm) ere dissolved in 30 ml of warm ethanol with supporting ultrasonic instrument . The re-crystallization process was performed using gently microwave assist to avoid any traces from applied solvent. The highly pure crystals were dried in oven the forwarded for structural investigations.

AFM-Nano-Structural Measurements

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. This process is new trend to get high resolution 3D-mapped surface for very small area~ 0.01 μm^2.

Fig 1_a 2D-AFM-non-contacting Tapping mode image captured for MOX antibiotic (1_b). 3D-AFM-non-contacting Tapping mode image for MOX antibiotic

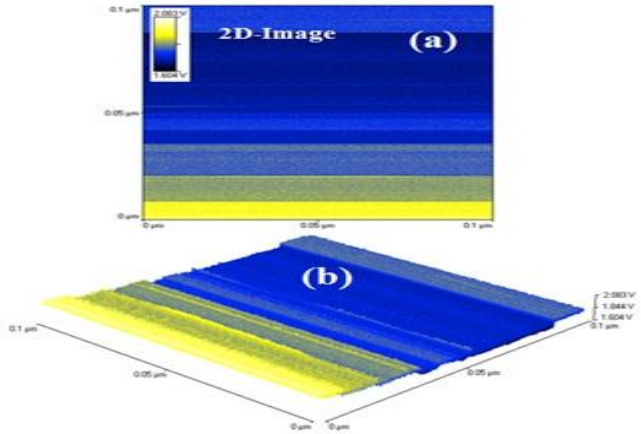


Fig 3. line array density of MOX.HCl antibiotic

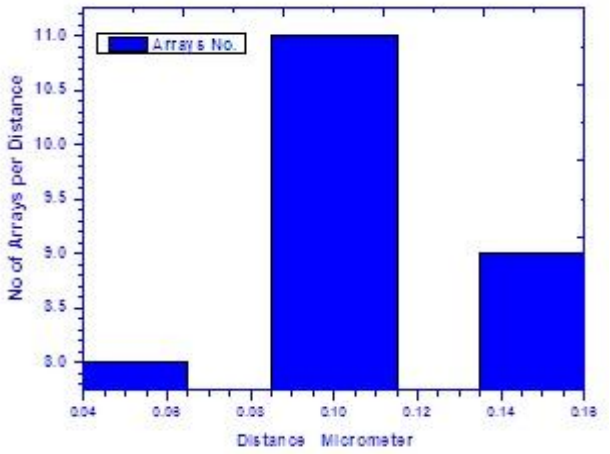


Fig 2a,b. TM-deflection AFM-imaging captured for MOX.HCl antibiotic with two different scanned area : 2_a : 0.2x0.2 μm^2scanned area , 2_b: 0.1x0.1 μm^2 scanned area

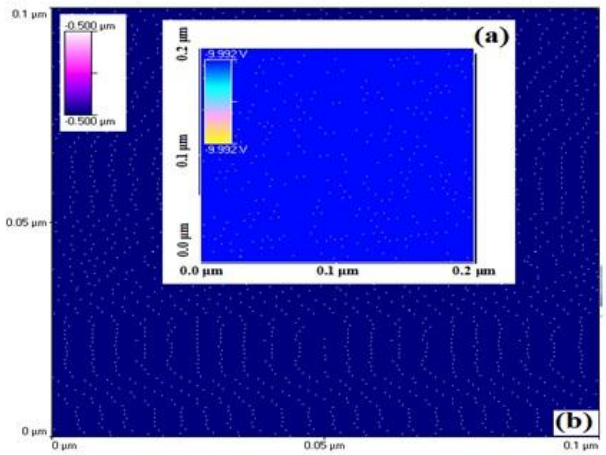
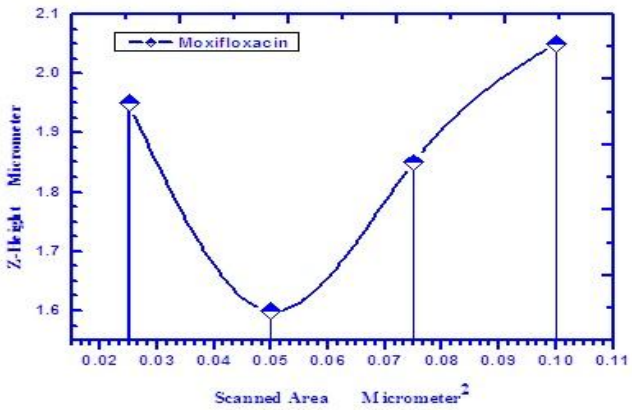


Fig 4. Gradient of heights on MOX.HCl antibacterial agent



RESULTS & DISCUSSION

Fig.$1_{a,b}$ displays two and three dimensional AFM-imaging applying non-contacting tapping mode for pure MOX hydrochloride .The analysis of image using AFM-Vecco soft wear indicated that the surface of MOX antibiotic drug is not unified and it can divided into three sectors as clear in Fig.$1_{a,b}$ the 1st sector is occupies region from zero until ~ 0.04μm with maximum height = 1.84 μm , 2nd region lies at distance from 0.04-0.09 μm with height ~ 1.6 μm as clear in figure 1b .The 3rd region occupies 0.09-0.1 μm with ultimate maximum height ~ 2.083 μm .

These observations are benefit to understand the efficiency and mechanistic steps of MOX drug as antibacterial agent from point of view surface area parameter as vital factor for MOX antibiotic specially if it is applied as cream/ointment antibiotic .

For evaluating internal arrays structure of surface topology of MOX.HCl antibiotic TM-deflection centers images were recorded as clear in Fig.$2_{a,b}$ .Analysis of Tm-deflection centers indicated that the array is repeated ~ 0.005 μm as clear in Fig.2b.

The Tm-deflection centers can be benefit to interpret conduction mechanism and compactness layer density of solid phase MOX.HCl if it is attitude as regular solid material regardless its pharmacological applications the average roughness was measured for MOX.HCl surface's and found to be 94 which is considerably highcompared with some other pharmaceutics matter

Fig.3 shows line array density per scanned area , as it clear number of arrays per 0.06 μm = 8 which is minimum value in contrast with distance (x-axis) 0.1 μm in which number of arrays are maximum = 11 line .These observations are conclusive and precise if it is comparable with data estimated from normal micro-structural instrument as scanning electron microscope (SEM) .The surface roughness is array density dependent i.e. as number of arrays per scanned distance increase roughness average increases . This is true only if the surface topology is not unified in heights (there are heights gradient as existed in our cas MOX.HCl antibiotic drug).

Fig.4 explains the surface topology of MOX.HCl drug, as it clear in Fig.4 the minimum height was recorded at 0.05x0.05 μm^2 = 1.6 μm while the maximum one with *z*-height ~ 2.04μm is recorded at 0.1x0.1 μm^2. These details of micro-structural data support chemical reaction reactivity of MOX.HCH on bases of surface area factor.

CONCLUSION

The present AFM-nano-structural investigations introduced informative precise data for the internal nano-properties of moxifloxacin solid /powder phase;

1- Grain sizes of moxifloxacin solid molecules were estimated and found to be ranged in between 200-390 nm and line array repeated regularly each ~0.005 μm.

2- .These micro/nano-structural data enhance manufacturer of pharmaceutics to formulate new powder technologies based on new estimated surface area reactivity.

3- Investigated nano-structural parameters enhance researcher and scientist to understand chemical reactivity of MOX.HCl antibiotic on the bases of huge exposure surface.

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