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A spectral study on the effect of the growth of micelles from a mixture of surfactants on the drug levofloxacin in the presence of nano-titanium oxide

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Abstract:

The study examined the physical and thermodynamic changes in combination with a mixture of surfactants that create filamentous micelles to determine the efficacy of levofloxacin and nano-titanium oxide.The investigation comprised combining two potent surfactants, CTAB and SDBS, in varying ratios and assessing the mixture's viscosity at different temperatures. The development of worm-like micelles was indicated by the measurement of the greatest viscosity value at a ratio of 7:3 between (CTAB) and (SDBS), respectively. Then, this ratio was combined with 200 ppm of nano-titanium oxide and 200 ppm of levofloxacin. The viscosity of the combination was assessed, and its thermodynamic functions were computed. Exothermic behavior, reduced unpredictability, and spontaneous nature were discovered in this process. The mix's impact on Salmonella bacteria was also investigated in this study.

Keywords: Levofloxacin, titanium dioxide nanoparticles, micelles, surfactants, CTAB, SDBS.

دراسة طيفية لتأثير نمو مذيلات مزيج من المواد الفعالة سطحيا على عقار الليفوفلوكساسين بوجود اوكسيد التيتانيوم النانوي

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مستخلص:

تضمن البحث دراسة فعالية مزيج من عقار الليفوفلوكساسين مع اوكسيد التيتانيوم النانوي من خلال دراسة التغيرات الفيزيائية والثرموداينميكية مع مزيج لمواد فعالة سطحيا لها القابلية على تكوين المذيلات الديدانية (الخيطية) .حيث تمت الدراسة مزج مادتين فعالتين سطحيتين وهما (CTAB) و(SDBS) وبأحجام مختلفة وحساب اللزوجة لهذا المزيج وبدرجات حرارية مختلفة ، حيث وجد ان اعلى قيمة للزوجة كانت عند نسبة (7:3) من (CTAB) و(SDBS) على التوالي والتي تشير الى تكوين المذيلات الديدانية (الخيطية) ثم مزج هذه النسبة مع (PPM200)من عقار الليفوفلوكساسين و (PPM200) من اوكسيد التيتانيوم النانوي ثم قيست اللزوجة وحسبت الدوال الثرموداينميكية لهذا المزيج وقد وجد ان لهذا التفاعل باعث للحرارة واقل عشوائية وتلقائي ودراسة تأثير هذا المزيج على بكتريا السالمونيلا.

الكلمات المفتاحية: ليفوفلوكساسين ، اوكسيد التيتانيوم النانوي ، المذيلات ، المواد الفعالة سطحيا ، CTAB، SDBS .

Introduction

Levofloxacin**:** The molecular formula of the antibiotic levofloxacin (LFX) is $C_{18}H_{20}FN_3O_4$. Levofloxacin (LFX), a medication, is an enantiomer. Figure (1) shows its structural chemical makeup[1].

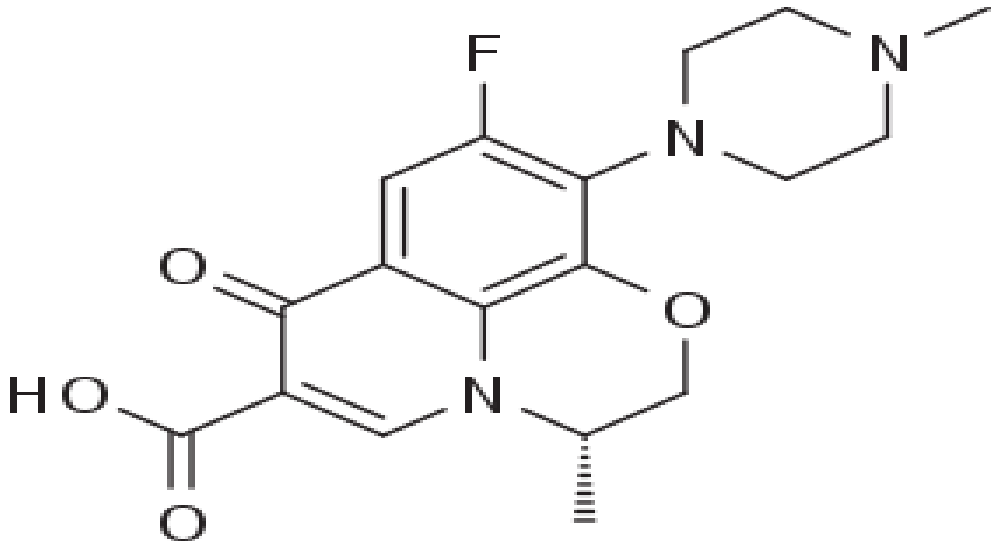

Figure (1): The structural composition of levofloxacin[1].

A medication of the fluoroquinolone group's third generation, levofloxacin is used to treat bacterial infections. The essential medications list of the World Health Organization includes this safe and effective treatment. It was granted a patent in 1987 and was later approved for medical use in the US in 1996 by the Food and Drug Administration (FDA) [2]. Patients with no other options for treatment who have acute bacterial sinusitis, acute exacerbation of chronic bronchitis, or urinary tract infections should only take it. To further prevent the growth of germs resistant to drugs, levofloxacin (LFX) is used. Levofloxacin is advised to be used exclusively in situations of severe bacterial infections, according to the U.S. Food and Drug Administration (FDA) [3].

Nano-titanium dioxide: Because of their affordability, durability, and bioactivity, studies have demonstrated that nano-titanium dioxide particles are among the best coverings for external surfaces that are resistant to bacteria and pathogens. This is explained by the characteristics of these particles, which include their large surface area, resistance to corrosion, and consistency in color.Particles of titanium dioxide find multiple uses, including surface disinfection, food, cosmetic, and water purification, and pharmaceutical manufacturing. Their non-toxicity has led to approval of their usage as food contact chemicals by the U.S. Food and Drug Administration (FDA)[4]. Titanium dioxide nanoparticles has the capacity to eradicate microorganisms, and their antibacterial action is mediated by a similar mechanism as other nanomaterials[5]. The mechanism by which titanium dioxide nanoparticles work as antibacterial agents against bacteria like E. coli, Salmonella intestinal bacteria, and Staphylococcus aureus is shown in Figure (2) [6].

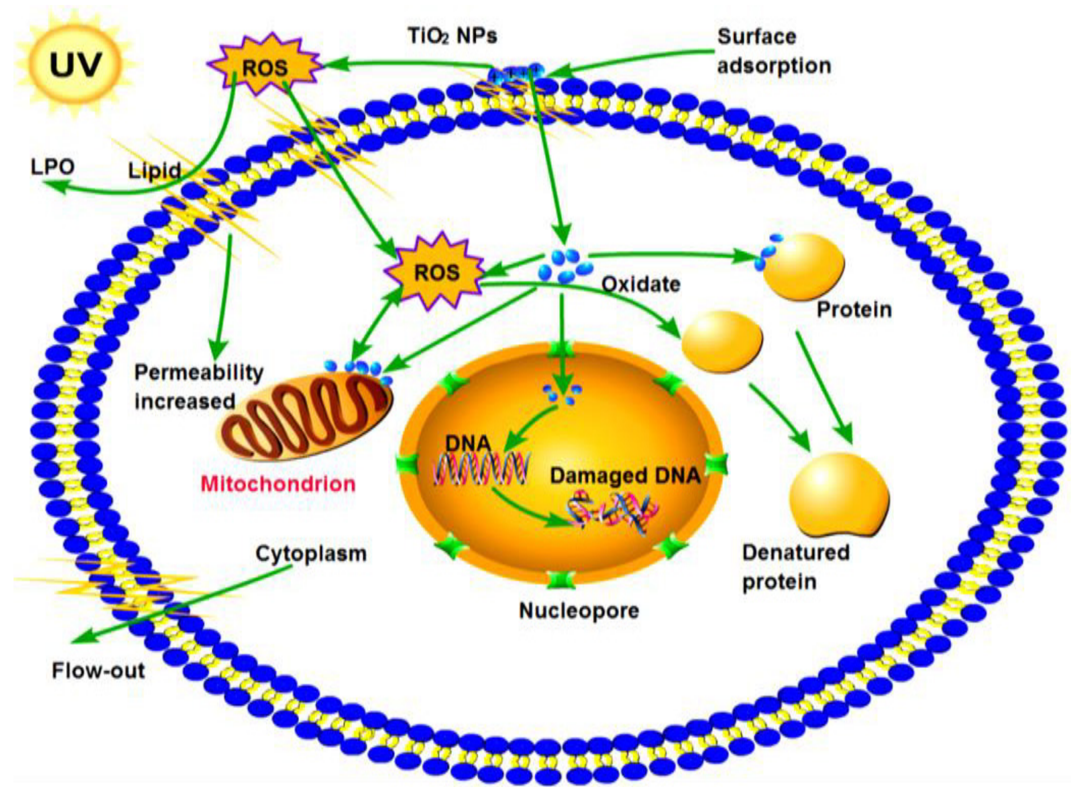

Figure (2): The process by which particles of titanium oxide have antibacterial properties[6].

The practical part.

1- preparing standard solutions for the active ingredients in surfactant-sAs a stock solution, a 100 ml solution containing 3% weight-based surfactant (SDBS) was created by dissolving 3.0928 g of the material in a volumetric flask containing a quantity of deionized distilled water. The volume was then filled to the required level using the same deionized distilled water. Similar to this, a stock solution of the surfactant (CTAB) with a concentration of 3% weight-weight was made in a 100 ml volumetric flask by dissolving 3.0928 g of the material in a volume of deionized distilled water, and then topping off the volume with more deionized distilled water.

2-Preparation of nanostructured titanium dioxide [7].

1. In a flask with an appropriate capacity (250 ml), 10g of synthetic titanium oxide (titania) was added to 50 ml of sodium hydroxide (NaOH) produced at a concentration of 10M.
2- Intermittently, the mixture is heated to a temperature of 100°C for 35 hours.

3- When the pH reaches 7, gradually add 10 milliliters of strong hydrochloric acid (HCl) and stir constantly. To obtain titanium dioxide nanoparticles, filter the precipitate and then put it in a drying oven set at 100°C for two hours. The dried titanium dioxide nanoparticles are depicted in Figure (3).

Figure (3): The prepared titanium dioxide nanoparticles.

3-Preparation of the drug solution. By dissolving 0.01 g of levofloxacin in a volume of distilled water and then filling the volumetric flask to the brim with distilled water, a 100 ml solution with a concentration of 100 ppm of the antibiotic was created.

4- Preparation of a mixture of surfactant solutions CTAB and SDBS with the drug and nano-titanium oxide. Specific volumes from the original CTAB and SDBS solutions were combined with specific volumes from the original levofloxacin solution to create a mixture of different solutions of these components in ten milliliters. As a result, while we obtain solutions with various combinations, the ultimate concentration of every mixture stays the same. Table (1) provides an illustration of the volume of the solutions that were taken out of the original solution for both drugs.

Table 1: Volume quantities following the addition of titanium dioxide nanoparticles at several concentrations to a combination of surfactants and the medication levofloxacin.

s.code	X1	X2	X3	4X
Conc.drug(ppm)	**25**	**50**	**100**	200
Conc (TiO_2) (ppm)	**25**	**50**	**100**	200
(TiO_2)(ml)	**1**	**1**	**1**	1
(SDBS)ml	**2.7**	**2.7**	**2.7**	2.7
(CTAB)ml	**6.3**	**6.3**	**6.3**	6.3
V.total(ml)	**10**	**10**	**10**	10

Viscosity measurements

The water bath is left until it achieves the specified measurement temperature after being adjusted to that level. Next, the sample to be measured is placed into the U-tube viscosity measurement equipment and submerged almost entirely in the water bath. The device is then left for five minutes, stirring from time to time. The model's descent time from the starting position to the endpoint indicated by the measuring equipment is then measured. This process is done roughly five to six times in order to get an average of many observations. This measurement is carried out at four different temperature points (283.15, 293.15, 310.15, and 323.15 K), and all of the solutions listed in Table (1) above are used in the experiment again. Equation (1) can be used to calculate the sample's viscosity.

$$\frac{\eta_1}{\eta_2} = \frac{\sigma_1 t_1}{\sigma_2 t_2} \quad ....(1)$$

Since σ_1, t_1, and η_1 represent the density, descent time, and viscosity of water, respectively. While σ_2, t_2, and η_2 represent the density, settling time, and viscosity of the surface-active substance solutions to be measured, respectively.

Figure (4): Viscosity measuring device (Estwald)

Results and Discussion

1-X-ray diffraction of nanostructured titanium oxide (TiO_2 Nps)

The generated titanium dioxide nanoparticles (TiO_2 Nps) are depicted in Figure (5) along with their X-ray diffraction (XRD) pattern. The size of the nanoparticles was determined using the Debye-Scherrer equation by knowing the angle of incidence and the peak width of one of the diffraction peaks. The range of the total particle size is 15.202 nm to 5.384 nm.

Table (2): Data of the six strongest peaks in the X-ray diffraction spectrum of nanostructured titanium oxide. (TiO_2 Nps)

Number of bege	2Θ	FWHM	D(nm)
1	**24.955**	**0.61**	14.205
2	**27.57**	**0.57**	15.202
3	**37.62**	**0.7**	12.215
4	**47.81**	**0.67**	13.796
5	**54.71**	**1.7**	5.384
6	**62.52**	**1.0**	9.542

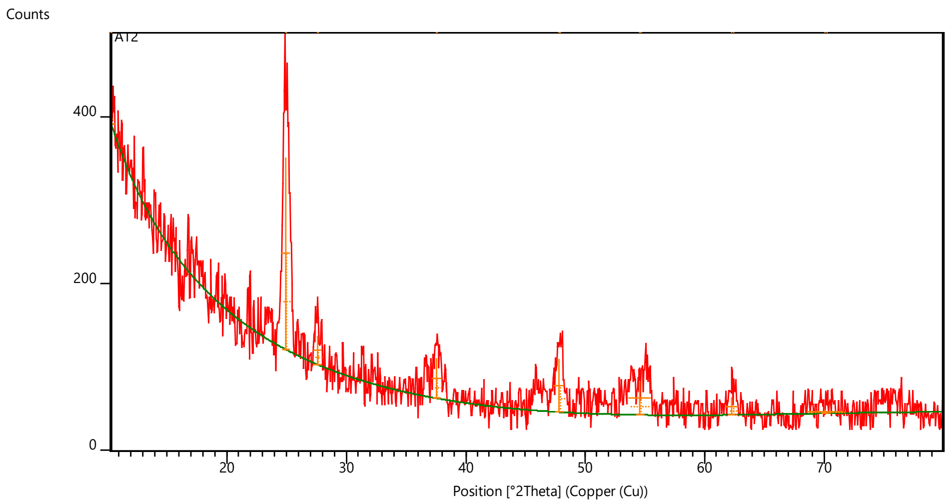

Figure (5): X-ray diffraction of nanostructured titanium oxide. (TiO_2 Nps)

2-Diagnosis of titanium dioxide nanoparticles using atomic force microscopy. Titanium dioxide (TiO_2 Nps) can be seen in two and three dimensions using an atomic force microscope. The greatest height of the titanium dioxide nanoparticles (TiO_2 Nps) was 3.36 µm, as depicted in figures (6, 7, 8). Important details regarding the size and distribution of the titanium dioxide nanoparticles (TiO_2 Nps) under study are shown in Figure (8), where each hue denotes a different height of the Nps. The total amount of nanoparticles was 1,932 with a density of 171,095,306 mm² for each particle. The greatest height was attained, and the average diameter measured 32.09 nm. (163.7 nm).

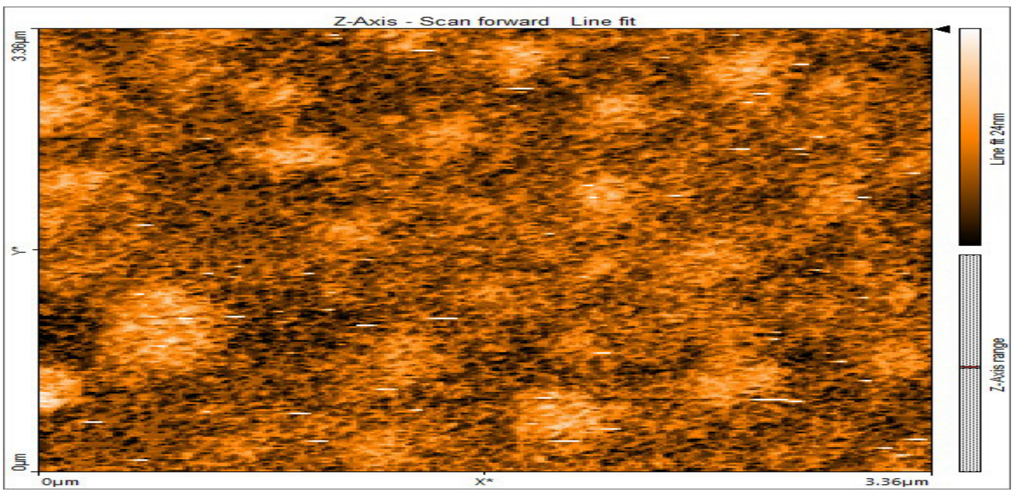

Figure (6): A two-dimensional image of nanostructured titanium dioxide (TiO_2 Nps)

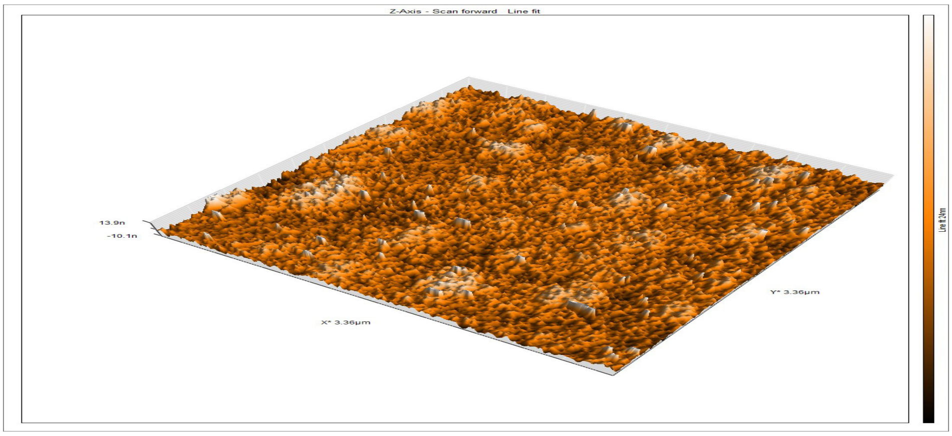

Figure (7): A three-dimensional image of nanostructured titanium dioxide. (TiO_2 Nps)

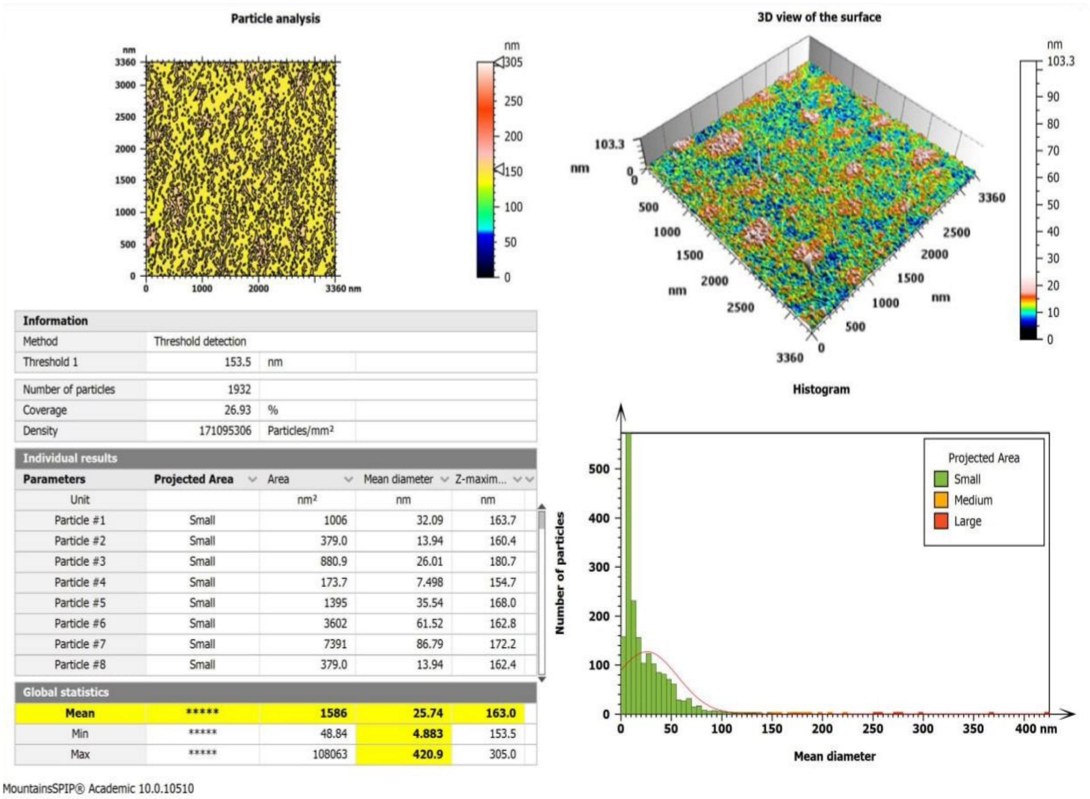

Figure (8): The percentage distribution of the diameters of titanium dioxide nanoparticles (TiO_2 Nps)

Study of the viscosity and thermodynamic variables of a binary mixture of surfactants.

A discernible rise in viscosity is caused by the production of filamentous or worm-like structures; hence, the formation of these structures is responsible for the observed increase in viscosity. Consequently, research has been done at various temperatures (283.15K, 293.15K, 303.15K, and 313.15K) on the capacity to form micelles from a binary mixture of surfactants (CTAB. SDBS).A mixture of (CTAB) at a percentage of 3 percent and (SDBS) at various mixing ratios is shown in Table 3.

Table (3): values of the mixture's viscosity and thermodynamic parameters when varying the surfactant ratio at various temperatures.

Sample code	SDBS	CTAP	η (Pa.s) ΔS° KJ.mol^{-1}.K^{-1} ΔG° KJ.mol^{-1}.K^{-1}				ΔH kJ.mol^{-1}
			T=283.15 K	**T=293.15 K**	**T=303.15 K**	**T=313.15 K**	
A1	**0**	**10**	**0.155 -15.25 4331.5**	**0.132 -15.331 4484.5**	**0.112 -15.336 4637.1**	**0.099 -15.339 4790.4**	**-11.01**
A2	**1**	**9**	**0.291 -10.290 2895.5**	**0.201 -10.291 2997.8**	**0.150 -10.62 3202.07**	**0.133 -9.96 3100.07**	**-19.23**
A3	**2**	**8**	**0.782 -1.89 576.7**	**0.319 -1.90 597.12**	**0.227 -1.907 617.49**	**0.147 -1.911 637.8**	**39.16**
A4	**3**	**7**	**2.696 8.0 -2330.5**	**1 8.008 -2412.8**	**0.285 8.01 -2495.1**	**0.211 8.022 -2577.4**	**-65.16**
A5	**4**	**6**	**1.684 4.14 -1226.4**	**0.482 4.149 -1269.8**	**0.233 4.147 -1310.6**	**0.192 4.16 -1356.4**	**-53.77**
A6	**5**	**5**	**1.036 0.136 -82.3**	**0.239 0.142 -85.3**	**0.183 0.147 -88.2**	**0.155 0.151 -91.1**	**-43.53**
A7	**6**	**4**	**0.924 -0.80 185.9**	**0.783 -0.802 192.5**	**0.351 -0.79 199.1**	**0.170 -0.792 205.6**	**-42.67**
A8	**7**	**3**	**0.245 -11.76 3309.8**	**0.149 -11.761 3426.7**	**0.126 -11.75 3543.6**	**0.091 -11.757 3660.5**	**-21.22**
A9	**8**	**2**	**0.235 -12. 06 3389.9**	**0.128 -12.065 3509.6**	**0.106 -12.061 3629.3**	**0.072 -12.05 3749.08**	**-27.43**
A10	**9**	**1**	**0.164 -15.07 4253.8**	**0.115 -15.071 4404.1**	**0.100 -15.069 4554.3**	**0.091 -15.0.65 4704.5**	**-14.05**
A11	**10**	**0**	**0.138 -16.52 4661.1**	**0.099 -16.524 4825.7**	**0.086 -16.522 4990.3**	**0.062 -16.520 5154.9**	**-18.44**

According to the findings, a rise in temperature allows the molecules in the solution to have more kinetic energy, which breaks down intermolecular interactions and resulting in a decrease in viscosity [8]. The interactions between the molecules of water are reduced as a result. As can also be seen from the viscosity values, which equal (1.684 pa.s) for sample (4A) at a temperature of 283.15K and a mixing ratio of (7:3) (CTAP-SDBS), the results also point to the development of micelles. These results are in line with earlier research [9.10]. Furthermore elucidated by this work is that the mixture ratio yields an exothermic reaction with a value of (ΔH=-65.16 KJ.mole-1), and that the reaction is spontaneous because the randomness rises with growing temperature at the same ratio.

***Study of the viscosity and thermodynamic variables of a binary mixture of surfactants and the drug with nano-titanium oxide together.**

An investigation was carried out on a combination of surfactants in a ratio of 7:3 (CTAP-SDBS), correspondingly, with different drug and nano-titanium oxide concentrations.

Table (5) : the viscosity values at different temperatures for this mixture.

Sample code	SDBS	CTAP	Conc.drug ppm	Conc .TiO_2 ppm	η (Pa.s)*١٠ ^{2} ΔS° $KJ.mol^{-1}.K^{-1}$ ΔG° $KJ.mol^{-1}.K^{-1}$				ΔH $kJ.mol^{-1}$
					T=283.15 K	**T=293.15 K**	**T=303.15 K**	**T=313.15 K**	
x4	**3**	**7**	**25**	**25**	**0.02727** **-267.89** **8.479**	**0.01101** **-267.29** **10.984**	**0.00288** **-270.86** **14.739**	**0.00199** **-275.63** **16.185**	**-67.37**
x4	**3**	**7**	**50**	**50**	**0.02816** **-267.12** **8.403**	**0.01105** **-269.26** **10.980**	**0.00289** **-272.76** **14.735**	**0.002010** **-268.62** **16.166**	**-67.95**
x4	**3**	**7**	**75**	**75**	**0.02893** **-266.90** **8.340**	**0.01109** **-266.77** **10.971**	**0.00297** **-270.16** **14.666**	**0.00212** **-265.88** **16.028**	**-67.23**
x4	**3**	**7**	**100**	**100**	**0.02961** **-263.49** **8.285**	**0.01114** **-263.63** **10.960**	**0.00301** **-267.05** **14.632**	**0.00226** **-262.44** **15.861**	**-66.32**

The results in Table (5) indicate that the viscosity values increased when using the drug levofloxacin and titanium dioxide nanoparticles compared to using the surfactant active ingredient mixture at a ratio of 7:3 alone and at all concentrations. It It was shown that viscosity reduces with a drop in temperature and increases when medication and titanium dioxide nanoparticle concentrations rise. This is explained by the fact that the mixture's molecular weight has increased, increasing the amount of large molecule aggregates as a result. Since the nanoparticles have a high surface area, their small size allows them to maintain their connections to one another at the micelle intersection, which increases the viscosity of the mixture [11].Reduced micelle intersections lead to a decrease in viscosity, which is achieved by raising the temperature of the drug and surfactant mixture in addition to the nanoscale titanium dioxide. At a temperature of 283.15 K, the mixture's viscosity value reached 2.992 Pa.s, with a higher degree of spontaneity (ΔG = -2.555 kJ.mole-1) when 200 ppm of levofloxacin and 200 ppm of nano-titanium oxide were used.The compound's polarity causes it to settle close to the micelle surface, which results in noteworthy spatial

Biological activity.

Salmonella (Typhi) bacteria were used to test the sample mixture (X4), which included (CTAB.SDBS) in a ratio of (7:3), along with (200 ppm) of levofloxacin and (200 ppm) of nanoscale titanium oxide. The Biotechnology Laboratory of Al-Nahrain University provided the bacterial isolates, and the United States Pharmacopeia (USP) was followed in the assessment process .The mixture was shown to be highly significant and to have outstanding results in inhibiting and killing Salmonella bacteria with an inhibition diameter of 25 mm. (9).It demonstrates this mixture's biological effectiveness.

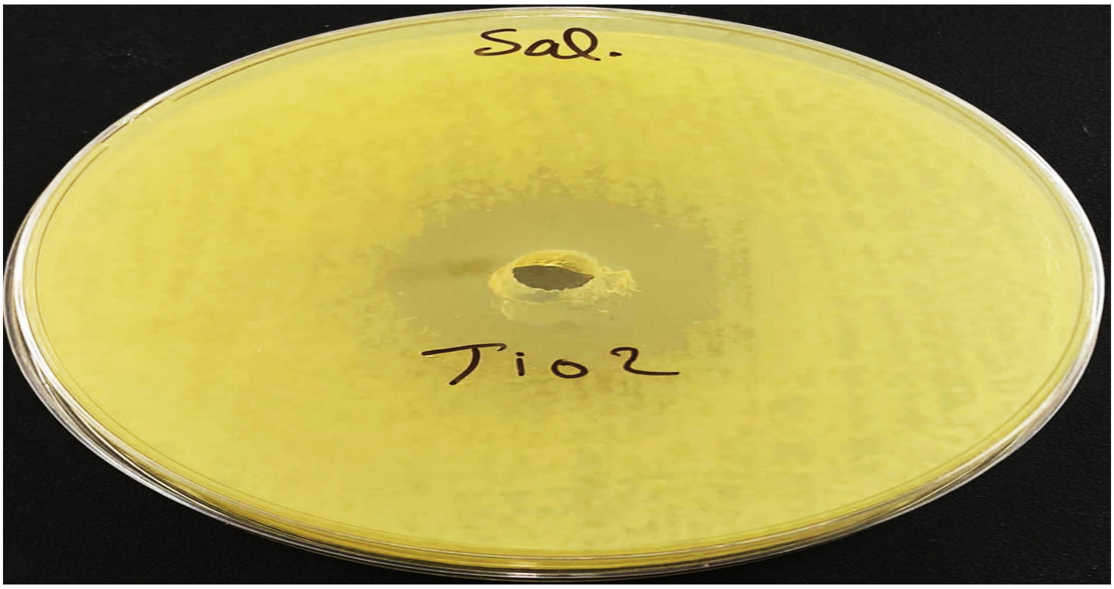

Figure (9): Inhibition of Salmonella bacteria using a mixture of surfactants and (200 ppm) of both levofloxacin and nano-titanium oxide (TiO_2 Nps)

The conclusions.

1-The highest viscosity was obtained by mixing two different volumes in a ratio of (7:3) of (CTAB.SDBS), respectively.
2-The viscosity decreases (the formation of nematode or thread-like structures) when temperatures rise.
3-The viscosity of the binary mixture of surfactant active substances increases more rapidly with the addition of (200 ppm) of levofloxacin and (200 ppm) of nanostructured titanium oxide, and decreases with the reduction of the concentrations of these two substances.
4-According to the calculated values of the thermodynamic functions, the reaction was more spontaneous and exothermic (ΔH = -66.324 KJ.mole-1) with a decrease in randomness.
5- The mixture of surfactants used in the study helps keep the nanoparticles from agglomerating, which enhances the biological efficacy of this prepared mixture.
6-This mixture has the ability to inhibit and kill Salmonella bacteria with very good results.

References

1- 62-Bush LM, Chaparro-Rojas F, Okeh V, Etienne J. Cumulative clinical experience from over a decade of use of levofloxacin in urinary tract infections: critical appraisal and role in therapy. Infect Drug Resist. 2011;4:177-89.

2- Yew WW, Chan CK, Chau CH, Tam CM, Leung CC, Wong PC, Lee J. Outcomes of patients with multi-drugresistant pulmonary tuberculosis treated with ofloxacin/levofloxacin-containing regimens. Chest. 2000 Mar;117(3):744-51.

3-Anderson VR, Perry CM. Levofloxacin : a review of its use as a high-dose, short-course treatment for bacterialinfection. Drugs. 2008;68(4):535-65.

4-Brandelli A, Ritter AC, Veras FF. Antimicrobial activities of metal-nanoparticles. In: Metal nanoparticles in pharma. Springer; 2017. p.337–63.

5-Kumaravel V, Nair KM, Mathew S, Bartlett J, Kennedy JE, Manning-HG, et al. Antimicrobial TiO2 nano-composite coatings for surfaces, dental and orthopaedic implants. Chem Eng J. 2021;129071.

6-Hou J, Wang L, Wang C, Zhang S, Liu H, Li S, et al. Toxicity andmechanisms of action of titanium dioxide nanoparticles in livingorganisms. J Environ Sci. 2019;75:40–53.

7-Shibaib KHAL. Study of the Antibacterial Activity by using Titanium-Dioxide Nanoparticles. Eng Technol J. 2016;34(6 Part (B) Scientific).

8-Fait, M. E., Bakas, L., Garrote, G. L., Morcelle, S. R. and Saparrat, M. C. N., (2019). Cationic surfactants as antifungal agents, Appl. Microbiol. Biotechnol., 103, 97-112.

9- Liu, J., Liu, Z., Yuan, T., Wang, C., Gao, R., Hu, G., Xu, J. and Zhao, J., (2020). Synthesis and properties of zwitterionic gemini surfactants for enhancing oil recovery, J. Mol. Liq., 311, 113179.

10-Godec, R. F., (2009). Effects of surfactants and their mixtures on inhibition of the corrosion process of ferritic stainless steel, Electrochimica Acta, 54, 2171-2179.

11-Kombade, Sarika, and Navneet Kaur. "Pathogenicity island in Salmonella." Salmonella spp.-A Global Challenge. IntechOpen, 2021.