Eurasian Chemical Communications

SAMI

FULL PAPER

Estimation and development of some biophysical characteristics of the drug Favipiravir used in the treatment of corona-virus using green chemistry technology

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This study included the preparation and identification of copper oxide nanoparticles (CuNPs) prepared from eucalyptus leaf extract using modern and advanced detection and analysis devices: XRD, AFM, SEM, UV-Vis, and TEM. The results of the tests indicated that the prepared particles are spherical and rod-shaped, with average diameters ranging from 32.55-37.94 nm, and the results showed that the copper oxide nanoparticles were within the nano-scale, and the wavelength of the drug is (322) nanometers. The factors affecting the loading of the drug (Favipiravir) at a concentration of (40 μg/mL) on the surface of activated charcoal prepared from eucalyptus leaves were studied, as well with a weight of 0.1 g and in the presence of copper oxide nanoparticles with different concentrations. It was found that the equilibrium time is 25 minutes, and the thermodynamic functions were calculated at different temperatures. The results illustrated that the loading process by using exothermic adsorption (physical adsorption), is less random process and spontaneously. The possibility of using the loaded substance (Favipiravir:CuNPs) to inhibit microorganisms such as viruses, bacteria, and fungi was studied, and by the presence of the surface active substance sodium dodecyl sulphate SDS, it was found that it has the ability to inhibit by 100%, as a result of the merging of the tail of the superficial active substances with the fatty membrane of the virus, the other microorganisms, its dismantling, and encapsulation of its parts. The vaccines and therapeutic drugs developed on the basis of nano-medicine, which are currently undergoing clinical trials, have the potential to become innovative alternatives to defeat COVID-19 in the future.

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Introduction

Favipiravir drug is one of the drugs used as anti-influenza virus and its scientific name is (6-fluoro-3-hydroxy-2-pyrazinecarboxamide) and its molar mass is 157.1 g/mole [1]. Figure 1 displays the chemical structure of the Favipiravir activity against the RNA of other viruses such as arenaviruses, bunyaviruses, and filo-viruses which makes it a potentially promising drug for incurable RNA virus infections, as well as being used to treat Ebola, Marburg, Nipah, and Zika viruses as well as Lassa fever [3,2].
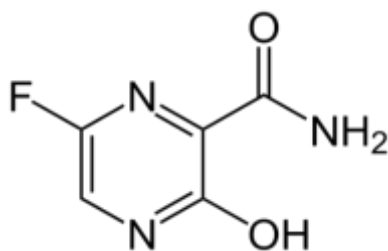
FIGURE 1 Chemical structure of Favipiravir

Favipiravir has been approved for new strains of pandemic influenza which do not respond to antiviral therapies in Japan [5,4]. Recently, studies have been conducted for experimental treatments against COVID-19 and it has been suggested as an effective treatment for this purpose [6].

Favipiravir is classified as a safe and effective treatment for influenza and patients with the emerging corona pandemic, however it needs more studies to know the side effects when using long-term, such as its effect on hyperuricemia, which has not yet been studied, so there is a need for more evidence in its use as a safe treatment [7]. Therefore, we used the green chemistry method to increase the drug effectiveness in addition to reduce the side effects by declining dose and adding nanomaterials by using biological extracts.

Green nanotechnology [8] is the development of clean technologies to reduce environmental products hazardous to human health associated with the manufacture and use of nano products and technologies, which have two goals: the first is to produce nanomaterials without harming the environment or humans, providing solutions to environmental problems, while the second goal involves developing products which benefit the environment, either directly or indirectly. Therefore, nanotechnology is the development of clean technologies to reduce the potential risks to environmental and human health. It works to reduce pollutants and harmful processes by confronting them directly or by changing their creation conditions. It is the technology which has been developed and used in an environmental friendly manner and to conserve natural resources.

This promising technology heralds a huge leap in all branches of science and engineering, and optimists believe that it will cast a shadow over all areas of modern medicine, the global economy and even the daily life of the modern individual, as it allows the possibilities of making anything by arranging molecules next to each other at the lowest possible ref.

Carbon-based nanomaterials are characterized by being materials with (pores) with diameters ranging from (2-50 nm) [9], and they have the ability to bind to many chemicals by adsorption, and they indicate a high activity that works to kill microorganisms present on the surface. Surfaces as a result of their porosity and adsorption properties, such as fighting different types of bacteria, such as Actinomycetals, Bacillus subtilis, E.coli, and others, as well as different types of viruses, such as the pseudo-rabies, the porcine reproductive, the respiratory syndrome virus, and others, and they can kill different types of fungi, such as the white mold fungus, black rhizocton (Rhizoctonia solani), (Magnaporthe grisea), and so forth, in addition to its ability to kill parasites, such as Leishmaniasis of all kinds [10,11,12].

Experimental part

The used instruments

Several devices were used, which are indicated in Table 1.

TABLE 1 The devices used and their origin

The device name	Company	Origin
UV-vis. Spectrophotometer Double Beam	Spectrophotometer-200705044	China
pH Meter	Jenway-3310	England
Stirrer Hotplate	LabTech – LMS -1300	Korea

Materials used

Chemicals were used in this study without performing the purification process, and the following companies were the source that supplied them (BDH, Aldrich, and Merk), as depicted in Table 2.

TABLE 2 Chemicals used in this research

No	Chemical materials	Molecular formula	Molecular Wight (g/mole)
1	Favipiravir	$C_5H_4FN_3O_2$	157.1
2	Aqueous blue copper sulfate	$CuSO_4.5H_2O$	249.68
3	SDS	$NaC_{12}H_{25}SO_4$	288.372
4	Hydrochloric acid	HCl	36.5
5	Sodium hydroxid	NaOH	40

Stock solution prepare

A standard solution of the drug Favipiravir under study was prepared at a concentration of 1000 µg/mL by dissolving 0.1 g of the drug in a 100 mL volumetric flask as a Stock solution, and from it the working solution was prepared at a concentration of 100 µg/mL by diluting 10 mL of it in a 100 mL volumetric flask, and the volume was filled up to the mark with distilled water.

Preparation of a solution of the medicinal preparation Samavir (200 mg) at a concentration of 100 µg/mL

10 tablets of the medicinal preparation Samavir (200 mg) were crushed, the equivalent of the weight of one tablet was taken and dissolved in a volumetric flask (200 mL), then the volume was completed to the mark with distilled water so that the concentration became 1000 µg/mL, and from this solution transferred 10 mL to a volumetric flask (100 mL) and the volume was completed to the mark with distilled water to obtain a concentration of 100 µg/mL.

Preparation of a sodium dodecyl sulfate solution

(25 mL) was prepared at a concentration of 0.1 M as a stock solution of SDS by dissolving (0.7209 g) in the least amount of distilled water for one time, then the volume was filled up to (25 mL) by using a volumetric flask, then it was used according to the work requirements.

Working method

Determine the wavelength for maximum absorption: The wavelength of the maximum absorption of the studied drug was determined by recording the absorption spectrum using UV-visible spectrometers.

Determine calibration curve for the drug under study: After determining the wavelength of the maximum absorbance λ_{max} of the solution (322 nm), a calibration curve was constructed by transferring volumes (0.5-6 mL) at a concentration of 100 µg/mL to a series of 10 mL volumetric flask and the volume was completed to the mark with distilled water and measuring the absorption at (322 nm) against water as a planck

solution, and the linear of concentrations were in compliance with the Beer-Lambert Law in the range (5-60) μg/mL.

Method application: The drug Favipiravir in the medicinal preparation was determined by using the direct method via measuring the absorption of three concentrations - from the solution of the drug Samavir (200 mg) in the form of tablets - falling within the calibration curve of (20, 40, and 60) μg/mL, and the straight-line equation was applied to them, and the results were with good accuracy and compatibility. Table 3 indicates the application of the direct method to the medicinal preparation Samavir (200 mg).

TABLE 3 Application of the direct method to the medicinal preparation Samavir (200 mg)

	Pharmaceutical	Taken ($\mu g.mL^{-1}$)	Found ($\mu g.mL^{-1}$)	Rec%	RSD* %
Direct method	**Samavir (tablet) 200 mg**	20	20.4634	102.3170	0.7101
		30	30.1585	100.5284	0.4613
		40	39.9146	99.7865	0.2784

* Six readings

Analytical data for the proposed method

The analytical data of the proposed method are summarized in Table 4 as follows.

TABLE 4 Analytical data for the proposed method

Method	λ_{max} (nm)	Linearity ($\mu g.mL^{-1}$)	L.O.D ($\mu g.mL^{-1}$)	L.O.Q ($\mu g.mL^{-1}$)	ε (L.mol-1.cm-1)	Sandell's index ($\mu g.cm^{-2}$)	Straight line equation	R^2
Suggested method	322	5-60	1.0558	3.5196	2576.44	0.0609	y = 0.0164x - 0.0226	0.9993

Preparation of copper oxide nanoparticles

Add 5 mL of Zubaidi truffle extract to 100 mL of aqueous blue copper sulfate solution. Put a hot plate magnetic stirrer for 7 hours .While stirring, add the extract, the light blue color appears after adding the extract to the light green color and then, the brownish dark green color after 7 hours. Then, leave it overnight as the solution appears brown. Put the prepared solution into a centrifuge at a speed of 3500 rpm for 20 minutes. The precipitate was taken and placed in a glass container and then, dried using an oven at 40 °C for 12 hours. The black precipitate was stored in closed tubes for the purpose of testing, as displayed in Figure 2.
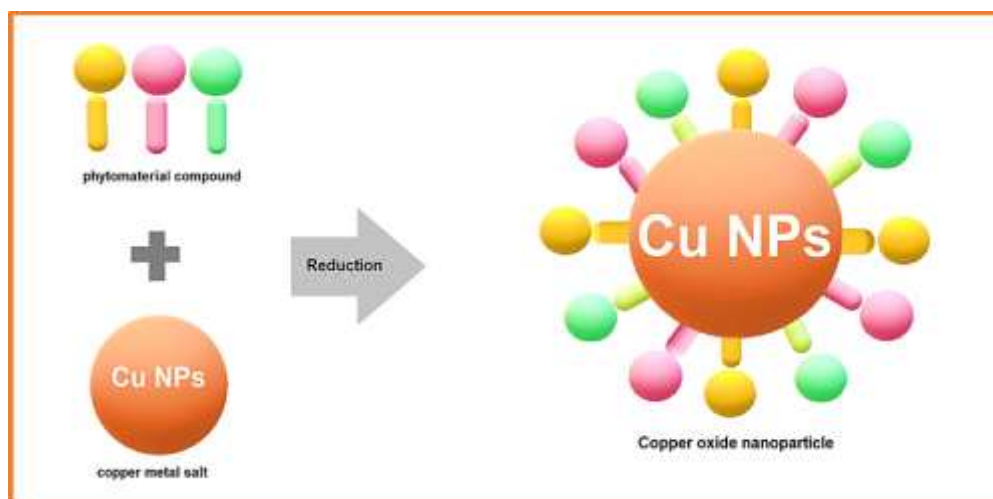
FIGURE 2 Preparation of copper nanoparticles by Zubaidi truffles

Preparation of activated charcoal from eucalyptus leaves

1-A quantity of eucalyptus leaves was taken, washed several times, and cleaned well from the dust stuck to it and grinded into very soft pieces, after which it was washed with deionized water repeatedly.

2- The charring was carried out by taking 100 g of chopped and dried eucalyptus leaves, put them in a ceramic dish and placed inside the incineration oven at a temperature of 600 degrees Celsius for one hour. Cool the charcoal, then grind well and place in an airtight container away from moisture.

3- The prepared charcoal was chemically activated with a weight of 20 g of the prepared charcoal powder and 15 mL of lemon juice was added to the charcoal powder, and mixed well inside the beaker. After cooling, the resulting activated charcoal is washed with deionized water several times to get rid of impurities. The process of its washing with deionized water is repeated to purify it from acid residues. The activated charcoal is dried for two hours at 110 °C. Some measurements are made to evaluate the specifications of the prepared activated charcoal, such as ash, moisture, and so on.

Adsorption

Estimation of adsorbate: The term adsorption capacity or its efficiency was used to express the amount of the adsorbent material by estimating the amount of the remaining substance from the solutions of the drug and then calculating the amount of the adsorbed substance, through the difference between the initial concentration of the drug solution and the amount of the remaining substance, depending on the calibration curve of the drug to calculate these concentrations. The adsorption capacity of the drug adsorbent substance is expressed by Equation No. (1). The percentage of the drug (Adsorbate) or the so-called adsorption efficiency was calculated through the use of Equation No. (1) [13,14,15].

$$Q_e = \frac{C_o - C_e}{M} \times V \qquad (1)$$

In which, C_o represents the value of the initial concentration of the drug in the liquid phase (mg/L) and C_e the drug concentration in the solution at equilibrium (mg/L)

$$\%Adsorption = \frac{C_o - C_e}{C_o} \times 100 \qquad (2)$$

Determination of an adsorbent dose: Three different weights of activated charcoal (0.03, 0.05, and 0.1) g and an initial concentration of (40 µg/mL) were selected for the drug

converter, while the temperature (25) °C and shaking time (30) minutes were adopted. The study proved the use of an adsorbent substance (activated carbon) of 0.1 g in the range of concentrations required to reach the state of equilibrium.

Determination time of equilibrium: Eight solutions were prepared containing fixed quantities of the adsorbate in equal concentrations (40 μg/mL) of the drug solution and adding the same amount of activated charcoal (0.1) g at temperatures (25) °C and the normal pH the bottles were placed in the shaker equipped with a water bath, and each bottle contained (10) mL. After continuous shaking, all solutions were separated using a centrifuge at different times (5, 10, 15, 20, 25, and 30) minutes, respectively. The filtrate absorbance was measured by the spectroscopic method (UV-Vis.) and the calibration curve of the drug. The results indicated that the equilibrium time of the drug was at 25 minutes.

Effect of temperature: The effect of temperature was studied by repeating the same previous steps mentioned in the concentration effect, with the same conditions and quantities, but at different temperatures (10, 20, 30, and 40) °C which were set by a thermometer, and the results of this study were used to calculate the thermodynamic functions.

Results and discussion

The first step in studying the adsorption process is to determine the maximum wavelength of the Favipiravir solution using UV-vis spectroscopy. It was found that the maximum wavelength of the solution of this drug is (322) nanometers, as displayed in Figure 3.

Then, a calibration curve was built at a range of dilute concentrations (5-60 μg/mL) to estimate the amount of favipiravir adsorbate remaining in the solution using the spectroscopic method, and according to Beer-Lambert Law [16] (A=ƐbC), the relationship between absorbance was drawn with concentration, it illustrated a linear relationship indicating that it is subject to Beer-Lambert law, as demonstrated in Figure 4.

The highest wavelength of nano-copper oxide was measured and it was found that it contains two peaks, the first at 233 nm and the second at 219 nm, as shown in Figure 5, as the highest wavelength peak depends on the type of extract and method of preparation [17].

Copper nanoparticles were diagnosed by several tests, including transmission electron microscopy and it was found that the prepared particles at a magnification of 100 nm are spherical and rod-shaped, as displayed in Figure 6.
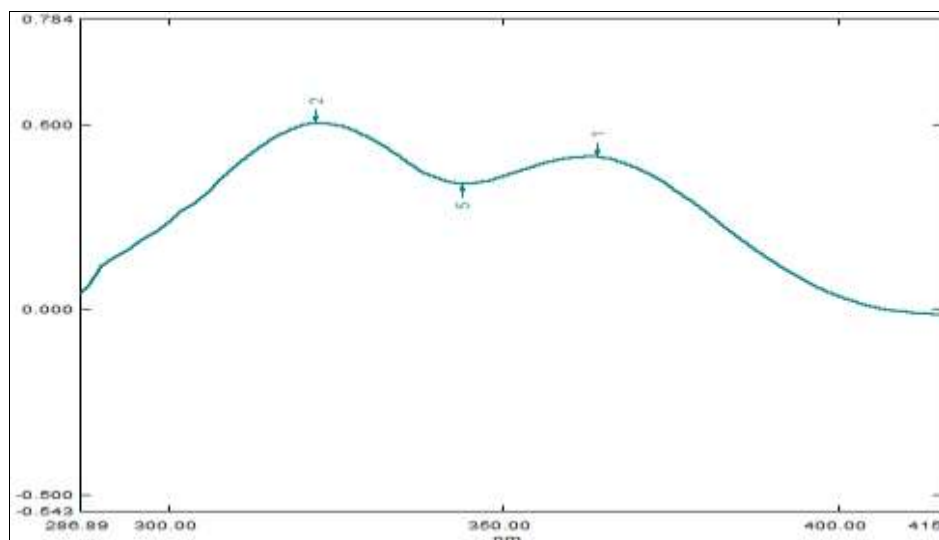
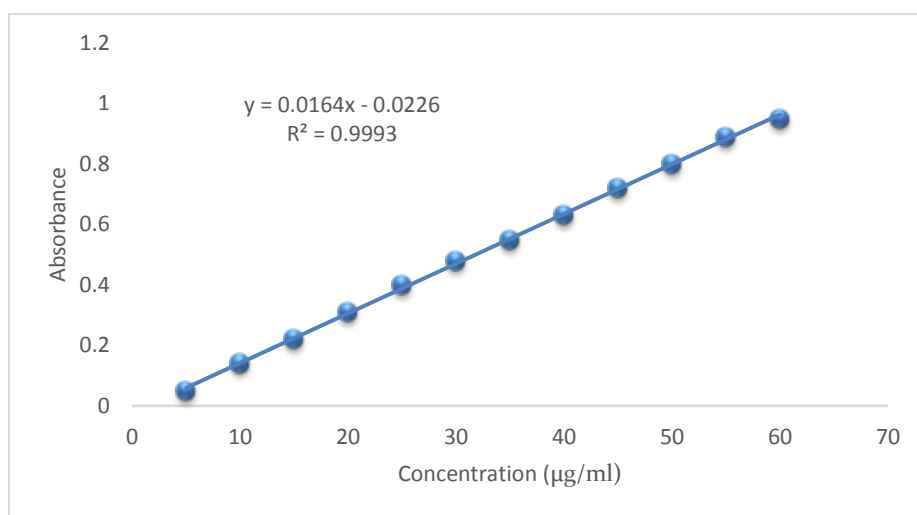**FIGURE 3** UV and visible spectrum of the drug under study

FIGURE 4 The calibration curve of the drug under study
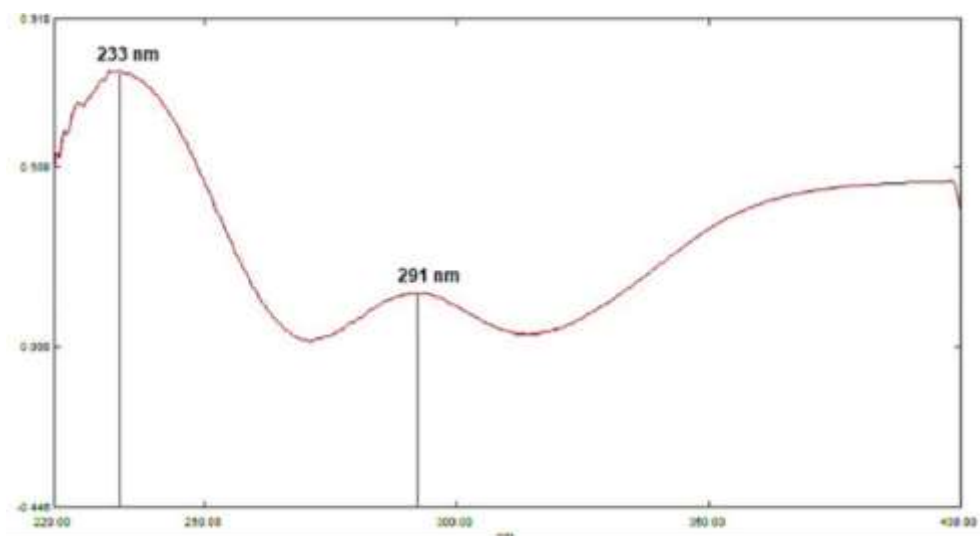

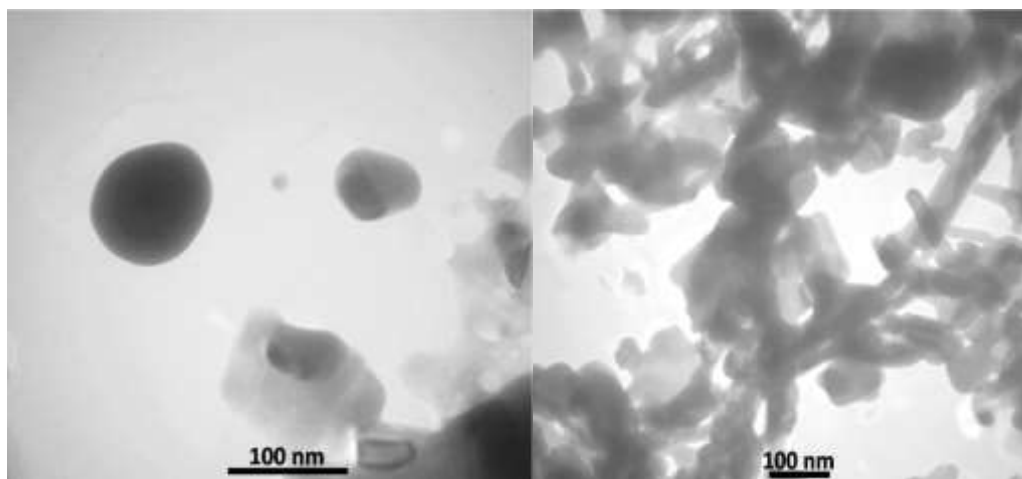**FIGURE 5** UV-visible spectrum of the prepared copper oxide particles

FIGURE 6 A transmission electron microscope image of the prepared copper oxide particles

The prepared nanoparticles were also diagnosed by a scanning electron microscope, and it was found that the prepared particles had diameters ranging from 32.55-37.94 nm.

They are spherical and rod-shaped, and this was confirmed by TEM microscopy, as depicted in Figure 7.
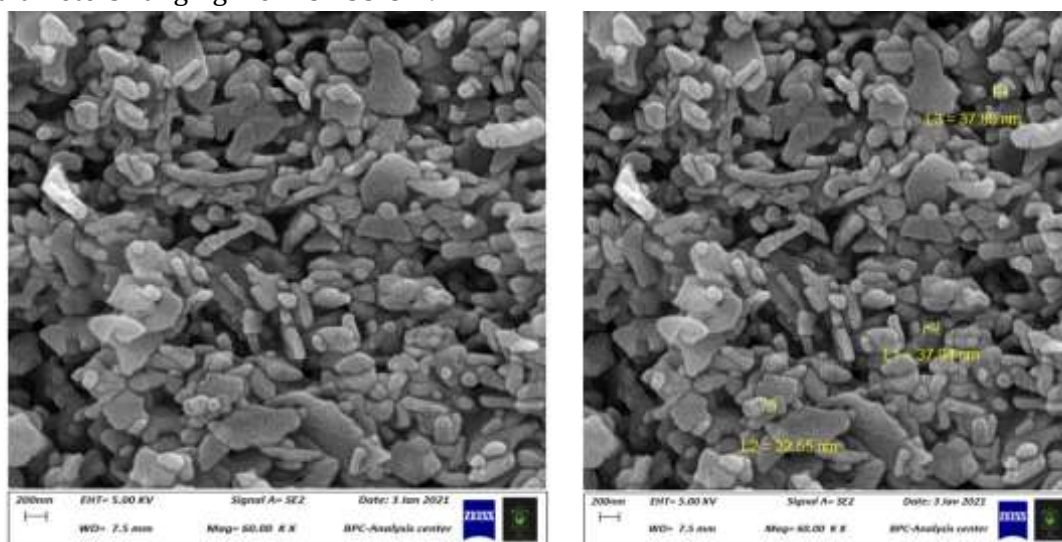

FIGURE 7 Scanning electron microscope image of the prepared copper oxide particles

Through the X-ray diffraction results of nanoparticles of copper oxide and by the Debye-Schirar equation, the size of the nanoparticles was calculated, where it was found that the particle size is about 2.6 nm, and the highest values obtained for the diffraction angles were 2θ are 38.8, 35.5, and 48.8, which correspond to the values 002, 111, and 202, respectively, likewise these values represent Miller indices of the material as shown in Figure 8.
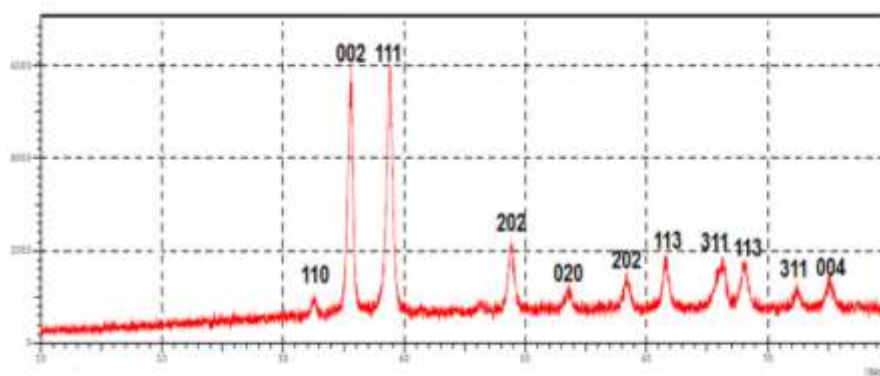
FIGURE 8 X-ray diffraction of copper oxide

From the measurements of the atomic force microscope and as it has been proven in references and literature [18], it is significantly possible to prepare copper oxide in the form of nanorods, where in this work the copper oxide was prepared in the form of nanorods. The size of these rods in the sample under examination is 22.89 nm as in Figure 9, which represents a three-dimensional image of the sample.

The relative abundance of Cu in the CuO nanoparticles is observed in Figure 10, in which this peak is observed at about 8 and is clearly as given in the measurement.
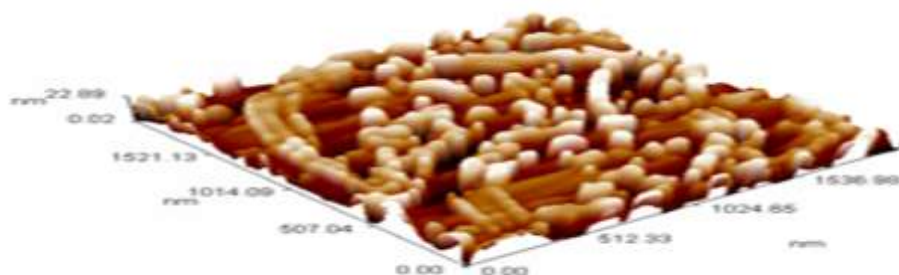

FIGURE 9 A picture under the atomic force microscope of the prepared copper oxide nanoparticles
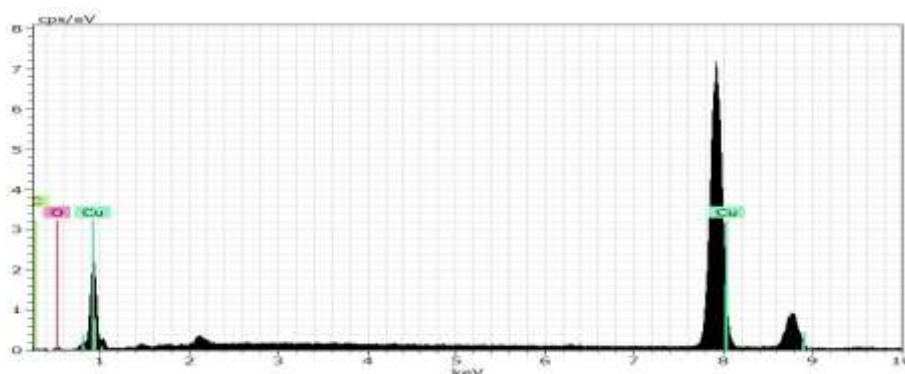

FIGURE 10 X-ray energy scattering spectrum of nanoparticles of copper oxide

Prepared charcoal diagnosis

Adsorption study

The Favipiravir concentration was monitored spectroscopically over time in order to determine the equilibrium time, knowing that this experiment was carried out with the use of a fixed concentration of Favipiravir (40 µg/mL) molar with a fixed weight of activated charcoal which is (0.1 g) and at the maximum

wavelength of the drug. Favipiravir (275 nm) at a temperature of 298.15 K and the speed of

the shaker was 100 (rpm). The results are indicated in the Table 5.

TABLE 5 The effect of time on adsorption efficiency and determination of equilibrium time

Tim(min)	Absorption	C_e (mg/L)	C_{Abs} (mg/L)	Absorption%
0*	0.611	-	-	-
5	0.226	15.15	24.842	62.105
10	0.166	11.5	28.5	71.25
15	0.118	8.573	31.427	76
20	0.096	7.231	32.769	81.9
25	0.096	7.231	32.769	81.9
30	0.143	10.09	29.91	74.7

*Before adding charcoal

It is noted from the results depicted in the Table 5 and Figure 11 that the absorbance value was (0.611) (without any addition) and it decreased during the first ten minutes by a large amount, as the adsorption process of Favipiravir occurred as a result of the adsorption by activated charcoal, as the adsorption efficiency reached (71.2%). This high efficiency is due to the availability of a huge amount of unoccupied adsorption sites as well as the large surface area possessed by the prepared charcoal and this is consistent with the kinetic theory, as the adsorption is fast in its beginning and then, becomes slow [14,19]. It is noted from the proven results that the adsorption efficiency has continued to increase with time, however by a small amount until reaching the equilibrium state at the time (25 minutes), where the adsorption efficiency at this time (81.9%), which is the highest value of the adsorption efficiency and at this time, the speed of the adsorption process is equal to the speed of the adsorption process, after which a slight increase in absorption and a decrease in the efficiency of adsorption is observed. The reason is due to the repulsion of the Favipiravir drug molecules and their return to the solution due to the saturation of the pores on the surface of the prepared activated charcoal [20].
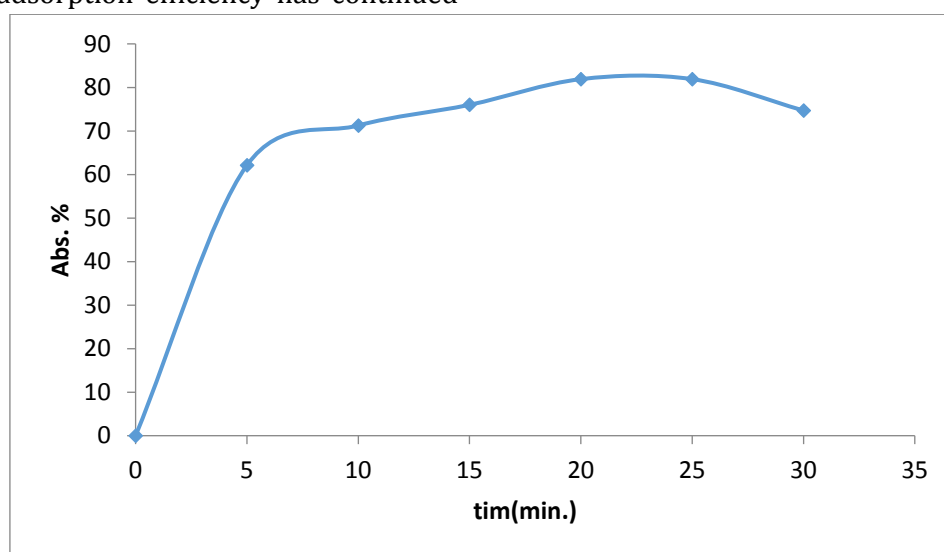

FIGURE 11 The change of Favipiravir adsorption efficiency with time

Effect of Favipiravir concentration: The prepared activated charcoal has a high

adsorption capacity in the adsorption of Favipiravir, so that during a short period of

time, removal or adsorption of a large amount of drug concentration will occur. In order to examine the effect of the change in concentration, adsorption was carried out on a group of different concentrations of Favipiravir, with fixation of other effecting conditions, in which the study was conducted at a temperature of 298.15 K and the speed of the shaker is (100 rpm).

The results in the Table 6 indicated that the adsorption efficiency decreases with the increase in the initial concentration of the drug under study, and this is due to the fact that the increase in the initial concentration leads to an increase in the number of adsorbable molecules on a fixed and specific number of sites eligible for adsorption that are present on the surface of the adsorbent, which it leads to a large amount of drug solution molecules being left in the solution at equilibrium and makes a decrease in the adsorption efficiency, so the best concentration was chosen as 40 µg/mL, which gives the best adsorption efficiency of (81.9%).

TABLE 6 The effect of the initial concentration of Favipiravir on the adsorption efficiency

Co (M)	Abs. Before Ads.	Abs. After Ads.	Ce (ppm)	Cads (mg/L)	Adsorption%
40	0.611	0.096	7.231	32.769	81.9
50	0.807	0.179	12.25	37.75	75
60	0.978	0.295	19.36	40.64	67

Effect of adsorbent weight: The effect of the weight of the prepared charcoal (adsorbent material) was studied on the efficiency of Favipiravir adsorption by using three weights of prepared activated charcoal (0.025, 0.05, and 0.1) grams, while maintaining all other variables of temperature (298.15 K) and shaker speed was 100 (rpm) and an equilibrium time (25 minutes) by the best concentration of (40 µg/mL), and the adsorption process was followed up spectroscopically. The obtained results illustrated that increasing the adsorbent weight increases the efficiency of adsorption (the adsorption percentage), as this is due to the fact that when the weight of the adsorbent is increased, an additional site is available for the adsorption of Favipiravir from its aqueous solution, in which it was found that the best weight of the adsorbent is (0.1 g), which gives the highest rate of adsorption efficiency, as indicated in Table 7 and Figure 12.

TABLE 7 The effect of the weight of the prepared activated charcoal on the adsorption efficiency

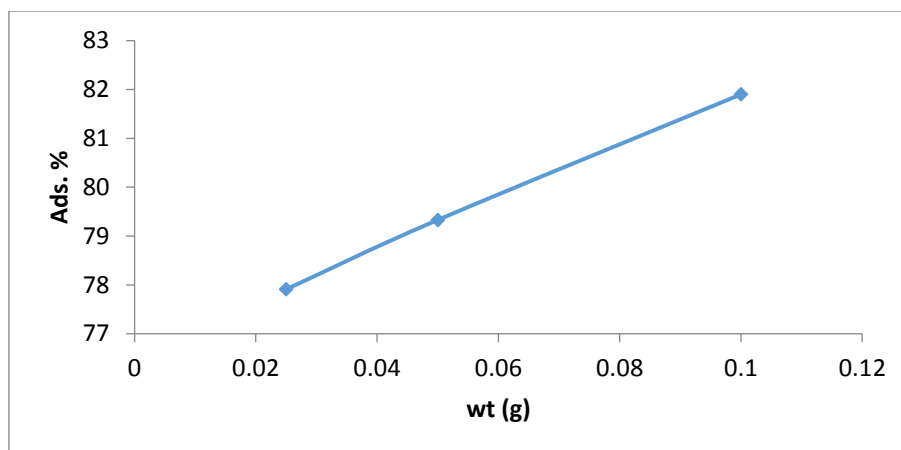| Weight of A.C (g)	Abs.	Adsorption%
0.025	0.127	77.91
0.05	0.113	79.33
0.1	0.096	81.9

FIGURE 12 The relationship between the effect of the adsorbent weight and the adsorption efficiency

The pH effect: The adsorption efficiency of different compounds, especially those which contain in their composition amino, phenolic or carbonic groups, and other groups are affected by the nature of the medium in which they are adsorbed, due to the change of these groups with the pH change of the medium in which they were adsorbed [21].

The adsorption efficiency of the solution (the drug only, the mixture of the drug with copper oxide nanoparticles) was studied by using the same conditions of temperature (298.15 K) and the drug concentration (it is 40 μg/mL) with (0.000015 M) for nano-copper oxide with (0.1 g) of activated charcoal, and the results were obtained as mentioned in Table 8.

TABLE 8 The pH effect on the percentages of adsorption using the prepared activated charcoal

(pH)	Ads.% For drug	Ads.% drug + nano copper oxide
Natural	81.9$_{(4.8)*}$	86.5$_{(4.87)*}$
7	77.6	79.8
9	72.3	76.09

*(4.8) The natural pH function of the drug

It was found from the percentage of adsorption of the prepared activated charcoal has increased in the neutral and acidic medium, that the reason for the increase in the adsorption efficiency in the neutral and acidic medium is the increase in the number of positive ions, which leads to an increase in the strength of the electrostatic attraction with the surface of the adsorbent material, while in the base medium the adsorption efficiency is decreasing because of the molecular interactions and the formation of hydrogen bonds, and likewise this will lead to a decrease in the adsorption efficiency [22].

As depicted in Table 8, the percentage of adsorption efficiency increases with the pH

increase. The reason for the variation in the adsorption efficiency from the acidic medium, then the neutral medium, the basic medium is that Favipiravir contains the amine group NH_2 which drives electrons and has a negative charge where it acquires the positive proton from the acidic medium and turns into the positively charged alany-lynyum ion, and the surface carries negative and positive charges, so electrostatic attraction will occur that will lead to an increase in the adsorption efficiency. As for the reason for the decrease in the neutral and basic medium, it is due to the fact that the amine group (NH2) will acquire a negative charge from the medium, which will lead to electrostatic repulsion and

thus, the adsorption efficiency will decrease [22,23].

Temperature effect of Favipiravir mixture with copper oxide nanoparticles: The effect of temperature on the adsorption process of Favipiravir and copper oxide particles on the surface of activated charcoal was studied at different temperatures by the best concentration of the drug is 40 μg/mL) and (0.000015 molar) of copper oxide and using the best weight of activated charcoal (0.1 g). Likewise, the speed of the shaker was 100 (rpm), in which the adsorption process was followed up spectroscopically at the equilibrium time (25 minutes). The results are indicated in Table 9 and Figure 13.

TABLE 9 The effect of temperature on the adsorption efficiency of the mixture of the drug and nano-copper oxide

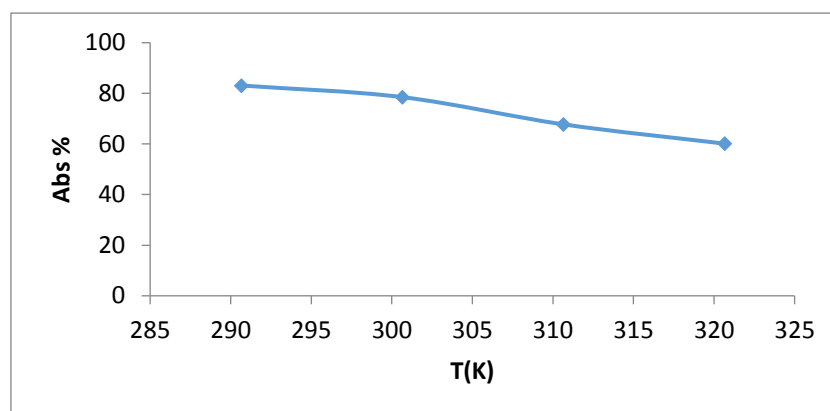| T(K)	Absorption	Qe(mg/g)	Adsorption%
290.65	0.088	6.743	83.1
300.65	0.118	8.573	78.5
310.65	0.189	12.902	67.74
320.65	0.239	15.951	60.12

FIGURE 13 Decreased adsorption efficiency with increasing temperature of the mixture of the drug and nano-copper oxide

From the results demonstrated in Table 9 and Figure 13, it was found that the adsorption efficiency decreases with increasing temperature, meaning that the adsorption process is exothermic process and this corresponds to the thermodynamic requirements of the adsorption process, meaning that increasing the temperature leads to an increase in the kinetic energy of the molecules present in the adsorbate solution (drug, nano-copper oxide) on the surface of the prepared activated charcoal, and thus a breakdown of the Vander-Waals bonding between the adsorbate molecules and the surface of the activated charcoal lead to an increase in their separation from the adsorbent surface and returns to the solution [21].

Calculation of thermodynamic functions: By studying the thermodynamic functions, it is possible to identify the nature of the studied system and the nature of the forces that control it, and that the value of the equilibrium constant (K_{eq}) at different temperatures represents the most important variables that we rely on in calculating the thermodynamic functions, as the K_{eq} values were calculated by using the following Equation [14,15]:

$$K_{aq} = \frac{X_{eq}}{a - X_{eq}} \qquad (3)$$

In which, a demonstrates the initial concentration of the adsorbate (mg/L),X_{eq} depicts the adsorbate concentration at equilibrium, and a-X_{eq} depicts the residual concentration of the adsorbate at equilibrium.

The values of (ΔG^o) were calculated by Equation 4.

$$\Delta G = -RT \ln K_{eq} \quad (4)$$

From the values of (ΔG^o) and (ΔH) that were calculated using the Vant-Hoff equation, which we obtain by drawing ($\ln K_{eq}$) with the temperature reciprocal $1/T$ as displayed in Figure 12, we calculate the (ΔS^o) values as follows:

$$\Delta G^o = (\Delta H - \Delta S^o)/T \quad (5)$$

It is worth noting that this study was conducted at the optimal conditions for adsorption by the best concentration of Favipiravir (40 µg/mL) with (0.000015 molar) of nano-copper oxide, the best weight of the adsorbent material (0.1 g) and at the equilibrium time (25 minutes), and thermodynamic values, as displayed in Figure 12 and Table 14.
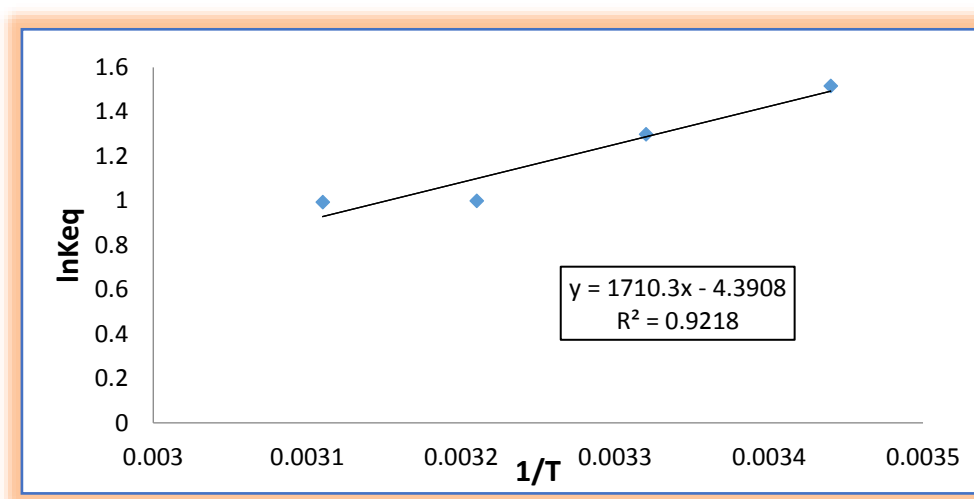

FIGURE 14 Van't Hof curve for adsorption of the mixture of Favipiravir with nano-copper oxide

TABLE 10 Thermodynamic functions of the drug mixture with copper oxide nanoparticles

T(K)	1/T (K^{-1})	Keq	lnKeq	ΔG^o (KJ/mol)	ΔH (KJ/mol)	ΔS^o (J/mol.K)
290.65	0.00344	4.932	1.5957	-3855.95		-35.65
300.65	0.00332	3.665	1.2988	-3246.48	-14219.43	-36.49
310.65	0.00321	1.507	0.9991	-2580.41		-37.46
320.65	0.00311	2.507	0.9941	-2650.15		-36.08

Biological study

The study was applied by applying the mixture of the drug and nano-copper oxide loaded on the surface of the prepared activated charcoal on the influenza virus and in the SDS presence, as the study proved the ability of the mixture to kill the virus [24] by 100%, as in Figure 15.
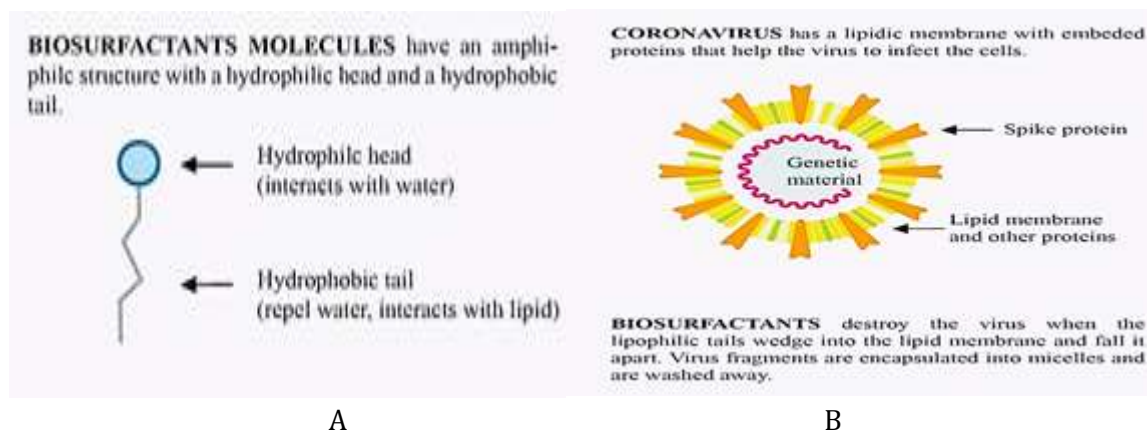
FIGURE 15 A- Surfactants A hydrophilic head and a hydrophobic tail for the surfactants [15]. B- The shape of the Covid-19 virus and the role of micelles of surfactants in its destruction.

It is noted from Figure 15 that the composition of surfactants which have a hydrophilic (lipophobic) head and a hydrophobic (lipophilic) tail, as micelles resulting from the process of mixing the surfactants destroy the Corona virus at the hydrophobic (lipophilic) tail, as a result of the tail merging of the surface-active substances with the fatty membrane of the virus (which causes cell injury, because it contains embedded proteins), dismantling it, encapsulating its parts, and removing it completely.

Likewise, the addition of nanomaterials to a mixture of surfactants increases the viscosity as a result of the increased crosslinking of micelles with each other, which ultimately leads to an increase in the duration of the anti-microbial activity on the surfaces.

Some nanomaterial's, such as carbon-based nanomaterials have also the ability to disperse the medium to a large extent, as it works to prevent the medium materials in it from gathering in a certain space without the other, which leads to exposing microorganisms to a larger surface area, and thus the anti-virus effectiveness will be to a greater extent [24,25,26].

The biological activity test was conducted by studying the ability of the sample mixture to kill the fungi (*Candida albicans*), as displayed in Figure 16. The results indicated that the antiviral drug is not effective against fungi when it is alone, however with the presence of the nano-material (copper oxide) and the drug under study loaded on the surface of the nano-carbon gave effectiveness against the virus [27] and fungi together, and thus the antiviral drug was developed with nano-materials that kill bacterial, as depicted in Figure 17.
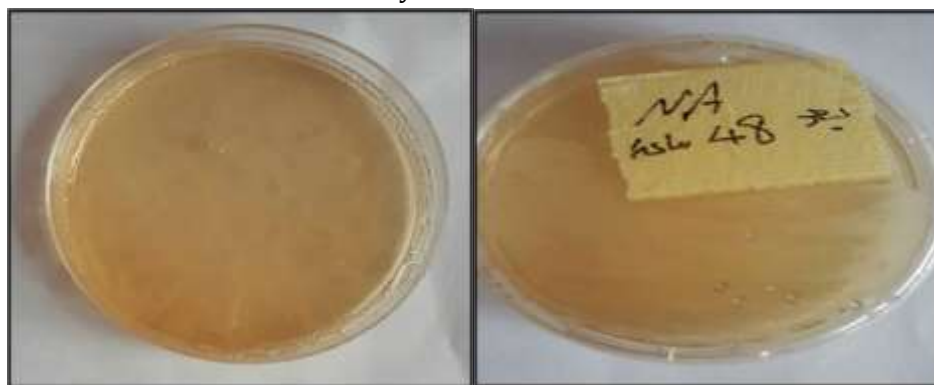

FIGURE 16 Fungi medium after (48) hours of sterilization with the drug under study

FIGURE 17 Fungi medium after (48) hours of sterilization with the drug mixture and nano-copper oxide loaded on the surface of the nano-carbon

Conclusion

- The equilibrium time is 25 minutes, and the adsorption efficiency increases when the natural pH of the drug.
- The adsorption system is an exothermic, spontaneously, and less random process.
- Improving and developing the drug under study by loading it on the surface of activated charcoal and in the presence of nano-copper oxide.
- The drug acts as an antiviral, and when loaded with nanomaterials, it becomes antifungal and antibacterial.

Acknowledgements

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