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Oxidative degradation of neomycin and streptomycin by cerium(IV) in sulphuric and perchloric acid solutions

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ABSTRACT

Degradation kinetics of antibiotics neomycin and streptomycin was explored spectrophotometrically via their oxidation by cerium(IV) in both sulphuric and perchloric acids. The oxidation reactions demonstrated a 1:8 stoichiometry (antibiotic:cerium(IV)). The kinetics of the reactions in the examined acidic media was first-order with respect to [cerium(IV)] and fractional-first orders with respect to examined antibiotics and H^+ concentrations. In the perchloric acid solution, the oxidation reactions of both antibiotics manifested fractional-first-order credence in $[H^+]$, whereas the reactions that occurred in sulphuric acid solutions displayed negative less than unit order rate with $[H^+]$. Additionally, different behaviours of the reactions in dissimilar acidic media regarding the influence of ionic strength were recorded. Tests for free radical involvement throughout the oxidation reactions were positive. Under the same circumstances, the rates of neomycin oxidation in both acidic media were lower than those of streptomycin, and those obtained in perchloric acid were higher than those of sulphuric acid for both antibiotic substrates. Conceivable oxidation mechanisms in both sulphuric and perchloric acids consistent with the obtained kinetic results were anticipated. Additionally, the derived rate-law expressions in both acids were in good accordance with the obtained kinetic results. The activation parameters of the oxidation reactions in the acidic media were assessed and debated.

1. Introduction

Pharmaceuticals (medical drugs) are organic compounds utilised in medicines to cure diseases in humans. However, these are foreign things in the human body and must be eliminated or removed from the body after performing their roles. Subsequently, the human body excretes them through a process known as drug metabolism, which takes place through several biochemical reactions, including oxidation, reduction, hydrolysis, and hydration. Generally, pharmaceuticals are discharged into or enter the environment through various ways such as via the excreta of humans or animals, wastewater effluent, and manufacturing processes. [1]. Furthermore, some pharmaceuticals are excreted without metabolic modifications [2,3]. The presence of even low concentrations of such pharmaceuticals in the environment may have toxic effects on microorganisms because these are complex organic compounds, which are difficult to decompose into simple final products. Therefore, they are regarded as one of the most dangerous pollutants in the environment and to human health [2,3], and their effects are continuously increasing. Because of their vigorous risks to the environment and humans, removal or degradation of pharmaceuticals via diverse media has become a substantial area of environmental research [4,5]. Several recent studies have specified that conventional treatment methods of pharmaceutical pollution based on biological treatment alone is not effective [5]. Thus, new methods must be developed for the reduction and elimination of these chemicals, which may be a combination of physical, biological, and chemical methods [5–10].

Antibiotics are amongst the most important groups of pharmaceutical drugs employed for treating humans and animals for bacterial and fungal infections. They are also utilised in such things as food preservation and processing, and scientific researches [11,12]. Aminoglycoside antibiotics are organic compounds containing amino cyclitol moieties to which amino sugars are linked glycosidically. These antibiotics are effective against gram+ve and gram-ve organisms, as well as mycoplasma. Neomycin and streptomycin are two significant examples of aminoglycoside antibiotics; their structures are illustrated in Fig. 1. Neomycin is used in a variety of pharmaceutical applications [13]. It is used to treat bacterial infections in the intestines and to treat hepatic coma [14]. Streptomycin is a widely used antibiotic, which can be used in the treatment of humans and domestic animals, as well as agriculture plants [15].

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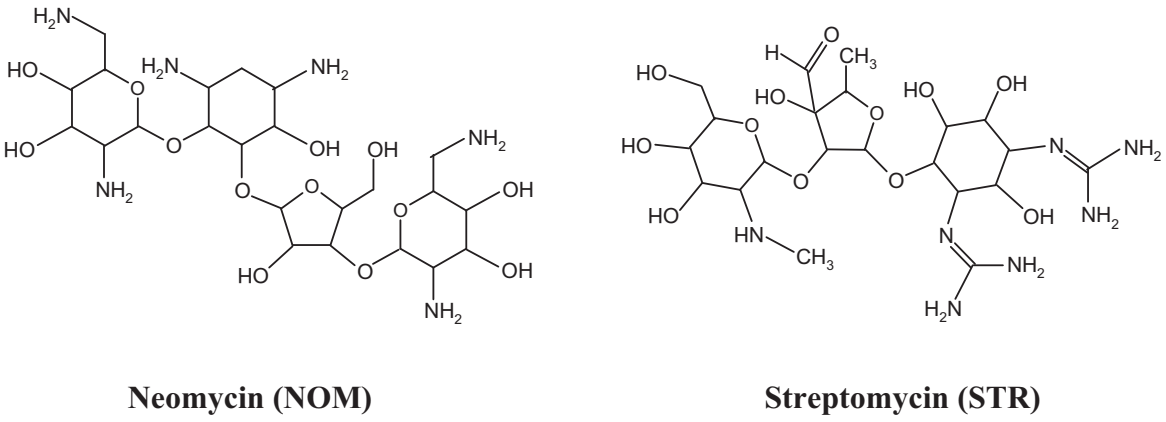

Fig. 1. Chemical structures of neomycin and streptomycin.

However, a wide range of antibiotics with diverse structures has been found in the environment, which are regarded to have low biodegradability and can affect living organisms. Several methods or techniques have been employed for the removal of antibiotics [5–11]. Chemical removal methods have been used, but the by-products that enter the environment are toxic pollutants. Physico-chemical techniques such as adsorption and electrolytic oxidation have been used for the treatment of pollutants in wastewater. However, chemical oxidation is a presumed method for antibiotic degradation in liquid and solid samples. Oxidation of medical drugs is important in the treatment processes of water and in understanding drug metabolism in pharmacokinetics studies [16–21]. Chemical oxidation may be regarded as a conceivable processing strategy for pharmaceutical drugs in wastewater, surface water, and groundwater. Through oxidation, the oxidiser transforms the toxic compounds into less harmful ones that are safe to discharge into the environment. Oxidation reactions of pharmaceutical drugs can be catalysed by oxygen, heavy metal ions, and light. However, in biochemical reactions, kinetic knowledge of medical drugs is needed for the optimisation of the reaction environment and to create a clear mechanistic picture of the metabolism of such drugs in biological systems. In certain cases, the rate constants of oxidation reactions amongst pharmaceutical compounds and oxidising agents may refer to the reactivity of these compounds during the treatment process and can be useful in the modelling of such processes [9,16].

Cerium(IV) in acidic media is a strong oxidant utilised in a variety of kinetic investigations [22–29], especially in sulphuric acid solutions [25,26], whereas oxidation reactions by cerium(IV) in perchloric acid are exceedingly rare [24,29]. However, the rates of oxidation reactions with cerium(IV) in perchloric acid are higher than those in sulphuric acid. The mechanism of oxidation by cerium(IV) was found to depend on the nature of the reductant and type of acid medium [27,28]. Despite the kinetics of cerium(IV), oxidation of some antibiotics has been investigated earlier [23,24], but no studies have been reported on the kinetics of cerium(IV) oxidation of neomycin and streptomycin drugs. Because of the lack of literature on the kinetics of oxidation of these antibiotics and our current interest in the elucidation of the mechanisms of the oxidation of antibiotics, the present study was conducted. In this study, we reported the kinetic, mechanistic, and thermodynamic aspects of oxidative degradation of neomycin and streptomycin by Ce^{IV} in dissimilar acidic media. The main goals of this investigation were to illuminate the selectivity of such antibiotics toward the cerium (IV) oxidant, to explore the effects of varying the antibiotic and acidic medium used on the reaction kinetics, to understand the kinetically reactive species in these redox reactions, to delineate a conceivable oxidation mechanism in both acidic media, and to establish rate-law expressions according to the kinetic results. This study introduces a promising treatment method, which may be a more convenient, inexpensive, rapid, and simple technique for antibiotic degradation to save the environment and human health, than previously published methods.

2. Experimental

2.1. Materials

The selected antibiotics utilised in this investigation (neomycin and streptomycin) were AK Scientific (UK) from Glentham Life Sciences and were used as supplied. Their stock solutions were prepared in bi-distilled water. Cerium(IV) solution was prepared fresh by dissolving a weighed sample (ceric ammonium sulphate, Sigma) in a 1.0 mol dm^{-3} sulphuric acid solution. It was then diluted with bi-distilled water and kept overnight in a brown glass bottle and was utilised after 24 h [26]. Cerium(III) solution was prepared by dissolving cerium(III) acetate hydrate (Sigma) in water. Sodium salts of both sulphate (Sigma-Aldrich) and perchlorate (Merck) were utilised to attain the required ionic strengths in sulphuric acid (98% Merck) and perchloric acid (70% Merck) media, respectively. Stock solutions of the remainder of the reagents were prepared by dissolving the required weights of Analar or Merck samples in bi-distilled water.

2.2. Kinetic measurements

All kinetic measurements in this investigation were conducted under a pseudo-first-order circumstance in which the examined antibiotics were initially present in substantial excess of that of the oxidant concentration, [Ce^{IV}]. The ionic strengths of the reaction mixtures were maintained constant, and the temperature was controlled at that desired within ±0.1 °C. The progress of the reactions was followed by estimating the decrease in the absorbance of cerium(IV) at its absorption maximum wavelength (λ_{max} = 316 nm) until at least two-half lives of the reactions were completed. All measurements were conducted in triplicate, and the rate constants were reproducible within ±3–5%. A Shimadzu UV-1800 automatic scanning double-beam spectrophotometer with a wavelength programme controller was used for all absorbance measurements. The reaction orders with respect to the examined antibiotics, as well as the acidic medium, were calculated from the slopes of logarithms of the observed first-order rate constants (log k_{obs}) versus log (concentration) by changing the concentrations of the antibiotic and the acid in turn, while the other constituents remained constant.

3. Results

3.1. Reactions stoichiometry

Stoichiometry of the oxidation reactions of neomycin and streptomycin antibiotics (A) with cerium(IV) (Ce^{IV}) in both sulphuric and perchloric acid media was investigated spectrophotometrically at a wavelength of 316 nm (the maximum absorption wavelength of Ce^{IV}). The recorded absorption values for a variety of reaction mixtures with dissimilar ratios of $[Ce^{IV}]/[A]$ at fixed $[H^+]$ and ionic strength (I) at room temperature (reacted for 24 h to complete the reactions) afforded a ratio of $\Delta[A]/\Delta[Ce^{IV}] = 1:(8 \pm 0.28)$. This outcome revealed that 8.0 mol of Ce^{IV} reacted with 1.0 mol of the antibiotic.

3.2. Time-resolved spectra

Time-resolved spectra during the cerium(IV) oxidation of neomycin (NOM) and streptomycin (STR) in sulphuric and perchloric acids are presented in Fig. 2(a)–(d). In both acidic solutions, the recorded spectra manifested regular decays of the cerium(IV) band at $\lambda_{max} = 316$ nm, as the reactions advanced because of the reduction of cerium(IV) to cerium(III) by the antibiotics. Under comparable conditions, the decay in cases of streptomycin in both acidic media was higher than that of neomycin and that acquired in perchloric acid was also higher than that in sulphuric acid for both antibiotics.

3.3. Dependence of the oxidation rates on cerium(IV) concentration

The order of the oxidation reactions of both neomycin and streptomycin by cerium(IV) was explored by investigating the oxidation rates at various initial concentrations of cerium(IV), $[Ce^{IV}]_0$, ranging between 1.0×10^{-4} and 8.0×10^{-4} mol dm^{-3} at fixed concentrations of antibiotic substrates and acidic media. The acquired results were first-order plots (ln absorbance vs. time) and were linear for reactions longer than two-half lives as shown in Fig. 3 (for neomycin in sulphuric acid solution as a representative example), with no significant variation in the observed first-order rate-constant values (k_{obs}) for different $[Ce^{IV}]$, as listed in Tables 1 and 2 for sulphuric and perchloric acid, respectively. Both the linearity of ln absorbance versus time plots, as well as the independence of k_{obs} values at various $[Ce^{IV}]$ confirmed that the oxidation reactions were first-order with $[Ce^{IV}]$.

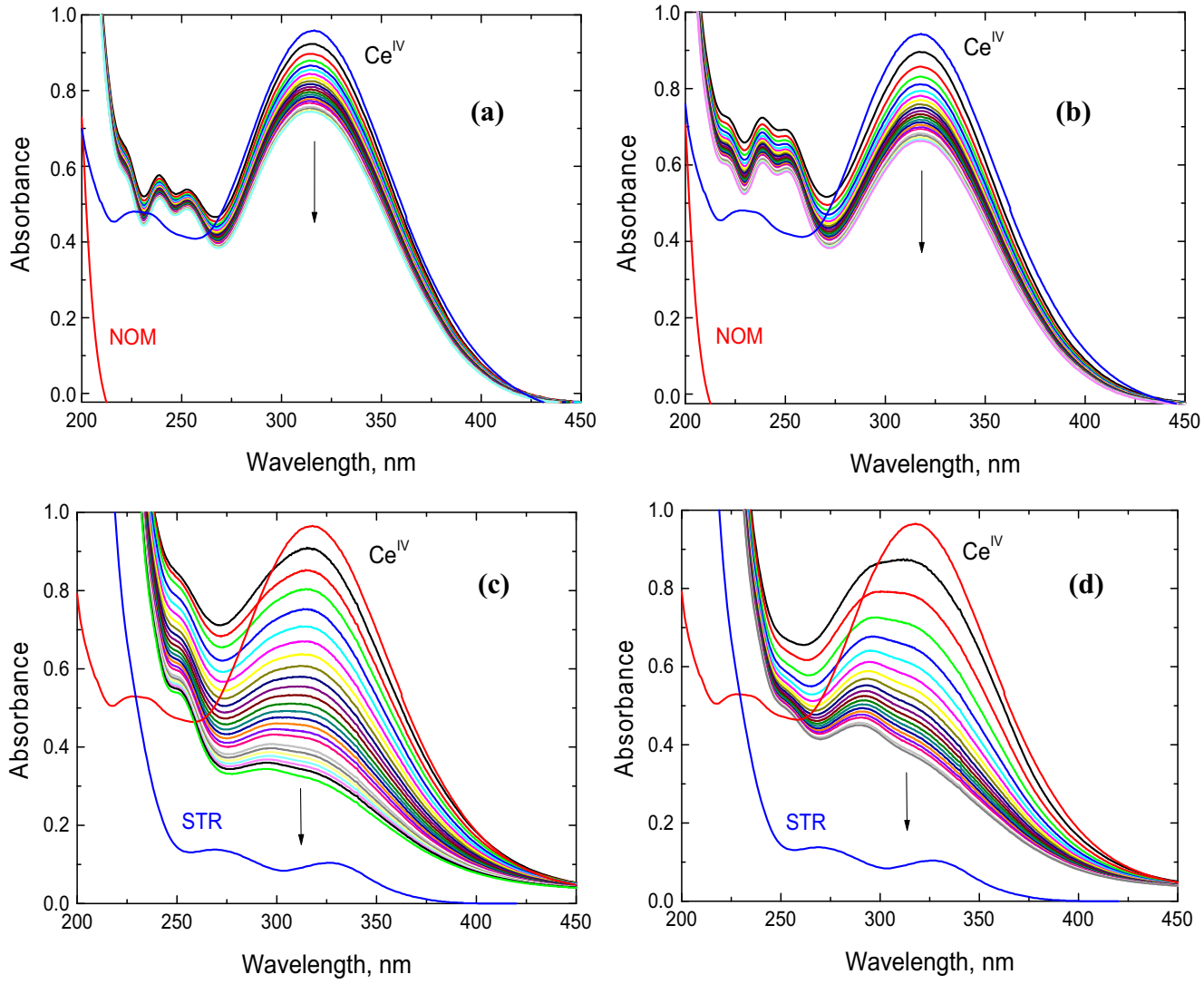

Fig. 2. Spectral changes during cerium(IV) oxidation of neomycin (NOM) in (a) sulphuric and (b) perchloric acid, and streptomycin (STR) in (c) sulphuric and (d) perchloric acid. $[Ce^{IV}] = 2.0 \times 10^{-4}$, $[A] = 1.5 \times 10^{-2}$, $[H^+] = 1.2$ and $I = 2.0$ mol dm^{-3} at 298 K.

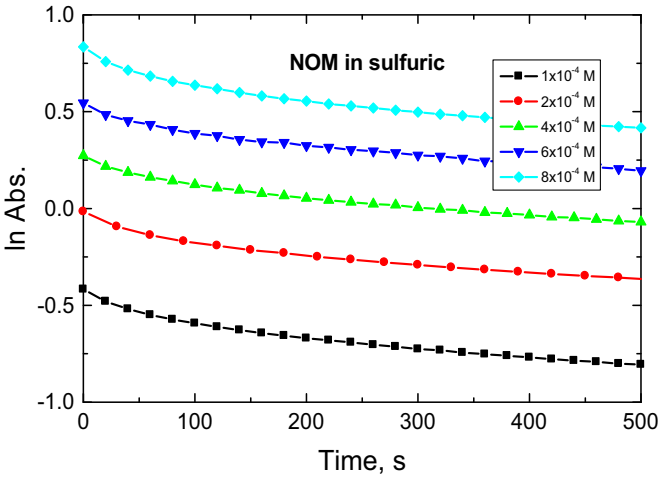

Fig. 3. Effect of [cerium(IV)] on the first-order rate-constant plot for the oxidation of neomycin (NOM) by cerium(IV) in sulphuric acid solution. [A] = 1.5×10^{-2}, [H^+] = 1.2, and I = 2.0 mol dm^{-3} at 298 K.

3.4. Dependence of the oxidation rates on the concentration of the antibiotics

In both acidic solutions, the effects of the concentration of the antibiotics, [A], were explored by recording the k_{obs} values at several [A] with fixed values for other constituents. The results indicated that an increase in [A] enhanced the oxidation rates, according to the values of k_{obs} listed in Tables 1 and 2. The reaction orders with regard to [A] were obtained as the gradients of log k_{obs} vs. log [A] plots, as presented in Fig. 4, which were 0.69 and 0.73 for neomycin, and 0.82 and 0.87 for streptomycin in sulphuric and perchloric acids, respectively, indicating less than a unit order rate in [A].

3.5. Dependence of the oxidation rates on acidic media concentrations

To examine the effects of [H^+] concentration on the rates of the oxidation reactions, kinetic runs were conducted at various [H^+] concentrations, whereas those of other variables were held constant. The results for both antibiotics showed that increasing [H^+] decreased the oxidation rates in sulphuric acid solutions but increased the rates in perchloric acid solutions as shown in the values of k_{obs} listed in Tables 1 and 2. Plots of k_{obs} vs. [H^+] were linear with negative slopes in the case of sulphuric acid solutions and positive slopes and intercepts in the case of perchloric acid solutions, as illustrated in Fig. 5(a) and (b) for neomycin and streptomycin, respectively, thus indicating negative and positive less than unit order dependences for [H^+] in sulphuric and perchloric acid, respectively. The orders of the reactions with respect to [H^+] in sulphuric acid solutions were −0.49 and −0.51 for neomycin and streptomycin, respectively, and those obtained in perchloric acid solutions were 0.54 and 0.58 for neomycin and streptomycin, respectively. These were calculated as the gradients of the plots of log k_{obs} versus log [H^+].

3.6. Dependence of the oxidation rates on the ionic strength

To illuminate the nature of the reacted ionic species, the rates of the reactions were examined at various ionic strengths of the reactions media (between 2.0 and 3.6 mol dm^{-3}) by supplementation of sodium sulphate in sulphuric acid solutions and sodium perchlorate in perchloric acid solutions. The results indicated that the reaction rates increased with increasing ionic strength in perchloric acid solutions, whereas they changed negligibly in cases of sulphuric acid solutions as determined by k_{obs} values at various ionic strengths (Tables 1 and 2). Thus, in cases of perchloric acid solutions, the Debye-Huckel plots were linear with positive slopes, as shown in Fig. 6.

3.7. Dependence of the oxidation rates on the dielectric constant of the reaction media

The influence of the dielectric constants (D) or relative permittivity of the reaction media on the oxidation rates was explored by changing the solvent composition (v/v %) of the water-miscible organic solvent, i.e., acetic acid, to water in the reaction media. The values of D were calculated from the Laidler and Eyring equation, Eq. (1):

$$D = D_w V_w + D_s V_s \quad (1)$$

where, D_w and D_s represent water and organic solvents, respectively, and V_w and V_s are the fractions of the component volume of water and solvent, respectively, in the total reaction mixture.

The experimental results showed that the rates of reactions in the perchloric acid solutions decreased with decreasing dielectric constants

Table 1
Effects of variations of [Ce^{IV}], [A], [H^+], and ionic strength, I, on the rate constants k_{obs} in the cerium(IV) oxidation of neomycin and streptomycin in sulphuric acid solutions at 298 K.

10^4 [Ce^{IV}] (mol dm^{-3})	10^2 [A] (mol dm^{-3})	[H^+] (mol dm^{-3})	I (mol dm^{-3})	10^4 k_{obs} (s^{-1})	
				Neomycin	Streptomycin
1.0	1.5	1.2	2.0	4.69	18.77
2.0	1.5	1.2	2.0	**4.10**	**18.12**
4.0	1.5	1.2	2.0	4.12	18.21
6.0	1.5	1.2	2.0	4.09	18.09
8.0	1.5	1.2	2.0	4.23	18.37
2.0	**0.5**	1.2	2.0	1.97	9.87
2.0	**1.0**	1.2	2.0	3.04	14.36
2.0	**1.5**	1.2	2.0	**4.10**	**18.12**
2.0	**2.0**	1.2	2.0	5.17	21.84
2.0	**2.5**	1.2	2.0	5.89	24.11
2.0	1.5	**0.6**	2.0	5.61	23.89
2.0	1.5	**0.9**	2.0	4.79	21.07
2.0	1.5	**1.2**	2.0	**4.10**	**18.12**
2.0	1.5	**1.5**	2.0	3.69	15.98
2.0	1.5	**1.8**	2.0	3.31	13.49
2.0	1.5	1.2	**2.0**	**4.10**	**18.12**
2.0	1.5	1.2	**2.4**	3.94	17.74
2.0	1.5	1.2	**2.8**	4.02	17.57
2.0	1.5	1.2	**3.2**	4.05	17.92
2.0	1.5	1.2	**3.6**	4.01	17.68

Experimental error ± 3%.

Table 2
Effects of variation of [Ce^{IV}], [A], [H^+], and ionic strength, *I*, on the rate-constant k_{obs} in the cerium(IV) oxidation of neomycin and streptomycin in perchloric acid solutions at 298 K.

10^4 [Ce^{IV}] (mol dm^{-3})	10^2 [A] (mol dm^{-3})	[H^+] (mol dm^{-3})	*I* (mol dm^{-3})	10^4 k_{obs} (s^{-1})	
				Neomycin	Streptomycin
1.0	1.5	1.2	2.0	7.87	30.12
2.0	1.5	1.2	2.0	**7.58**	**29.25**
4.0	1.5	1.2	2.0	7.63	29.51
6.0	1.5	1.2	2.0	7.48	29.27
8.0	1.5	1.2	2.0	7.59	29.62
2.0	**0.5**	1.2	2.0	3.45	13.81
2.0	**1.0**	1.2	2.0	5.67	20.87
2.0	**1.5**	1.2	2.0	**7.58**	**29.25**
2.0	**2.0**	1.2	2.0	9.39	37.78
2.0	**2.5**	1.2	2.0	11.24	45.81
2.0	1.5	**0.6**	2.0	5.21	19.76
2.0	1.5	**0.9**	2.0	6.52	25.11
2.0	1.5	**1.2**	2.0	**7.58**	**29.25**
2.0	1.5	**1.5**	2.0	8.62	33.23
2.0	1.5	**1.8**	2.0	9.39	36.84
2.0	1.5	1.2	**2.0**	**7.58**	**29.25**
2.0	1.5	1.2	**2.4**	8.77	44.32
2.0	1.5	1.2	**2.8**	10.02	55.47
2.0	1.5	1.2	**3.2**	11.14	66.67
2.0	1.5	1.2	**3.6**	12.23	79.41

Experimental error ± 4%.

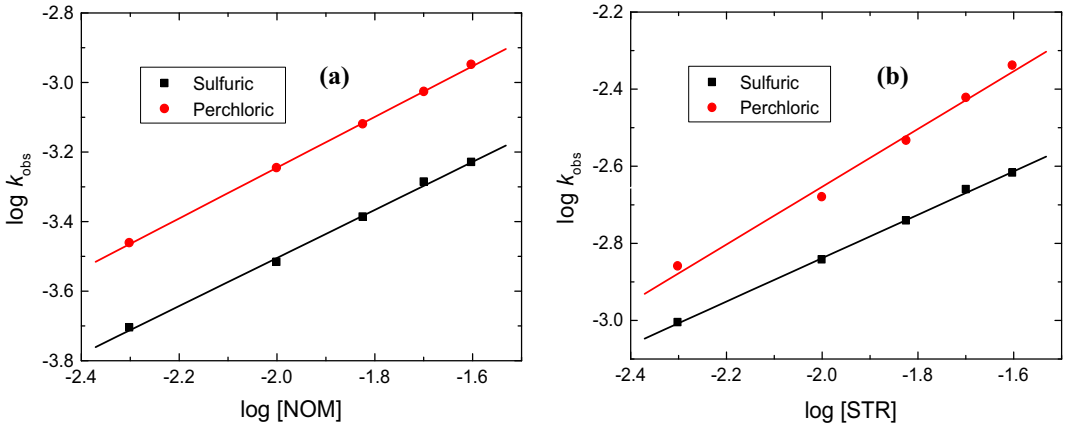

Fig. 4. Plots of log k_{obs} versus log [A] for the oxidation of (a) neomycin (NOM) and (b) streptomycin (STR) in sulphuric and perchloric acid solutions. [Ce^{IV}] = 2.0×10^{-4}, [H^+] = 1.2, and I = 2.0 mol dm^{-3} at 298 K.

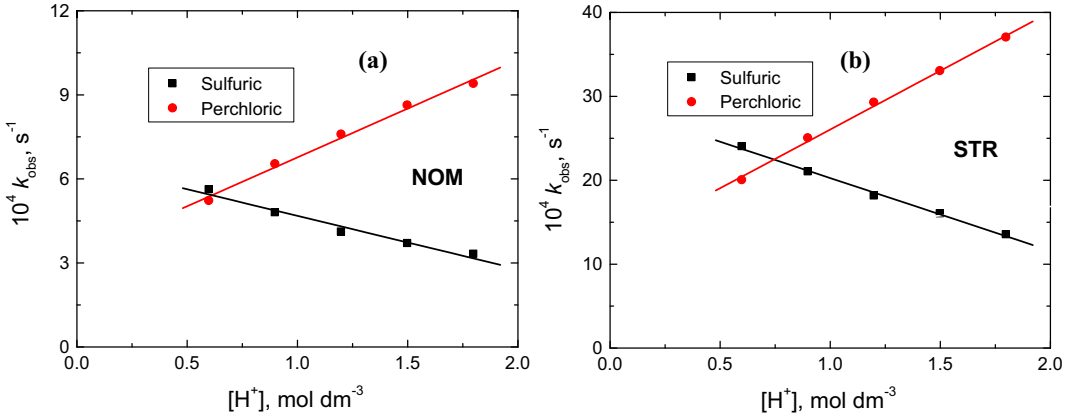

Fig. 5. Impact of [H^+] on the rate-constant k_{obs} for the oxidation of (a) neomycin (NOM) and (b) streptomycin (STR) in sulphuric and perchloric acid solutions. [A] = 1.5×10^{-2}, [Ce^{IV}] = 2.0×10^{-4}, and I = 2.0 mol dm^{-3} at 298 K.

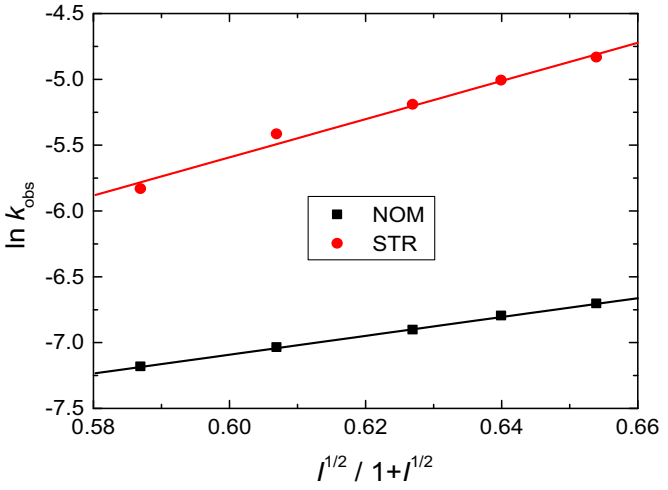

Fig. 6. Debye-Huckel plots in the cerium(IV) oxidation of neomycin (NOM) and streptomycin (STR) in perchloric acid solutions. [A] = 1.5×10^{-2}, [Ce^{IV}] = 2.0×10^{-4}, and [H^+] = 1.2 mol dm^{-3} at 298 K.

of the reaction medium (increasing acetic acid content). Plots of log k_{obs} versus $1/D$ were linear with negative slopes as illustrated in Fig. 7. In cases of sulphuric acid solutions, the rate constants were significantly unaffected by the decrease in the dielectric constant.

3.8. Dependence of the oxidation rates on temperature

Oxidation reactions in both acidic solutions were examined at five temperatures ranging between 288 and 328 K, while other constituents were held stable, viz. [Ce^{IV}] = 2.0×10^{-4}, [A] = 1.5×10^{-2}, [H^+] = 1.2, and I = 2.0 mol dm^{-3}. The oxidation rates were increased as the temperature increased as shown by the values of k_{obs} in Table 3. The activation parameters regarding the second-order rate constants (k') were computed from Eyring plots (Fig. 8) and Arrhenius plots (Fig. 9) and are presented in Table 4.

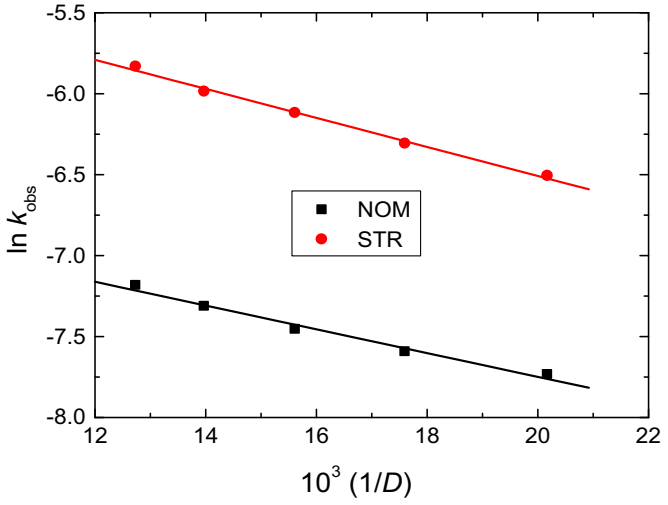

Fig. 7. Effects of dielectric constant on rates of cerium(IV) oxidation of neomycin (NOM) and streptomycin (STR) in perchloric acid solutions. [A] = 1.5×10^{-2}, [Ce^{IV}] = 2.0×10^{-4}, [H^+] = 1.2, and I = 2.0 mol dm^{-3} at 298 K.

Table 3
Effects of temperature on the rate-constant k_{obs} in the cerium (IV) oxidation of neomycin and streptomycin in sulphuric and perchloric acid solutions. [A] = 1.5×10^{-2}, [Ce^{IV}] = 2.0×10^{-4}, [H^+] = 1.2, and I = 2.0 mol dm^{-3}.

T (K)	10^4 k_{obs} (s^{-1})			
	Neomycin		Streptomycin	
	Sulphuric	Perchloric	Sulphuric	Perchloric
288	2.21	4.56	12.11	21.87
298	**4.10**	**7.58**	**18.12**	**29.25**
308	9.08	19.47	44.73	45.81
318	15.44	38.89	65.42	80.07
328	23.89	67.51	87.71	157.28

3.9. Effects of the initially added product on the oxidation rates

The effects of supplementation of cerium(III) ions as the predicted product of cerium(IV) reduction was examined in the range of concentrations from 1.0×10^{-4} to 8.0×10^{-4} mol dm^{-3} at fixed concentrations of cerium(IV), antibiotics, and acids. The results indicated that the addition of the Ce^{III} ion did not significantly change the rates of oxidation reactions in both acidic media.

3.10. Effects of [HSO_4^-]

Because of bisulphate ion was included in the cerium(IV) oxidation reactions in sulphuric acid solutions, the influence of the bisulphate ion was investigated by conducting the kinetic measurements at various concentrations with fixed levels of other constituents. The outcome indicated that increasing [HSO_4^-] decreased the rates of oxidation reactions. The plot of $1/k_{obs}$ versus [HSO_4^-] was linear with a positive intercept, as illustrated in Fig. 10.

3.11. Free radicals test

To illuminate the presence or absence of free radicals throughout the oxidation reactions, prerequisite quantities of acrylonitrile monomer (approximately 10% v/v) were added to a series of initially oxidised reaction mixtures (between the examined antibiotic and oxidant solutions) in deaerated vessels, which were preserved for approximately 60 min. Heavy white precipitates were established when these tests were negative and repeated in the absence of either antibiotics or oxidants under the same conditions. This indicated that the reactions proceeded via the generation of free radicals.

4. Discussion

4.1. The suggested reaction's mechanisms

4.1.1. Kinetically active cerium(IV) species in sulphuric and perchloric acid solutions

In sulphuric acid media, cerium(IV) ion forms various sulphate complexes, such as $Ce(SO_4)^{2+}$, $Ce(SO_4)_2$, $HCe(SO_4)_3^-$, and $H_3Ce(SO_4)_4^-$. The formation of such complexes depends on the concentrations of H^+, HSO_4^-, or H_2SO_4 [27,28]. The results indicated that increasing the concentrations of both H^+ and HSO_4^- ions decreased the rates of the reactions, suggesting that $HCe(SO_4)_3^-$ may be regarded as the kinetically active species of cerium(IV), according to the following equilibrium [30,31],

$$HCe(SO_4)_3^- + HSO_4^- + H^+ \overset{K_1}{\rightleftharpoons} H_3Ce(SO_4)_4^- \quad (2)$$

In perchloric acid, cerium(IV) ion may be present as either a free species, Ce^{4+}, a hydrolysed species, $Ce(OH)^{3+}$ or $Ce(OH)_2^{2+}$, or a dimeric species, $(Ce–O–Ce)^{6+}$ or $(HOCe–O–CeOH)^{4+}$ [32,33]. It was reported

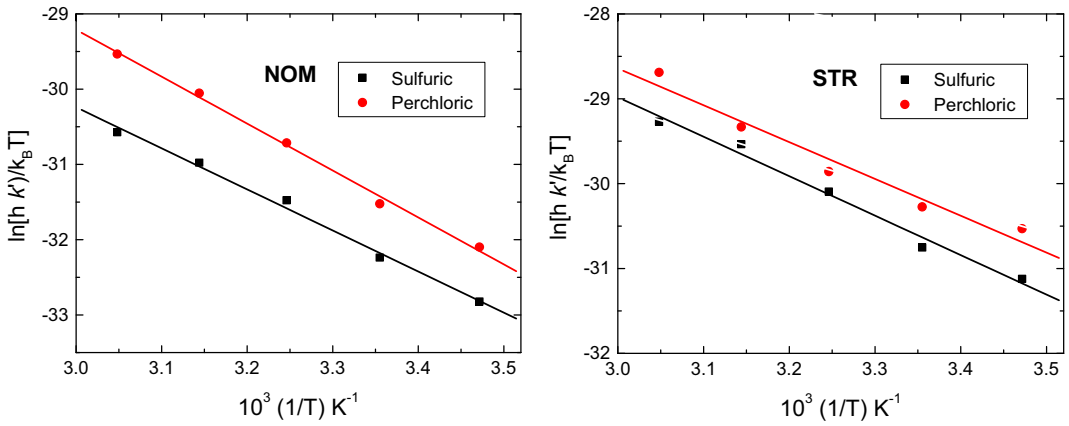

Fig. 8. Eyring plots of k' in the oxidation of neomycin (NOM) and streptomycin (STR) in sulphuric and perchloric acid solutions. [A] = 1.5×10^{-2}, [Ce^{IV}] = 2.0×10^{-4}, [H^+] = 1.2, and I = 2.0 mol dm^{-3}.

[34] that the free species, Ce^{4+}, is the predominant at [H^+] ≥ 1.0 and at [Ce^{IV}] up to 1.5×10^{-3} mol dm^{-3}. Thus, under the present conditions, as well as increasing the reaction rates with the increase in [H^+], Ce^{4+} may be regarded as the kinetically active species of cerium(IV).

4.1.2. Reactions mechanism in sulphuric acid

The reactions of neomycin and streptomycin (A) with cerium(IV) in sulphuric acid have a 1:8 (A:Ce^{IV}) stoichiometry. The reactions were first-order in [Ce^{IV}], fractional-first order in antibiotic concentration, [A], and negative less than unit order in both [H^+] and [HSO_4^-]. The rates were unchanged with ionic strength and the dielectric constant of the reaction medium. Tests for free radical intervention were positive. No effect of the added product, cerium(III), was observed.

In the light of foregoing aspects, the oxidation of antibiotic substrates (A) by cerium(IV) in sulphuric acid is proposed to proceed with the construction of a complex between the neutral antibiotic substrate and the kinetically active cerium(IV) species ($HCe(SO_4)_3^-$), which formed according to equilibrium (2). The free oxidation rates of both ionic strength and dielectric constants supported that the reactions were between a neutral substrate and an ion, i.e., between an antibiotic molecule (A) and a negatively charged cerium(IV) reactive species [36–38], as illustrated in the equilibrium:

$$A + HCe(SO_4)_3^- \overset{K_2}{\rightleftharpoons} [A{-}HCe(SO_4)_3^-](C_1) \quad (3)$$

Table 4
Activation parameters of k' in the cerium(IV) oxidation of neomycin and streptomycin in sulphuric and perchloric acid solutions. [A] = 1.5×10^{-2}, [Ce^{IV}] = 2.0×10^{-4}, [H^+] = 1.2, and I = 2.0 mol dm^{-3}.

Activation parameters	Neomycin		Streptomycin	
	Sulphuric	Perchloric	Sulphuric	Perchloric
ΔS^*, J mol^{-1} K^{-1}	−114.73	−87.30	−124.71	−129.69
ΔH^*, kJ mol^{-1}	45.31	51.80	38.66	36.08
ΔG^*_{298}, kJ mol^{-1}	79.50	77.81	75.82	74.73
E^*_a, kJ mol^{-1}	47.89	54.54	41.24	35.58

Complex formation occurred before the rate-determining step, which was supported by the obtained fractional-first-order kinetics with respect to antibiotic concentrations. Formation of complexes was also proved kinetically by the obtained non-zero intercepts of $1/k_{obs}$ vs. 1/[A] plots [35], as shown in Figs. 11 and 12 for neomycin and streptomycin, respectively.

The complex formed slowly decays in the rate-determining step to yield the antibiotic free radical (A•) and cerium(III),

$$[A{-}HCe(SO_4)_3^-](C_1) \underset{slow}{\overset{k_1}{\rightarrow}} A^{\cdot} + Ce^{3+} + 2SO_4^{2-} + HSO_4^- \quad (4)$$

This step is supported by the acquired negligible effect of the added cerium(III) ion [38].

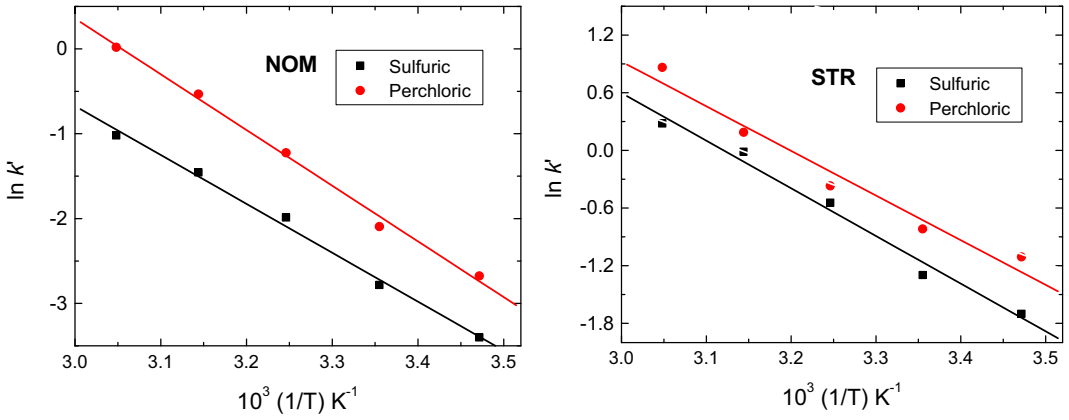

Fig. 9. Arrhenius plots of k' in the oxidation of neomycin (NOM) and streptomycin (STR) in sulphuric and perchloric acid solutions. [A] = 1.5×10^{-2}, [Ce^{IV}] = 2.0×10^{-4}, [H^+] = 1.2, and I = 2.0 mol dm^{-3}.

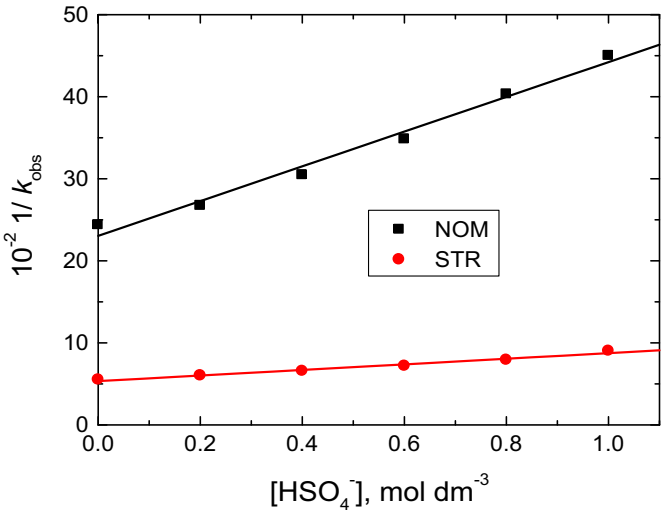

Fig. 10. Plots of $1/k_{obs}$ versus $[HSO_4^-]$ in the cerium(IV) oxidation of neomycin (NOM) and streptomycin in sulphuric acid solutions. [A] = 1.5×10^{-2}, $[Ce^{IV}] = 2.0 \times 10^{-4}$, $[H^+] = 1.2$, and $I = 2.0$ mol dm^{-3} at 298 K.

The antibiotic radical reacts rapidly with another $HCe(SO_4)_3^-$ species to form an intermediate oxidation product of antibiotic and cerium(III) species, as shown in the following equation:

$$A^{\cdot} + HCe(SO_4)_3^- \xrightarrow{fast} \text{Intermediate oxidation product of A} + Ce^{3+} \quad (5)$$

The intermediate oxidation product reacts with another cerium(IV) reactive species in subsequent fast steps to yield the final oxidation products.

The proposed reaction mechanism led to the derivation of the following relationship between k_{obs} and antibiotic, hydrogen ion, and bisulphate ion concentrations (see Appendix A in the Supplementary information),

$$k_{obs} = \frac{k_1 K_2 [A]}{1 + K_1 [HSO_4^-][H^+] + K_2 [A]} \quad (6)$$

and with rearrangement, the following equations are obtained,

$$\frac{1}{k_{obs}} = \left(\frac{1 + K_1 [HSO_4^-][H^+]}{k_1 K_2}\right)\frac{1}{[A]} + \frac{1}{k_1} \quad (7)$$

$$\frac{1}{k_{obs}} = \left(\frac{K_1}{k_1 K_2}\right)[HSO_4^-][H^+] + \frac{1}{k_1 K_2 [A]} + \frac{1}{k_1} \quad (8)$$

In light of the derived Eqs. (7) and (8), the plots of $1/k_{obs}$ vs. $1/[A]$ at fixed $[H^+]$, and $1/k_{obs}$ vs. $[H^+]$ at fixed [A] must be linear with positive intercepts as obtained experimentally and illustrated in Figs. 11 and 12 for neomycin and streptomycin, respectively. The values of the rate constant of the rate-determining step (k_1) and the equilibrium constants (K_1 and K_2) are calculated from the slopes and intercepts of these plots and are inserted in Table 5.

4.1.3. Reaction mechanism in perchloric acid

The kinetics of reduction of cerium(IV) by neomycin and streptomycin in perchloric acid was in good agreement with that noted for sulphuric acid with respect to reaction stoichiometry, reaction order in the oxidant and antibiotic concentrations, tests for free radicals and the influence of cerium(III) ions. However, perchloric acid reactions exhibited a less than a unit positive order change in $[H^+]$ with their rates augmented by raising both ionic strength and dielectric constants, which are in contrast with those obtained in sulphuric acid.

The positive fractional-first-order kinetics in $[H^+]$, as well as the literature background [39] and the structures of the examined antibiotics, suggested the protonation of the antibiotic substrate in the first step to constructing a more reactive species of the antibiotic, Eq. (9):

$$A + H^+ \overset{K_3}{\rightleftharpoons} AH^+ \quad (9)$$

Additionally, the obtained fraction of a unit order in [A] suggested the formation of a complex (C_2) between Ce^{4+} and AH^+, as represented by the equation,

$$Ce^{4+} + AH^+ \overset{K_4}{\rightleftharpoons} \left[AH^+ - Ce^{4+}\right](C_2) \quad (10)$$

Increasing the oxidation rates with the increase in both ionic strength and dielectric constant supports the reaction between two similarly charged ions [36–38], i.e., between Ce^{4+} and AH^+ (Eq. (10)).

The constructed complexes decayed in the rate-determining step of free radicals (A•) and Ce^{III},

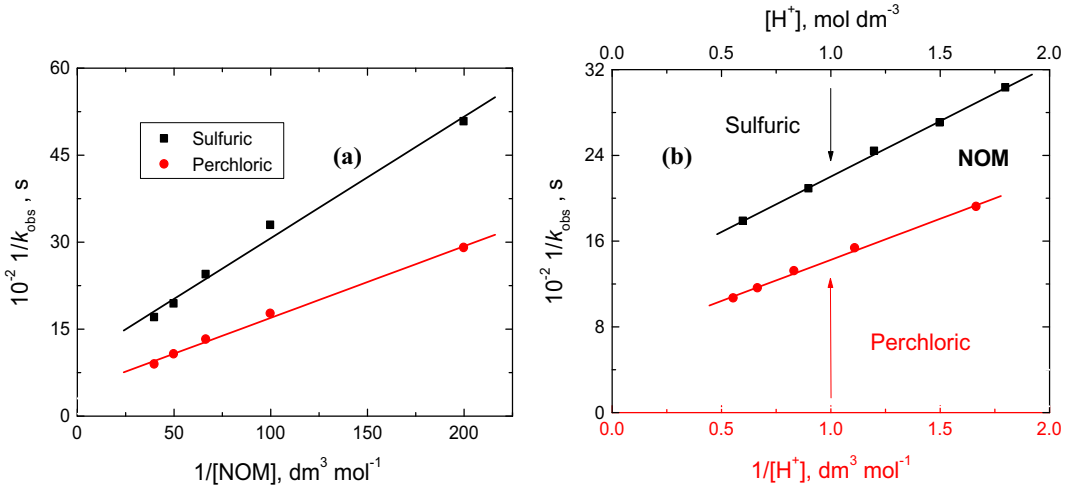

Fig. 11. Verification of (a) Eqs. (7) and (13), and (b) Eqs. (8) and (14) in the oxidation of neomycin (NOM) in sulphuric and perchloric acid solutions. $[Ce^{IV}] = 2.0 \times 10^{-4}$ and $I = 2.0$ mol dm^{-3} at 298 K.

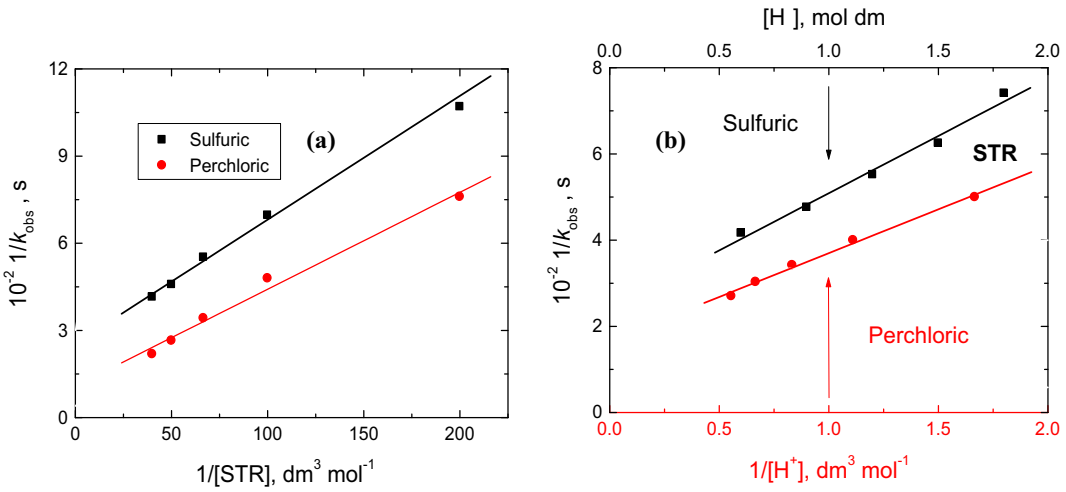

Fig. 12. Verification of (a) Eqs. (7) and (13), and (b) Eqs. (8) and (14) in the oxidation of streptomycin (STR) in sulphuric and perchloric acid solutions. $[Ce^{IV}] = 2.0 \times 10^{-4}$ and $I =$ 2.0 mol dm^{-3} at 298 K.

$$\left[AH^{+}-Ce^{4+}\right](C_2) \underset{slow}{\overset{k_2}{\rightarrow}} A^{\cdot} + Ce^{3+} \tag{11}$$

Furthermore, the antibiotic radical reacts rapidly with another Ce^{4+} species to form an intermediate oxidation product of antibiotics and Ce^{3+}. The formed intermediate product reacts with other Ce^{4+} species in subsequent rapid steps to yield the final oxidation products.

The suggested oxidation mechanism led to the following equation (see Appendix B in the Supplementary information),

$$k_{obs} = \frac{k_2 K_3 K_4 [A]\left[H^{+}\right]}{1 + K_3\left[H^{+}\right] + K_3 K_4 [A]\left[H^{+}\right]} \tag{12}$$

With the rearrangement of Eq. (12), Eqs. (13) and (14) were obtained,

$$\frac{1}{k_{obs}} = \left(\frac{1 + K_3\left[H^{+}\right]}{k_2 K_3 K_4\left[H^{+}\right]}\right)\frac{1}{[A]} + \frac{1}{k_2} \tag{13}$$

$$\frac{1}{k_{obs}} = \left(\frac{1}{k_2 K_3 K_4 [A]}\right)\frac{1}{\left[H^{+}\right]} + \left(\frac{1}{k_2 K_4 [A]} + \frac{1}{k_2}\right) \tag{14}$$

Regarding the derived Eqs. (13) and (14), the plots of $1/k_{obs}$ vs. $1/[A]$ at fixed $[H^+]$, and $1/k_{obs}$ vs. $1/[H^+]$ at fixed [A] should be linear with positive intercepts as obtained experimentally and shown in Figs. 11 and 12. The values of the rate-constant k_2 and the equilibrium constants K_3 and K_4 were computed and are also listed in Table 5.

Table 5
Values of the rate constants of the rate-determining steps and the equilibrium constants in the oxidation of neomycin and streptomycin in sulphuric and perchloric acid solutions. $[Ce^{IV}] = 2.0 \times 10^{-4}$ and $I = 2.0$ mol dm^{-3} at 298 K.

Acid medium	Rate and equilibrium constants	Neomycin	Streptomycin
Sulphuric	$10^2\ k_1$ (s^{-1})	10.32	40.52
	$10^2\ K_1$ (dm^3 mol^{-1})	19.05	3.76
	$10^{-2}\ K_2$ (dm^3 mol^{-1})	3.26	16.55
Perchloric	$10^2\ k_2$ (s^{-1})	21.69	92.58
	$10^2\ K_3$ (dm^3 mol^{-1})	20.85	47.70
	$10^{-2}\ K_4$ (dm^3 mol^{-1})	1.93	0.74

4.2. The activation parameters

The acquired activation parameters of k' presented in Table 5 can be debated as follows: the higher negative values of $\Delta S^{\#}$ illuminated construction of compressed intermediate complexes between the examined antibiotics and the oxidant cerium(IV) [40,41]. The acquired values of $\Delta H^{\neq}$ and $\Delta S^{\neq}$ are both in accordance with the electron transfer reactions. The positive values of both $\Delta H^{\neq}$ and $\Delta G^{\neq}$ specified that the establishment of the intermediate complexes were endothermic and non-spontaneous, respectively. Additionally, the higher activation energies $E_a^{\neq}$ indicated that the rate-determining step was the decay of the intermediate complexes into the oxidation products.

5. Conclusions

1) The kinetics and mechanistic aspects of oxidation of neomycin and streptomycin (A) by Ce^{IV} have been investigated using UV–Vis absorption spectra in both sulphuric and perchloric acid solutions.
2) The oxidation reactions demonstrated a 1:8 stoichiometry (A:Ce^{IV}).
3) Under the same conditions, the rates of streptomycin oxidation in both acidic media were higher than those of neomycin, and those acquired in perchloric acid were also higher than those of sulphuric acid for both antibiotic substrates.
4) In perchloric acid, the reactions showed a fractional positive unit order with $[H^+]$ and their rates were increased with increasing ionic strength and dielectric constants, which are in contrast with those obtained for sulphuric acid.
5) Conceivable oxidation mechanisms in both sulphuric and perchloric acids consistent with the obtained kinetic results were anticipated.
6) The derived rate-law expressions for both acids were consistent with the results.
7) The activation parameters for the oxidation of both antibiotics in the investigated acidic media were assessed and debated.
8) This study introduced a promising treatment method, which may be a more convenient, inexpensive, rapid, and simple method for antibiotics degradation and improve the environment and human health more than the previously published techniques.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.molliq.2020.113439.

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