History of Medicine, 2023, 9(2): 387–404
DOI: 10.17720/2409-5834.v9.2.2023.053

Spectrophotometric Determination of Stoichiometric-ratios and Kinetics study for the colored Azo-Drugs resulting from the interactions of three drugs: Tetracycline, Cefixime & Paracetamol with Diazotized (4-AminoBenzophenone) reagent

Banaan Ibrahim Taha Hassan Al-Sayadi[1], Mohammad Mahmoud Hussein Younes Al-Niemi[2], Ebtehag Zeki Sulyman Al-Halim[3]

[1] *Master's student in Chemistry, Department of Chemistry, College of Education for Girls, University of Mosul, Mosul, Iraq.*
Email: bananb957@gmail.com
[2] *Assistant Professor Doctor of Physical Chemistry, Department of Chemistry, College of Education for Pure Sciences, University of Mosul, Mosul, Iraq.*
Email: drmohammadalhusseiny@uomosul.edu.iq
[3] *Professor Doctor of Industrial Chemistry, Department of Chemistry, College of Education for Girls, University of Mosul, Mosul, Iraq.*
Email: ebthalim@uomosul.edu.iq

Received: 11 May 2023 **Accepted:** 10 June 2023

Citation: Al-Sayadi BITH, Al-Niemi MMHY, Al-Halim EZS (2022) Spectrophotometric Determination of Stoichiometric-ratios and Kinetics study for the colored Azo-Drugs resulting from the interactions of three drugs: Tetracycline, Cefixime & Paracetamol with Diazotized (4-AminoBenzophenone) reagent. History of Medicine 9(2): 387–404. https://doi.org/10.17720/2409-5834.v9.2.2023.053

Abstract

The spectroscopic (mole-ratio) method was used to determine the ratios of components (Stoichiometric-ratios) for the colored Azo-Drugs resulting from the interactions of three drugs: Tetracycline, Cefixime & Paracetamol with Diazotized(4-AminoBenzophenone) reagent. at different acidic media (pH=5,7&9). These colored drug complexes were formed from the interactions of electron-donor molecules such as: Tetracycline, Cefixime & Paracetamol with Diazotized(4-AminoBenziphenone) reagent molecule that accepts those electrons. It was found that the resulting three colored Azo-Drugs are of (1:1) type.

In this study, we concluded that the ratios of the components (Stoichiometric-ratios) are (1 Drug: 1 Diazotized reagent) for the all colored Azo-compounds formed do not depend on the pH of the medium, if it is acidic, neutral, and basic. That is, with pH values equal to 5,7&9, respectively, and also does not depend on changing the temperature.

The kinetics of the three colored Azo-compounds formed for a period of time (100 min.) at the three pH functions and at a temperature (20oC), and at optimal conditions and appropriate wavelengths ("max) for each of them, were studied. And it turned out that all of them are of the Pseudo-first-order in relation to the drug. As increasing the concentrations of Diazotized reagent to ten times or more than (the concentrations of the three drugs) does not affect the rate-constants for this reaction that were within the range (0.0351-0.0642 min-1.) nor the half-life-times of each of them, which were within the range (10.8-19.7) min.

Keywords

Stoichiometric ratios, Kinetics study, Azodyes, Paracetamol, Tetracycline, Diazotized 4-aminobenzophenone.

The attention of many researchers has recently turned to the preparation and study of a type of complexes known as (donor-accepter) complexes by using absorption spectra in the visible and ultraviolet regions of the spectrum because of the great importance of these complexes, especially in the medical and biological chemical fields. The ease and accuracy of the spectroscopic method and the availability of its requirements in many laboratories is what encouraged researchers to apply it in determining the proportions of the components of the different colored complexes.

Tetracycline[1-6], sold under various brand names, is an oral antibiotic in the tetracyclines family of medications, used to treat a number of infections, including acne, cholera, brucellosis, plague, malaria, and syphilis. Common side effects include vomiting, diarrhea, rash, and loss of appetite. Wikipedia, Formula: $C_{22}H_{24}N_2O_8$, CAS ID: 60-54-8, Molar mass: 444.435 g/mol, IUPAC ID: (4S,6S,12aS)-4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxonaphthacene-2-carboxamide.

Tetracycline[1-6] is used to treat infections caused by bacteria including pneumonia and other respiratory tract infections; ; certain infections of skin, eye, lymphatic, intestinal, genital and urinary systems; and certain other infections that are spread by ticks, lice, mites, and infected animals.Once inside the cell, tetracyclines bind reversibly to the 30S ribosomal subunit at a position that blocks the binding of the aminoacyl-tRNA to the acceptor site on the mRNA-ribosome complex. Protein synthesis is ultimately inhibited, leading to a bacteriostatic effect.

Tetracyclines[1-6] probably penetrate bacterial cells by passive diffusion and inhibit bacterial growth by interfering with protein synthesis or by destroying the membrane. A growing number of various bacterial species acquire resistance to the bacteriostatic activity of tetracycline. Discovered as natural products from actinomycetes soil bacteria, the tetracyclines were first reported in the scientific literature in 1948. They were noted for their broad spectrum antibacterial activity and were commercialized with clinical success beginning in the late 1940s to the early 1950s.

Cefixime[7-12], sold under the brand name Suprax among others, is an antibiotic medication used to treat a number of bacterial infections. These infections include otitis media, strep throat, pneumonia, urinary tract infections, gonorrhea, and Lyme disease. For gonorrhea typically only one dose is required. Molar mass: 453.452 g/mol. Cefixime is marketed under many trade names worldwide; examples include Pancef, Caricef, Taxim o, Texit,Ofex, Cef-3, Denvar, 3-C, Cefim, Magnett, Oroken, Ofiken, Fix-A, and Zifi. In India it is marketed as Zifi 200 and is commonly counterfeited.

Suprax[7-12] is indicated in the treatment of adults and pediatric patients six months of age or older with pharyngitis and tonsillitis caused by susceptible isolates of Streptococcus pyogenes. (Note: Penicillin is the usual drug of choice in the treatment of Streptococcus pyogenes infections. A broad-spectrum, third-generation cephalosporin antibiotic derived semisynthetically from the marine fungus Cephalosporium acremonium with antibacterial activity.

Paracetamol[13-21], also known as acetaminophen, is a medication used to treat fever and mild to moderate pain. Common brand names include Tylenol and Panadol. Formula: $C_8H_9NO_2$, Density: 1.26 g/cm^3., Molar mass: 151.163 g/mol. , Melting point: 169 °C. , Boiling point: 420 °C , IUPAC ID: N-(4-hydroxyphenyl)acetamide, N-(4-hydroxyphenyl)ethanamide , Soluble in : Water, Acetone.

Why is this medication prescribed? Acetaminophen is used to relieve mild to moderate pain from headaches, muscle aches, menstrual periods, colds and sore throats, toothaches, backaches, and reactions to vaccinations (shots), and to reduce fever. Conclusions Acetaminophen was highly effective for treating pain, functional disability, photophobia, and phonophobia in a population-based sample of persons with migraine, excluding the most disabled persons with migraine. The drug also had an excellent safety profile and was well tolerated[13-21].

In our research, we reacted the aforementioned three drugs with Diazotized(4-AminoBenzi

phenone)reagent to form three colored Azo-Drugs at optimal conditions for each of them, and then determined the proportions of the components of these three resulting complexes, and then followed up their kinetics and found the rate-constant and half-life-times for each of Azo-compound.

Researcher Dr. Mohammad M. H. Y. Al-Niemi conducted several separate studies[22-34]. Part of it included following up the kinetics of formation of

colored (donor-acceptor) complexes resulting from the interaction of some Schiff bases with nitrogenous reagents or interaction of drugs with nitrogenous reagents after determining the proportions of the components of the aforementioned complexes at the optimum conditions for each of them. The results confirmed that the ratios of the complexes are of the type (1 electron donor: 1 electron acceptor).

The other section included thermodynamic studies of the stability constants of the colored (donor-acceptor) complexes resulting from the interaction of some Schiff bases with nitrogenous reagents or the interaction of drugs with nitrogenous reagents after determining the proportions of the components of the aforementioned complexes at the optimum conditions for each of them. The results confirmed that the ratios of the complexes are of the type (1 donor: 1 acceptor of electrons), with a study of the factors affecting them, as well as calculating the thermodynamic variables (ΔH, ΔG^{o}, and ΔS^{o}) at different temperatures and at different acidic media. In all the aforementioned studies, the photometric method proved to be simple, accurate and accurate.

Dr. Mohammad M. H. Y. Al-Niemi also carried out two studies: the first was concerned with determining the structural bodies of the fifteen imines derived from 2,4- dihydroxybenzaldehyde by chemical and physical methods. The second is to determine the optimal conditions for some phenolic Azo-imine dyes resulting from the reaction of the imines mentioned with the reagent of azotized sulfanilic acid.

The spectral measurements are characterized by being very simple, sensitive, fast, and less costly in estimating the elements in the types of models, and more accurate than traditional analytical methods, especially for colored models. And that what was mentioned above is a small part of what the literature contains of this type of studies, and that we limited ourselves to mentioning this very brief number of these studies because of the narrowness of the field with a certain number of research pages, and we limited ourselves to mentioning what is recent of them, and that there are Many sources can be consulted in the literature for those interested in this type of study[22-34].

Experimental part

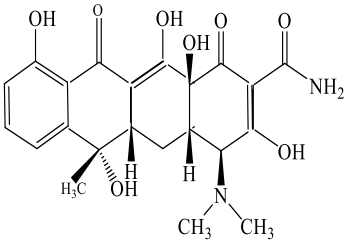
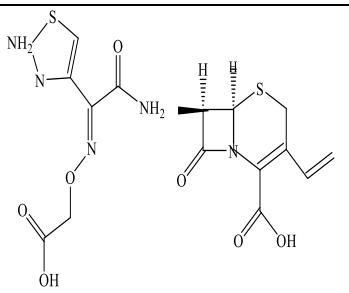
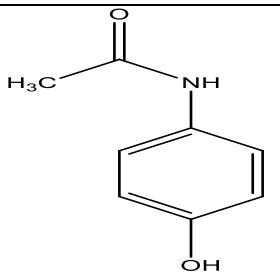
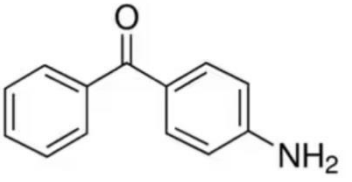
The chemicals used during the research were supplied by the companies: Swiss-Fluka, British-BDH, Spanish-PRS and the Nineveh Pharmaceutical Factory, which are: 4-AminoBenzophenone, sodium carbonate Na_2CO_3, hydrochloric acid HCl, sodium hydroxide NaOH, ethanol. It has been used as is without additional treatments. While the solutions were prepared as follows:

1- (10^{-3}M) of Diazotized(4-Aminobenzophenone)reagent was prepared as in the known standard preparation methods for other diazotized reagents in previous studies[22-34] with a weight of (0.179gm) of 4-AminoBenzophenone and dissolved in (50ml) of distilled water, then (20ml) of a solution (1M) of HCl was added to it and heated. Then the solution transferred to a volumetric flask of (250ml), then cooled to a temperature (0-5°C) in an ice bath. Then (8.65ml) of 1% of $NaNO_2$ is added to the solution, then stirred, and after 5 minutes the solution is supplemented to the mark with cold water in the volumetric flask, then the solution is kept in the refrigerator in a dark flask.

2- Solutions of basic salt (sodium carbonate) and (2N) of hydrochloric acid were prepared by standard methods[22-34], and these solutions are used to control the acidity functions of the colored Azo-Drug complexes at the values required for research[22-34], which are shown in Table (2).

3- (10^{-3}M) was prepared from solutions of the three drugs: (Tetracycline, Cefixime & Paracetamol) by dissolving the appropriate grams calculated from the molarity law of their powders separately in three volumetric bottles with a capacity of (250 ml), and then all of them were supplemented to the mark with distilled water[22-34]. The following table (1) shows the numbers, names, symbols, and some physical properties of the three drugs and the diazotized reagent with their structure.

Table(1): Numbers, names, symbols and some physical properties of the three drugs and the diazotized reagent with their structures.

Comp. No.	Symbol of Drugs or Reagent	Nomenclature	Color	λmax (nm.)	Structure
1	TC	Tetracycline	yellow Crystals	358	
2	CEF	Cefixime	White Powder	294	
3	PARAC	Paracetamol	White Crystal Powder	286	
4	D4AB	Diazotized(4-Amino Benzophenone) Reagent	Yellow	306	

Results and Discussion

The progress in scientific research in various fields of life, including chemistry, has led to interest in studying and preparing many types of Azo-Dyes of great importance from an industrial point of view, depending on the electronic spectra (U.V + Visible) technology). Our research initially focused on finding the most important optimal conditions for the formation of each AzoDye of the three dyes under study from the reaction of tetracycline, cefixime, and paracetamol with the diazotized(4-aminobensphenone) reagent, as well as determining the optimal proportions of its components. The best optimal conditions for dye formation included: optimum initial wavelength, optimum volume of reagent, optimum order of addition and thus optimum final wavelength (λmax) for dye formation at optimal conditions, as reported in our previous studies[22-34]. The following table shows the final optimal conditions for the three Azo-Drugs prepared under study at a temperature of (293 K) and at different acidic functions (pH5,7&9).

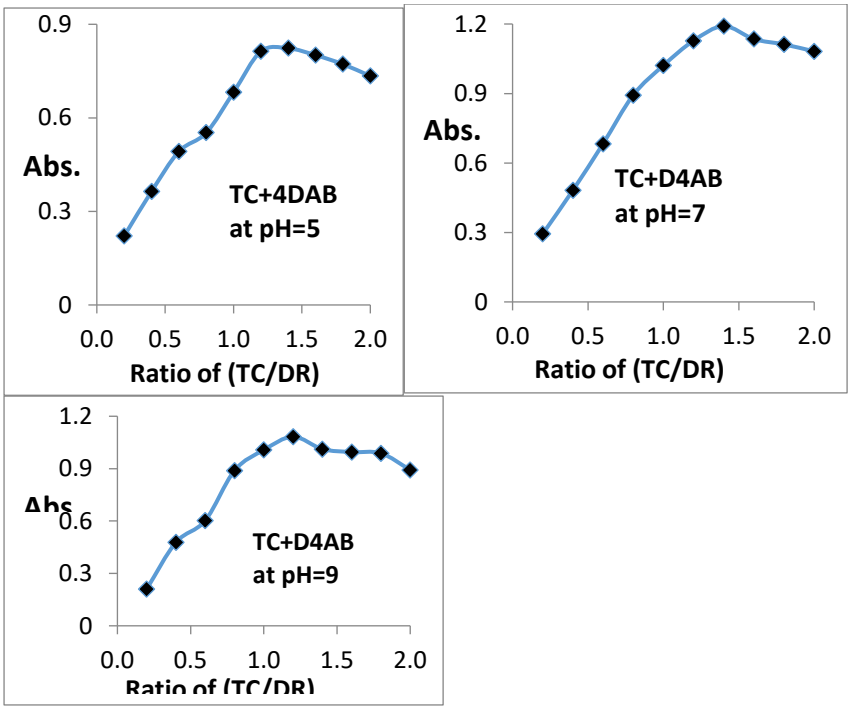
Table(2): The final optimal conditions for the three Azo-Drugs prepared under study at a temperature of (293°K) and at different acidic functions (pH5,7&9).

Comp. No.	Symbol of prepared Azo-Drug	pH	Final Optimal Conditions of prepared Azo-Drug	Final λmax (nm.) of prepared Azo-Drug
1	TC+D4AB	5	0.60ml(0.1M-BS)+ 0. 5ml(10^{-3}M-TC)+ 0.7ml(10^{-3}M-DR)	418
		7	0.75ml(0.1M-BS)+ 0.7ml(10^{-3}M-DR)+ 0.5ml(10^{-3}M-TC)	426
		9	0.5ml(10^{-3}M-TC)+ 0.7ml(10^{-3}M-DR)+ 0.95ml(0.1M-BS)	422
2	CEF +D4AB	5	0.6ml(10^{-3}M-DR)+ 0.45ml(0.1M-BS)+ 0.5ml(10^{-3}M-CEF)	366
		7	0.65ml(0.1M-BS)+ 0.5ml(10^{-3}M-CEF)+ 0.6ml(10^{-3}M-DR)	382
		9	0.5ml(10^{-3}M-CEF)+ 0.6ml(10^{-3}M-DR)+ 0.8ml(0.1M-BS)	362
3	PARAC+D4AB	5	0.5ml(10^{-3}M-PARC)+ 0.5ml(0.1M-BS)+ 0.6ml(10^{-3}M-DR)	426
		7	0.5ml(10^{-3}M-PARC)+ 0.7ml(0.1M-BS)+ 0.6ml(10^{-3}M-DR)	444
		9	0.5ml(10^{-3}M-PARC)+ 0.9ml(0.1M-BS)+ 0.6ml(10^{-3}M-DR)	434

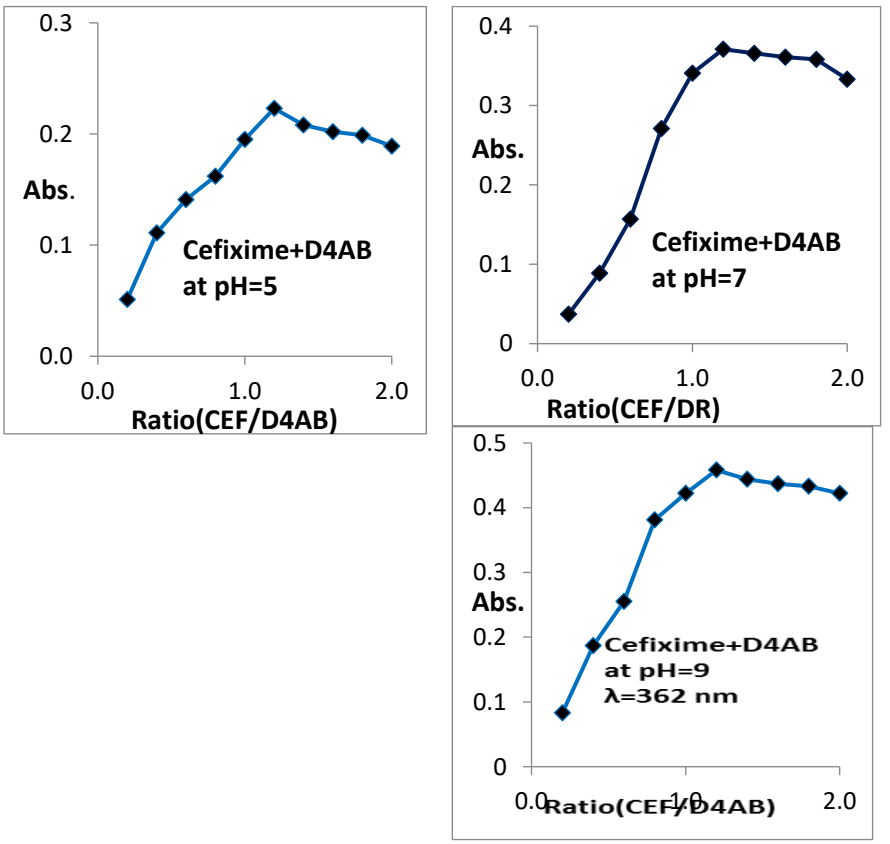
Note: DR stands for Diazotized Reagent, BS stands for Basic Salt of Sodium Carbonate, and D stands for Drug.

1-The ratios of the components (Stoichiometric-Ratios) of the Drug-Azo-Compounds:

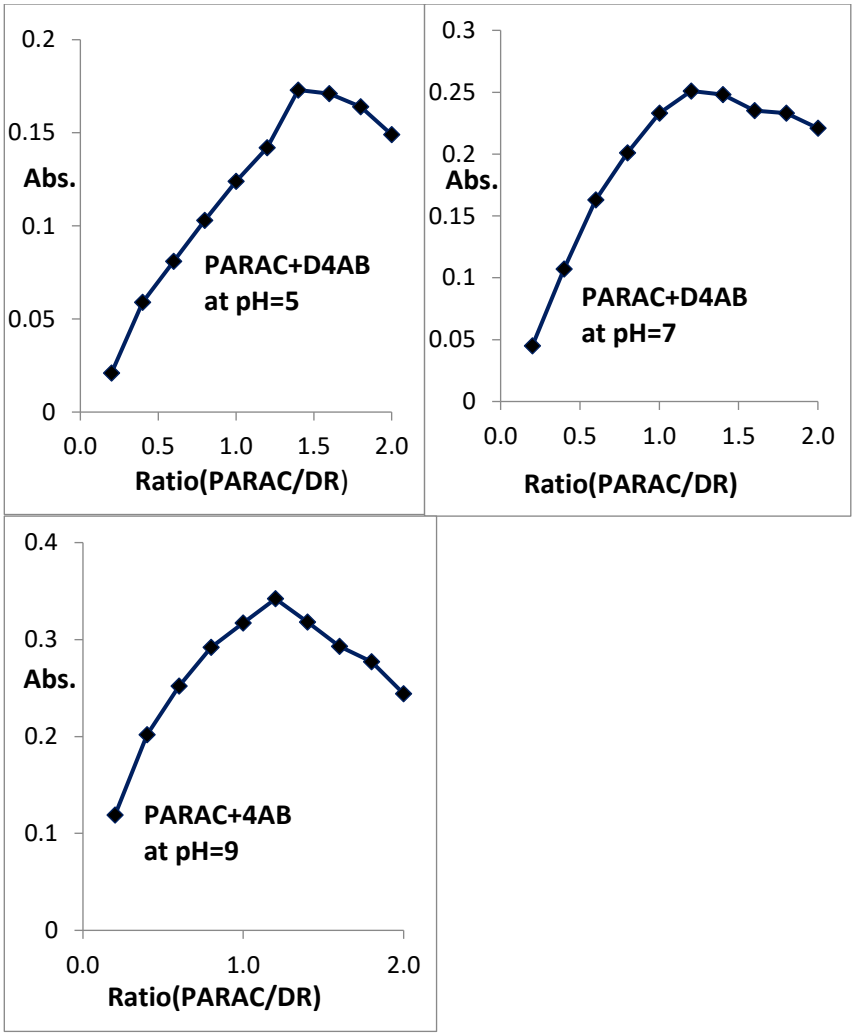
Since our study was specific to the liquid state only, we used the spectrophotometric method in the calculations, which is one of the methods of automated analysis. Various research studies[22-34] have confirmed that the latter method includes three different methods: the Job method, the mole-ratio method, and the propensity ratio method. Research studies have confirmed that the mole-ratio method is the most common and can be applied to different systems. Therefore, the mole-ratio method was used in this research to determine the proportions of the components of the colored azo-drug complexes. This is done by preparing a number of solutions in which the amount of (drug) is fixed, and the amount of (reagent) is variable, and the absorbance of these solutions is measured against the stock solution and at the pH functions (5,7 and 9), and as in the following figures. Then the proportions of the component's Stoichiometric ratios of all the three complexes were found at three pH levels, so it was found that they are all of the type (1 Drug :1 Diazotized reagent).



Figure(1): The mole-ratio of the dark Yellow Azo-Drug (TC+D4AB) at different pH levels and at a temperature of (293K).



Figure(2): The mole-ratio of the dark Yellow Azo-Drug (CEF+D4AB) at different pH levels and at a temperature of (293K).



Figure(3): The mole-ratio of the dark Yellow Azo-Drug (PARAC+D4AB) at different pH levels and at a temperature of (293K).

It is noted from the above figures first that there is a direct relationship between the absorbance's of the dark yellow drug complexes against the mole-ratios of the diazotized reagent and when the temperature is constant, which is (20)°C. This relationship continues until reaching the maximum values, which represent the proportions of the components for the complexes at any pH under study (pH = 5,7 and 9). Secondly, the relationship referred to above turns into an inverse or a negative deviation. It was also shown from the three figures above that the mole-ratios of the dark yellow produced compounds at a temperature of (293K) and at all pH levels were: (1 drug: 1 diazotized reagent). It is also noted from the three figures (1-3) that the mole-ratio (1Drug:1Diazotized Reagent) was not affected by the change in the acidity function of the resulting dye solutions.

2- The kinetic study:

The basis of this study is based on determining the order of the reaction by following up the kinetics of the formation of the above three dyes spectrally at the optimal conditions for each formed Azo-dye. Absorption of the resulting colored dye for (100) minutes. And then calculate the rate constant (k_1), and the half-life-time($t_{1/2}$) for each reaction at a temperature (293K) and three acidic media: neutral, basic, and acidic.

The solutions shown in Table(2) above were prepared first at a temperature (293 K), but with an increase in the concentration of the reagent ten times the concentration of the drug. It was proved that increasing the concentration of the reagent to ten times its original concentration did not affect the reaction rate. And we followed up the absorption of the

formation of each dye kinetically at the optimal conditions for each Azo-dye formed, and at its best wavelength, with an increase in the concentration of the reagent tenfold, until the end of the reaction or reaching the maximum absorption value (A∞), and set the value of the reaction end time (t∞), as in Tables (3-5). After that, the kinetic equation for the pseudo-first-order reaction was applied after the failure of applying the second-order equation in both the equal and different concentrations. In this study, we used the integration method to follow up the kinetics of the formation reactions of the resulting dyes. When applying the following pseudo-first-order equation to all the obtained kinetic results:

$$\mathbf{Ln\{A\infty/(A\infty-At)\}= k_1.t} \text{ ----------(1)}$$

And by plotting the graph between Ln{A∞/(A∞-At) against time (in minutes), we obtained good straight lines with high correlation coefficient (R^2) values that ranged in the range (0.9069-0.9641) for all the dyes under study, and with a slope equal to the R^2 constants. The speed (k_1) of their interactions. The latter indicates that the resulting of forming reaction for Azo-dye is pseudo-first-order with respect to the drug, as in Figures(4-6). Thus, the rate constant was calculated for each formed compound, which enabled us to calculate the values of the half-life-time($t_{1/2}$) for each reaction, which represents the time required to consume half of the reactants, which was calculated from the following second equation:

$$\mathbf{t_{1/2}=Ln2/k_1} \text{----------(2)}$$

These results were consistent with previous studies[22-34] on the reaction kinetics of the formation of Azo-compounds. The following tables (3-6) represent a Monitoring kinetics for the absorbance of the three produced Azo-dyes under study against time at a temperature of (293°K), at (pH5, pH7 and pH9), and at the optimum wavelength for each of pH.

Table(3): Monitoring kinetics for absorbance of produced (TC+D4AB) against time at a temperature of (293°K), at (pH5, pH7 and pH9), and at the optimum wavelength for each of pH.

Time (min.)	pH=5 , λmax=418nm.			LN(A∞/(A∞-At))	$t_{1/2}$(min.)
	Abs.	A∞-At	A∞/(A∞-At)		
0	0.000	0.710	1.000	0.000	10.8
2	0.342	0.368	1.929	0.657	
5	0.355	0.355	2.000	0.693	
7	0.401	0.309	2.298	0.832	
10	0.444	0.266	2.669	0.982	
13	0.495	0.215	3.302	1.195	
15	0.521	0.189	3.757	1.324	
17	0.537	0.173	4.104	1.412	
20	0.542	0.168	4.226	1.441	
23	0.563	0.147	4.830	1.575	
25	0.584	0.126	5.635	1.729	
27	0.595	0.115	6.174	1.820	
30	0.619	0.091	7.802	2.054	
35	0.637	0.073	9.726	2.275	
40	0.651	0.059	12.034	2.488	
45	0.662	0.048	14.792	2.694	
50	0.670	0.040	17.750	2.876	
55	0.674	0.036	19.722	2.982	
60	0.699	0.011	64.545	4.167	
65	0.710	0.000	∞	∞	
70	0.365	0.345	2.058	0.722	
75	0.355	0.355	2.000	0.693	
80	0.332	0.378	1.878	0.630	
85	0.312	0.398	1.784	0.579	
90	0.301	0.409	1.736	0.552	
95	0.294	0.416	1.707	0.535	

100	0.277	0.433	1.640	0.495	
Time (min.)	pH=7 , λmax=426nm.			LN(A∞/(A∞-At))	$t_{1/2}$(min.)
	Abs.	A∞-At	A∞/(A∞-At)		
0	0.000	0.882	1.000	0.000	19.7
2	0.120	0.762	1.157	0.146	
5	0.235	0.647	1.363	0.310	
7	0.333	0.549	1.607	0.474	
10	0.422	0.460	1.917	0.651	
13	0.440	0.442	1.995	0.691	
15	0.482	0.400	2.205	0.791	
17	0.523	0.359	2.457	0.899	
20	0.540	0.342	2.579	0.947	
23	0.556	0.326	2.706	0.995	
25	0.569	0.313	2.818	1.036	
27	0.597	0.285	3.095	1.130	
30	0.619	0.263	3.354	1.210	
35	0.637	0.245	3.600	1.281	
40	0.651	0.231	3.818	1.340	
45	0.673	0.209	4.220	1.440	
50	0.690	0.192	4.594	1.525	
55	0.732	0.150	5.880	1.772	
60	0.751	0.131	6.733	1.907	
65	0.782	0.100	8.820	2.177	
70	0.812	0.070	12.600	2.534	
75	0.882	0.000	∞	∞	
80	0.422	0.460	1.917	0.651	
85	0.380	0.502	1.757	0.564	
90	0.397	0.485	1.819	0.598	
95	0.467	0.415	2.125	0.754	
100	0.477	0.405	2.178	0.778	
Time (min.)	pH=9 , λmax=422nm.			LN(A∞/(A∞-At))	$t_{1/2}$(min.)
	Abs.	A∞-At	A∞/(A∞-At)		
0	0.000	1.082	1.000	0.000	12.3
2	0.555	0.527	2.053	0.719	
5	0.573	0.509	2.126	0.754	
7	0.592	0.490	2.208	0.792	
10	0.664	0.418	2.589	0.951	
13	0.681	0.401	2.698	0.993	
15	0.698	0.384	2.818	1.036	
17	0.777	0.305	3.548	1.266	
20	0.794	0.288	3.757	1.324	
23	0.822	0.260	4.162	1.426	
25	0.844	0.238	4.546	1.514	
27	0.881	0.201	5.383	1.683	
30	0.923	0.159	6.805	1.918	
35	0.947	0.135	8.015	2.081	
40	0.961	0.121	8.942	2.191	
45	0.982	0.100	10.820	2.381	
50	0.999	0.083	13.036	2.568	
55	1.021	0.061	17.738	2.876	
60	1.032	0.050	21.640	3.075	

65	1.044	0.038	28.474	3.349	
70	1.054	0.028	38.643	3.654	
75	1.066	0.016	67.625	4.214	
80	1.076	0.006	180.333	5.195	
85	1.082	0.000	∞	∞	
90	0.989	0.093	11.634	2.454	
95	0.978	0.104	10.404	2.342	
100	0.955	0.127	8.520	2.142	

Table(4): Monitoring kinetics for absorbance of produced (CEF+D4AB) against time at a temperature of (293°K), at (pH5, pH7 and pH9), and at the optimum wavelength for each of pH.

Time (min.)	pH=5, λmax=366nm.			LN(A∞/(A∞-At))	$t_{1/2}$ (min.)
	Abs.	A∞-At	A∞/(A∞-At)		
0	0.000	0.330	1.000	0.000	13.9
2	0.030	0.300	1.100	0.095	
5	0.050	0.280	1.179	0.164	
7	0.070	0.260	1.269	0.238	
10	0.090	0.240	1.375	0.318	
13	0.110	0.220	1.500	0.405	
15	0.140	0.190	1.737	0.552	
17	0.160	0.170	1.941	0.663	
20	0.180	0.150	2.200	0.788	
23	0.210	0.120	2.750	1.012	
25	0.230	0.100	3.300	1.194	
27	0.250	0.080	4.125	1.417	
30	0.270	0.060	5.500	1.705	
35	0.290	0.040	8.250	2.110	
40	0.330	0.000	∞	∞	
45	0.270	0.060	5.500	1.705	
50	0.240	0.090	3.667	1.299	
55	0.210	0.120	2.750	1.012	
60	0.170	0.160	2.063	0.724	
65	0.160	0.170	1.941	0.663	
70	0.150	0.180	1.833	0.606	
75	0.130	0.200	1.650	0.501	
80	0.110	0.220	1.500	0.405	
85	0.000	0.330	1.000	0.000	
90	0.050	0.280	1.179	0.164	
95	0.040	0.290	1.138	0.129	
100	0.030	0.300	1.100	0.095	
Time (min.)	pH=7, λmax=382nm.			LN(A∞/(A∞-At))	$t_{1/2}$ (min.)
	Abs.	A∞-At	A∞/(A∞-At)		
0	0.000	0.510	1.000	0.000	14.1
2	0.110	0.400	1.275	0.243	
5	0.140	0.370	1.378	0.321	
7	0.160	0.350	1.457	0.376	
10	0.180	0.330	1.545	0.435	
13	0.210	0.300	1.700	0.531	
15	0.250	0.260	1.962	0.674	
17	0.270	0.240	2.125	0.754	
20	0.280	0.230	2.217	0.796	

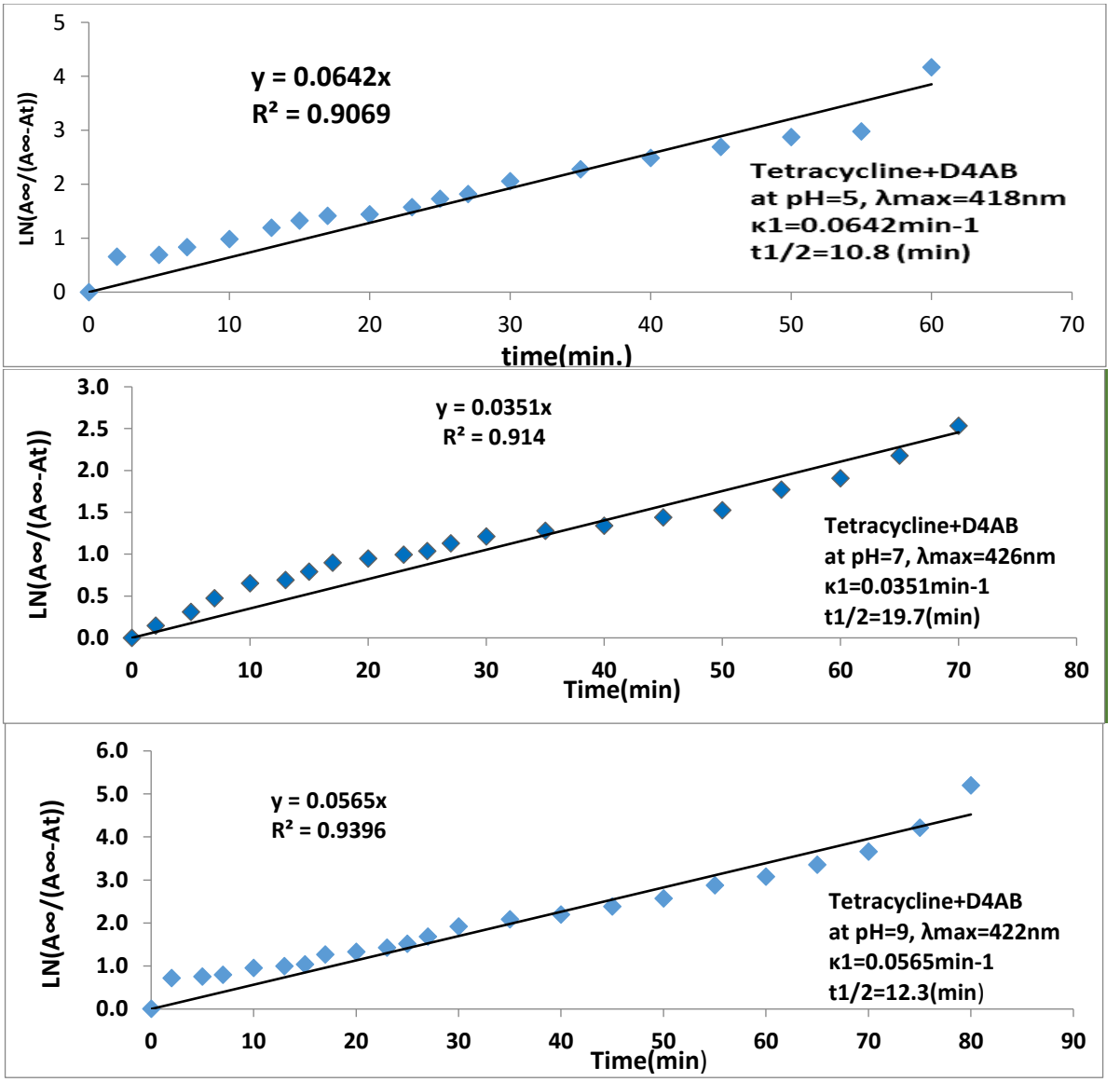
23	0.320	0.190	2.684	0.987	
25	0.350	0.160	3.188	1.159	
27	0.370	0.140	3.643	1.293	
30	0.390	0.120	4.250	1.447	
35	0.420	0.090	5.667	1.735	
40	0.460	0.050	10.200	2.322	
45	0.510	0.000	∞	∞	
50	0.470	0.040	12.750	2.546	
55	0.440	0.070	7.286	1.986	
60	0.410	0.100	5.100	1.629	
65	0.380	0.130	3.923	1.367	
70	0.360	0.150	3.400	1.224	
75	0.310	0.200	2.550	0.936	
80	0.280	0.230	2.217	0.796	
85	0.260	0.250	2.040	0.713	
90	0.240	0.270	1.889	0.636	
95	0.210	0.300	1.700	0.531	
100	0.180	0.330	1.545	0.435	
Time (min.)	pH=9, λmax=362nm.			LN(A∞/(A∞-At))	$t_{1/2}$ (min.)
	Abs.	A∞-At	A∞/(A∞-At)		
0	0.000	0.670	1.000	0.000	12.8
2	0.220	0.450	1.489	0.398	
5	0.250	0.420	1.595	0.467	
7	0.270	0.400	1.675	0.516	
10	0.310	0.360	1.861	0.621	
13	0.350	0.320	2.094	0.739	
15	0.360	0.310	2.161	0.771	
17	0.390	0.280	2.393	0.872	
20	0.410	0.260	2.577	0.947	
23	0.430	0.240	2.792	1.027	
25	0.460	0.210	3.190	1.160	
27	0.480	0.190	3.526	1.260	
30	0.520	0.150	4.467	1.497	
35	0.560	0.110	6.091	1.807	
40	0.580	0.090	7.444	2.007	
45	0.640	0.030	22.333	3.106	
50	0.670	0.000	∞	∞	
55	0.580	0.090	7.444	2.007	
60	0.540	0.130	5.154	1.640	
65	0.510	0.160	4.188	1.432	
70	0.480	0.190	3.526	1.260	
75	0.460	0.210	3.190	1.160	
80	0.410	0.260	2.577	0.947	
85	0.380	0.290	2.310	0.837	
90	0.350	0.320	2.094	0.739	
95	0.310	0.360	1.861	0.621	
100	0.270	0.400	1.675	0.516	

Table(5): Monitoring kinetics for absorbance of produced (PARAC+D4AB) against time at a temperature of (293°K), at (pH5, pH7 and pH9), and at the optimum wavelength for each of pH.

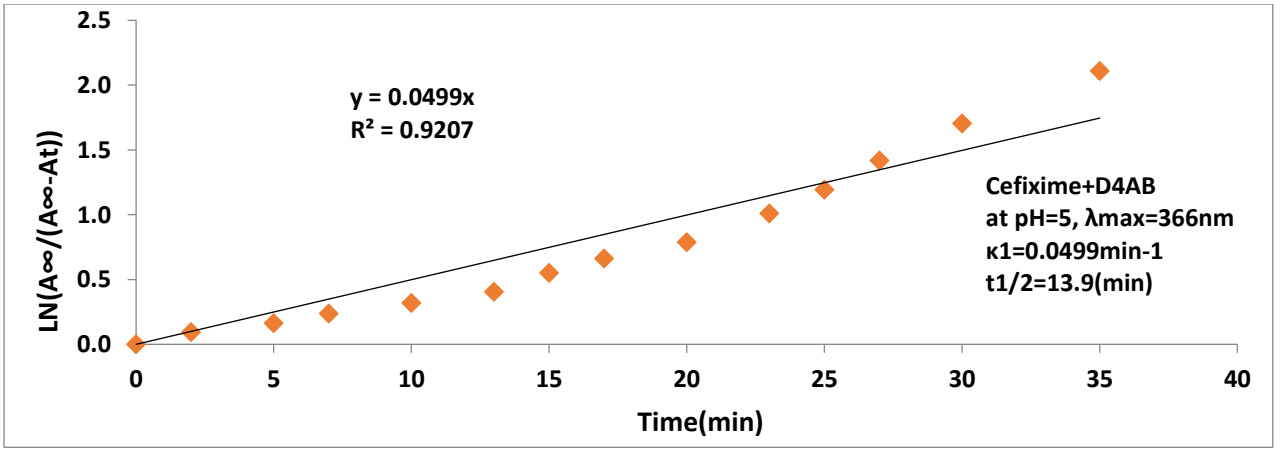
Time (min.)	pH = 5, λmax=426nm.			LN(A∞/(A∞-At))	$t_{1/2}$ (min.)
	Abs.	A∞-At	A∞/(A∞-At)		
0	0.000	0.242	1.000	0.000	12.2
2	0.070	0.172	1.407	0.341	
5	0.087	0.155	1.561	0.446	
7	0.096	0.146	1.658	0.505	
10	0.111	0.131	1.847	0.614	
13	0.120	0.122	1.984	0.685	
15	0.132	0.110	2.200	0.788	
17	0.144	0.098	2.469	0.904	
20	0.156	0.086	2.814	1.035	
23	0.164	0.078	3.103	1.132	
25	0.177	0.065	3.723	1.315	
27	0.185	0.057	4.246	1.446	
30	0.193	0.049	4.939	1.597	
35	0.203	0.039	6.205	1.825	
40	0.213	0.029	8.345	2.122	
45	0.224	0.018	13.444	2.599	
50	0.233	0.009	26.889	3.292	
55	0.242	0.000	∞	∞	
60	0.212	0.030	8.067	2.088	
65	0.204	0.038	6.368	1.851	
70	0.188	0.054	4.481	1.500	
75	0.164	0.078	3.103	1.132	
80	0.145	0.097	2.495	0.914	
85	0.132	0.110	2.200	0.788	
90	0.112	0.130	1.862	0.621	
95	0.096	0.146	1.658	0.505	
100	0.088	0.154	1.571	0.452	
Time (min.)	pH=7, λmax=444nm.			LN(A∞/(A∞-At))	$t_{1/2}$ (min.)
	Abs.	A∞-At	A∞/(A∞-At)		
0	0.000	0.499	1.000	0.000	12.22
2	0.100	0.399	1.251	0.224	
5	0.202	0.297	1.680	0.519	
7	0.243	0.256	1.949	0.667	
10	0.173	0.326	1.531	0.426	
13	0.303	0.196	2.546	0.934	
15	0.319	0.180	2.772	1.020	
17	0.332	0.167	2.988	1.095	
20	0.325	0.174	2.868	1.054	
23	0.367	0.132	3.780	1.330	
25	0.383	0.116	4.302	1.459	
27	0.404	0.095	5.253	1.659	
30	0.419	0.080	6.238	1.831	
35	0.433	0.066	7.561	2.023	
40	0.452	0.047	10.617	2.362	
45	0.464	0.035	14.257	2.657	
50	0.469	0.030	16.633	2.811	
55	0.464	0.035	14.257	2.657	
60	0.499	0.000	∞	∞	
65	0.465	0.034	14.676	2.686	

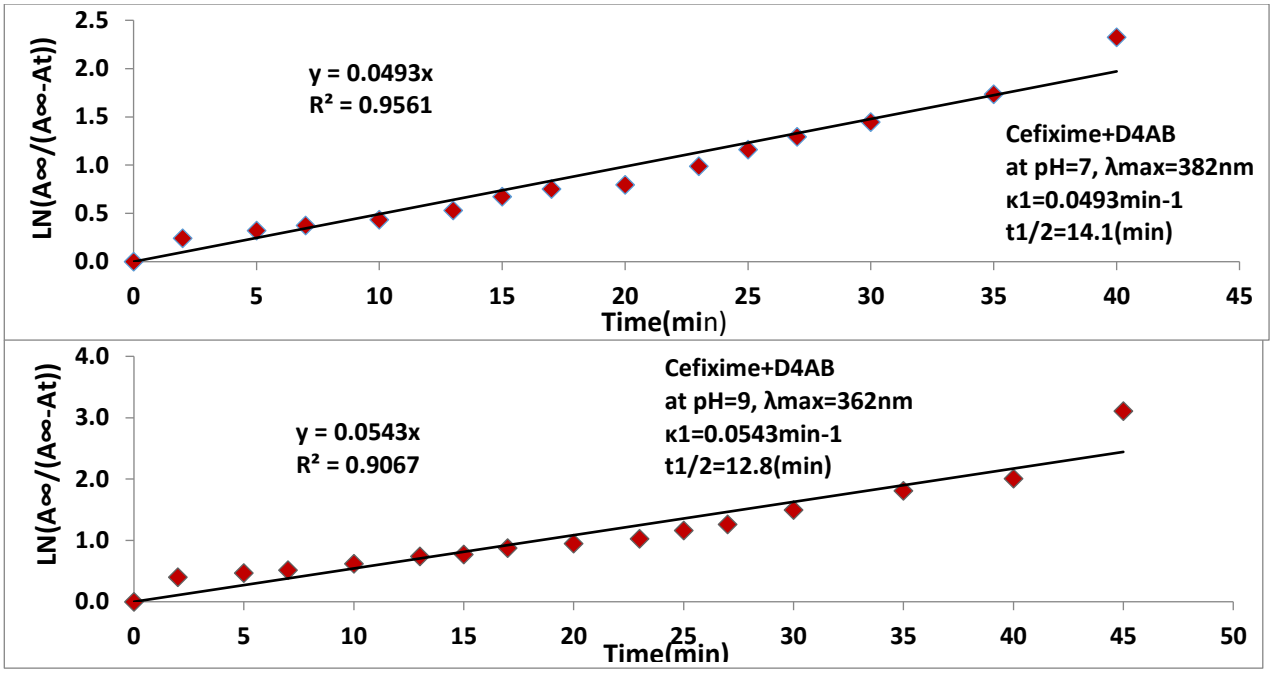
70	0.446	0.053	9.415	2.242	
75	0.334	0.165	3.024	1.107	
80	0.323	0.176	2.835	1.042	
85	0.321	0.178	2.803	1.031	
90	0.311	0.188	2.654	0.976	
95	0.289	0.210	2.376	0.865	
100	0.265	0.234	2.132	0.757	
Time (min.)	pH=9, λmax=434nm.			LN(A∞/(A∞-At))	$t_{1/2}$ (min.)
	Abs.	A∞-At	A∞/(A∞-At)		
0	0.000	0.688	1.000	0.000	14.7
2	0.170	0.518	1.328	0.284	
5	0.202	0.486	1.416	0.348	
7	0.243	0.445	1.546	0.436	
10	0.267	0.421	1.634	0.491	
13	0.405	0.283	2.431	0.888	
15	0.422	0.266	2.586	0.950	
17	0.435	0.253	2.719	1.000	
20	0.442	0.246	2.797	1.028	
23	0.465	0.223	3.085	1.127	
25	0.487	0.201	3.423	1.230	
27	0.498	0.190	3.621	1.287	
30	0.512	0.176	3.909	1.363	
35	0.534	0.154	4.468	1.497	
40	0.554	0.134	5.134	1.636	
45	0.576	0.112	6.143	1.815	
50	0.597	0.091	7.560	2.023	
55	0.622	0.066	10.424	2.344	
60	0.634	0.054	12.741	2.545	
65	0.652	0.036	19.111	2.950	
70	0.678	0.010	68.800	4.231	
75	0.688	0.000	∞	∞	
80	0.444	0.244	2.820	1.037	
85	0.433	0.255	2.698	0.993	
90	0.412	0.276	2.493	0.913	
95	0.398	0.290	2.372	0.864	
100	0.365	0.323	2.130	0.756	

And when we plotted between Ln(A∞/(A∞-At)) against time (in minutes), we got good straight lines with high correlation coefficient (R^2) values for all the dyes under study, as in Figures (4-6), which represent absorption kinetics of the three prepared Azo-dyes against time for a period of (100min.) at a temperature (293K), and at an optimal wavelength (λmax) for each dye and at each pH.

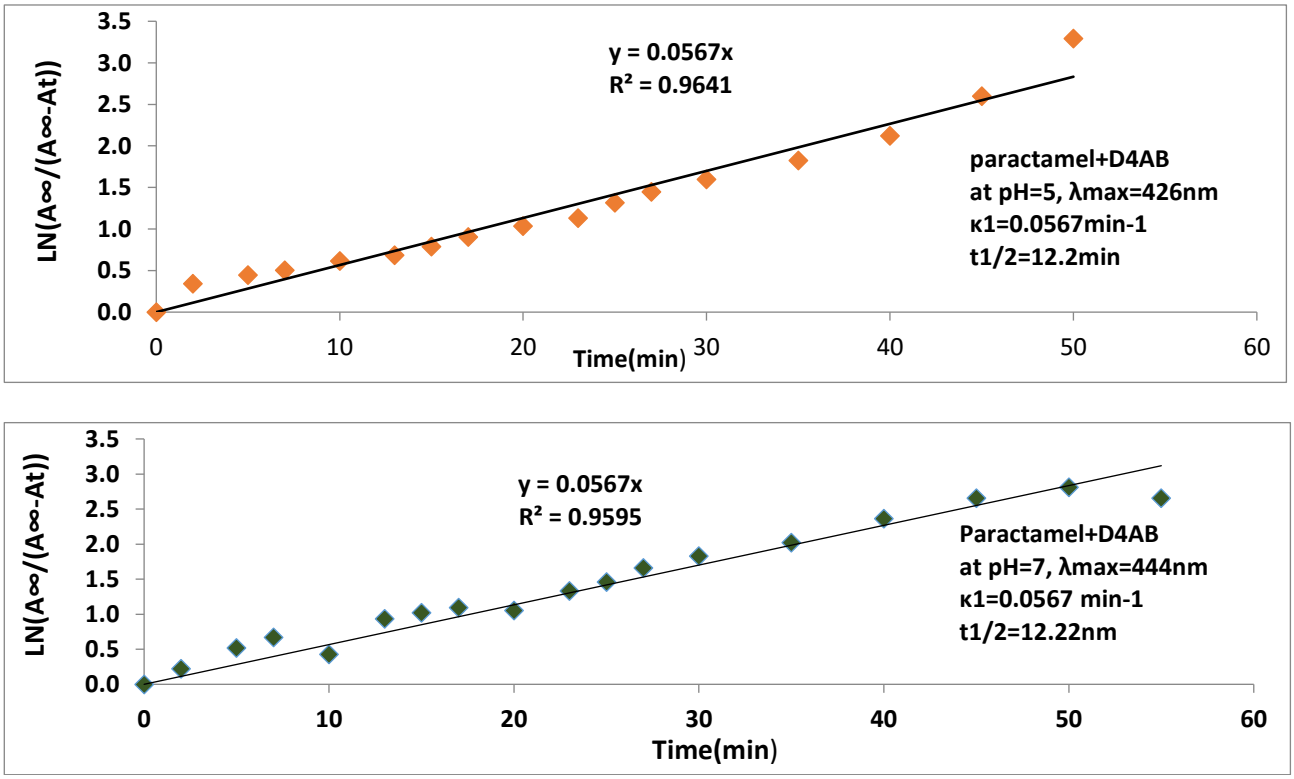


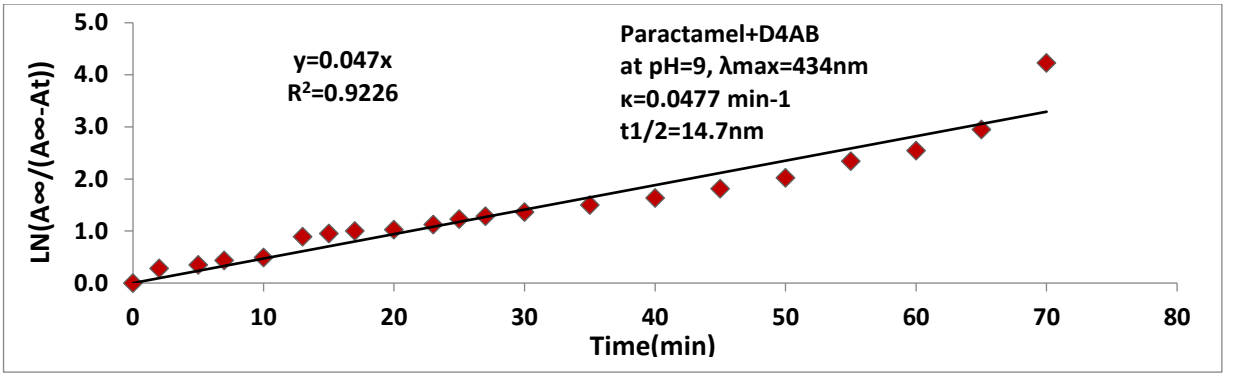
Figure(4): Absorption kinetics of the prepared (TC+D4AB) against time for a period of (100min.) at a temperature of (293°K), at (pH5, pH7 and pH9), and at the optimum wavelength for each of pH.





Figure(5): Absorption kinetics of the prepared (CEF+D4AB) against time for a period of (100min.) at a temperature of (293°K), at (pH5, pH7 and pH9), and at the optimum wavelength for each of pH.





Figure(6): Absorption kinetics of the prepared (PARAC+D4AB) against time for a period of (100min.) at a temperature of (293°K), at (pH5, pH7 and pH9), and at the optimum wavelength for each of pH.

Figures (4-6) show that there is a direct relationship between the absorption of the formation of the three Azo-dyes with time. It was also observed that there was a continuous increase in absorption after (75) minutes after the formation of the first dye (TC+D4AB), after (45) minutes after the formation of the second dye (CEF+D4AB), and after (60) minutes after the formation of the third dye (PARAC+D4AB), and then a sudden drop in absorption due to the completion of the formation of the resulting dye and the end of the reaction. The latter does not affect the values of (λmax) of the compound formed after these times (t∞), due to the end of the reaction, and this is confirmed by the values of the half-life-time($t_{1/2}$), which were: (19.7) minutes from the formation of the first dye (TC+D4AB), and after (14.1) minutes from the formation of the second dye (CEF+D4AB), and after (12.2) minutes from the formation of the third dye (PARAC+D4AB). And as in Table (6).

From the three tables (3-5), the highest absorption (A∞) was obtained for the formation of each dye of all dyes, the expiration times for their formation (t∞), the rate constants for their formation (k_1), as well as the half-life-time for each of them ($t_{1/2}$). It is also noted from figures (4-6) above, that an increase in the reaction rate constant for dyes inevitably leads to a decrease in the half-life-times, as shown in the following table(6), which represents the values of infinite absorption (A∞), and the expiration time Formation (t∞), half-life-time ($t_{1/2}$), and reaction rate constant (k_1) for the formation of each of the three prepared Azo-dyes at a temperature of (293°K), at (pH5, pH7 and pH9), and at the optimum wavelength for each of pH.

Table(6): The values of infinite absorption (A∞), the formation completion time (t∞), the half-life ($t_{1/2}$), and the reaction rate constant (k_1) for the formation of each of the three prepared Azo-dyes at a temperature of (293°K), at (pH5, pH7 and pH9), and at the optimum wavelength for each of pH.

No. of Azo-Compound	Symbol of Azo-Compound	pH	λ_{max} (nm.)	t_∞ (min.)	A_∞	k_1 (min.$^{-1}$)	($t_{1/2}$) (min.)
1	(TC+D4AB)	5	418	65	0.710	0.0642	10.08
		7	426	75	0.882	0.0351	19.7
		9	422	85	1.082	0.0565	12.3
2	(CEF+D4AB)	5	366	40	0.330	0.0429	13.1
		7	382	45	0.510	0.0493	14.1
		9	362	50	0.670	0.0543	12.8
3	(PARAC+D4AB)	5	426	55	0.242	0.0567	12.2
		7	444	60	0.499	0.0567	12.22
		9	434	75	0.688	0.0477	14.7

From table(6), the following appears:

1- The rate constant of the reaction of the formation of the resulting Azo-dye under study at a temperature and three acidic functions is of the pseudo-first-order relative to the drug, and the highest value of the Azo-dye was equal to (0.0642min.$^{-1}$), meaning

that it is the fastest reaction. The lowest value of the Azo-dye was equal to (0.0350min.$^{-1}$), that is, it is the slowest reaction. This was consistent with previous kinetic studies of different interactions in the literature[22-34].

2- The rate constant values (k_1) for the formation of Azo-dyes differ according to the structure of the drug.
3- The values of the reaction rate constants (k_1) for dye formation are inversely proportional to the half-life-times($t_{1/2}$) of each Azo-dye.
4- The wavelength of the compound (λmax) changes with the difference in the structure of the drug that forms the dye.

Conclusions

We can conclude from this study the following:

1- When determining the optimal conditions for each formed Azo-dye, it was found that the optimal ratios for its components were (1:10) for (1Drug:10Reagent), respectively. That is, the concentration of the reagent is ten times the concentration of the drug concentration, and this indicates that increasing the concentration of the reagent does not affect the rate of the formation reaction for Azo-dye. That is why it is called the pseudo-first-order.
2- The values of the rate constants (k_1) for the formation of all the three dyes under study depend on the structure of the drug constituting each dye, at the temperature and the three pH parameters.
3- The best wavelength of the compound (λmax) changes with the difference in the structure of the drug that forms the dye.
4- The values of the half-life-time($t_{1/2}$) for the formation reaction for each of Azo-dye were completely opposite to the rate constant values (k_1) of the reaction for the produced same dye under the same conditions. This indicates that the faster reaction is completed in less time.
5- The acidic media used during this study for the formation of the colored produced drug-compounds were acidic (pH5), neutral (pH7), and basic (pH9), and no effect of these different media on the proportions of the components of the colored produced drug-compounds under study was recorded.

References

1- Bhattacharya SK., (2007). "An evaluation of current cholera treatment", National Institute of Cholera and Enteric Diseases (2003). Expert Opin Pharmacother, 4(2), pp.141–6Viera, MH, Perez, OA, Berman, B (2007). "Incyclinide". Drugs of the Future. 32(3), pp.209–214.

2-Ryan M. E., Usman A., Ramamurthy N. S., Golub L. M. and Greenwald R. A. (2001). "Excessive matrix metalloproteinase activity in diabetes: Inhibition by tetracycline analogues with zinc reactivity", Current medicinal chemistry, 8(3), pp.305–316.

3-Richards C., Pantanowitz L. and Dezube B. J. (2011). "Antimicrobial and non-antimicrobial tetracyclines in human cancer trials". Pharmacological Research, 63(2), pp.151–156.

4-Piscitelli Stephen C. and Keith Rodvold , (2005). "Drug Interactions in Infectious Diseases". Humana Press.

5-Olson MW., Ruzin A., Feyfant E., Rush TS., O'Connell J. and Bradford PA., (2007). "Functional, biophysical, and structural bases for antibacterial activity of tigecycline", Antimicrobial agents and chemotherapy, 50(6), pp.2156–2166.

6-SAMUEL D., (2017). "Archaeology of ancient Egypt beer", Journal of the American Society of Brewing Chemists, 54(1), pp.3-12.

7-Chow A.W., Benninger M.S. and Brook I., (2012). "Clinical practice guideline for acute bacterial rhinosinusitis in children and adults", Clin. Infect. Dis., 54, pp.72-112.

8-Wald E.R., Applegate K.E. and Bordley C., (2013). "Clinical Practice Guideline for the Diagnosis and Management of Acute Bacterial Sinusitis in Children Aged 1 to 18 Years. Pediatrics".

9-Allen V.G., Mitterni L. and Seah C., (2013). "Neisseria gonorrhoeae treatment failure and susceptibility to cefixime in Toronto", Canada. JAMA., 309, pp.163-70.

10-Kirkcaldy R.D., Bolan G.A. And Wasserheit J.N., (2013). "Cephalosporin-resistant gonorrhea in North America", JAMA., 309, pp.185-7.

11-Kirkcaldy R.D., Zaidi A. and Hook E.W., (2013). "Neisseria gonorrhoeae antimicrobial resistance among men who have sex with men and men who have sex exclusively with women: the Gonococcal Isolate Surveillance Project", Ann Intern. Med., 158, pp.321-8.

12-Mc. Evoy G.K., (2003). "Drug Information", Cephalosporins General Statement., American Society of Health-System Pharmacists, pp.125-39.

13-Daly F.F., Fountain J.S., L., Murray A. Graudins and Buckley N.A., (2008). "Guidelines for the management of paracetamol poisoning in Australia and New Zealand-explanation and elaboration. A consensus statement from clinical toxicologists consulting to the Australasian poisons information centres", Med. J. Aust., 188(5), pp. 296–301.

14-Khashab M., Tector A.J. and Kwo P.Y., (2007). "Epidemiology of acute liver failure", Curr. Gastroenterol Rep., 9(1), pp. 66–73.

15-Hawkins L.C., Edwards J.N. and Dargan P.I., (2007). "Impact of restricting paracetamol pack sizes on

paracetamol poisoning in the United Kingdom: a review of the literature", Drug Saf., 30(6), pp. 465-479.

16-Larson A. M., Polson J. and Fontana R. J., (2005). "Acetaminophen-induced acute liver failure: results of a United States multicenter, prospective study", Hepatology, 42(6), pp.1364–1372.

17-(2022). "Why paracetamol (acetaminophen) is a suitable first choice for treating mild to moderate acute pain in adults with liver", kidney or cardiovascular disease, gastrointestinal disorders, asthma, or who are older", Current Medical Research and Opinion, 38, (5), pp.811–825.

18-"Paracetamol - the best selling antipyretic analgesic in the world". An introduction to pharmaceutical sciences", production chemistry, techniques and technology. Oxford: Biohealthcare, ISBN., 978(1), p.270.(2021).

19-Thérapeutiques. En ligne, (2006). Patrice Queneau, La Saga du paracétamol. Médecine, 2(4), pp.158-159.

20-Kis B., Snipes J.A. and Busija D.W., (2005). "Acetaminophen and the cyclooxygenase -3 puzzle: sorting out facts, fictions, and uncertainties". J. Pharmacol. Exp. Ther., 315(1), pp.1–7.

21-Johnston J., Savarie P., Primus T., Eisemann J., Hurley J. and Kohler D., (2002). "Risk assessment of an acetaminophen baiting program for chemical control of brown tree snakes on Guam: evaluation of baits, snake residues, and potential primary and secondary hazards". Environ Sci. Technol., 36(17), pp.3827–3833.

22-A. Azzouz and A. O. Agha, "The Influence of Temperature, pH and the Type of Oxime Isomer on the Stability Constant Values of Some Azo Dyes Formations Between Oximes and the Diazotized Sulfanilic Acid Salt," Iraqi National Journal Of Chemistry, no. 30, 2008.

23-A. Azzouz and M. Al-Niemi, "Influence of structures on the stability constants values for some dyes formation formed by reactions of imines and the diazotized sulphanilic sodium salt," Iraqi National Journal of Chemistry, vol. 42, p. 177, 2011.

24-R. S. Al-Saffar, S. A. Zakaria, and N. S. Othman, "Spectrophotometric Determination of p-aminobenzoic acid via Diazotization and Coupling reaction," Research Journal of Pharmacy and Technology, vol. 14, no. 10, pp. 5313-5318, 2021.

25-G. Wyasu and B. Myek, "Synthesis of an azo dye and its cobalt complex derived from 3-aminophenol," Communication in Physical Sciences, vol. 6, no. 1, 2020.

26-A. H. Al-Marsumi and M. M. Al-Niemi, "Determination of thermodynamic parameters and studying the stability of some aromatic complexes derived from 4-dimethyl aminobenzaldehyde with dinitro aniline reagent," EDITORIAL BOARD-2021, vol. 16, no. 2-3, p. 19, 2021.

27-A. H. Ali Mohsin, H. Al-Niemi, and M. Mahmoud, "Thermodynamic study for the stability of aromatic complexes formation derived from the reaction of 4-dimethyl amino benzaldehyde with diazotized dinitro aniline reagents," Egyptian Journal of Chemistry, vol. 65, no. 2, pp. 421-437, 2022. 10.21608/EJCHEM.2021.87003.4241

28-A. Azzouz and A. Obed Agha, "The influence of surfactants and solvents on the stability constant value of some azo dyes formation between oximes and the diazotized Sulphanilic acid salt," Journal of Education and Science, vol. 17, no. 2, pp. 10-16, 2005.

29-M. M. H. AL-Niemi, "Study of the effect of temperature on the kinetics of the reactions of dyes produced from the reactance of 2,4-dihydroxy benzaldehyde, syn and anti-4,2-dihydroxybenzaldehyde with electron-donating (diazotized sulfanilic acid sodium salt) reagent", J.Edu. and Sci.,25(2), pp.27-43.,2012.

30-M. M. H. AL-Niemi, "Study the effect of acidity function on the kinetic of the two complexes formation produced from the reaction of salicylic acid with two diazotized reagents", Natural Volatiles and Essential Oils, NVEO., 8(5), pp. 8850-8860.,2021.

31-M. M. H. Al-Niemi, "Calculation of kinetic parameters to activate the formation of azoimine dyes derived from the reaction of substituents of ortho-2,4-dihydroxybenzylidene aniline with the diazotized sulfanilic acid sodium", Journal of Education and Science, Mosul university, Iraq, 24(2), pp. 29-44., 2011.

32-M. M. H. Al-Niemi, "Study of the effect of temperature on the kinetics of the reactions of dyes produced from the reactance of 2,4-dihydroxy benzaldehyde, syn and anti-2,4-dihydroxybenzaldehyde with electron-donating (diazotized sulfanilic acid sodium salt) reagent", J.Edu. and Sci., 25(2), pp. 27-43., 2012.

33-M. M. H. Y. Al-Niemi, "KINETIC STUDY FOR THE REACTIONS OF PARACETAMOL WITH DIAZOTIZED (P-NITROANILINE & SULFANILIC ACID SODIUM SALT)", Egyptian Journal of Chemistry (SCOPUS), 66(2), pp.535-542., 2023.

34-M. M. H. Y. Al-Niemi, "Determination of rate constants and half-life times of complexes derived from coupling reaction 2, 4-dinitroaniline and two electron-donating compounds", Egyptian Journal of Chemistry (SCOPUS), 66(2), pp.339-347., 2023.