Influence of pH, light and temperature on the stability of Amoxicillin and Triprolidine .HCl .

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Abstract :

The stability of two drugs Amoxicillin and Triprolidine . HCl was studied in aqueous solution . The results show that Amoxicillin was stable in pH range (2-8), while it decomposed at pH more than (6) . The same results have been shown when the solution temperature was varied between 25-100C^{o} , the decomposition occurred at a temperature above 60C^{o} . When Amoxicillin exposed to UV light in presence of O_2 gas , it was unstable , but was relatively stable in the absence of O_2 gas . Triprolidine .HCl was stable under the same above condition and factors .

UV- Visible spectrometer was used to follow the spectrum of two drugs.

الخلاصة:

درست استقرارية المادتين الدوائيتين الاموكسيسلين وترابرولدين هيدروكلورايد في محاليلها المائية. اثبتت النتائج ان الاموكسيسلين مستقر في مدى الدالة الحامضية(8-2) الا انه يتحلل في الوسط القاعدي(6<pH) . كذلك اثبتت هذه الدراسة استقرارية الاموكسيسلين في مدى درجات الحرارة الاعتيادية60-25 م° ويتحطم الدواء في درجات الحرارة القاسية في المدى(100-70) م°. وعند تعريض المحلول المائي لدواء الاموكسيسلين للاشعة فوق البنفسجية فأنه مستقر نسبياً الا انه يتحلل عند امرار غاز الاوكسجين. وتمت متابعة عملية الاكسدة الضوئية حركياً واثبتت النتائج انها في المرتبة الاولى وتم حساب ثابت السرعة النوعي لهذه العملية وكذلك عمر النصف. اما دواء الترابرولدين هيدروكلورايد فأنه مستقر تحت نفس المتغيرات المبينة اعلاه. استخدم جهاز الاشعة فوق البنفسجية

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Introduction :

Amoxicillin is a simisynthetic pencillin and has a similar antibacterial spectrum to ampicillin. Triprolidine.HCL is antihistamine drugs and described under promethazine.HCL[1].

Yunqi and Reza[2] studied the stability of metronidazole, tetracycline HCL and famotidine in solid and liquid states. They found that elevated temperature accelerated the degradation of all these drugs but light was not a factor for the degradation. Also these drugs are relatively stable at pH=4.0.

The stability of the drugs active ingredients are important factor in the drugs industry . The drugs can undergo degradation processes such as hydrolysis , oxidation and photolysis. Other factors such as presence of heavy metals and humidity also influence the drugs degradation[3].

Studding the effect of light an heat on the stability of furacilin , procaine. HCL and nitro furazone drugs have been done by many authors[4].

They found that the degradation rate were obeys first- order kinetics. Studies[5] with ketoconazole have been shown that photodegradation occurs after 24 hrs. of UV light exposure . Therefore these drugs should be packaged and stored in closed am be red color container and should be also protected from moisture .

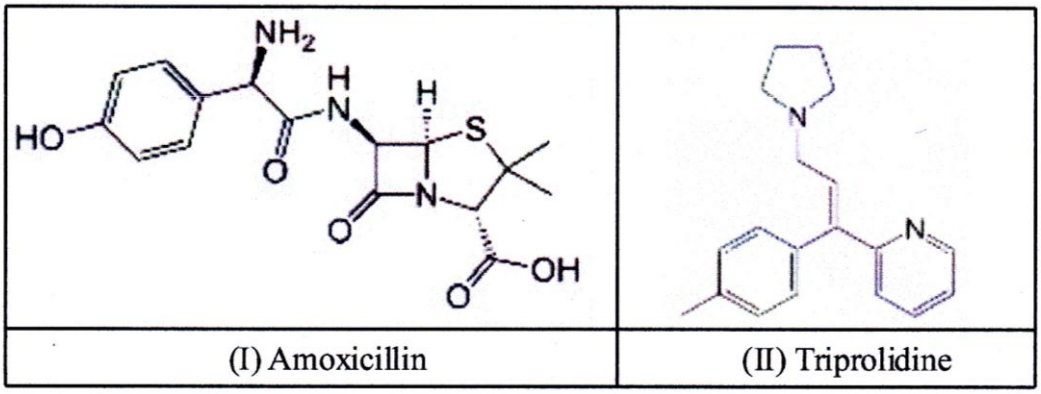
In this work the influence of different factors such as pH, light and temperature on the rate of decomposition of Amoxicillin and Triprolidine . HCL in aqueous solution have been studied.

Experimental :

A-Materials :

Amoxicillin and Triprolidine . HCL with 99.99 % purity, were

purchased from SDI company. Their structural formula were shown in figure (1).



(I) Amoxicillin | (II) Triprolidine

Figure (1) : Structural formula for (I) Amoxicillin (II) Triprolidine- HCL.

HCL and NaOH solutions were purchased from BDH company and were used to adjust the pH solution between 2-12.

B-Apparatus :

UV-Visible spectrophotometer from CARY company ;Medium pressure mercury lamp (MPML) with a maximum wavelength 365 nm ,150w,model PHYWE ; Magnetic stirrer model Buchi and thermostated water bath circulator model Haake FE2 were also used in this research.

Result and Discussion:

3-1 UV-Visible spectra of drugs

UV-Visible spectra of drugs Amoxicillin in 0.1 N HCL and Triprolidine. HCL in distilled water shown in figure (1) and (2).

3-2 Factors influencing drugs degradation:

A- pH :

The acidity or the alkalinity of a solution has a profound influence on the decomposition of work drug compound ; so in this work ; variation

of solution PH from 2-12 at 25°C were performed to study the stability of Amoxicillin and Triprolidine. HCL .

The results indicate that Amoxicillin was stable in the pH range 2-8 while it decomposed in pH range 8-12(alkaline solution) especially in pH=12 , Amoxicillin was completely hydrolyzed by OH^- ion according to the following equation :

Amoxicillin like penicillin are hydrolyzed by OH^- / H_2O via amide group and also beta lactam ring of antibiotics is highly reactive and can be inactivating the drug molecule[6].

The same result has been found in the case of Aspirin[7] and the decomposition rate was rapidly increases in the pH of 10 . Other drugs such as niacinemide,phenethicillin barbiturates and chloramphenicol have been reported to degrade by amide hydrolysis[8].

In the case of aqueous solution of triprolidine.HCL it was found that this drug was stable under the wide range of pH solution (2-12).

B -Temperature :

Temperature has a high degree of influence on the chemical reactions and usually they are accelerated by a raise in temperature. It is know that 10°C increase in temperature produces a 2- 5fold increase in decomposition.

The thermal hydrolysis of amoxicillin aqueous solution was studied in the temperature range of 25-l00°C. The results show that amoxicillin was stable in the temperature range 25-60°C. while studying at elevated temperature 70-100°C to perform the assess thermal stability; amoxicillin was decomposed to a yellow solid compound. Figure (3) shows UV-Visible spectrum of the unknown compound which a new band was appeared at 375 nm. This band increased in intensity with increasing time heating (2hrs),but it became stable at 100°C during 30 min of heating .

Triprolidine. HCL was stable in the all temperature range 25- 100°C.

C- Light :

In this work the photo stability of amoxicillin and Triprolidine .HCL in aqueous solution have been studied.

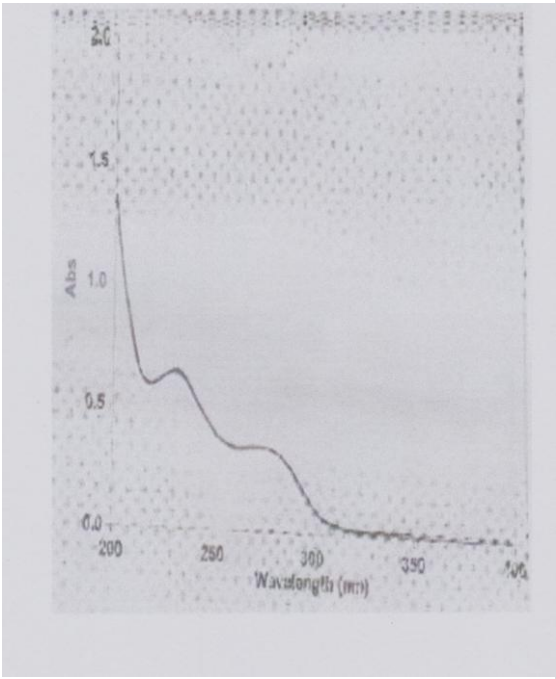
The results indicate that amoxicillin was unstable by photolysis in presence of oxygen gas passing throughout , the aqueous solution and the solution color became yellowish during photo oxidation process and anew band at 375 nm was appeared as shown in figure(4&5) .While in the absence of oxygen amoxicillin was stable under exposure of UV light.

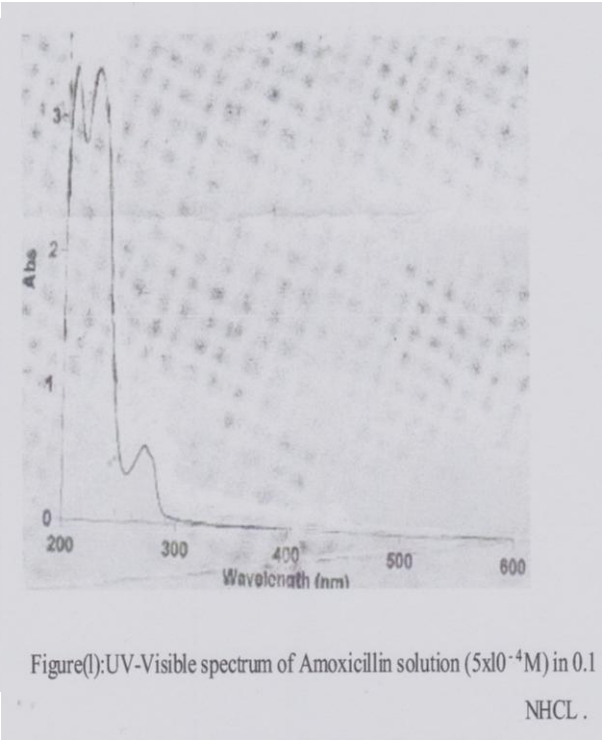
The band at 375 nm was increased in intensity during time of irradiation. Plotting a concentration Vs. time gave a non linear relationship as shown in figure (6).

While fig (7) gave a linear relation ship between In(a-x) Vs. time which indicate a first order reaction .From the slope of the straight line a first order rate constant and $t_{1/2}$ have been determined which is $1x10^{-3}$ min^{-1} while $t_{1/2}$ was 693 min. In this process, oxygen free radicals O_2 and OH were formed and these radicals were decomposed the drug substances .

Therefore oxidation is the most important path way of drug decomposition because oxygen is present every where in the atmosphere and lead to auto oxidation.

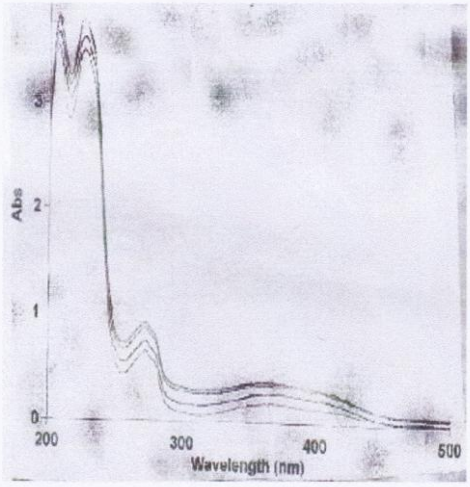
These closed and tight containers should be used to store the drug. Triprolidine. HCL was stable under photolytic process in the presence or absence of oxygen gas.



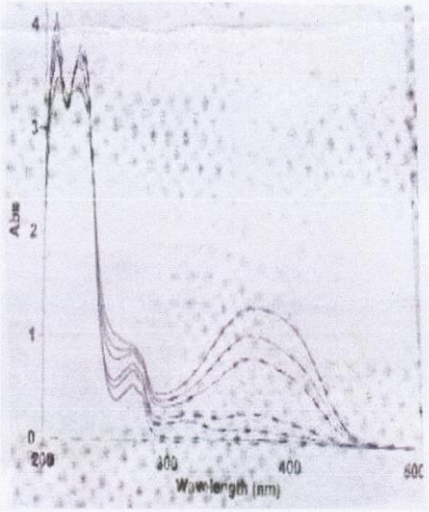


Figure(l):UV-Visible spectrum of Amoxicillin solution (5xl0^{-4}M) in 0.1 NHCL .

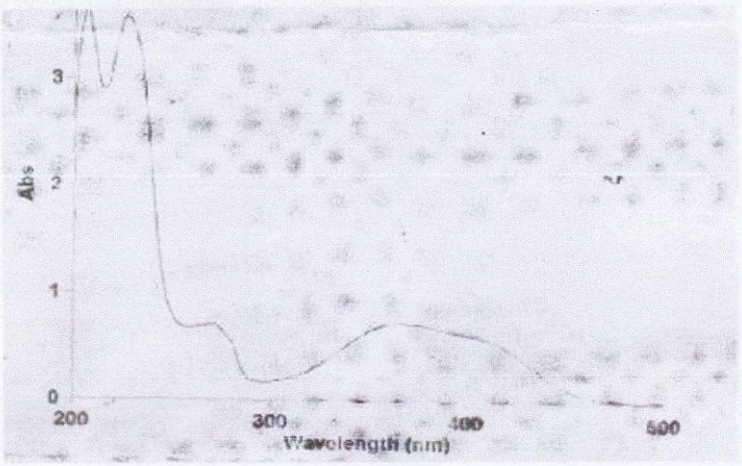
Figure(3):UV-Visible spectra of Amoxicillin solution (5x10 M) in 0.1 N HCL during different time of heating at 70°C.



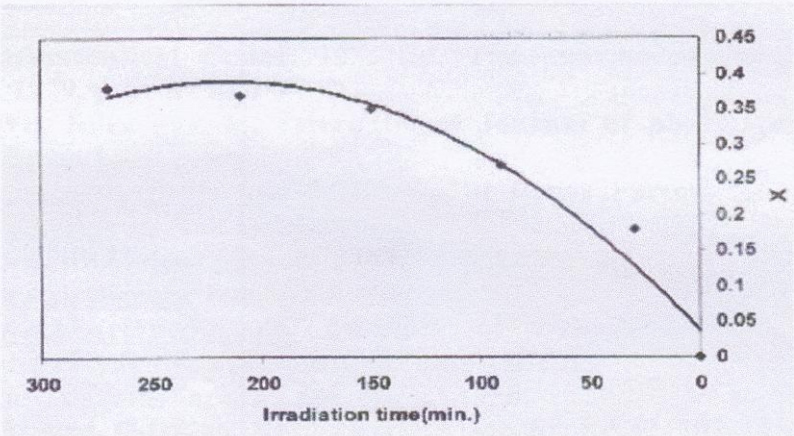
Figure(2):UV-Visible spectrum of Triprolidine.HCL (5xl0^{5}M) in distilled water.



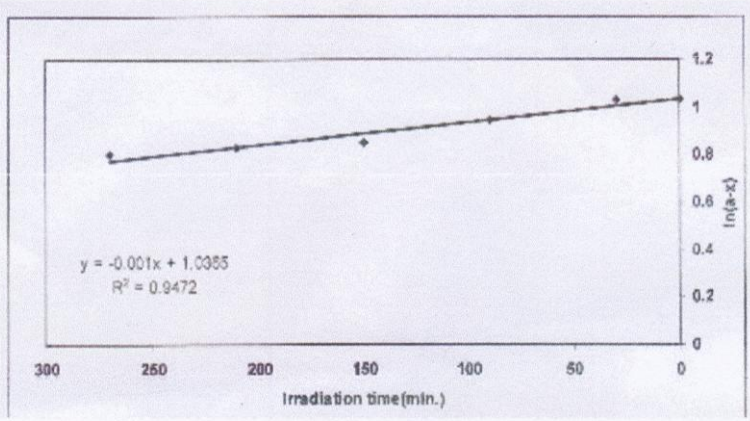
Figure(4):UV-Visible spectra of Amoxicillin solution ($5x10^{-4}$M) in 0.1 N HCL during different time of irradiation in presence of oxygen.



Figure(5):UV-Visible spectra of photolytic product for Amoxicillin solution ($5x10^{-4}$M) in 0.1 N HCL.



Figure(6): Relation between the concentration of photolytic product for Amoxicillin at Amax=375nm at different intervals time of photolysis



Figure(7): First order relationship for the photolytic product for Amoxicillin solution during intervals time of irradiation

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