

Introduction

Epirubicin (EPI) is the 4'-epimer of doxorubicin and is a member of the anthracycline class of antibiotics. Epirubicin produces less side effects than doxorubicin and so it can be used in higher doses. This has been used in the treatment of breast, gastric, ovarian, colorectal carcinomas. Prior studies have shown that stability of drug may be influenced by environmental factors relative and air humidity. The stability of epirubicin is important to be investigated both in the solutions and in solid phase.

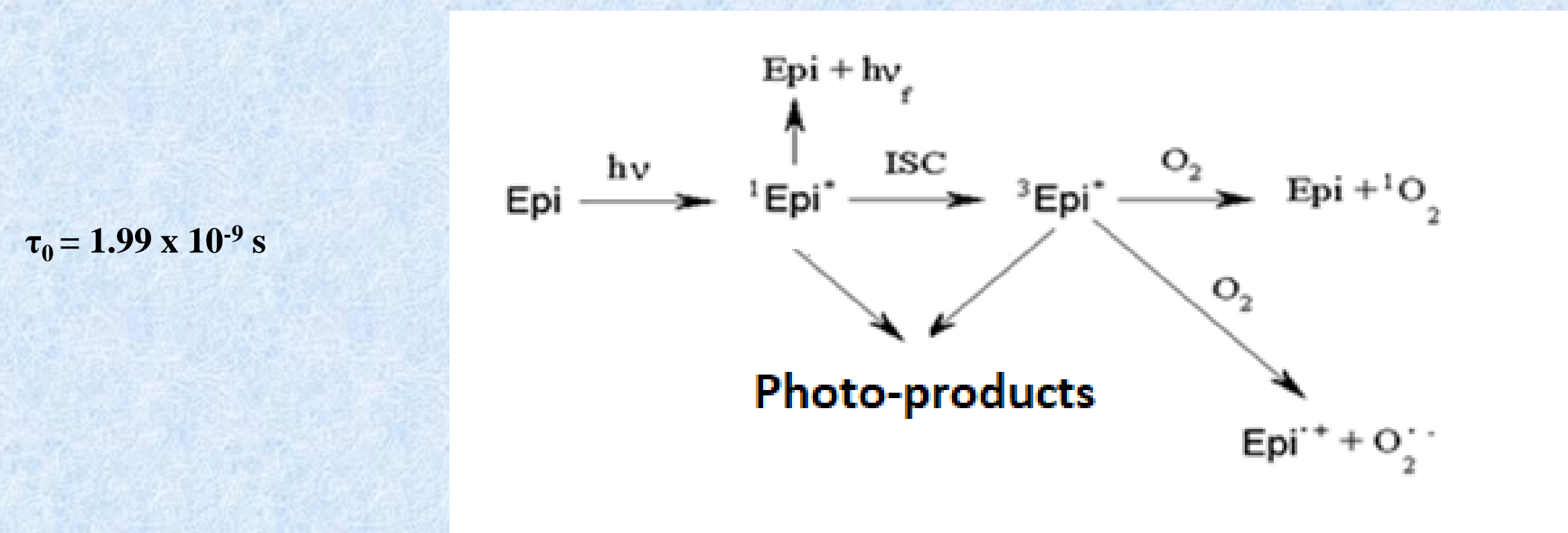
Experimental

- The photodegradation experiments were carried out in a laboratory scale UV reactor using a low-pressure mercury lamp which emits at $\lambda = 254$ nm
- For Visible range were used medium-pressure mercury lamp with power 150 and 250 W, respectively. The lamp equipped with an UV-VIS radiation transparent glass water cooling jacket is immersed in the centre of the reactor containing the drug solution.
- The UV-vis spectra of drug were recorded at room temperature from 200 to 700 nm using a Jasco V-530 spectrophotometer with a spectrometric quartz cell (1 cm path length).

Results

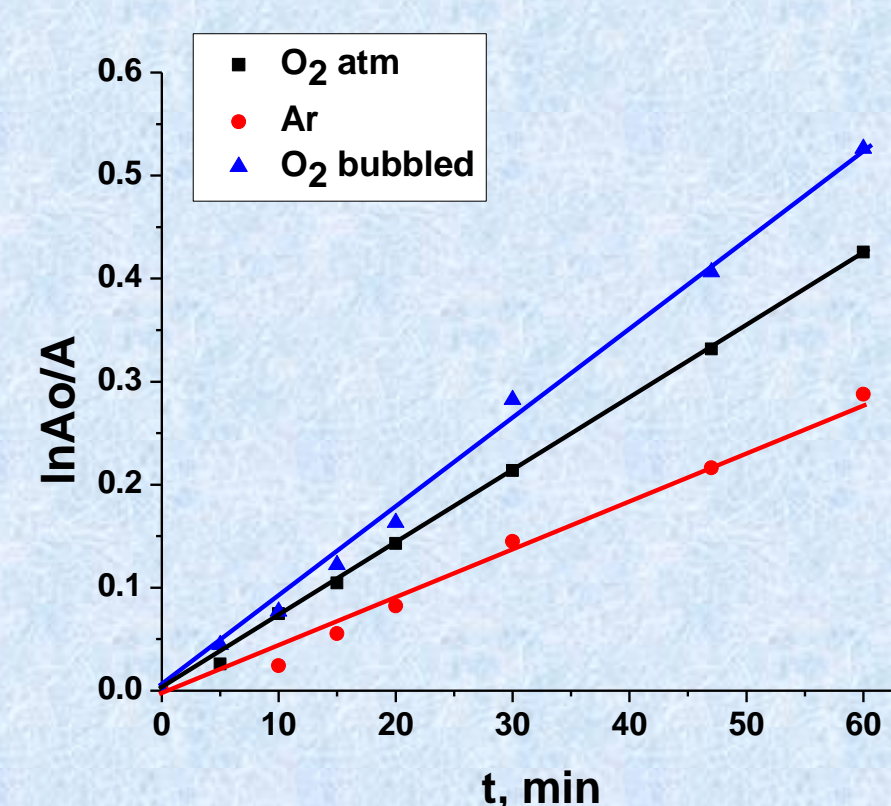
Major reaction pathways

Our experimental results correlated with the available literature information led us to the following mechanism of the primary process:

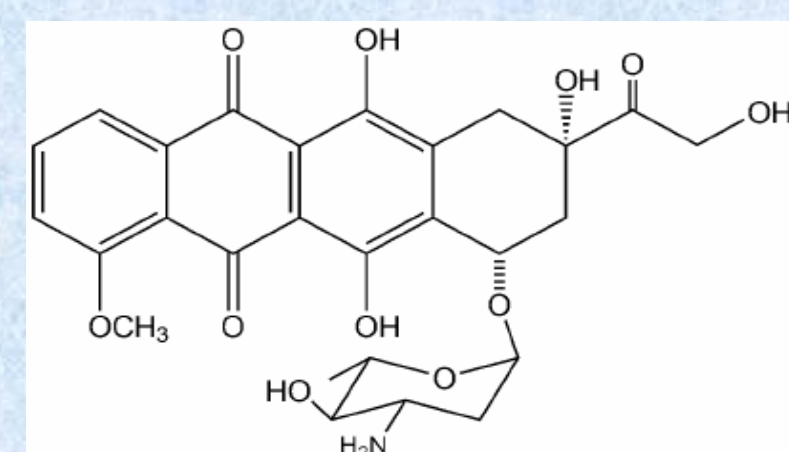
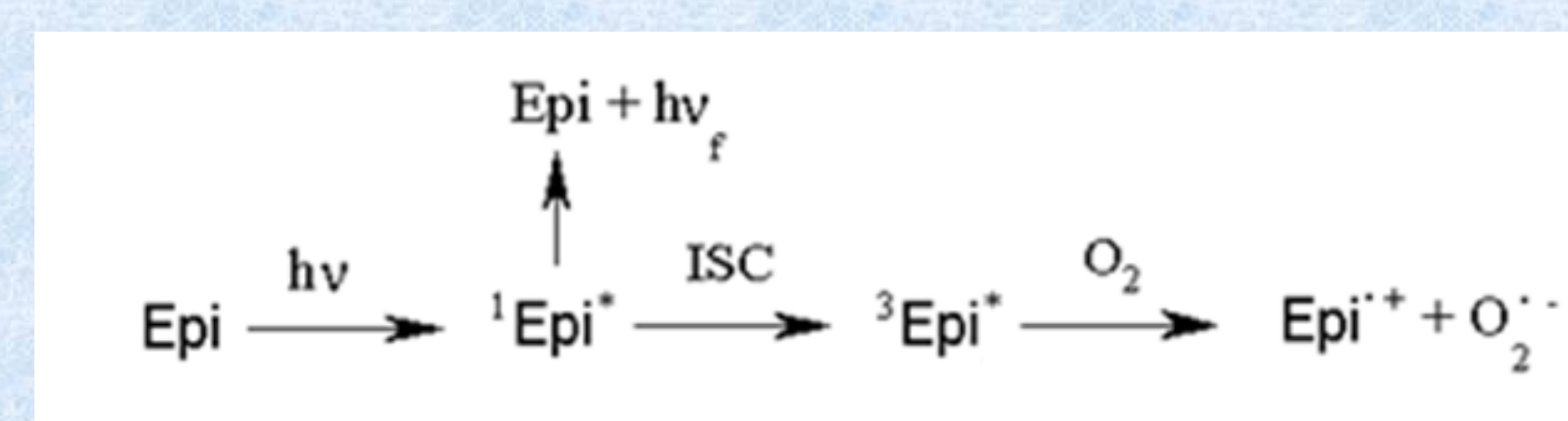


The excited singlet state $^1\text{Epi}^*$ may be deactivated by fluorescence emission, hemolytic or heterolytic bond scission and intersystem crossing (ISC) process with the appearance of $^3\text{Epi}^*$. The low quantum yields determined experimentally show that only the last process takes place whereas the recombination in the solvent cage, leading to the initial molecule occurs with high probability.

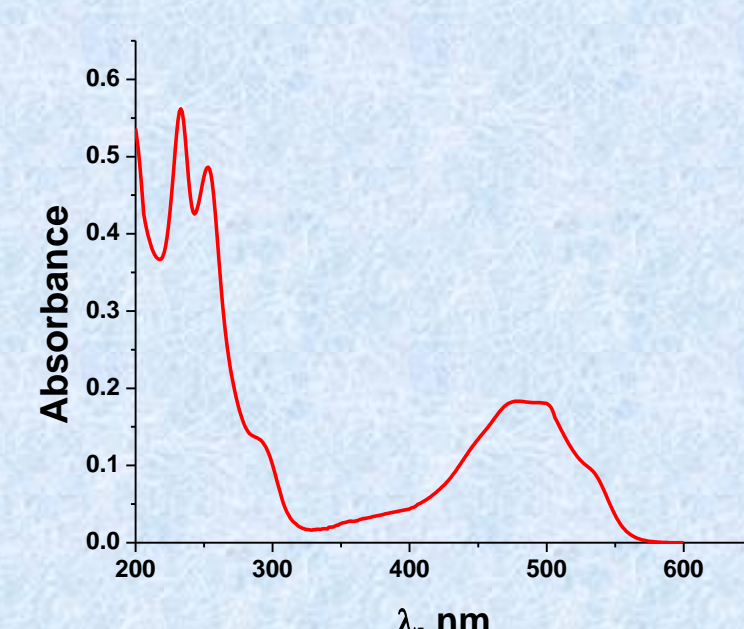
Influence of O₂



Condition	k, min ⁻¹
Ar	0.0046
O ₂ atm	0.0071
O ₂ bubbled	0.0087

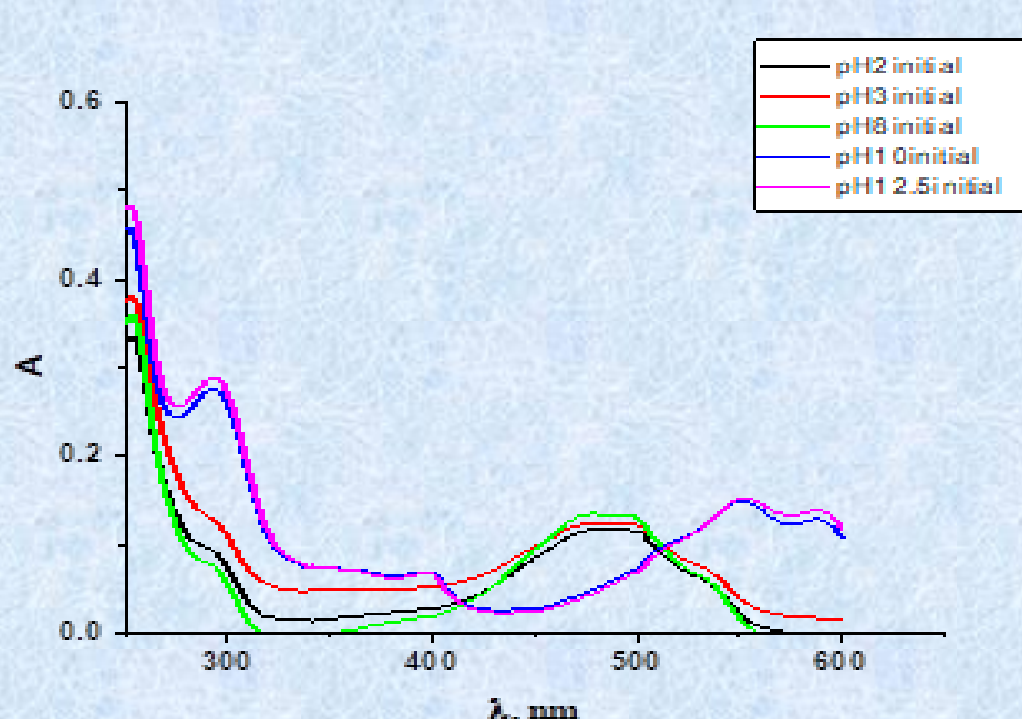


Epi structure

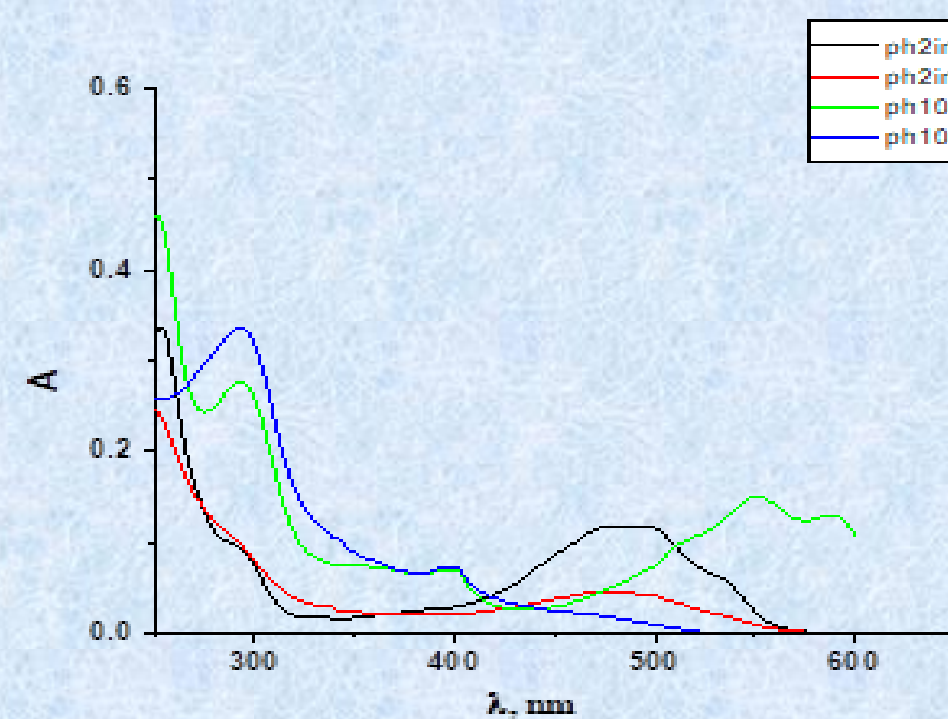


The absorption spectrum of Epirubicin

Influence of pH

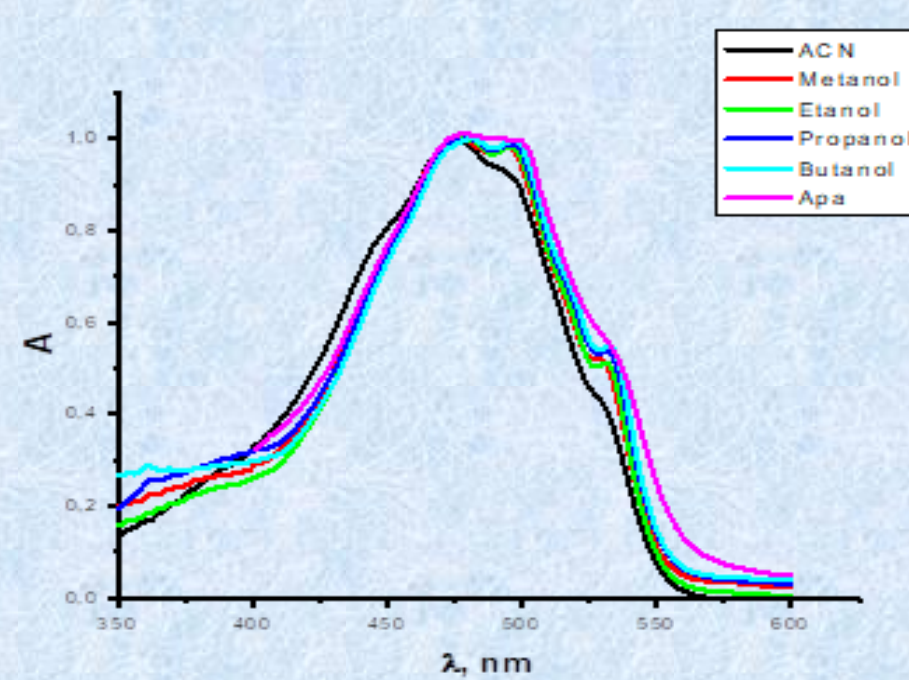


The evolution of absorption spectrum with the pH value



The absorption spectrum for pH=2 and pH=10 after 20 and 10 minutes of irradiation

Influence of solvents

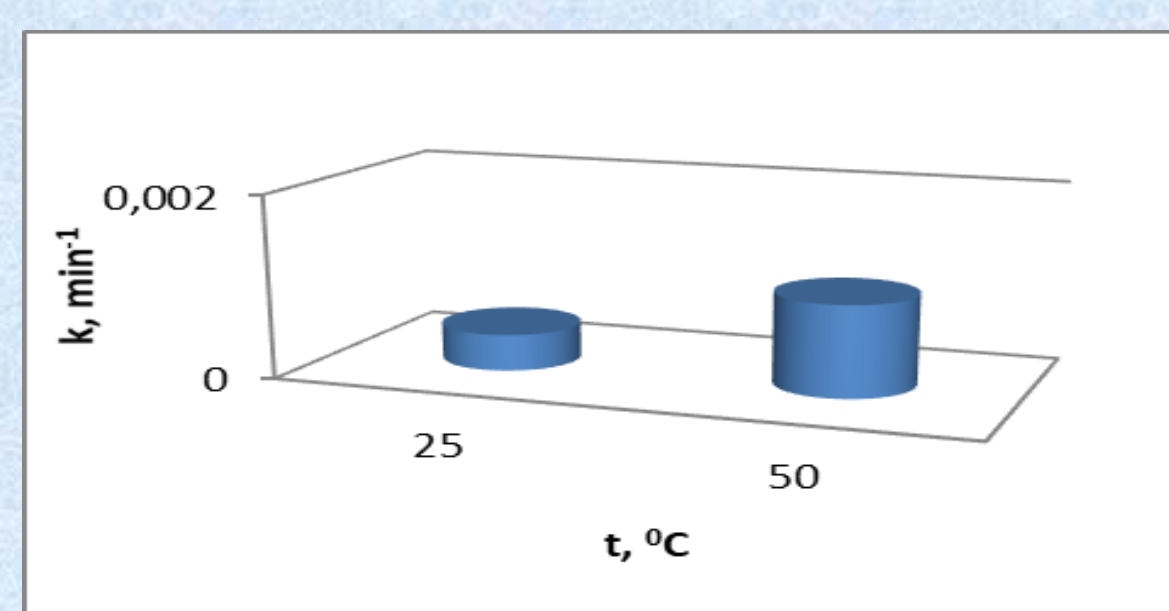


The absorption spectrum of Epirubicin in different organic solvents

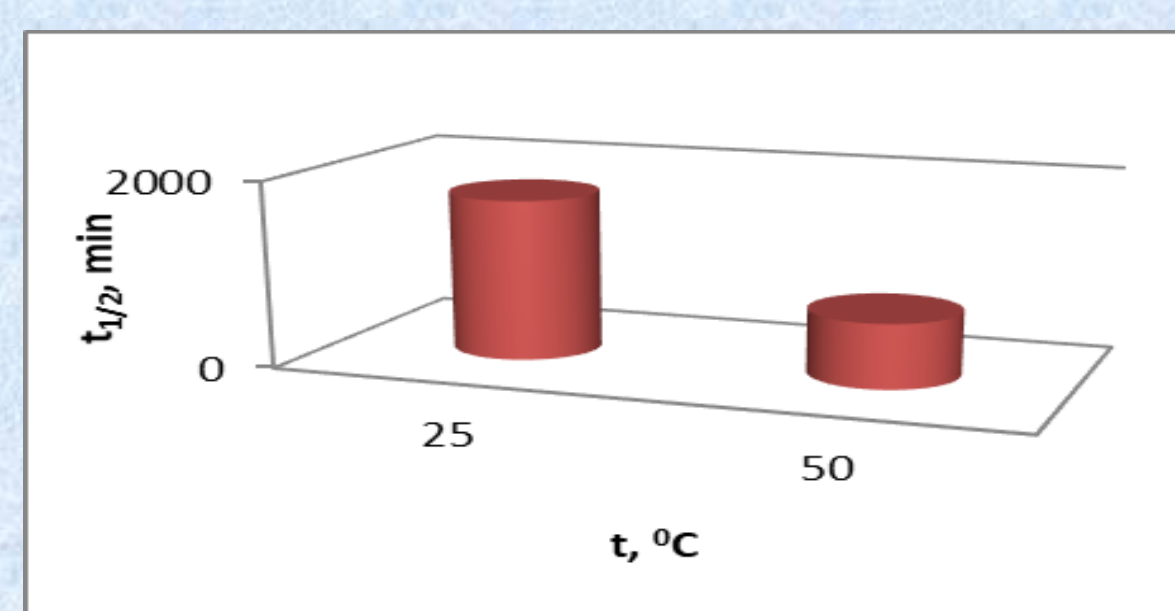
Photochemical parameters in different solvents

Solvents	k_p, s^{-1}	k_{sp}, s^{-1}	τ, s	$\phi_{em}(575\text{ nm})$	$\phi_{em}(580\text{ nm})$
Water	7.15E+06	7.23E+07	1.20E-08	0.09	0.13
Methanol	2.49E+06	1.06E+07	7.63E-08	0.19	0.27
Ethanol	2.35E+06	8.83E+06	8.95E-08	0.21	0.31
Butanol	2.13E+06	9.72E+06	8.44E-08	0.18	0.27
Acetonitrile	2.14E+06	9.11E+06	8.89E-08	0.19	0.28

Influence of temperature



The influence of temperature on the rate constant



Influence of temperature on half-life

Conclusions

- ✓ Epirubicin is unstable in alkaline pH even in the absence of radiation.
- ✓ The presence of O₂ in the studied system plays an important role ($k_{Ar} < k_{O_2\text{-atm}} < k_{O_2\text{-bubbled}}$).
- ✓ Increasing the temperature leads to increased degradation efficiency.
- ✓ The addition of organic solvents may increase the stability of epirubicin.