

¹Chair and Department of Applied Pharmacy,
²Chair and Department of Synthesis and Chemical Technology of Pharmaceutical Substances,
Faculty of Pharmacy, Medical University in Lublin, Poland

MARIA ZUŃ¹, PIOTR BELNIAK¹, DOROTA DWORNICKA¹,
REGINA KASPEREK¹, SYLWIA WOŚKO¹, MARZENA RZĄDKOWSKA²,
EWA POLESZAK¹

*Influence of concentration of the urea on the hydrogen
peroxide content in 3% aqueous and non-aqueous solutions
stored at different temperatures*

Wpływ stężenia mocznika na zawartość nadtlenu wodoru w 3% roztworach wodnych
i niewodnych przechowywanych w różnych temperaturach

Hydrogen peroxide is widely used in medicine and in industry [1,7,12-14]. It is used as an antiseptic [8], disinfectant [1], whitening [3], oxidizing [2]. The aqueous solutions of 3%, 6% and 10% are most frequently used. Because of its strong oxidizing properties it is unstable. Various substances as: acetanilide, hydroxyquinoline, sodium pyrophosphate and acids are used for stabilization [2]. According to literature data, the stable complexes of hydrogen peroxide and urea are obtained, which are produced in solid form: powders, tablets [6]. Therefore, the question is if the solutions of hydrogen peroxide with urea for external use are enough stable. That is why the aim of the study was determining the influence of different amounts of urea on hydrogen peroxide stability in the dilutions stored at different temperatures.

MATERIALS AND METHODS

R e a g e n t s. Hydrogen peroxide (30%), sulfate acid OD (98g/l), potassium permanganate (0.02 mol/l RM); glycerine (Poch., Gliwice), polyethylene glycol 300 (LOBA – Chemie, Wien – Fischened (PEG – 300), 1,2-propylene glycol (Ph.Eur., Fuke (Chemie) (PPG-1,2).

E x p e r i m e n t a l p r o c e d u r e s. Prepared solutions were poured into the bottles of dark, amber glass, closed cup of polyethylene and stored in the dark place at room temperature and in the thermostat at 30°C and 40°C. The content of hydrogen peroxide in the solutions was determined according to FP VI.

D e t e r m i n a t i o n o f 3 % H₂O₂ s o l u t i o n s. Each time 1g of the solution was weighed, 9 ml of water and 20 ml sulfate acid (98g/l) were added, then titrated with KMnO₄ (0.02mol/l) until the color changes to pink. The content of hydrogen peroxide in the sample was calculated by the following equation:

$$X\% = v \cdot 1.7 \cdot 100/1000 = 0.17 \cdot v ;$$

where 1ml KMnO_4 corresponds to 1.7mg H_2O_2 .

Solutions preparation. To study the kinetics of aging the aqueous solutions of hydrogen peroxide (3%) with and without urea were prepared. In addition, for comparative study the solutions of hydrogen peroxide (3%) with non-aqueous solvents (polyethylenoglicole-300; 1,2-propanediol and glyceride) were also prepared. The solutions 3% MO were obtained. Ten grams of hydrogen peroxide (30%) was weighed and supplemented to 100g with distilled water, or PEG-300, or PPG-1,2, or glycerine. The solutions with addition of urea were made by weighing 2,4, 6, 8, 10g of urea, then dissolving in small amount of water and adding to the diluted with water solution of hydrogen peroxide. Finally, everything was supplemented with distilled water to 100g. The solutions: 3%M2, 3% M4, 3%M6, 3%M8, 3%M10 were obtained. In the same way, non-aqueous solutions of hydrogen peroxide (30%) and urea were prepared by mixing 10g of hydrogen peroxide (30%) and 6g of urea. PEG-300, PPG-1,2 or glycerine were used as a solvent.

The hydrogen peroxide content of 3% solutions at 20°C, 30°C and 40°C versus time of storage was shown on Fig. 1-4. The data contained on figures show that decomposition of hydrogen peroxide proceeds according to first-order, with a slight delay. Based on the equation of rate constant of the first-order reaction, the decomposition rate constants of hydrogen peroxide at, 20°C, 30°C, 40°C was calculated.

Logarithms of the constants presented to the inverse absolute temperature give linear graphs in the temperature range 20-40°C (Fig. 4). It allows to determine the activation energy (E_a) and check the compatibility of experimentally determined decomposition rate constants of the hydrogen peroxide at 20°C and constants calculated from the transformed Arrhenius's equation [11].

$$E_a = \frac{\ln K_1 - \ln K_2}{T_2 - T_1} \cdot 1.9872 \cdot T_1 \cdot T_2$$

$$\ln K_{20} = \ln K_2 = \frac{E(T_2 - T_{20})}{1.9872 \cdot T_2 \cdot T_{20}}$$

$$K_1 > K_2, T_2 > T_1, T_2 > T_{20}$$

1.9872- – gas constant

K_{20} – decomposition rate constant at 20°C

K_1, K_2 – decomposition rate constants determined experimentally

The stability of hydrogen peroxide ($t_{10\%}$) in the solutions stored at room temperature was calculated from the equation :

$$t_{10\%} = \frac{0.1053}{K_{20}}$$

$t_{10\%}$ - time decomposition of the 10% of active substance

K_{20} – decomposition rate constant at 20°C

The calculation results of the activation energy E_a and the time decomposition of 10% of active substance are given in Table 1.

Table 1. Kinetics of the hydrogen peroxide decomposition in 3% aqueous solutions

Solution	Decomposition rate constants K_{exp} (day ⁻¹)			Activation energy (cal·mol ⁻¹)	Decomposition rate constants at 20°C K_{exp} (day ⁻¹)	Decomposition time of 10% active substance at 20°C (day)	
	temperature					experimental	calculated
	20°C	30°C	40°C				
M0	$5.50 \cdot 10^{-4}$	$5.3 \cdot 10^{-3}$	$3 \cdot 10^{-2}$	38922.32	$5.14 \cdot 10^{-4}$	191.45	204.86
M2	$5.47 \cdot 10^{-2}$	$3.79 \cdot 10^{-1}$	-	34150.28	-	-	-
M4	$6.55 \cdot 10^{-2}$	$4.32 \cdot 10^{-2}$	-	33290.76	-	-	-
M6	$7.19 \cdot 10^{-2}$	$4.34 \cdot 10^{-2}$	-	31720.76	-	-	-
M8	$8.57 \cdot 10^{-2}$	$4.44 \cdot 10^{-2}$	-	29012.54	-	-	-
M10	$9.88 \cdot 10^{-2}$	$4.82 \cdot 10^{-2}$	-	27971.82	-	-	-

RESULTS AND DISCUSSION

The stability of the medical preparations is often undertaken subject associated with therapeutic effect of the medical substance and the conditions of storage. Oxidizing properties of hydrogen peroxide require the addition of different stabilizers, which prolong the stability of the active substance. The urea is one of the used stabilizers, mainly in combination of solid dosage forms of hydrogen peroxide. Medical 3% solutions of hydrogen peroxide should be enough stable to enable the application on mucous membranes of the skin. That is why the aim of the study was the determination of the properties of hydrogen peroxide in aqueous and non-aqueous solutions at different storage temperatures in the presence of the urea.

The aqueous solutions containing 3% of hydrogen peroxide with different amounts of urea were stored for 80 days, at 20°C, 30°C, 40°C. Based on the tests and the results, it was found, that the decomposition of hydrogen peroxide is proceeding according to first-order, starting with a little delay. In studies it has not observed the stabilizing effect of the urea in the aqueous solutions on hydrogen peroxide, in comparison to the solid complexes of this substance described in literature, where this effect has been observed [6].

During the storage at 20°C, within 21 days the solutions were quite stable and showed a slight decrease of active substance content: M0(99,02%), M2(94,4%), M4(99,3%), M6 (99,8%), M8(97,4%), M10(84,1%). At low concentrations of the urea (2-6%), the decrease of amounts of active substance was inversely proportional to the concentration of urea, at 8 and 10% concentrations the decomposition increased with the amount of urea in the solution.

During further storage of these solutions (80 days) the decomposition process has accelerated significantly and has been proportional to the amount of urea in the solution, as illustrated by constants first-order: K_{20} (3%M0)=0.00055d⁻¹, K_{20} (3%M2)= 0.05466d⁻¹, K_{20} (3%M4)=0.06552d⁻¹, K_{20} (3%M6)=0.07195d⁻¹, K_{20} (3%M8)=0.08568d⁻¹, K_{20} (3%M10)= 0.09885d⁻¹. Similar relationships were observed in the solutions stored at 30°C, but the decomposition rate constants

of hydrogen peroxide were much higher, which indicates a faster decomposition of substances in these solutions [$K_{30(3\%M)}=0.00573d^{-1}$, $K_{30(3\%M2)}=0.37872d^{-1}$, $K_{30(3\%M4)}=0.432435d^{-1}$, $K_{30(3\%M6)}=0.434376d^{-1}$, $K_{30(3\%M8)}=0.443690d^{-1}$, $K_{30(3\%M10)}=0.482540d^{-1}$]. The decomposition rate constant of hydrogen peroxide, in solutions stored at 40°C could be determined only in 3% solution without urea $K_{40(3\%M)}=0.03004d^{-1}$. In other solutions the decomposition of hydrogen peroxide was observed within one week. Fig.6. shows the dependence of constant decomposition of hydrogen peroxide on the concentration of added urea.

The evaluation of stability of active substance was carried out by determining the value of activation energy of the ongoing reaction. Calculated from Arrhenius' s equation, activation energy of hydrogen peroxide (E_a) decreased with the increase of concentration of urea and with the increase of decomposition constant (K). The highest value was observed in the solution without urea (39019.57 cal·mol⁻¹), the lowest at 10% concentration of urea (279711.82 cal·mol⁻¹).

The next criterion of stability was the evaluation of the decomposition time of 10% of hydrogen peroxide. This time was varied depending on used decomposition constant (K calculated or K determined) at 20°C. These values were similar and were 204.86 and 191.45 days.

In addition, for comparison purposes 3% solutions of hydrogen peroxide with glycerine, polypropylene glycol and polyethylene glycol with addition of 6% urea, were examined. It was noted, that the decomposition of hydrogen peroxide with glycerine and polypropylene glycol followed immediately after the preparing the solutions.

In the solutions prepared with polyethylene glycol, the decomposition of the active substance proceeded according to first-order without delay. Decomposition rate constants were increasing with increase of temperature from $1.75 \cdot 10^{-3}d^{-1}(20^\circ C) < 4.1 \cdot 10^{-3}d^{-1}(30^\circ C) < 5.3 \cdot 10^{-3}d^{-1}(40^\circ C)$, but they were lower than in similar 3% aqueous solutions. Moreover, the activation energy calculated for hydrogen peroxide in non-aqueous solutions with polyethylene glycol was 12581.2 cal·mol⁻¹ and it was lower about three times.

Summarizing, the use of non-aqueous solutions as antiseptics on the skin and mucous membranes can be more successful than aqueous ones, which evaporate from the skin surface and mucous membranes very fast, are irritating and less stable.

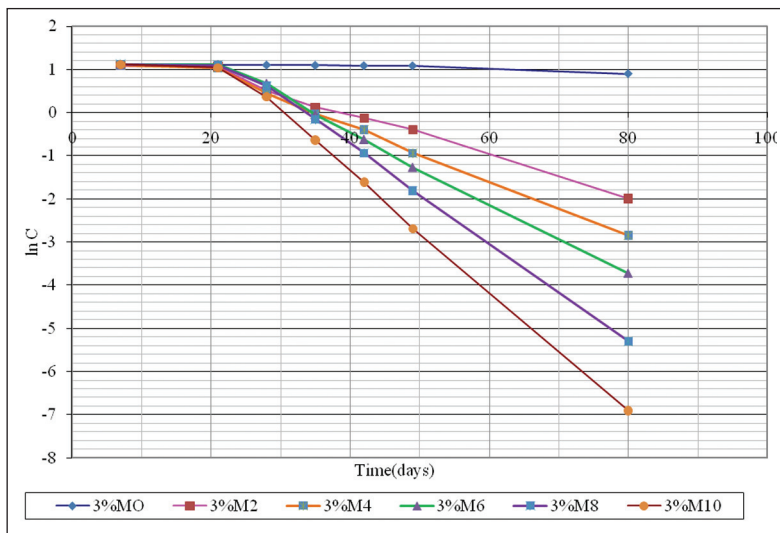


Fig.1. Effect of storage time at 20°C on the concentrations of hydrogen peroxide in 3% aqueous solutions with and without urea

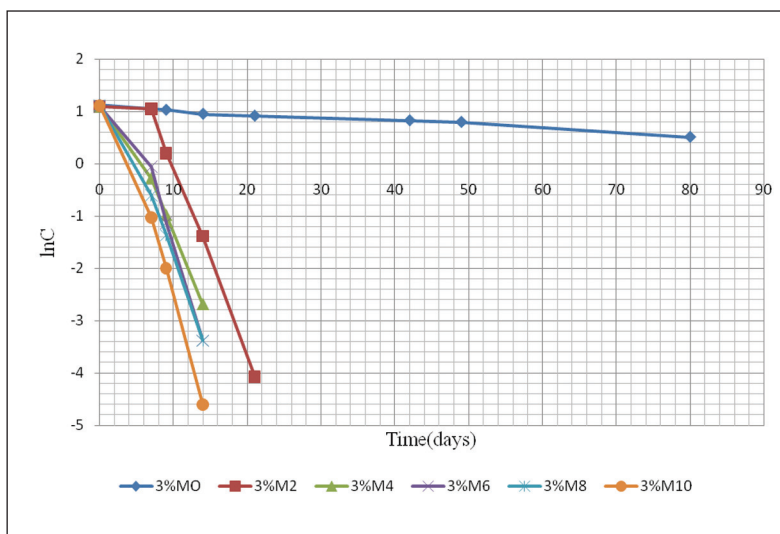


Fig. 2. Effect of storage time at 30°C on the concentrations of hydrogen peroxide in 3% aqueous solutions with and without urea

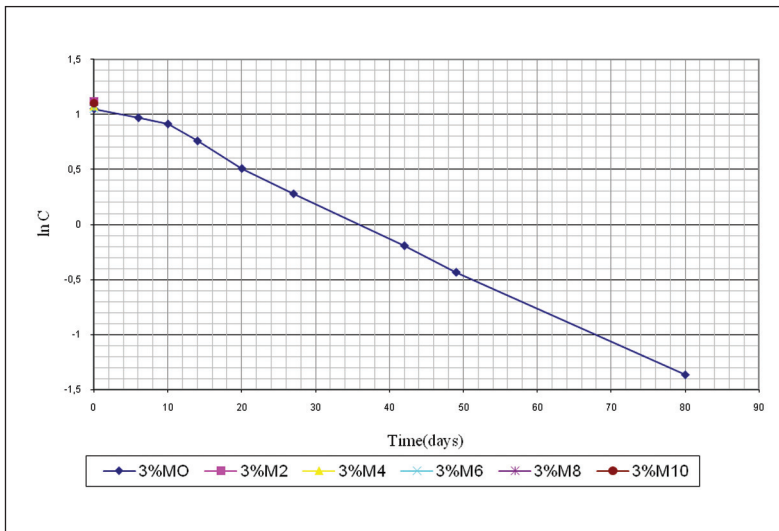


Fig. 3. Effect of storage time at 40°C on the concentrations of hydrogen peroxide in 3% aqueous solutions with and without urea

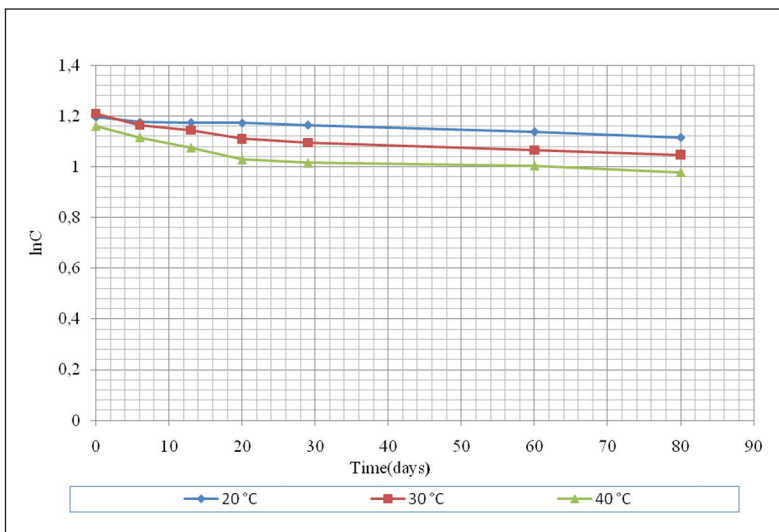


Fig. 4. Effect of storage time at 20°C, 30°C, 40°C on the concentrations of hydrogen peroxide in 3% non-aqueous solutions with 6% urea

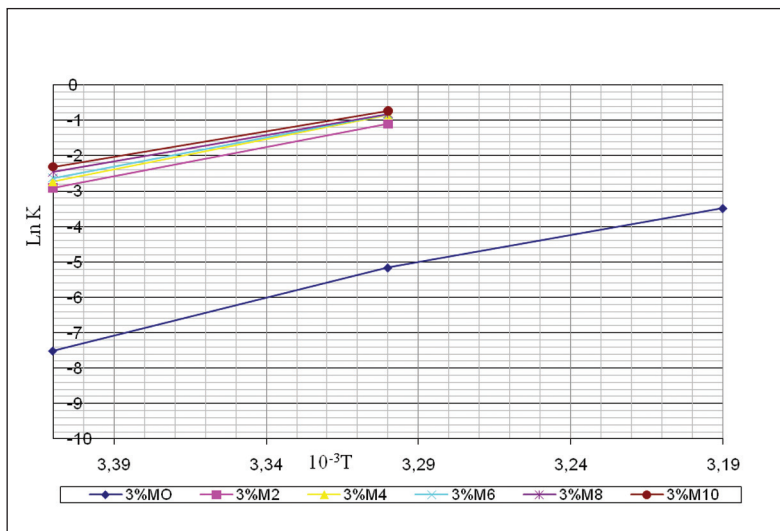


Fig. 5. Dependence decomposition rate constants of hydrogen peroxide in 3% aqueous solution (M0-M10) from temperature of storage

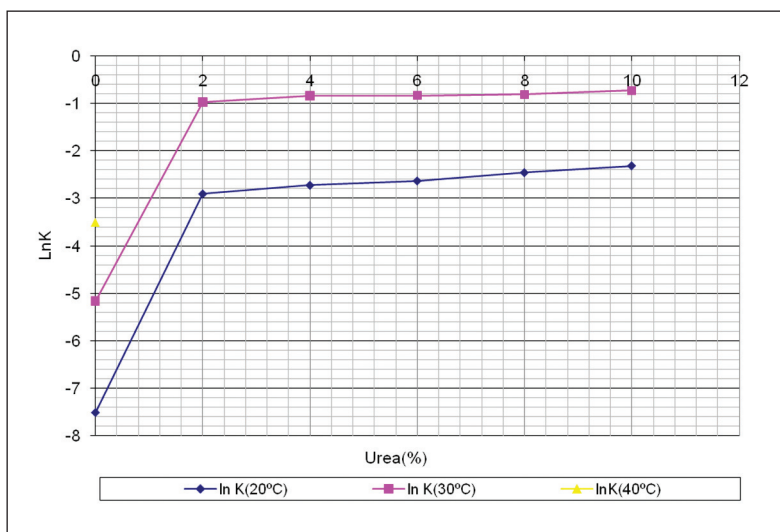


Fig. 6. Dependence decomposition rate constants of hydrogen peroxide from the concentration of urea

CONCLUSIONS

1. The addition of urea to 3% solutions of the hydrogen peroxide cause the acceleration of decomposition rate of active substance.
2. The decomposition rate constants of the hydrogen peroxide increase with the storage temperature of the solutions.
3. Based on the tests and obtained results it was found that glycerin and polypropylene glycol are not suitable for the hydrogen peroxide solutions.
4. Polyethylene glycol 300 is a good solvent, and 3% solutions stabilized with 6% addition of urea are enough stable.

REFERENCES

1. Ahmad S.: Control of skin infections by a combined action of ultraviolet A (from sun or UVA lamp) and hydrogen peroxide (HUVA therapy), with special emphasis on leprosy. *Med. Hypotheses.*, 57, 484, 2001.
2. Alfa M., Jackson M.: A new hydrogen peroxide-based medical-device detergent with germicidal properties : comparison with enzymatic cleaners. *Am. J. Infect. Control.*, 29, 168, 2001.
3. Azrak B. et al.: Influence of bleaching agents on surface roughness of sound or eroded dental enamel specimens. *J. Esthet. Restor. Dent.*, 22,391,2010.
4. Berger S. et al.: Changes in the stiffness of demineralized dentin following application of tooth whitening agents. *Acta Odontol. Scand.*, 15,1,2011.
5. Biss R. et al.: Process for producing PVP-hydrogen peroxide complex. *PCT Int. Appl. WO 92 17,158 (Cl. A61K7/40)*, 15 Oct 1992, *US Appl. 683, 467*, 8 Apr 1991.
6. Bradecka B., Krystek A.: Preparation of stable sodium percarbonate, an ecologically safe bleach. *Przem. Chem.*, 70, 430, 1991.
7. Christensen O., Anehus S.: Hydrogen peroxide cream: An alternative to topical antibiotics in the treatment of impetigo contaginosa. *Acta. Derm. Venereol.*, 74, 460, 1994.
8. Polish Pharmacopoeia VI. Warsaw 1992.
9. Fatakawala H., Uhland S.: Hydrogen peroxide mediated transvaginal drug delivery. *Int. J. Pharm.*, 16, 409, 2011.
10. Gerlach R. et al.: Initial color change and color retention with a hydrogen peroxide bleaching strip. *Am. J. Dent.*, 15, 3, 2002.
11. Militly I. et al.: Improved parameter estimation in Arrhenius typy models. *Termochim.Acta.*, 92, 77, 1985.
12. Mishra N. et al.: Study on antioxidant activity of common dry fruits. *Food Chem. Toxicol.*, 48, 3316, 2010.
13. Muangrat R. et al.: Alkaline subcritical water gasification of dairy industry waste (Whey). *Bioresour. Technol.*, 102, 6331, 2011.
14. Sankar M. et al.: Oxidation of glycerol to glycolate by using supported gold and palladium nanoparticles. *Chem.Sus.Chem.*, 2, 1145, 2009.
15. Zhang W., Qu G.: Synthesis and application prospect of ureaperoxide. *Shanghai Huagong.*, 23, 36, 1998.

SUMMARY

In this study, the stability of the hydrogen peroxide in 3% aqueous and non-aqueous solutions with different amount of urea (2-10%) was examined. The solutions were stored at 20-40° C. The decomposition process proceeded according to first-order. The decomposition rate constant of the hydrogen peroxide increased with the increase of urea and the activation energy decreased. The storage temperature also had influence on decomposition of the active substance. Solutions of the hydrogen peroxide prepared with polyethylene glycol 300, stabilized with 6% addition of urea were more stable than analogous aqueous solutions.

Keywords: hydrogen peroxide, urea, stability, activation energy, storage

STRESZCZENIE

W pracy zbadano trwałość nadtlenu wodoru w 3% roztworach wodnych i bezwodnych z różną zawartością mocznika (2-10%). Roztwory przechowywano w temperaturach 20-40°C. Rozkład nadtlenu wodoru przebiegał we wszystkich roztworach zgodnie z procesem I-rzędu. Wraz ze wzrostem ilości mocznika w roztworach, wzrastała stała rozkładu nadtlenu wodoru a spadała energia aktywacji. Także temperatura przechowywania miała wpływ na rozkład substancji leczniczej. Roztwory nadtlenu wodoru sporządzone na PEG 300, stabilizowane dodatkiem 6 % mocznika były bardziej trwałe niż analogiczne roztwory wodne.

Słowa kluczowe: nadtlenek wodoru, mocznik, trwałość, energia aktywacji, przechowywanie